
Risk-based Estimate of Effect of Foodborne Diseases on Public Health, Greece

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The public health effect of illness caused by foodborne pathogens in Greece during 1996–2006 was quantified by using publicly available surveillance data, hospital statistics, and literature. Results were expressed as the incidence of different disease outcomes and as disability-adjusted life years (DALY), a health indicator combining illness and death estimates into a single metric. It has been estimated that each year ≈370,000 illnesses/million inhabitants are likely caused because of eating contaminated food; 900 of these illnesses are severe and 3 fatal, corresponding to 896 DALY/million inhabitants. Ill-defined intestinal infections accounted for the greatest part of reported cases and 27% of the DALY. Brucellosis, echinococcosis, salmonellosis, and toxoplasmosis were found to be the most common known causes of foodborne illnesses, being responsible for 70% of the DALY. Overall, the DALY metric provided a quantitative perspective on the impact of foodborne illness that may be useful for prioritizing food safety management targets.

To initiate and sustain efforts for prevention and control of foodborne diseases, it is essential to determine the extent and dimensions of the problem (1). Accurate knowledge of disease incidence and severity is invaluable to competent national authorities for use in selecting appropriate management actions to reduce the overall public health impact. However, much of the

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information collated regarding foodborne illnesses by different systems cannot be directly translated into policy (2) for 3 main reasons. First, not all cases are reported to health authorities, and estimates of underreporting result in considerable uncertainty in burden of illness studies, which limits the interpretation and analysis of available information (3,4). Second, often only a fraction of illnesses caused by food-related pathogens are actually foodborne because transmission can also be through the environment, direct contact with animals, or from person to person (5). Third, foodborne illnesses may vary not only in their incidence but also in their severity, resulting in widely different clinical manifestations and potentially involving long-term sequelae, although for their accurate description and quantification a uniform health measure would be needed (6).

To circumvent the latter issue, the World Health Organization (WHO) recommends using disability-adjusted life years (DALY) as a metric to express the public health effects of foodborne diseases (2), and DALY is increasingly used for a wide variety of illnesses (6–8). The aim of this study was to test the feasibility of using publicly available relevant data sources combined with the DALY metric to quantify the annual impact of foodborne illnesses in a country in a format useful for policy decisions. The country selected was Greece. The study used available surveillance data, hospital statistics from 1996 through 2006, and literature. In an attempt to address the first 2 limitations of the types of study mentioned above, we account in our estimates for uncertainty caused by underreporting and food attribution by using probability distributions to describe a range of plausible values for these parameters. Results are also expressed as cases in the general population, reported or estimated severe cases, and deaths to enable comparisons with similar studies in other countries.

Methods

The various steps taken to estimate the incidence and impact of foodborne illness in Greece are shown in Figure 1. Reported cases of illnesses that may be transmitted through food were for the larger part collected from the Hellenic Statistical Authority (ELSTAT) (9) and the Hellenic Center for Infectious Diseases Control (HCIDC) (10). A limited number of data were obtained from WHO disease surveillance reports where HCIDC was mentioned to be the source (11,12) for better transparency and from other literature when no other information was available (13). The study included the period 1996–2006 for which data were available from both national sources. ELSTAT collects information regarding hospitalizations for patients who have a duration of stay ≥ 1 day based on the Basic Tabulation List (BTL) of the International Classification of Diseases, 9th Revision. ELSTAT data are based on sampling of hospitalized patients' bulletins.

This sampling includes bulletins of deceased patients, although these bulletins are not recorded separately. Hospitalizations recorded by the ELSTAT are likely to vary in their severity because the population in Greece had free access to hospital centers where it was possible to be treated even for minor health issues (14). HCIDC collects information on notified cases from hospital microbiologic laboratories and district health authorities (11) and also performs active surveillance on the general incidence of gastroenteritis through physicians' reports (10). HCIDC data can thus be representative of hospitalizations or visits to physicians and are a mixture of laboratory-confirmed and symptom-based notified cases. In the absence of a study validating these 2 systems of collecting information on disease incidence, we considered ELSTAT and HCIDC data to be representative of reported (severe) cases of illness. Corrections for undernotification or overnotification were not made because this would require a country-specific study that is not currently available. For the few illnesses for which data were available from both systems, ELSTAT data were preferred. For cryptosporidiosis, giardiasis, and toxoplasmosis, cases were estimated indirectly taking into account studies on prevalence of these parasites in the general population (15,16). The mean and standard deviation of reported and estimated cases for 1996–2006 were used to create normal distributions, which were considered representative of the annual incidence of these illnesses (17).

Deciding on a precise estimate of the proportion of cases that can be attributed to food is complicated (5). Because of differences in food production, consumption, and the ecology of pathogens, the percentage of foodborne transmission is expected to vary among countries and constitutes a major area of uncertainty. To make an adjustment for food attribution, PERT distributions were

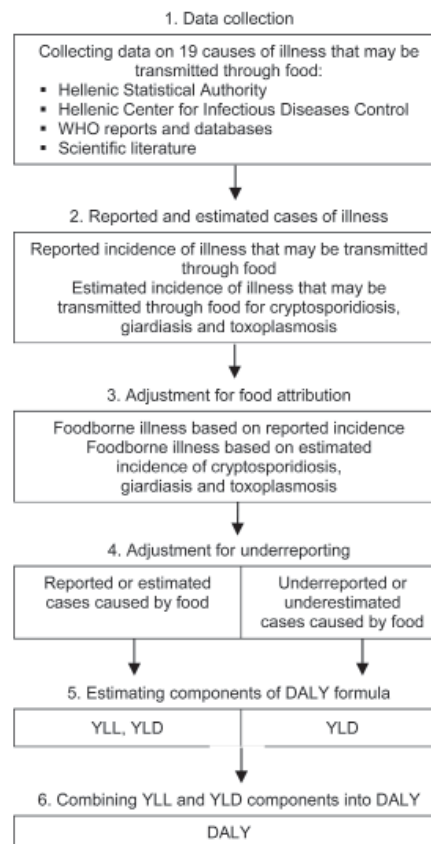


Figure 1. Working scheme for estimating the incidence and effects of foodborne illness in Greece. For cryptosporidiosis and giardiasis, because estimated cases are on the same level of the surveillance pyramid as reported cases, the cases occurring in the community (underestimated cases) were based on underreporting factors suitable for these pathogens. In the case of toxoplasmosis, disability-adjusted life years (DALY) are calculated only on the basis of estimated cases which cover the entire population. WHO, World Health Organization; YLL, years of life lost caused by premature death in the population; YLD, years lived with disability for incident cases of the health condition.

used as multipliers (18) (Table 1). Minimum and maximum parameters of PERT distributions were based on a literature search covering the range of potential values. Most likely values were based on data most relevant to Greece and Europe because endemicity of illnesses is often related to specific regions (19,20).

Not all cases of foodborne illness are reported to health authorities (3), and the degree of underreporting varies greatly among diseases between countries or within 1 country in different periods (21). To make an adjustment for underreporting, PERT distributions were used as multipliers (18) and extremes were selected to cover the full range of values found in literature. Most likely values were set at the middle of this range to give equal weight to extremes of each distribution (Table 1). We assumed that

Table 1. Parameters of the PERT distributions used to describe foodborne transmission, underreporting, and case-fatality rate for foodborne illnesses, Greece, 1996–2006*

Illness	Minimum, most likely, maximum†		
	Food attribution, %	Underreporting	Case-fatality rate, %
Bacterial			
Botulism	80, 100, 100	1.625, 1.8125, 2	3, 10.15, 17.3
Brucellosis	50, 84, 100	2, 10.85, 19.7	0.9, 2, 5
Campylobacteriosis	30, 55, 80	7.6, 274.8, 542	0.1, 0.1265, 0.153
Enterohemorrhagic <i>Escherichia coli</i>	40, 51, 90	2, 14.05, 26.1	0.25, 0.54, 0.83
Leptospirosis	1, 5, 49	10, 15, 20	5, 10, 15
Listeriosis	69, 99, 100	1.1, 1.7, 2.3	10, 30, 44
Salmonellosis	55, 95, 95	3.2, 51.45, 99.7	0.5, 0.701, 0.902
Shigellosis	8.2, 10, 31	3.4, 18.35, 33.3	0.1, 0.13, 0.16
Typhoid and paratyphoid fever	55, 80, 95	2, 7.65, 13.3	0.4, 0.95, 1.5
Food poisoning	87, 100, 100	29.3, 185.65, 342	0, 0.025, 0.05
Parasitic			
Amebiasis	10, 50, 100	9.2, 9.6, 10	0.1, 0.2, 0.3
Cryptosporidiosis	5.6, 5.6, 8	7.4, 53, 98.6	0.07, 0.335, 0.6
Echinococcosis	30, 30, 100	2, 3, 4	1, 2.24, 3
Giardiasis	5, 10, 30	4.6, 25.45, 46.3	0, 0.05, 0.1
Toxoplasmosis	30, 50, 63	NA	3.3, 3.75, 4.8
Viral: acute hepatitis A			
	5, 8, 11	2, 5.55, 9.1	0.3, 1.35, 2.4
Mixed/ill-defined causes			
Other helminthiasis	30, 90, 100	4.6, 51.6, 98.6	3.37‡
Intestinal infections due to other specified microorganism	1, 36, 70	2, 402, 1,562	0.25‡
Ill-defined intestinal infections	1, 36, 50	2, 402, 1,562	0.0045‡

*NA, not applicable.

†Minimum, most likely (mean), and maximum parameters of each PERT distribution. More information, including an expanded version of this table, can be found in the online Technical Appendix (www.cdc.gov/EID/content/17/9/101766-Techapp.pdf).

‡For these illnesses, an average fixed value was used for the case-fatality rates estimated by using data from the World Health Organization Mortality Database on the deaths and incidence data from the Hellenic Statistical Authority.

underreporting factors primarily represent underreported cases of serious illnesses that result in physician visits, and underreporting factors for gastrointestinal illnesses are primarily associated with cases not resulting in physician visits. Although in some studies an arbitrarily assigned factor is used to cover for misdiagnosed or undiagnosed hospitalizations and deaths (3,18), it was omitted in the absence of specific data for Greece and underreported cases caused by this phenomenon were considered to be included in the “ill-defined intestinal infections” BTL code as suggested by other authors (17). We also assumed that all reported cases were diagnosed and coded correctly.

DALY values were calculated as $DALY = YLL + YLD$, where YLL are the years of life lost because of premature death in the population and YLD are the years lived with disability for incident cases of the health condition (22). YLD was estimated for reported or estimated cases and underreported cases, and YLL was estimated based only on reported or estimated cases. The rationale for this was that fatal cases contributing to YLL occur at the top of the surveillance pyramid and, if diagnosed, most likely are notified, particularly for obligatory notifiable diseases such as most of the ones examined here. Moreover, for illnesses contributing to YLD such as gastrointestinal illnesses, underreported

cases not resulting in hospitalization are not expected to have fatal outcomes. The sole exception was listeriosis, in DALY values mainly accounted for through YLL (23), because it has been under surveillance only since 2004. Thus, even serious cases of this infection were expected to be considerably undernotified in part of the period under study because physicians and laboratories might not immediately be aware of the new reporting requirements. Therefore, to avoid underestimation of deaths, YLD for listeriosis was estimated on the basis of reported and underreported cases.

The individual components of the DALY formula are estimated as follows: $YLL = d \times e$, where d is the number of deaths and e is the expected individual life span at the age of death in years; $YLD = n \times t \times w$, where n is the number of cases of a specific illness, t is its duration in years and w is a weight factor (disability weight) that reflects its severity on a scale from 0 (perfect health) to 1 (death) (22,24). In calculating YLL, the number of deaths (d) was estimated by multiplying reported or estimated cases caused by foodborne infection for each illness with a PERT distribution describing a plausible range of pathogen-specific case-fatality rates (18) on the basis of literature data from other industrialized countries (Table 1). Selected case-fatality rates were always from

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the same level of the surveillance pyramid as reported for estimated cases. For some generic BTL codes (e.g., “Other helminthiases,” “Intestinal infections due to other specified microorganism,” and “Ill-defined intestinal infections”), the number of deaths was based on data from the WHO Mortality Database (25).

Regarding the expected individual life span at the age of death in years (*e*), the age of death was estimated on the basis of data collected by the HCIDC and ELSTAT on patients’ age in reported cases. When no explicit information was available in these sources, which was the case for 5 illnesses, age at time of death was assumed to

Table 2. Disability weights related to the diseases included in study of the effects of foodborne infections, Greece, 1996–2006

Illness	Disability weights	
	Reported or estimated cases	Underreported cases
Bacterial		
Botulism		
Moderate cases	0.600	0.600
Severe cases	0.906	0.906
Brucellosis	0.200	0.200
Campylobacteriosis		
Gastroenteritis	0.393	
Reactive arthritis	0.140	
Guillain-Barré syndrome, first year*	0.250	
Guillain-Barré syndrome, long-term sequelae	0.160	
Inflammatory bowel disease	0.260	
Irritable bowel syndrome	0.042	
Enterohemorrhagic <i>Escherichia coli</i>		
Watery diarrhea and hemorrhagic colitis	0.393	0.067
Hemolytic uremic syndrome and end-stage renal disease	†	
Leptospirosis	0.920	0.096
Listeriosis	‡	‡
Salmonellosis		
Gastroenteritis	0.393	
Inflammatory bowel disease	0.260	
Irritable bowel syndrome	0.042	
Reactive arthritis	0.150	
Shigellosis		
Irritable bowel syndrome	0.220	0.096
Irritable bowel syndrome	0.042	
Typhoid and paratyphoid fever	0.600	0.096
Food poisoning	0.220	0.067
Parasitic		
Amebiasis		
Cured	0.400	0.067
Cryptosporidiosis		
Cured	0.393	0.067
Echinococcosis		
Cured	0.200	0.200
Postsurgical conditions	0.239	0.239
Relapse	0.809	0.809
Undiagnosed	0.200	0.200
Giardiasis		
Cured	0.393	0.067
Toxoplasmosis		
Clinical symptoms in the first year of life§	0.140	¶
Asymptomatic at birth, chorioretinitis later in life	0.080	¶
Viral: acute hepatitis A		
Cured	0.500	0.500
Mixed/ill-defined causes		
Other helminthiases		
Intestinal infections caused by other specified microorganism	0.463	0.067
Intestinal infections caused by other specified microorganism	0.400	0.067
Ill-defined intestinal infections	0.400	0.067

*For an explanation of this selection, see the online Technical Appendix (www.cdc.gov/EID/content/17/9/101766-Techapp.pdf).

†For hemolytic uremic syndrome (including end-stage renal disease as a sequela), it is estimated that every case corresponds to 1.05 years lived with disability (24).

‡Not applicable for listeriosis because the high case-fatality rate (>95%) of the disability-adjusted life year estimates is composed of years of life lost (24) that mainly determine the burden of the disease. Therefore, no years lived with disability were estimated.

§Clinical symptoms in the first year of life include chorioretinitis, intracranial calcifications, hydrocephalus, and central nervous system abnormalities that lead to neurologic deficiencies such as mental retardation.

¶Toxoplasmosis cases are estimates for the entire population. Consequently, underreporting does not apply.

be 40 years. To check the impact of this assumption on the ranking of foodborne risks, we tested both extremes by assuming 0 years as the age at death and by assuming YLL to be 0. For “Other helminthiases,” data from the WHO Mortality Database were used. General life expectancy was based on the life table for Greece for 2000 (22). For comparison, estimates were also made by using the WHO standard West Level 26 life table (22).

In calculating YLD, duration of illness (t) was based on data collected by ELSTAT and on literature regarding serious and mild forms of each cause of illness. Different disability weights (w) were used for each disease based on the severity of its sequelae and whether estimated cases likely reach the health system or not (Table 2). All underreported cases were assumed to be mild or self-limiting for gastroenteritis-related illnesses. For serious, non-self-limiting diseases such as brucellosis or echinococcosis that are not related to gastroenteritis, nonreported cases were considered to be as severe as reported or estimated cases.

All estimations were performed by using the @RISK 5.7 software (Palisade Corporation, Ithaca, NY, USA) as an add-in in Microsoft Excel 2010 (Microsoft, Redmond,

WA, USA). Full details regarding estimations of DALY, selection of input distributions and simulation settings can be found in the online Technical Appendix (www.cdc.gov/EID/content/17/9/101766-Techapp.pdf).

Results

Annual Incidence of Foodborne Illnesses

For 1996–2006, we estimated 369,305 (95% credible interval [CrI] 68,283–910,608) illnesses per million inhabitants per year attributable to eating contaminated food, at least 905 of which (95% CrI 499–1,340) are reported or estimated to be severe and 3 fatal (95% CrI 2.0–4.8) (Table 3). Ill-defined intestinal infections accounted for most (94%) cases (sum of reported/estimated and underreported cases). Regarding reported/estimated cases, ill-defined intestinal infections were responsible again for the greatest part (72%), followed by salmonellosis (8.2%), brucellosis (7.1%), food poisoning (4.0%), and echinococcosis (2.7%). Most deaths (48%) were estimated to be caused by brucellosis, although salmonellosis, echinococcosis, listeriosis, and toxoplasmosis also contributed substantially to deaths.

Table 3. Mean estimated incidence of total foodborne illnesses, reported/estimated illnesses, and deaths attributed to food in Greece per 1 million inhabitants, 1996–2006*

Illnesses	Incidence per million inhabitants					
	Total illnesses		Reported/estimated illnesses		Deaths	
	Mean†	95% CrI‡	Mean†	95% CrI‡	Mean†	95% CrI‡
Bacterial						
Botulism	0.13	0.011–0.28	0.066	0.056–0.15	0.0067	0.00052–0.017
Brucellosis	699	225–1,378	64	30–102	1.5	0.52–3.0
Campylobacteriosis	3,571	851–7,733	13	5.6–22	0.016	0.0069–0.029
EHEC	1.0	0.069–2.8	0.072	0.0058–0.17	0.00039	0.000030–0.00098
Leptospirosis	4.0	0.34–13	0.27	0.023–0.84	0.027	0.0022–0.087
Listeriosis	0.89	0.11–1.9	0.41	0.049–0.85	0.19	0.021–0.45
Salmonellosis	3,793	750–8,350	74	22–128	0.52	0.15–0.93
Shigellosis	25	1.1–77	1.4	0.068–3.8	0.0018	0.000088–0.0050
Typhoid and paratyphoid fever	37	3.3–92	4.8	0.47–10	0.046	0.0043–0.11
Food poisoning	6,636	450–17,569	36	2.8–80	0.0089	0.00055–0.025
Parasitic						
Amebiasis	13	1.9–29	1.3	0.19–3.0	0.0026	0.00037–0.0064
Cryptosporidiosis	197	71–360	3.7	2.4–5.3	0.013	0.0050–0.022
Echinococcosis	72	29–140	24	10–45	0.52	0.19–1.0
Giardiasis	159	47–358	6.3	2.7–12	0.0031	0.00069–0.0074
Toxoplasmosis	3.4	2.5–4.1	3.2	2.4–4.0	0.12	0.090–0.16
Other helminthiases	137	22–322	2.7	0.56–5.1	0.089	0.019–0.17
Viral: hepatitis A	6.9	1.4–15	1.2	0.27–2.4	0.017	0.0031–0.038
Mixed/ill-defined causes						
Intestinal infections caused by other specified microorganism	7,394	354–25,558	14	1.2–36	0.035	0.031–0.091
Ill-defined intestinal infections	346,558	45,985–886,276	655	256–1,082	0.030	0.012–0.049
Total of gastroenteritis	368,520	67,536–909,457	812	408–1,245	0.95	0.52–1.4
Total	369,305	68,283–910,608	905	499–1,340	3.1	2.0–4.8

*Values have been rounded to include significant digits and thus not all summations necessarily tally. **Boldface** indicates the top 5 contributors to each estimate category. EHEC, enterohemorrhagic *Escherichia coli*; CrI, credible interval.

†These estimates correspond to the mean of the output distributions.

‡95% CrI representative of the 2.5 and 97.5 percentiles.

Public Health Impact of Foodborne Illnesses Expressed as DALY

Foodborne illnesses accounted for ≈896 DALY per 1 million inhabitants annually (95% CrI 470–1,461), of which 14% were attributable to YLL and 86% to YLD (Table 4). As much as 34% of the estimated effects of foodborne disease in Greece could be attributed to gastroenteritis-related illnesses, and the remaining 66% was unevenly split among 6 non–gastroenteritis-related illnesses (brucellosis, echinococcosis, toxoplasmosis, leptospirosis, hepatitis A, and botulism). Notwithstanding attendant uncertainty (Figure 2), the most serious foodborne illness in Greece was brucellosis, representing ≈55% of the estimated DALY and contributing greatly to illness (>88%). Ill-defined intestinal infections were the second most serious contributor to disease burden (≈27% of DALY), followed by echinococcosis (7.8%) and salmonellosis (4.6%) as known causes of illness.

Discussion

The DALY metric provided a different view on the effects of foodborne illnesses on public health in comparison to incidence estimates (Table 5). Although

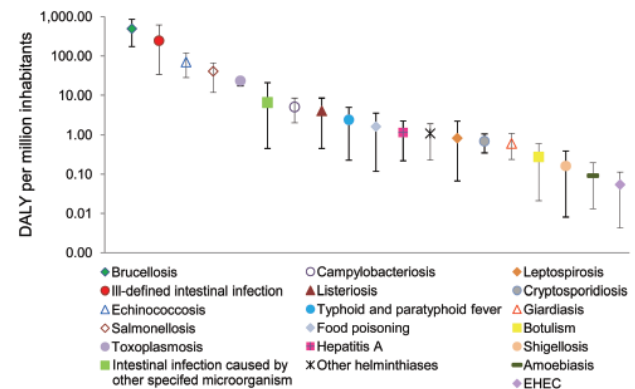


Figure 2. Disability-adjusted life years (DALY) caused by different foodborne diseases per million inhabitants in the course of an average year in Greece, including uncertainty. Estimates are presented on a logarithmic scale on the y-axis. Whiskers represent 95% credible intervals. EHEC, enterohemorrhagic *Escherichia coli*.

salmonellosis was captured as a major contributor by all 4 rankings, there was variation regarding other causes of illness. Interestingly, diseases that have the highest effect on public health either in terms of illness (ill-

Table 4. Estimates of YLL, YLD, and DALY caused by foodborne illnesses in an average year in Greece per 1 million inhabitants, including plausible range attributable to uncertainty*

Illnesses	Estimated YLL (95% CrI)†	Estimated YLD (95% CrI)†	Estimated DALY (95% CrI)†
Bacterial			
Botulism	0.27 (0.021–0.67)	0.0066 (0.00056–0.015)	0.28 (0.021–0.69)
Brucellosis	59 (21–121)	434 (140–856)	493 (174–943)
Campylobacteriosis	1.2 (0.51–2.1)	3.9 (1.5–7.5)	5.14 (2.0–9.4)
Enterohemorrhagic <i>Escherichia coli</i>	0.016 (0.0012–0.039)	0.039 (0.0031–0.091)	0.054 (0.0043–0.13)
Leptospirosis	0.81 (0.066–2.7)	0.015 (0.0013–0.046)	0.83 (0.067–2.7)
Listeriosis	4.1 (0.45–9.7)	‡	4.1 (0.45–9.7)
Salmonellosis	31 (8.7–55)	10 (2.9–19)	41 (12–72)
Shigellosis	0.12 (0.060–0.34)	4.1 (0.0021–0.12)	0.16 (0.0081–0.46)
Typhoid and paratyphoid fever	2.3 (0.21–5.4)	0.17 (0.016–0.38)	2.4 (0.23–5.7)
Food poisoning	0.36 (0.022–0.98)	1.3 (0.088–3.3)	1.6 (0.12–4.1)
Parasitic			
Amebiasis	0.079 (0.011–0.20)	0.013 (0.0019–0.030)	0.092 (0.013–0.22)
Cryptosporidiosis	0.50 (0.20–0.88)	0.20 (0.10–0.32)	0.69 (0.35–1.2)
Echinococcosis	16 (5.9–31)	54 (22–106)	70 (28–135)
Giardiasis	0.12 (0.028–0.29)	0.48 (0.18–0.99)	0.61 (0.24–1.2)
Toxoplasmosis	9.7 (7.0–13)	14 (10–17)	23 (17–29)
Other helminthiasis	0.92 (0.19–1.8)	0.17 (0.029–0.38)	1.1 (0.23–2.1)
Viral: hepatitis A			
hepatitis A	1.1 (0.20–2.4)	0.089 (0.018–0.19)	1.2 (0.22–2.6)
Mixed/ill-defined causes			
Intestinal infections caused by other specified microorganism	1.4 (0.12–3.6)	5.2 (0.26–18.0)	6.6 (0.45–21)
Ill-defined intestinal infections	1.2 (0.5–2.0)	243 (33–621)	245 (34–622)
Total of gastroenteritis§	43 (20–68)	265 (55–643)	308 (94–687)
Total	130 (81–196)	767 (361–1,308)	896 (470–1,461)

*Values have been rounded to include significant digits and thus not all summations necessarily tally. **Boldface** indicates the top 5 contributors to each estimate category. YLL, years of life lost; YLD, years lived with disability; DALY, disability-adjusted life years; CrI, credible interval.

†95% CrI representative of the 2.5 and 97.5 percentiles.

‡DALY due to listeriosis are mainly determined by the YLL (23); therefore, no YLD were estimated.

§Gastroenteritis-related illnesses are considered to be all of the above except: botulism, brucellosis, leptospirosis, echinococcosis, hepatitis A, and toxoplasmosis.

Table 5. Ranking of the top 5 causes contributing to the effects of foodborne illness in Greece as estimated on the basis of individual incidence parameters and disability-adjusted life years, 1996–2006

Rank	Incidence estimates			
	All foodborne illnesses	Reported/estimated illnesses	Deaths	Disability-adjusted life years
1	Ill-defined intestinal infections	Ill-defined intestinal infections	Brucellosis	Brucellosis
2	Intestinal infections due to other specified causes	Salmonellosis	Salmonellosis	Ill-defined intestinal infections
3	Food poisoning	Brucellosis	Echinococcosis	Echinococcosis
4	Salmonellosis	Food poisoning	Listeriosis	Salmonellosis
5	Campylobacteriosis	Echinococcosis	Toxoplasmosis	Toxoplasmosis

defined intestinal infections), death (toxoplasmosis) or both (brucellosis) are not identified in the ranking based on a single individual incidence parameter, but they are captured by DALY, which has the advantage of enabling comparisons between different disease endpoints. For instance, although toxoplasmosis is not among the 5 major contributors on the basis of the total incidence or on reported/estimated cases, it is given more prominence through using the DALY metric because this also accounts for severe outcomes and sequelae of this disease. Although self-limiting diseases may appear to be essential in terms of incidence, on the basis of DALY they do not greatly contribute to either illness or death. Therefore, use of the DALY metric gives a different and risk-based perspective of the influence of foodborne illnesses on the health of a country's population because it is estimated on the basis of the diseases' frequency (incidence) and severity (health effect).

Most of the foodborne illness cases in Greece were caused by ill-defined intestinal infections (Table 3). This finding is consistent with results from similar studies in other countries (3,17). Using the current Greek surveillance system, we cannot attribute this burden to known causes of gastroenteritis other than the ones included in this study. Noroviruses could be the etiologic agents in a large proportion of these ill-defined intestinal infections because they have been considered the most likely agent of foodborne illness caused by unknown agents (26) and have been found in other studies to be a most common cause of foodborne illness due to known agents (17,18). Outbreak data found for these pathogens were scarce (27) and therefore not included in this study. A considerable part of this category might also have been caused by other unknown agents of illness or known agents that have been misdiagnosed. For instance, campylobacteriosis is expected to be undiagnosed to a great extent in Greece because few laboratories in the country have the ability to identify the pathogen (10). This finding could partially explain the high underreporting factor estimated for this illness for Greece, based on the approach of Ekdahl and Giesecke (28) compared with results for other Western countries (3,29).

Brucellosis was found to be the leading cause of illness and death in Greece. Although its incidence showed

a reasonably consistent decline during the period of this study, it still constitutes a serious public health problem (Figure 3). The disease is most common in rural areas of the country, and risk factors for its contraction are occupational contact with animals and the consumption of unpasteurized milk and milk products (30,31).

Echinococcosis was the second most notable foodborne illness. This disease has been recognized as a serious health problem in the country (32) and linked with contaminated food (10,33). Echinococcosis caused by *Echinococcus granulosus* (cystic echinococcosis) is the dominant form in Greece (32), where the infection is hyperendemic (19). Although its incidence has gradually decreased since 1984 as a result of a long anti-echinococcosis campaign and general improvements in living and hygiene standards (32), it still is a serious health risk for the population (Figure 3).

Salmonellosis was the third most serious foodborne illness of known etiology in terms of public health impact, and it also was the most prominent gastroenteritis-related illness of identified cause (Table 3). This finding is consistent with it being a noteworthy zoonosis, which contributes to a high prevalence of gastrointestinal illness in the European Union (34), and the most often reported causative agent of outbreaks of an identified etiologic agent worldwide (35).

After salmonellosis, congenital toxoplasmosis was also a major contributor to the disease burden, although in terms of incidence it is an uncommon illness with <4 cases per million inhabitants. The disease has not been

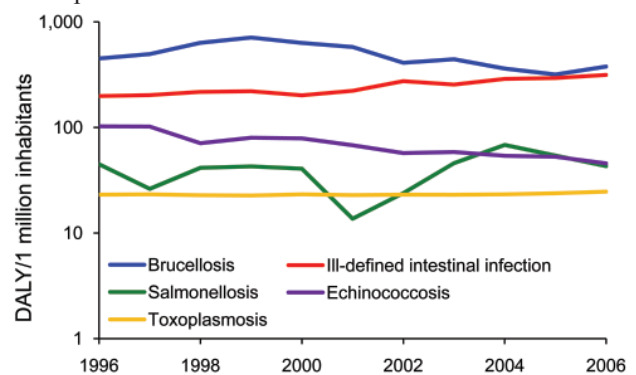


Figure 3. Trends for the top 5 contributors to the burden of foodborne diseases in Greece, 1996–2006. DALY, disability-adjusted life years.

recognized as a major foodborne illness in the country, although its serious health consequences have been well documented (36).

There are 4 major factors that add to the uncertainty in our estimates that are not independent: 1) underreporting, 2) food attribution, 3) the quality of incidence data, and 4) value choices in the DALY formula. Given the limited data available for Greece, data from other countries have been used to create multipliers for underreporting and foodborne transmission (online Technical Appendix); these data were of variable quality and representativeness. For instance, in the case of campylobacteriosis and salmonellosis, underreporting factors based on tourist studies (28,37) have been included in the multipliers, which were higher than underreporting factors from other Western countries for the same pathogens (4,18). Such underreporting factors might not be completely representative of the difference between reported cases resulting in physician visits and cases in the general population because these studies can be subject to several biases (e.g., tourists differ from natives in exposure) (28), although at the same time they cover for phenomena such as undernotification and misdiagnosis of illnesses that were beyond our intention. As a consequence of including data derived by using different method approaches, the plausible range of these multipliers was wide, which resulted in DALY estimates with similarly wide credible intervals (Figure 2). However, despite this limitation, our estimates can still be used for risk ranking purposes.

Uncertainty is also an inherent property of incidence data. Specifically, data for reported cases in Greece (and elsewhere) rely on insufficiently detailed codes, there is incomplete or lacking separate surveillance for many foodborne pathogens, and a specific diagnosis is not given for most episodes of enteric illness requiring hospitalization. These factors result in the greater part of reported cases of gastroenteritis being attributed to ill-defined causes. As with other studies of this kind, assumptions had to be made, notably considering the age of death. Although this assumption did not change the 5 major foodborne risks, it had considerable impact on the individual estimates. We also had to assume that serious cases of illness that have been reported because of a specific agent have been diagnosed and coded correctly or notified to the appropriate authorities. This assumption might not always be the case because at least some of these illnesses are expected to be part of the ill-defined illnesses. A correction for misdiagnosis and undernotification cannot be included for the reported illnesses until country specific data are available. Assigning an arbitrary factor as in other studies (3) introduces new uncertainties and, unlike incidence data in the case of DALY, can affect the ranking of foodborne risks. Thus, our estimates are based only on the illnesses that the surveillance system in Greece currently exposes,

and the estimates' robustness can only be further improved through improved surveillance.

As for uncertainty resulting from value choices in the DALY formula itself, in the present study no age-weighting or discounting were used because their combined use has been criticized as attributing considerably fewer disease impacts and effects to younger age groups (38), and disability weights were carefully selected. For policy-making purposes, ideally, disability weights should be based on the opinion of the general public because they should reflect preferences of the society being studied (21). Conceivably, use of the DALY metric could help reduce a considerable part of overall uncertainty by accounting for sequelae, which are not normally taken into consideration in studies focusing solely on incidence of foodborne illness yet do constitute a substantial part of the overall effects on a population. In our study, all well-defined sequelae for which information existed in literature were used for DALY calculations, but our findings could be subject to change when new insights become publicly available. For instance, rates of posthospitalization morbidity related to gastrointestinal illnesses have not been taken into account in the absence of a specific study, although the duration of illness can be longer than the actual hospital stay.

Finally, selection of life tables is another factor that can influence the DALY estimates. When our estimates could be based on West Level 26 life tables, total burden of illness expressed as DALY increased by only 0.0042%, although individual estimates for illnesses could differ by up to 5.0% (results not shown).

Regarding the total incidence of foodborne illnesses, our estimates were in the same range as the estimates for Australia (Table 6), although somewhat higher because the study by Hall et al. was restricted to gastroenteritis-related foodborne illnesses (17). Our estimates of severe reported or estimated cases are between the range of hospitalization rates mentioned for different countries, and the same is the case for our case-fatality rates. Our DALY estimates were higher than estimates for the Netherlands (7) or New Zealand (39), although our estimated overall impact for gastrointestinal illnesses is still comparable to the one from the Netherlands where brucellosis is not a major foodborne risk.

Our finding that brucellosis, salmonellosis, echinococcosis, and toxoplasmosis together accounted for $\approx 70\%$ of annual DALY means that these diseases might be major targets for policy making regarding appropriate food safety management actions, especially because their causative agents and likely transmission routes are generally known. Overall, the approach may be of interest to competent authorities in other countries requiring risk-based estimates ranking the impact of foodborne pathogens on public health to prioritize risk management actions.

Table 6. Comparison of foodborne illness effects on public health in Greece with estimates from other countries*

Country (reference)	Target	Disease estimates per 1 million inhabitants			
		All illnesses†	Hospitalizations	Deaths	DALY
United States (3)	All causes	270,057	1,155	18	NA
United States (18)	Known agents	31,438 (90% CrI 22,074–42,475)	187 (90% CrI 132–253)	5 (90% CrI 2–8)	NA
United States (40)	Unspecified agents	128,404 (90% CrI 66,318–204,670)	240 (90% CrI 33–526)	6 (90% CrI 1–11)	NA
England and Wales (29)	All causes	26,161	406	9	NA
Australia (17)	Gastro	281,250 (95% CrI 208,333–359,375)	766 (95% CrI 594–922)	4 (95% CrI 2–6)	NA
The Netherlands (7)	All causes	79,725–104,256	NA	1–12	184–613
New Zealand (39)	6 agents‡	128,421 (95% CrI 34,801–330,075)	NA	NA	632 (95% CrI 344–1,066)
Greece (this study)	All causes	369,305 (95% CrI 68,283–910,608)	905 (95% CrI 499–1,340)§	3.1 (95% CrI 2.0–4.8)	896 (95% CrI 470–1,461)
Greece (this study)	Gastro only	368,520 (95% CrI 67,536–909,457)	812 (95% CrI 408–1,245)§	0.95 (95% CrI 0.52–1.4)	308 (95% CrI 94–687)

*Data have been normalized for population differences and are expressed per million inhabitants. DALY, disability-adjusted life years; NA, not available; CrI, credible interval; gastro, gastroenteritis.

†Credible interval not available for all studies.

‡The study was limited to campylobacteriosis, salmonellosis, listeriosis, infection with Shiga toxin-producing *Escherichia coli*, yersiniosis, and infection with norovirus.

§The reported/estimated cases of severe illness in this study can be considered to be approximately the same as hospitalizations.

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Ms Gkogka is a PhD student in the Laboratory of Food Microbiology of Wageningen University. She is interested in food safety management, risks caused by foodborne illnesses, and approaches for assessing risk-based decision making.

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Risk-based Estimate of Effect of Foodborne Diseases on Public Health, Greece

Technical Appendix

SELECTION OF INPUT DISTRIBUTIONS AND OTHER PARAMETERS FOR THE DISABILITY-ADJUSTED LIFE YEAR ESTIMATES

Reported cases: Reported cases of illnesses that may be transmitted through food were for the larger part collected from the Hellenic Statistical Authority (ELSTAT) (1) and the Hellenic Center for Infectious Diseases Control (HCIDC) (2). A limited number of data were obtained from WHO disease surveillance reports where HCIDC was mentioned to be the source (3,4) for better transparency and from other literature when no other information was available (5). The study included the period 1996 through 2006 for which data were available from both national sources (Technical Appendix Technical Appendix Table 1). ELSTAT collects information regarding hospitalizations for cases that have a duration of stay of at least 1 day based on the Basic Tabulation List (BTL) of the International Classification of Diseases, Ninth Revision (ICD-9). ELSTAT data are based on sampling of hospitalized patients' bulletins. This sampling includes bulletins of deceased patients though the latter are not recorded separately. Recorded hospitalizations by the ELSTAT are likely to differ in their severity as Greece's population had free access to hospital centers during the period of the study where it was possible to be treated even for minor health complaints (6). HCIDC collects information on notified cases from hospital microbiological laboratories and district health authorities (3) while it also performs active surveillance on the general incidence of gastroenteritis in the country through physicians (2). HCIDC data can thus be representative of hospitalizations or visits to physicians and they are a mixture of laboratory confirmed and symptom based notified cases. For the few gastrointestinal illnesses (shigellosis, typhoid and paratyphoid fever) for which data were available from both sources, cases were usually more for hospitalizations (ELSTAT data) than for notified cases (HCIDC data). Among the non-gastrointestinal illnesses (echinococcosis and brucellosis) this was always the case. This could be due to the fact that either there is serious

undernotification (both by hospitals and physicians) to the HCIDC or extended repetition of tests and prescriptions in hospitals as suggested by Mossialos et al. (6) that could result in more than one bulletin for the same person. For the purpose of our estimates, we considered both ELSTAT and HCIDC data to be representative of reported (severe) cases of illness and we decided not to include undernotification (or possible overnotification) because a correction for these phenomena would require a country specific study on the validation of the 2 systems, which is not available. For the four illnesses for which data were available from both systems, ELSTAT data were preferred because they are based on sampling of bulletins directly from hospitals while part of the HCIDC data are collected indirectly through district health authorities (3).

Percentage foodborne: To cover for the uncertainty associated with food attribution, program evaluation and review technique (PERT) distributions were used as multipliers (7). The minimum and maximum parameters of the PERT distributions were based on a literature search covering the range of potential values for this factor for every illness, and the most likely values were based on data most relevant to Greece/Europe as the endemicity of illnesses is often related to a specific region (8–10). When no European data could be found, data from other industrialized countries (7,11) and in the absence of the latter expert elicitation data (12) were used. When no other information was available to construct an upper limit for foodborne transmission a value of 100% was assumed as in the case of brucellosis, echinococcosis, amoebiasis and other helminthiasis. A synopsis of the selected parameters accompanied by the country of origin of the data are provided in Technical Appendix Table 2. More detailed information about the range of values found for every illness during the literature search is provided below.

Underreporting: To cover for the uncertainty associated with under-reporting, Pert distributions were used as multipliers (7). The minimum and maximum parameters of these distributions were selected to cover the full range of values found in literature for this factor and the most likely values were set at the middle of this range for every illness since unlike food attribution there is no particular reason to consider European data more representative than data from other industrialized countries for this phenomenon. A synopsis of the selected parameters accompanied by the country of origin of the data are provided in Technical Appendix Table 2. More detailed information about the range of values found for every illness during the literature search is provided below.

Case-fatality rate: To cover for the uncertainty associated with the case-fatality ratio, PERT distributions were also used as multipliers. The minimum and maximum parameters of these distributions were selected so as to cover the range of values found in literature for this factor and the most likely values were set at the middle of this range for every illness. The literature search was focused on reviews for specific pathogens, outbreak studies and national burden of disease studies. The selected case fatality ratios from these studies were always based on reported cases of serious illness resulting in physician visits so that they are on the same level of the surveillance pyramid as the cases reported in Greece's surveillance system. In some instances few national data were available to estimate case fatality rates for generic codes ("Ill-defined intestinal infections," "Other helminthiases" and "Intestinal infections due to other specified microorganism") found in the WHO Mortality Database (13). A synopsis of the selected parameters accompanied by the country of origin of the data are provided in Technical Appendix Technical Appendix Table 2. More detailed information about the range of values found for every illness during the literature search is provided below.

Disability weights: To select the disability weights, studies were collected from literature in which the burden of every illness was quantified by using disability-adjusted life years (DALYs). Selected studies involved review studies on the global burden of specific illnesses (e.g., echinococcosis [14], brucellosis [15]) or on the burden of foodborne pathogens in the European Union (EU) or the Netherlands and other countries where the same indicator was used (16–19). For generic codes involving gastrointestinal illness due to various causes (e.g., "Other helminthiases") or unknown causes (e.g., "Ill-defined intestinal infections") disability weights were selected conservatively by using the classification system by Murray (20) in such a way that they would coincide with the upper range of every disability weight class. For example in the case of the ill-defined illness a disability weight of 0.4 was selected which corresponds to the upper range of class 3 disability weights (ranging from 0.220–0.4) used to describe severe gastrointestinal illness in other studies (e.g., 0.393 for severe gastroenteritis due to enterohemorrhagic *Escherichia coli* (EHEC) and giardiasis [16,18]). For underreported mild cases of gastrointestinal illness when no data on disability weights could be found in literature (e.g., "Ill-defined intestinal infections" or "Amebiasis") given the similarity of mild diarrheal symptoms of infectious origin (21) a disability weight of 0.067 was chosen as in other studies

where weights are assigned to mild diarrheal symptoms (18,22). A synopsis of all the selected disability weights is provided in Technical Appendix Technical Appendix Table 3.

SOFTWARE

We performed all estimations using the @RISK 5.7 software (Palisade Corporation, Ithaca, NY, USA) as an add-in in Microsoft Excel 2010 (Microsoft, Redmond, WA, USA) based on one simulation of 100,000 iterations, performed by applying the Latin Hypercube technique using a fixed seed value of 1 to enable our results to be reproduced by others and to make possible comparisons between alternative inputs.

BACTERIAL DISEASES

Botulism

Reported cases: Based on HCIDC data (Technical Appendix Technical Appendix Table 1).

Percentage foodborne: According to Abgueguen et al., 80%–100% of cases of botulism in the EU are foodborne (23) and 100% of the cases in France have been attributed to food (24). Given the fact that wound botulism, which is the only form of the disease not related with food, occurs very rarely in Europe (25) the estimate of 100% was chosen for Greece.

Case-fatality rate: The most likely case-fatality rate was considered to be 10.15%, the average of the range suggested by US data (3%–17.3%) (7,26).

Disability weight: It is estimated that ≈25% of the patients have to be intubated (severe cases) (26) and the remaining 75% are considered to be moderate cases. Disability weights of 0.906 were assigned to the severe cases and 0.6 to the moderate cases based on the description of the symptoms of the latter by Mann et al. (27) and the definitions of disability weights by Murray (20).

Duration of illness: The duration of illness was estimated to be 60 days for the patients ending up in need of mechanical help for respiration according to EU studies (23,28) while for the moderate cases the reported hospitalization time is 1 (27) to 2 weeks (29). The latter value was considered to be more reliable since it is based on estimates from a much larger outbreak of botulism that did not involve any pending legal actions unlike the former value.

Underreporting: A factor of 1.8125 was considered which is in the middle of the range 1.625–2 (11,25).

Note: The reported cases for Greece during 1998–2007 do not involve any incidents of infant botulism (2). Reported and underreported cases were considered to be equally severe. Although mild cases of botulism can also occur and they have often been reported during outbreaks, they were not considered here because affected persons seldom seek medical care and are not normally captured by surveillance unless they are part of an outbreak (7). Annually reported cases in Greece are ≤ 1 and they do not fit the outbreak definition (≥ 2 cases) (30).

Brucellosis

Reported cases: Based on ELSTAT data (ICD-9 code 023; BTL code 031) (Technical Appendix Technical Appendix Table 1).

Percentage foodborne: In a Greek study foodborne transmission was mentioned to be 84% (31) and in US studies 50% (7,11). Given the fact that brucellosis is a disease that is considered to have a high transmission rate through food (32) the value from the Greek study was selected to represent the mean of the PERT distribution. The minimum value of the distribution was based on the US studies, and the maximum value on an arbitrarily assigned conservative value of 100% since no other upper limit has been found in literature.

Case-fatality rate: The case-fatality rate of brucellosis is 5% based on Mead et al. (11) but on the HCIDC Web site it is stated that the mortality rate for the disease is less than 2% (2) and Roth et al. mention that the mortality rate is negligible although the disease can last for several years (15). A case-fatality rate of 2% was finally selected since it was considered to be closer to the situation in Greece (33). We considered 0.9% as a lower limit for the case-fatality rate based on recent US data (7).

Disability weight: A disability weight of 0.2 was assigned as in the study by Roth et al. based on the fact that the disease is perceived as painful and affecting occupational ability even during periods of remission (15).

Duration of illness: The median duration of the disease (clinical manifestation) is 3.11 years based on Roth et al. (15).

Underreporting: Given the seriousness of the disease whose clinical manifestations can last for years the underreporting factor would in theory be expected to be low (e.g., 2) as suggested for serious illnesses (11). Nonetheless, it can be as high as 19.7 based on estimates for the annual incidence of the disease in certain regions in Greece (34) and the average annual incidence of hospitalizations due to brucellosis during 1996–2005 (1). The average of these extremes was selected (10.85).

Note: Reported and underreported cases were considered to be equally severe.

Campylobacteriosis

Reported cases: Based on HCIDC data (Technical Appendix Technical Appendix Table 1).

Percentage foodborne: The percentage of cases of campylobacteriosis that can be attributed to food ranges from 30% to 80% based on various European studies summarized by Havelaar et al. (12). Although some of these studies mention 80% of the cases to be foodborne (11,35) data from a recent publication of the European Food Safety Authority on campylobacteriosis in the EU point out toward lower food attribution values, since only 35% of outbreaks and less than 50% of outbreak cases based on this study are due to food and drinking water (36) and the same is the case for another recent expert elicitation study according to which only 42% of the cases are due to food (12). Therefore, given this large variation among studies the average of the reported range of food attribution values in the European studies was selected as the most likely value for the PERT distribution (55%).

Case-fatality rate: A case fatality rate of 0.1265% was selected, which is in the middle of the observed range 0.1–0.153 for reported cases (7,11,35).

Disability weight: Different disability weights were assigned to each of the potential outcomes for reported cases of campylobacteriosis based on van Lier and Havelaar (16) and Haagsma et al. (37) as can be seen in Technical Appendix Technical Appendix Table 4. All underreported cases were assumed to be cases of self-limiting gastroenteritis and were thus assigned a disability weight of 0.067 (38).

Duration of illness: The estimated duration of each outcome for the reported cases can be seen in Technical Appendix Technical Appendix Table 4. The underreported cases were

assumed to have a duration of 3.48 days, which corresponds to gastroenteritis due to *Campylobacter* that does not result in a visit to GP (22).

Underreporting: Mead et al. mention that the disease is under-reported by a factor of 38 (11). According to European studies under-reporting of campylobacteriosis is estimated to be much lower; 7.6 based on Wheeler et al. (39) and 10.3 based on Adak et al. (35). However, taking into account that in Greece very few laboratories have the ability to identify the pathogen (2) the underreporting is expected to be higher than in other European countries and this was indeed found to be the case in a study by Ekdahl and Giesecke (40). However, in the latter study the incidence data for campylobacteriosis in Greece used to derive the underreporting factor where much lower than what is known for the year 2000 based on WHO data. Therefore by repeating the calculations for the correct national data the under-reporting factor was estimated as:

$$\frac{\left(\frac{\text{risk per 100,000 inhabitants in Finland}}{\text{risk per 100,000 travellers returning from Finland}} \right)}{\left(\frac{\text{risk per 100,000 inhabitants in Greece}}{\text{risk per 100,000 travellers returning from Greece}} \right)} = \frac{\left(\frac{68.2}{0.9} \right)}{\left(\frac{2.473}{17.7} \right)} = 542$$

To cover for uncertainty due to this parameter the whole range of under-reporting factors was considered (7.6–542) and the most likely value (274.8) was considered to be at the middle of this range.

EHEC

Reported cases: Based on HCIDC data (Technical Appendix Technical Appendix Table 1).

Percentage foodborne: Approximately 51% of the sources of EHEC outbreaks are foodborne or waterborne in Europe according to a study by Ammon for 1992–1996 (41). The range of values for this percentage could be larger (40%–90%) (12).

Case-fatality rate: The case-fatality rate for *E. coli* O157 has been estimated to be in the middle of the range suggested for EHEC O157 (0.25%–0.83%) (11,42).

Disability weight: There are four major conditions related with EHEC infection that determine the burden of the disease, watery diarrhea, hemorrhagic colitis, hemolytic-ureamic

syndrome (HUS) (43) and end-stage renal disease (ESRD). For watery diarrhea and hemorrhagic colitis a disability weight of 0.393 was assigned based on van Lier and Havelaar (16). It was also considered that for every reported case of EHEC, 0.5 cases of HUS occur, and that every case of HUS (including ESRD as a sequela) corresponds to 1.05 YLD (16). All underreported cases were considered to be cases of mild gastroenteritis for which a disability weight of 0.067 was selected (38).

Duration of illness: The duration of EHEC-related gastroenteritis varies between 2–9 days (44). Here, an average duration of 5.6 days was selected for watery diarrhea and hemorrhagic colitis due to EHEC infection according to van Lier and Havelaar (16). For the under-reported cases a duration of 3 days was assumed based on the median duration of non-bloody shiga toxigenic *Escherichia Coli* (STEC) O157 gastroenteritis (22).

Underreporting: An underreporting factor of 2 has been mentioned for verocytotoxin producing *Escherichia coli* (VTEC) in England and Wales (35) and 26.1 has been mentioned for the United States. (7). The most likely value (14.05) was considered to be in the middle of this range. Given the fact that cases of EHEC have only recently started to be under surveillance in Greece (2) undernotification of EHEC is also possible.

Leptospirosis

Reported cases: Based on HCIDC data (Technical Appendix Technical Appendix Table 1).

Percentage foodborne: Leptospirosis is contracted by direct or indirect contact with the urine of an infected animal (45) and thus common vehicles of the infection are contaminated food, water and soil (46). Though leptospirosis is considered to be a foodborne disease (46,47) estimating an actual percentage of cases that can be attributed to food is complicated since this disease has various ways of transmission (46). In a recent review of leptospirosis in the north of Greece, the source of the infection had been identified in only 51% of the cases studied where it was found to be non-food related (48). This means that the percentage of cases that can be attributed to food is anywhere between 1 and 49%. Taking into account another review of the disease in Germany where different types of exposure are mentioned (49) it can be concluded that food is not a common vehicle of the disease but keeping in mind that the only outbreak of leptospirosis in Greece reported in literature was foodborne (involved drinking water at a cafe)

(45) we assumed a very low food attribution of 5% which is in the same range as the one of hepatitis A or *Rotavirus* infections (12).

Case-fatality rate: The severity of the disease caused by leptospirosis can vary considerably, ranging from a subclinical infection to a severe syndrome of multi-organ infection with high mortality (45). Among those that become ill, leptospirosis has two clinically recognizable syndromes, the anicteric form (90% of patients) and the icteric form or Weil syndrome (50). Deaths from the anicteric form of the disease have been reported as rare (50) or almost nil (45) and in the $\approx 10\%$ of the patients that have the icteric form there is an associated 10% mortality rate (ranging from 5% to 10%) (45,50). In our study we assumed all reported cases to be representative of the icteric form of the disease and thus the latter case fatality rate was considered.

Disability weight: The anicteric form includes the great majority of infections which are either subclinical or of very mild severity for which we assumed a class 1 disability weight of 0.096 (20). The icteric form of the disease is very severe and is characterized by impaired renal and hepatic function, hemorrhage, vascular collapse, and mental status changes (50) and can have severe sequelae like acute renal failure, which occurs in 16 to 40% of the cases (45). Thus, for icteric leptospirosis a class 6 disability weight of 0.920 was assumed (20).

Duration of illness: Leptospirosis is listed in the ICD 10 coding system under code A27. Based on the average of countries that have submitted information in the EHMD for this disease in the years 2004–2006 we have considered the average duration of hospitalization to be ≈ 12 days (51). The underreported cases are assumed to belong to people that present the anicteric form of the disease which is not likely to result in medical consultation and lasts for about a week (45).

Underreporting: We assumed that all reported cases belong to the icteric form of the disease which is serious and that all underreported cases can be attributed to the anicteric form of the disease. Thus, an under-reporting factor of 15 was applied since the ratio of icteric/anicteric leptospirosis has a possible range between 1/20 and 1/10 (45).

Listeriosis

Reported cases: Based on HCIDC data. For 2001 and 2002 data from a European report on listeriosis in EU countries (5) were used since no data were available from the HCIDC for these years (Technical Appendix Table 1).

Percentage foodborne: 99% of the cases were considered to be foodborne (35). Other authors, however, mention this percentage being in the range of 69%–99% (12) or 100% (7).

Case-fatality rate: The case-fatality rate can range between 10% and 44% based on outbreak data covering both perinatal and other outbreak cases of severe listeriosis tabulated by Schlech (52). The average of these extreme values was considered (27%)

Disability weight: No disability weight was assigned to this disease since the burden of illness is determined mainly by the fatal cases (22). Moreover given the variety of symptoms related with either postnatal or adult acquired listeriosis (meningitis, sepsis, septicemia, pneumonia, abortion to mention but a few) assigning a uniform disability weight is extremely complex.

Duration of illness: For the same reason, as mentioned for disability weight, no assumptions were made regarding the duration of illness.

Underreporting: An underreporting factor of 1.7 was selected, which is in the middle of the range found in literature for this pathogen 1.1–2.3 (7,53) Under-reported cases were assumed to have the same severity as reported cases. Listeriosis is also the only disease in our study for which underreported cases were also used in estimating the total number of deaths. The reason for this is that the disease has only recently started to be under surveillance in Greece by the HCIDC and it is thus expected to be under-notified. Given again the fact that the DALY due to listeriosis are defined by the fatal cases any under-notification of the disease is likely to lead to a considerable underestimation of its true impact on the health of a population. Thus deaths are also estimated based on the expected number of underreported cases.

Note: mild cases of listeriosis resulting in diarrhea are not considered in this study.

Salmonellosis

Reported cases: Based on HCIDC data (Technical Appendix Table 1).

Percentage foodborne: 95% of the cases are considered to be foodborne (11,24). However, this value may also be considered to be 55%–95% (12).

Case fatality: The case fatality rate is considered to be 0.701% which is in the middle of the range 0.5%–0.902% suggested for laboratory confirmed cases (7,35).

Disability weight: According to other studies on the burden of illness (16,37) salmonellosis has 4 potential outcomes: gastroenteritis, inflammatory bowel disease, irritable bowel syndrome and reactive arthritis for which the incidence and disability weights are presented in Technical Appendix Table 5. For the underreported cases, which we assumed that they did not result in a visit to a physician, a disability weight of 0.067 was selected (22).

Duration of illness: The duration of illness for reported cases of illness is shown in Technical Appendix Table 5. For the under-reported cases a duration of 5.58 days was assumed based on the median duration of gastroenteritis in salmonellosis patients that do not visit a GP (22).

Under-reporting: Mead et al. mention that the disease is under-reported by a factor of 38 (11) and in European studies underreporting factors of 3.2 (39) or 3.9 (35) are mentioned though in a recent study by de Jong and Ekdahl the underreporting factor for several other European countries was mentioned to be much higher and in particular for Greece 99.7 (54). Thus the whole range was considered (3.2–99.7) with a most likely value set at the middle of the extreme values (51.45).

Shigellosis

Reported cases: Based on HCIDC and ELSTAT data (ICD-9 code 004; BTL code 012) (Technical Appendix Table 1). HCIDC data were not available for 1996–2003 and then ELSTAT data were used. For the remainder years (2004–2006) data from the HCIDC were used.

Percentage foodborne: 10% of the cases were considered as foodborne (24). This value may nonetheless range between 8.2 based on data from England (35) and 31% based on recent US data (7).

Case-fatality rate: The case-fatality rate was considered to be 0.1%–0.16% (7,11) with the average (0.13%) as the most likely value.

Disability weight: A disability weight of 0.22 was selected based on Wijewardene and Spohr (19). For the under-reported cases a disability weight of 0.067 was selected (22). To describe sequelae related with irritable bowel syndrome the same disability weight as for campylobacteriosis and salmonellosis derived IBS was used (37).

Duration of illness: The duration of hospitalizations (4.6 days) is based on data from the ELSTAT. For the under-reported cases the duration of illness was assumed to be the same as for *E. coli* O157 i.e., 3 days (22). For irritable bowel syndrome the same duration as for campylobacteriosis and salmonellosis derived IBS was used (37).

Under-reporting: Scallan et al. mention an under-reporting factor of 33.3 (7) and Adak et al. report a factor of 3.4 (35). The whole range was considered (3.4–33.3) with a most likely value set at the middle of the extreme values (18.35).

Typhoid and paratyphoid fever

The clinical manifestation of paratyphoid fever is very similar to the one of typhoid fever though usually milder (55). Nonetheless, given the fact that these infections are discussed together we also decided to treat them as one when estimating their health burden.

Reported cases: Based on HCIDC and ELSTAT data (ICD-9 code 002; BTL code 011) (Technical Appendix Table 1).

Percentage foodborne: 80% of the total cases are estimated to be foodborne based on data from England and Wales (35). Nonetheless, variation could be much greater if we accept the range of what is considered foodborne for *Salmonella* spp. (55%–95%) (12).

Case fatality: Is in the range of 0.4%–1.5%. The average of these extremes (0.95%) was considered to be the most likely value (11,24).

Disability weight: A disability weight of 0.096 has been selected by Wijewardene et al. (19). However, considering that the disability weight for non typhoidal gastroenteritis due to salmonellosis is 0.393 only for hospitalized cases according to van Lier and Havelaar (16) a disability weight of 0.096 does not reflect the severity of the disease. Therefore it was decided to arbitrarily assign a class 4 disability weight of 0.6 to severe cases of typhoid fever (hospitalizations) and a class 1 disability weight of 0.096 to uncomplicated cases that can be

treated at home since no other studies regarding the severity weight of this disease have been found in literature (20).

Duration of illness: Acute cases were assumed to last ≈ 2 weeks and uncomplicated cases usually 1 week (55,56).

Under-reporting: An under-reporting factor of 2 has been used for typhoid fever (11, 35) but a factor of 13.3 has also been suggested (7). The most likely value was set at the middle of this range (7.65).

Food poisoning

Reported cases: Based on ELSTAT data (ICD-9 codes 003, 005; BTL code 013) (Technical Appendix Table 1).

The BTL code under this item includes the following two ICD-9 codes (57):

Other salmonella infections (003) and

Other food poisoning (bacterial) (005). The latter category includes:

- Staphylococcal food poisoning
- Botulism
- *Cl. perfringens* food poisoning
- Food poisoning due to other *Clostridium* species
- Food poisoning due to *Vibrio parahemolyticus*
- Other microbial food poisoning (*B. cereus* food poisoning)
- Other unspecified food poisoning

Since we have separate data for the category “other salmonella infections” and “botulism” though the HCIDC, these have been used separately to estimate disease burden due to salmonellosis and botulism. Given the fact that fish and shellfish are always consumed cooked in Greece *V. parahemolyticus* is not expected to be a pathogen of concern to the public health although it has been isolated from fresh fish in the country (58) and is currently not included in the microorganisms that are notified to the HCIDC. *Bacillus cereus*, *Staphylococcus aureus*, and

Clostridium perfringens are mentioned as the most frequent causes of food poisoning in different countries (59–63) and thus it was assumed that the DALY due to food poisoning are defined by these three microorganisms. The short duration of hospitalization in Greece for food poisoning (weighted average of 4 days based on data from 1998–2005 that include cases of salmonellosis and botulism that are known to last longer) supports this assumption.

Percentage foodborne: By definition 100% is foodborne. Nonetheless, in some studies the percentage foodborne of the diseases caused by *S. aureus*, *B. cereus* and *C. perfringens* is somewhat lower ranging from 87%–91% (12).

Case fatality: Food poisoning due to the above microorganisms is generally self-limiting with an extremely low case fatality ratio, that ranges from 0 to 0.05% for these 3 pathogens (11,64). The average of this range (0.025%) was considered as the most likely value.

Disability weight: *B. cereus*, *St. aureus* and *Cl. perfringens* cause mild, self-limiting illnesses (65) so a class 1 disability weight of 0.067 was assigned to under-reported cases to match the disability weights of other underreported gastrointestinal illnesses included in this study and a class 2 disability weight of 0.220 to reported cases based on Murray, 1994 (20).

Duration of illness: Recovery from this kind of food poisoning is rapid and ranges usually from 1 to 3 days (44,66). The highest observed duration of illness (3 days) was selected for hospitalized cases and the lowest 1 day for under-reported cases.

Under-reporting: An under-reporting factor was difficult to establish since we do not know the relative incidence of *B. cereus*, *S. aureus* and *C. perfringens* food poisoning cases in this item. Nonetheless, since *S. aureus* has been mentioned to be responsible for more than half of documented food poisoning cases (59) an under-reporting factor of 185.65 was selected which is in the middle of the range found for this pathogen 29.3–342 (7,53).

PARASITIC DISEASES

Amebiasis

Reported cases: Based on ELSTAT data (ICD-9 code 006; BTL code 014) (Technical Appendix Table 1).

Percentage foodborne: Infection is initiated by ingestion of faecally contaminated food or water (43) and water, food and food-handlers have been reported to be the sources of infections (67) so in theory 100% of cases can be foodborne. However, the cysts of *Entamoeba histolytica* can survive in water (68) meaning that swimming in pools and beaches can also result in infections (69) and venereal transmission has also been observed (70). Moreover, the role of insects in the transmission of the disease has not been properly investigated (71). Given these uncertainties we assumed that 50% of the cases are due to food. In theory this percentage could be as low as 10% which was the case for foodborne transmission of *Giardia lamblia* which like *E. histolytica* is also transmitted by water, food and food handlers (67) but has been reported to be more often transmitted by faecally contaminated water than food (72).

Case fatality: The case fatality rate was considered to be $\approx 0.2\%$ based on tabulated data by Walsh (21) regarding the global prevalence and incidence of amoebiasis (range: 0.1%–0.3%).

Disability weight: A value of 0.4 was selected based on Wijewardene et al. (19). For the cases that go under-reported a disability weight of 0.067 was selected (22) based on similarity of the mild diarrheal syndrome of amoebiasis with salmonellosis, giardiasis, toxigenic *E. coli* diarrhea, many other diarrheas of infectious origin, or the irritable bowel syndrome (21).

Duration of illness: Based on ELSTAT data the average duration of the illness was assumed to be 4.74 days based on the average duration of hospitalization according to the ELSTAT (1). For the under-reported cases the duration of diarrhea was assumed to be 3 days based on the same rationale of the disability weight selection and the fact that non-bloody diarrhea by STEC O157 lasts for 3 days (22).

Under-reporting: An under-reporting factor of 10 is plausible as suggested for protozoan infections by Casemore (73). According to Evangelopoulos et al, 2001 (74) the prevalence of *E. histolytica* in Greece is 1 in every 38 immigrants. Considering that the total population of immigrants (people of foreign nationality) in Greece in 2001 was 796,713 based on the ELSTAT (1), infected persons were 20,966. Approximately 10% of infected persons have symptoms, and out of these persons 2%–20% (average 11%) have symptoms related with the invasion of *E.*

histolytica beyond the intestinal mucosa (68) which are presumed to require hospitalization. Therefore ≈ 230 persons with amebiasis in 2001 are presumed to have required hospitalization. Nevertheless in 2001 only 25 people sought medical care (1) which means that the underreporting factor is at least 9.2. However, this is a conservative estimate based on the prevalence of the pathogen in only one (although the largest) of the high risk groups in developed countries (immigrants, travelers, migrant workers, immunocompromised persons, institutionalized persons, and sexually active homosexuals) (68). Here a factor of 9.6 was selected which is in the middle of the range (9.2–10).

Cryptosporidiosis

Estimated cases: No data are available for cryptosporidiosis so the number of cases is estimated indirectly as follows. The prevalence of *Cryptosporidium parvum* infection in the Greek population is 2.7% based on data collected from Papazahariadou et al. (75) which is in line with the available information on the incidence of this parasitic infection in Europe (68). We assumed that this rate of infection applies to all patients getting hospitalized for gastroenteritis where a protozoan infection could be the cause according to ELSTAT data (BTL Code 015, “intestinal infections due to other specified microorganism” and BTL code 016, “ill-defined intestinal infections”).

Percentage foodborne: Based on the study for the United States (11) 10% of the cases are foodborne while based on a study for England and Wales (35) 5.6% of the cases are attributed to food. The data resulting from the European study were considered to be more relevant for Greece.

Case-fatality rate: A range of 0.07%–0.6% has been mentioned (18,35) and the average has been considered to be the most likely value.

Disability weight: A disability weight of 0.393 was selected since in our scenario we estimated the cases of the disease as a proportion of the cases that result in visits to a physician for gastroenteritis or hospitalization. A disability weight of 0.067 was selected for the under-reported cases (18).

Duration of illness: The average duration of illness was considered to be 18.4 days for cases resulting in hospitalization and 3.5 days for cases not resulting in a visit to a physician (18).

Underreporting: The underreporting factors for *Cryptosporidium parvum* infections range from 7.4 (35) to 98.6 (7). We set the most likely value for under-reporting at the middle of this range.

Echinococcosis

It is assumed that all cases in Greece are due to *Echinococcus granulosus* which causes cystic echinococcosis that is easier to treat and has a lower case fatality than alveolar echinococcosis caused by *E. multilocularis* (76). This assumption is based on the fact that alveolar echinococcosis is a rare form of echinococcosis in Greece since this country is not among the endemic regions of *E. multilocularis* (77) and only one case has been reported between 1981 and 2000 (78). Moreover, according to a recent review on echinococcosis in Greece (79) it is rather certain that the majority if not all of the cases of the disease in humans in the country are due to *E. granulosus*. Additionally it is assumed that all cases of cystic echinococcosis are treated with surgery which still remains the only potentially curative treatment for cystic echinococcosis (80).

Reported cases: Based on ELSTAT data (ICD-9 code 122; BTL code 073) (Technical Appendix Table 1). Though HCIDC data were also available for the same period, ELSTAT data were used instead as they were considered of better quality. This was because the officially reported cases (through the HCIDC) have been found to be few in comparison to the actual number of diagnosed cases in hospitals in the country as mentioned by Sotiraki et al. (79).

Percentage foodborne: Cystic echinococcosis requires ingestion of the eggs (76) which can be the result of handling hosts of the parasite or ingesting food contaminated with eggs (9). The exact percentage of cases that can be attributed to food is not known (32). According to WHO (81), as much as 30% of cystic echinococcosis is transmitted through food by contamination with parasite eggs. Given the fact that the disease is hyperendemic in Greece (9) contamination of food from the environment can be high, so in our study 30% of the cases were considered to be foodborne. In theory though since *E. granulosus* is a helminth, foodborne transmission could be as high as 100% (see disease category “other helminthiases”).

Case-fatality rate: A case fatality rate of 2.24% was selected that corresponds to all cases receiving surgery in Greece and the neighboring countries (14). A wider range of 1%–3% is also possible (76,82) and was considered in the form of a Pert distribution.

Disability weight: Several disability weights were selected depending on the outcome of surgery for cystic echinococcosis according to Budke et al. (14) and are presented in Technical Appendix Table 6.

Duration of illness: The selected values are based on the recovery time reported for each possible outcome of surgery for cystic echinococcosis (14) and are shown in Technical Appendix Table 6.

Underreporting: Budke et al. (14) suggest an underreporting factor of 4 on a global level, this was not found to be very realistic for a western developed country given the seriousness of the disease. Moreover, echinococcosis is considered to be a serious health problem in Greece and the notification of the disease is obligatory in both humans and animals. An under-reporting factor of 2 based on the rationale of Mead et al. (11) for serious diseases is also possible. Given the fact that the reliability of official data was questioned in a recent review of the disease in the country (79) it was finally decided to select a factor of 3 which is in the middle of the above range. It was also assumed that 10% of the total cases are undiagnosed and thus do not receive medical treatment. These cases were assigned a disability weight of 0.2 for 10 years (14). Lastly, reported and under-reported cases were assumed to have the same severity.

Giardiasis

Estimated cases: No data are available for giardiasis so the number of cases is estimated indirectly as follows. The prevalence of the parasite in the Greek population according to a recent study is 2.3% (75) which is in line with what has been mentioned about the rates of detection of this parasite in industrialized countries (68). We assumed that this rate of infection applies to all patients getting hospitalized for gastroenteritis where a protozoan infection could be the cause (BTL Code 015, “intestinal infections due to other specified microorganism” and BTL code 016, “Ill-defined intestinal infections”).

Percentage foodborne: Mentioned anywhere between 5 and 30% (12). Here a value of 10% was assumed as in (35).

Case fatality: The case fatality rate is very low according to Mead et al. (11) or zero according to Vijgen et al. (18) and this seems also to be the case in a more recent study by Adak et al. (35). However based on more recent U.S. data it can be 0.1% for laboratory confirmed cases (7). Thus a most likely value of 0.05% was considered which is in the middle of this range (0%–0.1%).

Disability weight: A disability weight of 0.393 was selected for hospitalized cases and 0.067 for under-reported cases (18).

Duration of illness: It was considered to be 10 days for people not visiting a physician and 30 days for hospitalized persons (18).

Under-reporting: This factor is in the range of 4.6–46.3 (7,35) and the average has been considered to be the most likely value.

Toxoplasmosis

Estimated cases: The disease has only recently started to be reported to the HCIDC (since 2004) and almost no cases were notified in the period 2004–2008 for which information is available (2). At the same time there are hospital studies on congenital toxoplasmosis that point out toward a much higher incidence of the disease in the country (83,84). Given this situation, it was considered more logical to estimate the total number of cases by multiplying the number of pregnancies for each year of the study with the percentage of seronegative women of reproductive age (~70%), the incidence of primary infection among pregnant women (0.51%) and the maternofetal transmission rate (19.4%) (83,85,86) (see Technical Appendix Table 7 of the Annex). The number of cases found in this way is in agreement with what is known so far regarding the incidence of the disease in developed countries which ranges between 1 and 10 cases per 10,000 births (17).

Percentage foodborne: In a European study by Cook et al. foodborne transmission for toxoplasmosis has been mentioned to be in the range of 30 to 63% (87). Here 50% of the cases were assumed to be foodborne since this value is approximately in the middle of the above range and has been used in other national studies as well (7,11,24).

Case fatality: The case-fatality rate is 2.3% according to Gibbs based on the percentage of stillbirths or neonatal deaths observed when toxoplasmosis occurs during pregnancy (88)

while according to Havelaar et al. (17) the incidence of fetal loss or neonatal death is 3.75% (3.3%–4.8%) among cases of congenital toxoplasmosis in the Netherlands. The case fatality rates by Havelaar et al. were selected for this study because they are more recent and derived through traceable and better quality data.

Disability weight: Toxoplasmosis can have various outcomes (fetal loss, neonatal death, chorioretinitis, abnormalities of the central nervous system that lead to neurologic deficiencies such as psychomotor, convulsions and mental retardation, hydrocephalus and intracranial calcifications) which differ in their severity and incidence. These data are presented in Technical Appendix Table 8 of the Annex.

Duration of illness: All outcomes of toxoplasmosis are considered to be life-long sequelae of the disease. Their duration is summarized in Technical Appendix Table 8 of the Annex.

Under-reporting: Not applicable.

Note: The study of Diza et al. (85) dealt with the seroprevalence of *Toxoplasma gondii* on the North of Greece and it was assumed that the seroprevalence of the parasite is the same for the whole of Greece. However, this is not the case since in rural areas and in the island of Crete the percentage of sero-positive persons appears to be higher (89).

Other Helminthiasis

Reported cases: Based on ELSTAT data (ICD-9 codes 121, 123, 124, 127–129; BTL code 076) (Technical Appendix Table 1).

Percentage foodborne: All of the helminthic parasites included in this category of diseases (57) have been reported to be transmitted through food (44,67,71,90–95). However, it is not possible to make a precise estimate of the actual percentage of cases that are transmitted through food since this information is not available for many of the sub-categories of diseases included under this classification while the relative importance of each in this BTL code is not very clear. For some of these diseases (trichinellosis, taeniasis, anisakiasis) the percentage foodborne is mentioned to be 100% (11, 24) and thus all the cases under this general category of diseases can be considered to be 100% foodborne. On the other hand certain species of helminthes included in this category have also been reported to have different modes of

transmission i.e., *Strongyloides stercoralis* can enter the body through the skin (96) and since many of them can be found in contaminated water in pools (97) they can be transmitted by swimming in such waters. Finally, helminthic infections are also known to have a venereal mode of transmission (98). Nonetheless, the above modes of transmission are not expected to be the case for most of the species in this category and thus 90% of the cases were assumed to be foodborne. In a very conservative scenario, only 30% of the cases were assumed to be foodborne as in the case of the tapeworm *Echinococcus granulosus*.

Case fatality: A case fatality of $\approx 3.4\%$ has been estimated for this group of illnesses based on the number of deaths among hospitalized cases (13) and the total number of hospitalizations for the period 1996–2006 (1).

Disability weight: Most of the helminthic intestinal infections in the Greek native population are caused by the species *Enterobius vermicularis*, *Ascaris lumbricoides*, *Strongyloides stercoralis* and *Taenia* sp. (75,99). However autochthonous cases of helminthic infections have been mentioned to be extremely rare in Greece and most of the reported cases of helminthiasis are imported following the influx of immigrants in the country (99). The helminthic infection most commonly identified in the foreign population (emigrants and refugees) is ancylostomiasis (caused by *Ancylostoma* sp.) (75, 99) while other species found in foreigners are *Trichuris trichiura*, *Ascaris lumbricoides*, *Strongyloides stercoralis*, *Taenia* sp., *Enterobius vermicularis* and *Schistostoma mansonii* (75). Helminthic infections due to *Ancylostoma* sp. and *Schistostoma* sp. are part of other BTL codes (075 and 072) (57) while *Strongyloides stercoralis* is not transmitted through food but cutaneously (96) so only the rest of the species mentioned above are of relevance for this item. Though all of the remaining helminthic species are primarily associated with gastrointestinal symptoms (100–103) they can also be associated with sequelae such as nutrient deficiencies and anemia or even epilepsy (100,104). The disability weights for these illnesses and their sequelae according to Lopez et al. (105) range from 0–0.463. Here the upper value of this range was considered to be of relevance for the reported cases and for the underreported cases which we assumed to be related with gastrointestinal symptoms a disability weight of 0.067 was selected (22).

Duration of illness: The duration of the disease was assumed to be 5.67 days based on ELSTAT data (1). In the absence of any more closely related numbers, for the under-reported

cases the median duration of diarrhea before visiting a GP in the Netherlands (6 days) was selected (106).

Under reporting: This factor could also be in the range of 4.6–98.6 based on what is known for the under-reporting of protozoan parasites (7,53). We set the most likely value for under-reporting at the middle of this range.

VIRAL DISEASES

Acute hepatitis A

Reported cases: Based on HCIDC data (Technical Appendix Table 1).

Percentage foodborne: 8% of the total cases were considered to be food-borne which is the average of the range suggested by a recent expert study (5%–11%) (12).

Case fatality: A case fatality rate of 0.4% was estimated by taking into account the age of acute hepatitis A patients in Greece and the case fatality rates for different age groups as presented in the HCIDC Web site (2).

Disability weight: A disability weight of 0.5 was selected for cases of acute hepatitis A (107). Reported and underreported cases were assumed to have the same severity.

Duration of illness: The duration of acute cases of hepatitis A is considered to be 9.5 days for both reported and underreported cases according to the average duration of hospitalizations in EU countries for which information could be found in the European Health For All Database (HFA-DB) (Technical Appendix Table 9).

Under-reporting: An under-reporting factor of 2 is possible based on the seriousness of the disease (11) though it can be as high as 9.1 (7). We set the most likely value for under-reporting at the middle of this range.

DISEASES DUE TO MIXED ILL-DEFINED CAUSES

Intestinal infections due to other specified microorganism

Reported cases: Based on ELSTAT data (ICD-9 codes 007, 008; BTL code 015) (Technical Appendix Table 1).

Percentage foodborne: 36% based on the relative frequency of foodborne transmission for known pathogens (11). In theory looking at the microorganisms included in this category (Technical Appendix Table 10) and at the percentages foodborne mentioned for some of these in literature this figure may vary between 1 and 70%.

Case fatality: To estimate mortality due to this category of diseases data for Greece from the WHO Mortality Database were used (13). According to this database mortality is very low for this particular ICD code ranging between 0 and 1 cases per year for the whole country population. The upper limit was considered more realistic although it is still likely to result in under-estimating of the real situation since the quality of data in this particular source has been mentioned to be low (108). Given the very generic nature of this category assuming a case-fatality rate is not possible.

Disability weight: Since the reported cases correspond to patients that were hospitalized, a class 3 disability weight of 0.4 was assigned (20). For the under-reported cases a class 1 disability weight of 0.067 was assigned (22).

Duration of illness: The average hospitalization time for these diseases in Greece (3.84 days) was considered (1). For the under-reported cases the duration of illness before visiting a GP for *Norovirus* was considered (3.8 days) (22).

Under-reporting: It was estimated by multiplying two separate under-reporting factors: the first underreporting factor covers the underreporting of gastroenteritis related illnesses between hospitalizations (ELSTAT data (1)) and visits to physicians (HCIDC data (S. Bonovas, T. Panagiotopoulos, E. Triantafillou, pers. comm.)) and the second one is used to cover the underreporting between visits to physicians for gastroenteritis and cases in the community (35). In this way four different underreporting factors were estimated for the period 2006–2003. For the rest of the years for which no information was available to estimate the first underreporting factor, the average of the estimated underreporting factors for the period 2005–2003 was used. In theory these under-reporting factors could be anywhere between 2 and 1562 based on what is

mentioned about the underreporting of some of the pathogens included in this category (Technical Appendix Table 10).

Ill-defined intestinal infections

Reported cases: Based on ELSTAT data (ICD-9 code 009; BTL code 016) (Technical Appendix Table 1).

Percentage foodborne: A value of 36% was selected for foodborne transmission as in cases of acute gastroenteritis due to unknown etiology (11). Given the fact that the nature of microorganisms in this category is not known this percentage could range between 1 and 100%.

Case fatality: The mortality rate was considered to be 1 case per year for the whole country population based again on the WHO Mortality Database (13) as in the previous item.

Disability weight: Since the reported cases correspond to patients that were hospitalized a class 3 disability weight of 0.4 was assigned (20). For the under-reported cases a class 1 disability weight of 0.067 was assigned (22).

Duration of illness: The average hospitalization time for these diseases in Greece (3 days) was considered (1). For the under-reported cases the duration of illness before visiting a GP for *Norovirus* was considered (3.8 days) (22).

Under-reporting: The same under-reporting rate as for the previous category was assumed. Nonetheless, the range of underreporting can vary a lot in theory given what we have so far observed regarding the range of under-reporting factors for foodborne pathogens (2–1562).

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Technical Appendix Table 1. Reported cases of illness that may be transmitted through food in Greece in the period 1996–2006 based on the Hellenic Centre of Infectious Diseases Control (HCIDC) and the Hellenic Statistical Authority (ELSTAT). Data are expressed as cases per million inhabitants by using population yearly figures collected from the ELSTAT. Values have been rounded to include significant digits

Diseases	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	Average	SD
Bacterial													
Botulism	–*	–*	0	0	0	0.091	0.091	0.091	0.091	0.090	0.090	0.061	0.045
Brucellosis	73	80	102	115	102	93	66	71	58	51	61	79	21
Campylobacteriosis	–*	–*	13	28	24	–*	–*	–*	31	21	26	24	6.4
EHEC†	–*	–*	–*	–*	–*	–*	–*	0.18	0.18	0	0.090	0.11	0.087
Leptospirosis	–*	–*	1.1	2.1	1.2	1.9	1.8	4.4	2.9	3.0	1.9	2.3	1.0
Listeriosis‡	–*	–*	0.093	0.64	0.55	0.27	0.46	0.091	0.27	0.72	0.63	0.42	0.24
Salmonellosis	92	54	85	88	84	28	49	94	140	111	89	83	31
Shigellosis	32	2.2	8.5	8.6	6.7	1.1	1.5	0.73	5.8	2.4	2.8	6.6	9.0
Typhoid and paratyphoid fever	11	10	9.8	10	2.9	5.0	1.6	2.9	3.6	3.7	1.6	5.6	3.7
Food poisoning§	13	46	15	26	23	86	68	24	25	16	4.1	31	25
Parasitic													
Amoebiasis	3.2	4.2	3.8	3.0	1.7	3.0	0.73	1.6	2.3	2.9	0.81	2.5	1.2
Echinococcosis	84	84	58	66	65	56	47	48	44	43	37	57	16
Viral: acute hepatitis A	10	12	24	24	15	19	22	7.0	6.5	16	12	15	6.4
Mixed/ill-defined causes													
Other helminthiases	2.6	2.0	2.4	3.0	3.7	6.0	4.0	3.0	4.4	0.72	3.6	3.2	1.4
Other specified microorganism§	94	45	37	23	39	41	17	45	11	30	19	37	23
Ill-defined infections	1635	1672	1790	1819	1663	1834	2266	2099	2378	2424	2595	2016	349

*Data for these years were not available.

† EHEC, enterohemorrhagic *Escherichia coli*.

‡ For the years 2001 and 2002 data from a European report on listeriosis in EU countries were used (5).

§Reported cases by the ELSTAT were in some instances part of very generic BTL codes (“Food poisoning” and “Intestinal infections due to other specified microorganisms”) that include illnesses due to different kinds of microorganisms some of which are reported separately by the HCIDC (campylobacteriosis, EHEC, botulism and salmonellosis) or estimated indirectly (giardiasis, cryptosporidiosis). When this kind of over-lapping was observed, the reported cases due to specified causes were subtracted from the corresponding BTL code to prevent overestimating the impact of these illnesses.

Technical Appendix Table 2. Parameters of the Pert distributions used to describe foodborne transmission, under-reporting and case fatality of foodborne illnesses

Diseases	Food attribution (%)			Under-reporting			Case-fatality (%)		
	min, mean, max*	Data origin†	Source	min, mean, max*	Data origin†#	Source	min, mean, max*	Data origin†#	Source
Bacterial									
Botulism	80, 100, 100	EU,EU,EU	(23, 24)	1.625, 1.8125, 2	EU/U.S.	(11, 25)	3, 10.15, 17.3	U.S./U.S.	(7, 26)
Brucellosis	50,84,100	U.S., GR, other	(7, 11, 31)	2, 10.85, 19.7	other¶¶	-	0.9, 2, 5	U.S./GR/U.S	(7, 11, 33)
Campylobacteriosis	30, 55, 80	EU/EU‡/EU	(12)	7.6, 274.8, 542	UK/EU	(39, 40)	0.1, 0.1265, 0.153	U.S./UK	(7, 11, 35)
EHEC§	40, 51, 90	EU/EU/EU	(12, 41)	2, 14.05, 26.1	UK/U.S.	(7, 35)	0.25, 0.54, 0.83	U.S./U.S.	(11, 42)
Leptospirosis	1, 5, 49	GR,other,GR	(48)	10, 15, 20	other¶¶	(45)	5, 10, 15	U.S./U.S.	(45)
Listeriosis	69, 99, 100	EU/EU/U.S.	(7, 12, 35)	1.1, 1.7, 2.3	EU/U.S.	(7, 53)	10, 30, 44	U.S./U.S.	(52)
Salmonellosis	55, 95, 95	EU/EU/EU	(12, 24)	3.2, 51.45, 99.7	EU/EU	(39, 54)	0.5, 0.701, 0.902	U.S./UK	(7, 35)
Shigellosis	8.2, 10, 31	EU/EU/U.S.	(7, 24, 35)	3.4, 18.35, 33.3	EU/U.S.	(7, 35)	0.1, 0.13, 0.16	U.S./U.S.	(7, 11)
Typhoid and paratyphoid fever	55, 80, 95	EU/EU/EU	(12, 35)	2, 7.65, 13.3	EU/U.S.	(7, 35)	0.4, 0.95, 1.5	U.S./EU	(11, 24)
Food Poisoning	87, 100, 100	EU/EU/EU	(12, 35)	29.3, 185.65, 342	U.S./EU	(7, 53)	0, 0.025, 0.05	EU/U.S.	(11, 64)
Parasitic									
Amoebiasis	10, 50, 100	other¶¶	-	9.2, 9.6, 10	other¶¶	(73)	0.1, 0.2, 0.3	GL/GL	(21)
Cryptosporidiosis	5.6, 5.6, 8	EU/EU/U.S.	(11, 35)	7.4, 53, 98.6	EU/U.S.	(7, 35)	0.07, 0.335, 0.6	EU/EU	(18, 35)
Echinococcosis	30, 30, 100	GL/GL/other	(81)	2, 3, 4	other/GL	(14)	1, 2.24, 3	GL/GR/GR	(14, 76, 82)
Giardiasis	5, 10, 30	EU/EU/EU	(12, 35)	4.6, 25.45, 46.3	EU/U.S.	(7, 35)	0, 0.05, 0.1	EU/U.S.	(7, 18)
Toxoplasmosis	30, 50, 63	EU/EU/EU	(24, 87)	n.a.	-	-	3.3, 3.75, 4.8	EU/EU	(17)
Viral: acute hepatitis A	5, 8, 11	EU/EU‡/EU	(12)	2, 5.55, 9.1	other/U.S.	(7)	0.3, 1.35, 2.4	U.S./U.S.	(7, 11)
Mixed/ill-defined causes									
Other helminthiases	30, 90, 100	other¶¶	-	4.6, 51.6, 98.6	EU/U.S.	(7, 53)	3.37	GR	(13)
Intestinal infections due to other specified microorganism	1, 36, 70	other¶¶	-	2, 402, 1562	other¶¶	-	**	GR	(13)
Ill-defined intestinal infections	1, 36, 50	other¶¶	-	2, 402, 1562	other¶¶	-	**	GR	(13)

*Minimum (min), most likely (mean), and maximum (max) parameters of each Pert distribution.

†Origin of the data selected to describe the minimum, most likely and maximum value of each Pert distribution; GR = Greece, EU = Europe, U.S. = United States, GL = global data, other = assumption when no other data have been found

‡The average of the range of values mentioned in European studies was selected.

§EHEC, enterohemorrhagic *Escherichia coli*.

¶¶No or very few data have been found so a range is considered to cover all possibilities after performing a review of existing literature on possible transmission routes or underreporting factors.

#For the under-reporting factors and the case-fatality rates the most likely value is set in the middle of the range so the origin of the data represents only the extremes of the range (minimum and maximum values) unless stated otherwise.

**For these illnesses YLL were estimated by using the yearly reported number of deaths from Greece in the WHO Mortality Database.

Technical Appendix Table 3. Disability weights related to the diseases included in the present study

Diseases	Disability weights			
	Reported or estimated cases	Source	Under-reported cases	Source
Bacterial				
Botulism				
moderate cases	0.600	(20)	0.600	(20)
severe cases	0.906	(20)	0.906	(20)
Brucellosis	0.200	(15)	0.200	(15)
Campylobacteriosis			0.067	(38)
gastroenteritis	0.393	(16)		
reactive arthritis	0.140	(16)		
GBS 1st year*	0.250	(16)		
GBS long term sequelae	0.160	(16)		
IBD†	0.260	(16)		
IBS‡	0.042	(37)		
EHEC§			0.067	(38)
watery diarrhea and hemorrhagic colitis	0.393	(16)		
HUS¶ and ESRD#	–**			
Leptospirosis	0.920	(20)	0.096	(20)
Listeriosis	–††		–††	
Salmonellosis			0.067	(22)
gastroenteritis	0.393	(16)		
IBD†	0.260	(16)		
IBS‡	0.042	(37)		
reactive arthritis	0.150	(16)		
Shigellosis	0.220	(19)	0.096	(20)
IBS‡	0.042	(37)		
Typhoid and paratyphoid fever	0.600	(20)	0.096	(20)
Food poisoning	0.220	(20)	0.067	(20)
Parasitic				
Amoebiasis	0.400	(19)	0.067	(22)
Cryptosporidiosis	0.393	(18)	0.067	(18)
Echinococcosis				
cured	0.200	(14)	0.200	(14)
post surgical conditions	0.239	(14)	0.239	(14)
relapse	0.809	(14)	0.809	(14)
undiagnosed	0.200	(14)	0.200	(14)
Giardiasis	0.393	(18)	0.067	(18)
Toxoplasmosis				
clinical symptoms in the 1st year of life ††	0.140	(17)	–§§	
asymptomatic at birth, chorioretinitis later in life	0.080	(17)	–§§	
Viral: acute hepatitis A	0.500	(107)	0.500	(107)
Mixed/ill-defined causes				
Other helminthiases	0.463	(105)	0.067	(22)
Intestinal infections due to other specified microorganism	0.400	(20)	0.067	(20)
Ill-defined intestinal infections	0.400	(20)	0.067	(20)

*GBS, Guillain-Barré Syndrome.

†IBD, Inflammatory Bowel Disease.

‡IBS, Irritable Bowel Syndrome.

§EHEC, enterohemorrhagic *Escherichia coli*.

¶HUS, hemolytic-uraemic syndrome.

#ESRD, end-stage renal disease.

**For HUS (including ESRD as a sequela) it is estimated that every case corresponds to 1.05 YLD (16).

††Not applicable. In the case of listeriosis due to its high case fatality ratio, >95% of the DALY estimates is composed of YLL (22) that mainly determine the burden of the disease and therefore no YLD were estimated.

‡‡Clinical symptoms in the first year of life include chorioretinitis, intracranial calcifications, hydrocephalus and CNS abnormalities that lead to neurologic deficiencies such as mental retardation.

§§Toxoplasmosis cases are estimates for the entire population. Consequently under-reporting does not apply.

Technical Appendix Table 4. Disability weights and average duration of illness for different outcomes of reported cases of campylobacteriosis according to van Lier and Havelaar (16) and Haagsma (37)

Outcome	Disability weight	Incidence	Duration (years)
Gastroenteritis	0.393	reported cases	0.027
Reactive arthritis	0.14	0.16 per reported case	0.61
GBS 1 st year	0.25	0.009 per reported case	1
GBS following years (long term sequela)	0.16	0.009 per reported case	29.26
Inflammatory bowel disease	0.26	0.0035 per reported case	44.36
Irritable bowel syndrome	0.042	0.088 per reported case	5 y

Technical Appendix Table 5. Disability weights, duration of illness and incidence for different outcomes of reported cases of salmonellosis according to van Lier and Havelaar (16) and Haagsma (37)

Outcome	Disability weight	Incidence	Duration
Gastroenteritis	0.393	all reported cases	11.2 d
Inflammatory bowel disease	0.26	0.003 per reported case	50.52 y
Irritable bowel syndrome	0.042	0.088 per reported case	5 y
Reactive arthritis	0.15	0.18 per reported case	0.61 y

Technical Appendix Table 6. Incidence, disability weights and duration for different outcomes of surgery for the treatment of cystic echinococcosis (14)

Surgery outcome	Incidence (%)	Disability weight	Duration (years)
Cured	74.755	0.2	1
Morbidity	16.550	0.239	5
Relapse	6.452	0.809	5
Death	2.244	–	–
*Undiagnosed	10	0.2	10

*It is assumed that 10% of all cases are undiagnosed and thus do not receive medical treatment.

Technical Appendix Table 7. Number of births during the period 1996–2006 and cases of toxoplasmosis based on the percentage of seronegative women of reproductive age (~70%), the incidence of primary infection among pregnant women (0.51%) and the maternofetal transmission rate (19.4%) (83, 85, 86)

Year	Pregnancies/year	Cases of toxoplasmosis
1996	100718	70
1997	102038	71
1998	100894	70
1999	100643	70
2000	103274	72
2001	102282	71
2002	103569	72
2003	104420	72
2004	105655	73
2005	107545	75
2006	112042	78

Technical Appendix Table 8. Possible outcomes of congenital toxoplasmosis, incidence among patients, duration of illness and disability weights. The duration of illness has been adjusted based on the life expectancy of the Greek population. Source: Havelaar et al. (17)

	Incidence (%)	Disability weights	Duration (years)
Fetal loss	3	1	78.2
Clinical symptoms in the first year of life			
Chorioretinitis	14	0.17	78.2
Intracranial calcification	11.4	0.01	78.2
Hydrocephalus	1.9	0.36	78.2
CNS abnormalities*	2.7	0.36	78.2
Neonatal death	0.75	1	78.2
Asymptomatic at birth, chorioretinitis later in life	16.9	0.08	68.2

*Includes abnormalities of the central nervous system that lead to neurologic deficiencies, that is psychomotor or other neurologic deficiencies, convulsions and mental retardation.

Technical Appendix Table 9. Average duration of acute hepatitis A based on data regarding the average length of stay in hospitals for 8 EU countries in 2006 according to the HFA-DB (109)

Country	Duration of illness (days)
Czech Republic	16.1
Austria	6.9
Slovenia	6.1
Cyprus	7.0
Croatia	12.7
Denmark	5.5
Finland	6.6
Slovakia	15.2
Average	9.5

Technical Appendix Table 10. Microorganisms included in BTL code "015 – Intestinal infections due to other specified microorganism accompanied by the percentage foodborne and under-reported rates found for each species in literature

Disease (microorganism)	Percentage foodborne	Under-reporting factor (reference)
Protozoal infections		
<i>Balantidium coli</i>	–	≥10 (73)
<i>Giardia lamblia</i>	5%–30% (12)	≥10 (73)
Coccidiosis (<i>Isospora belli</i> , <i>Isospora hominis</i>)	–	≥10 (73)
Trichomoniasis	0 (not foodborne)	–
Other intestinal diseases due to protozoa	–	≥10 (73)
Undefined protozoal diarrhea/dysentery	–	≥10 (73)
Intestinal infections		
<i>Escherichia coli</i>	30–70 (11)	38 (11)
Arizona group of paracolon bacilli	–	–
<i>Aerobacter aerogenes</i>	–	–
<i>Proteus mirabilis</i> , <i>P. morganii</i>	–	–
Other defined microorganisms (staphylococcal enterocolitis)	–	–
Microbial enteritis (undefined)	–	–
Enteritis due to specified virus (adenovirus, enterovirus)	6%–10% based on what is known for <i>Enterovirus</i> (12) and <i>Astrovirus/Adenovirus</i> (110)	721.3 (for astrovirus) (35)
Other microorganisms that cannot be classified elsewhere (viral gastroenteritis and enteritis)	1%–40% (12) (based on what is known for <i>Norovirus</i> and <i>Rotavirus</i>)	21.5–1562 (based on data for <i>Norovirus</i> and <i>Rotavirus</i>) (35,39)