CHAPTER

Health and economic burden of *Campylobacter*

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2.1 INTRODUCTION

Burden assessment plays an increasingly important and accepted role in food safety decision making. Burden assessment is a top–down approach that uses available epidemiological data, for example, generated through surveillance systems, to generate estimates of the health and economic impact of the concerned foodborne disease. These estimates can be used to generate an evidence-based ranking of the impact of foodborne diseases (i.e., risk ranking). Increasingly, these estimates are used to provide justification for the need to strengthen support for increased surveillance and prevention of foodborne diseases by national or international organizations, such as the World Health Organization (WHO). By generating burden estimates at multiple time points, it becomes possible to monitor and evaluate food safety measures over time, as well (Buzby and Roberts, 2009). Finally, health and economic impact may be combined in cost-effectiveness studies that allow to determine the intervention that offers the best value for money invested, so that resources are appropriately allocated (Oostvogels et al., 2015).

In this Chapter we review studies on the health and economic impact of *Campylobacter* at a global and national level.

2.2 HEALTH IMPACT OF *CAMPYLOBACTER*

2.2.1 QUANTIFYING HEALTH IMPACT

Quantifying health impact may be based on disease occurrence (prevalence or incidence), or on the number of deaths (mortality). However, these simple measures of population health do not provide a complete picture of the impact of foodborne

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diseases on human health (Mangen et al., 2010; Devleesschauwer et al., 2015). On the one hand, these measures either quantify the impacts of morbidity or mortality, thus prohibiting a comparative ranking of highly morbid but not necessarily fatal diseases and highly lethal diseases. On the other hand, they only quantify occurrence of illness or death, but not severity of illness or death. Indeed, foodborne illnesses may differ in clinical impact and duration of the concerned symptoms. Likewise, ignoring the age at which people die, and thus not considering how many years of healthy life might be lost due to death, does not fairly capture the impact of mortality.

To overcome the limitations of these simple measures, summary measures of population health (SMPHs) have been developed as an additional source of information for measuring disease burden. The disability-adjusted life year (DALY) is currently the most widely used SMPH in public health research. Originally developed to quantify and compare the burden of diseases, injuries, and risk factors within and across countries, the DALY summarizes the occurrence and impact of morbidity and mortality in a single measure (Murray and Lopez, 2013; Devleesschauwer et al., 2014a). The DALY is the key measure in the global burden of disease (GBD) studies, and is officially adopted by the WHO for reporting on health information (Murray et al., 2012; WHO, 2013).

The DALY is a health gap measure, measuring the healthy life years lost due to diseases or injury in a population. DALYs are calculated by adding the number of years of life lost due to premature mortality (YLLs) and the number of years lived with disability, adjusted for severity (YLDs). YLLs are the product of the number of deaths and the residual life expectancy at the age of death. Following an incidence perspective, YLDs are defined as the product of the number of incident cases, the duration until remission or death, and the disability weight that reflects the reduction in health-related quality of life on a scale from zero (full health) to one (death). The incidence perspective assigns all health outcomes, including those in future years, to the initial event (e.g., *Campylobacter* infection). This approach therefore reflects the future burden of disease resulting from current events. An alternative formula for calculating YLDs follows a prevalence perspective, and defines YLDs as the product of the number of prevalent cases with the disability weight (Murray et al., 2012). In this prevalence perspective, the health status of a population is assessed at a specific point in time, and prevalent diseases are attributed to events that happened in the past. This approach thus reflects the current burden of disease resulting from previous events. Although both perspectives are valid, the incidence perspective is more sensitive to current epidemiological trends (Murray, 1994), including the effects of intervention measures, and therefore often preferred for assessment of the burden of foodborne diseases (Devleesschauwer et al., 2015).

Different approaches can be taken for calculating DALYs, depending on whether the interest lies in quantifying the burden of a health outcome, a hazard, or a risk factor (Devleesschauwer et al., 2014b). A natural choice for quantifying the health impact of foodborne diseases is the hazard-based approach. This approach defines the burden of a specific foodborne disease as that resulting from all health states,

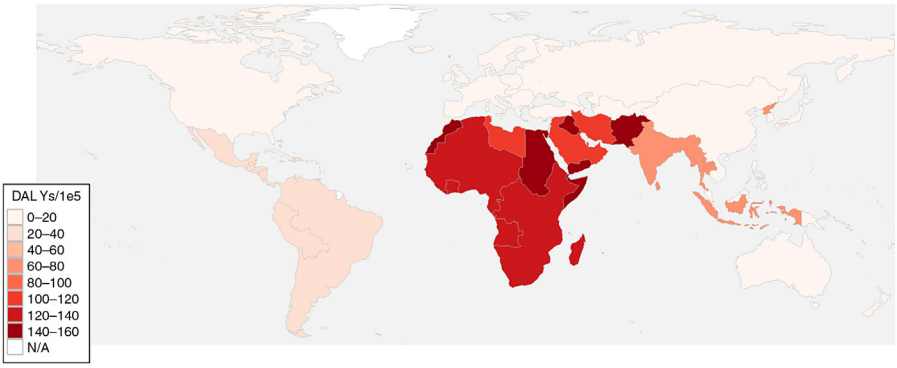

FIGURE 2.1 ***Campylobacter*** **DALY Per 100,000 People by Subregion, 2010 (Havelaar et al., 2015)**

that is, acute symptoms, chronic sequelae, and death, that are causally related to the concerned hazard, and that may become manifest at different time scales, or have different severity levels (Mangen et al., 2013). The starting point for quantifying DALYs therefore is typically the construction of a disease model or outcome tree that is a schematic representation of the various health states associated with the concerned hazard, and the possible transitions between these states (Devleesschauwer et al., 2014b). As reviewed in Chapter 1, the most important sequelae associated with *Campylobacter* infection are Guillain–Barré syndrome (GBS), reactive arthritis (ReA), inflammatory bowel disease (IBD), and irritable bowel syndrome (IBS).

2.2.2 GLOBAL BURDEN OF *CAMPYLOBACTER*

To date, the most comprehensive assessment of the global burden of campylobacteriosis is the one performed by the Foodborne Disease Burden Epidemiology Reference Group (FERG) of the WHO (Havelaar et al., 2015). FERG estimated that, in 2010, *Campylobacter* was responsible for 166 million [95% Uncertainty Interval (UI) 92–301 million] diarrheal illnesses (of a total of nearly 2 billion attributed diarrheal illnesses), and 31,700 (95% UI 25,400–40,200) GBS cases. These illnesses resulted in 37,600 deaths (95% UI 27,700–55,100), and 3.7 million DALYs [95% UI 2.9–5.2 million; equivalent to 54 (95% UI 42–77) DALYs/100,000] (Kirk et al., 2015). Foodborne transmission was estimated to contribute to 58% (44–69%) of the global disease burden (Hald et al., 2016).

Fig. 2.1 shows the regional variation of the *Campylobacter* burden. The African regions bore nearly half of the global burden, followed by the South-East Asian regions. Of note, while *Campylobacter* was only the sixth most important contributor to the global burden of foodborne disease, it was the most important foodborne hazard in the high-income countries of the American and Western Pacific regions, and the second most important foodborne hazard in the high-income countries of the European region (Havelaar et al., 2015).

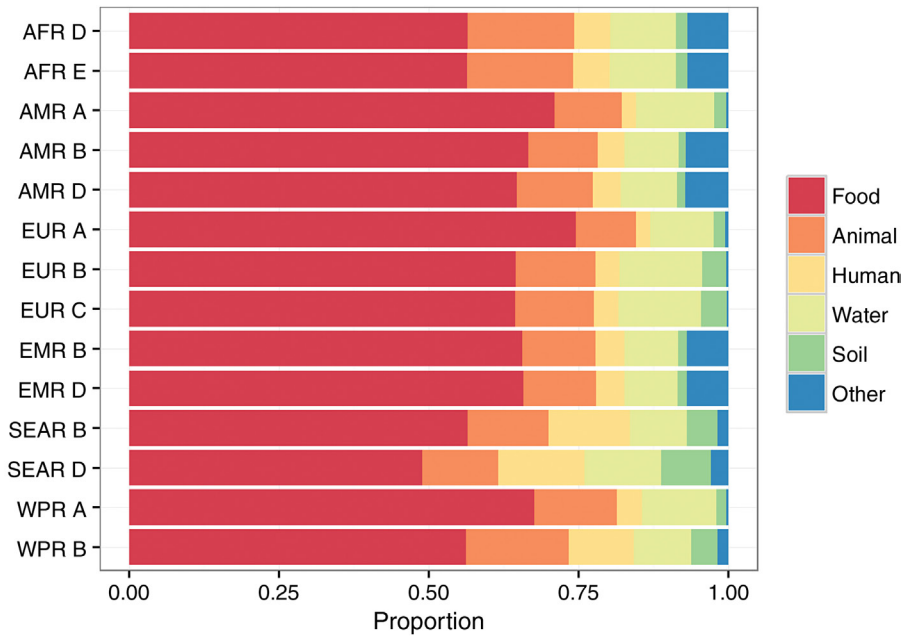

FIGURE 2.2 ***Campylobacter*** **Exposure Routes by Subregion, 2010** (Hald et al., 2016)

To estimate the global burden of campylobacteriosis, FERG attributed diarrheal incidence and mortality rates to *Campylobacter* using etiological fractions obtained through metaanalysis (Pires et al., 2015). This information was combined with *Campylobacter* incidence and mortality estimates available for high-income countries. Furthermore, it was estimated that 31% (range 28–45%) of GBS cases globally were associated with antecedent *Campylobacter* infection, and that the GBS case–fatality ratio was 4.1% (range 2.4–6.0%) (Kirk et al., 2015). Other sequelae, such as reactive arthritis, inflammatory bowel disease, and irritable bowel syndrome, were not included in the FERG estimates due to a lack of global data. As national burden studies have shown that sequelae add significantly to the *Campylobacter* disease burden (Mangen et al., 2015), the FERG estimates thus underestimate the true global burden of *Campylobacter*. The contribution of different transmission routes to the *Campylobacter* burden was assessed through a structured expert elicitation study (Hald et al., 2016). Fig. 2.2 shows the resulting regional attribution estimates, highlighting the importance of food as a major transmission route, followed by water, and direct animal contact. Within the foodborne transmission route, poultry was considered to be the dominant source of infection in all regions (Fig. 2.3).

A second source of GBD estimates of *Campylobacter* is the GBD 2013 study conducted by the Institute for Health Metrics and Evaluation. In GBD 2013, only *Campylobacter* enteritis was included. In 2013, *Campylobacter* enteritis was estimated

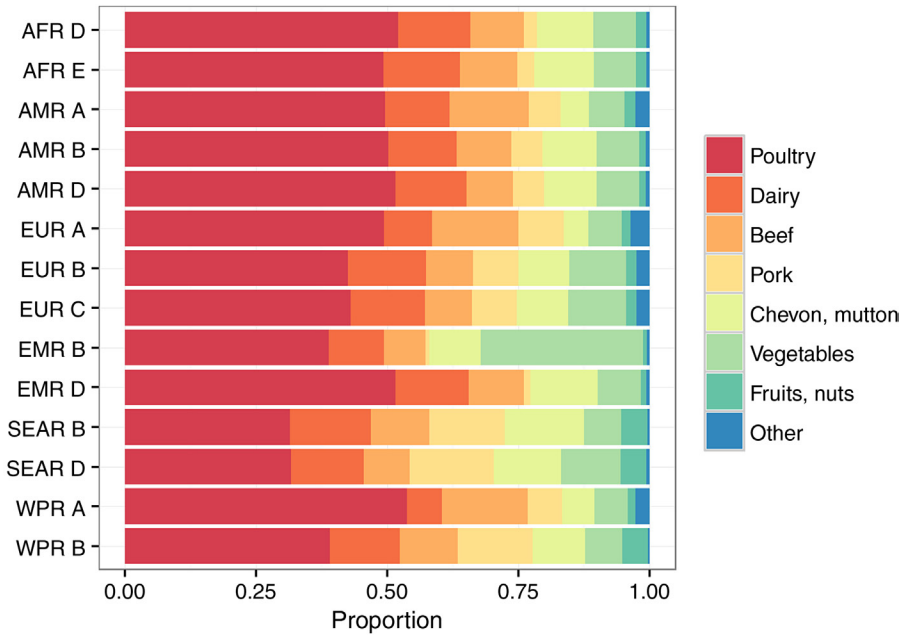

FIGURE 2.3 Sources of Foodborne *Campylobacter* Infection by Subregion, 2010 (Hald et al., 2016)

to be responsible for 14,100 deaths (95% UI 6900–22,400), and 1 million DALYs (95% UI 0.5–1.6 million), or 1.1% (95% UI 0.6–1.8%) of global diarrhea deaths, and 1.4% (95% UI 0.7–2.2%) of global diarrhea DALYs. Of note, the burden of *Campylobacter* enteritis appears to have halved since 1990, where it was estimated to be responsible for 28,400 deaths (95% UI 16,400–42,800), and 2.1 million DALYs (95% UI 1.2–3.2 million).

2.2.3 NATIONAL BURDEN OF *CAMPYLOBACTER*

Since the first national DALY calculation for *Campylobacter* published by Havelaar et al. (2000), several authors have estimated the burden of *Campylobacter* at a national or regional level. Table 2.1 provides an overview of available studies. All studies were performed in high-income countries, and confirmed the importance of *Campylobacter* as a foodborne pathogen. Indeed, when DALY estimates were used to rank multiple foodborne diseases, *Campylobacter* was consistently ranked first or second, with the exception of Greece, where it was ranked seventh (Gkogka et al., 2011). At a population level, the estimated burden of *Campylobacter* ranged from 0 DALYs/100,000 in Cyprus to 82 DALYs/100,000 in Australia. Comparisons across studies should nevertheless be done with caution, given the methodological differences, such as the comprehensiveness of data sources, or the nature of included

Table 2.1 National *Campylobacter* Burden Studies

References	Setting	Included Symptoms and Sequelae	DALY/ 100,000	DALY/ Case
Havelaar et al. (2000)	Netherlands	AGE; GBS; ReA	9.1	0.005
van den Brandhof et al. (2004)	Netherlands	AGE	8.5	0.014
Mangen et al. (2005)	Netherlands	AGE; GBS; ReA; IBD	7.5	0.015
van Lier et al. (2007); Kretzschmar et al. (2012)	Europe (20 countries)	AGE; GBS; ReA; IBD	5.3 (ranging from 0 in Cyprus to 28 in Czech Republic)	0.112
Haagsma et al. (2010)	The Netherlands	IBS	8.6	0.018
Lake et al. (2010)	New Zealand	AGE; GBS; ReA; IBD	4.0	0.013
Ruzante et al. (2010)	Canada, associated with chicken consumption	AGE; GBS	2.3	0.005
Gkogka et al. (2011)	Greece	AGE; GBS; ReA; IBD; IBS	0.5	0.001
Havelaar et al. (2012)	The Netherlands	AGE; GBS; ReA; IBD; IBS	20	0.041
Hoffmann et al. (2012); Batz et al. (2012, 2014)	USA	AGE; GBS	4.6[a]	0.016[a]
Toljander et al. (2012)	Sweden	AGE; GBS; ReA	2.8	0.004
Werber et al. (2013)	Germany	Only years of life lost were estimated	0.4	0.001
Kwong et al. (2012)	Canada		0.5	0.002
Gibney et al. (2014)	Australia	AGE; GBS; ReA; IBS	82	0.024
Kumagai et al. (2015)	Japan	AGE; GBS; ReA; IBD	4.8	0.051
Mangen et al. (2015)	The Netherlands	AGE; GBS; ReA; IBD; IBS	22	0.039
Scallan et al. (2015)	USA	AGE; GBS; ReA; IBS	7.5	0.027

[a]*Estimates are QALY losses instead of DALYs*

sequelae. Indeed, nearly all studies included GBS as a sequela, whereas the inclusion of ReA, IBD, and IBS was more variable. Haagsma et al. (2010) specifically looked at the burden of postinfectious IBS in The Netherlands, estimated to occur in 9% of *Campylobacter* patients, and found that including IBS doubled the burden estimate for *Campylobacter*. Across studies, the estimated DALY/case ranged from 0.001 to 0.112, corresponding to an average loss of less than 1 to 41 days of healthy life. However, for individual patients with specific sequelae, the health loss can be much more significant. Residual symptoms of GBS are, for instance, estimated to result in a loss of more than 6 years of healthy life (Havelaar et al., 2000).

2.3 ECONOMIC IMPACT OF *CAMPYLOBACTER*

2.3.1 COST-OF-ILLNESS

Foodborne diseases incur costs associated with illness and death, and impose an economic burden to the food industry, and the regulatory and public health sectors (Buzby and Roberts, 2009). Historically, however, most economic impact assessments only focused on the societal cost of human illness and death (Mangen et al., 2015). In these cost-of-illness (COI) studies, a distinction is typically made between direct and indirect costs, on the one hand, and healthcare and nonhealthcare costs, on the other (Mangen et al., 2010). Direct healthcare costs relate to the resources provided by the healthcare sector, such as healthcare provider consultations, diagnosis, medication, and hospitalization. Direct nonhealthcare costs (also called patient costs) relate to the resources used for healthcare borne by the patient and/or his family, such as over-the-counter medications, patient copayments for healthcare, and travel expenses to visit a healthcare provider. Indirect nonhealthcare costs mostly include productivity losses due to absenteeism, or job loss of patients and their caregivers. Indirect healthcare costs relate to medical consumption in life-years gained due to life-saving or death-postponing interventions, and are therefore by definition not included in COI studies.

COI estimates for *Campylobacter* have been generated since the 1980s (Todd, 1989), yet no estimate of the global economic impact of *Campylobacter* is available. Table 2.2 gives an overview of available *Campylobacter* COI estimates. All studies were performed in developed countries. Across countries, the indirect nonhealthcare costs (i.e., mostly productivity losses) appear to be the greatest contributor to the overall *Campylobacter* COI (Buzby et al., 1997; Roberts et al., 2003; Lake et al., 2010; Mangen et al., 2015). As for health impact assessment studies, it is important to include chronic sequelae in COI studies, as they can result in high individual and total costs (Buzby and Roberts, 2009; Mangen et al., 2015). Buzby et al. (1997) appear to be to first to evaluate COI of *Campylobacter*-associated GBS. They estimated that in 1995, in the USA, *Campylobacter* resulted in a total annual cost of US $1.5–8.0 billion, of which US $0.2–1.8 billion was due to *Campylobacter*-associated GBS (or around US $470,000/patient). The productivity cost of GBS patients not able to resume work was the largest contributor to the overall COI of *Campylobacter*-associated GBS.

However, comparison between studies is difficult. There exists, for example, no universally accepted method to estimate productivity losses in case of illness-related death or permanent disability (Buzby et al., 1997). The more frequently used methodology for estimating productivity losses due to absence from paid and unpaid work is the human capital approach, based on neoclassical labor theory. In the human capital approach, the value of potential lost income because of illness-related death or permanent disability is estimated, starting from the age of death or permanent disability, up to the age of retirement. However, arguing that the neoclassical labor theory is out of line with reality to current labor markets, Koopmanschap et al. (1995) introduced the friction cost approach. In this approach, productivity losses are only

Table 2.2 National *Campylobacter* Cost-of-Illness (COI) Studies

References	Setting	Reference Year	Included Symptoms and Sequelae	Included Cost Components	Total COI	COI/Case
Todd (1989), Roberts (1986)	United States	Not indicated	AGE	DHC; PL_H and intangible cost (death)	Up to US $1.4 billion	Up to US $666
Buzby et al. (1997)	USA	1995	AGE; GBS	DHC; PL_H and intangible costs (death/disability)	US $1.5–8.0 billion	US $750–800
Withington and Chambers (1997)	New Zealand	1995	AGE; GBS; ReA	DHC; DNHC; PL_H	NZ $4.5 million	NZ $596
Scott et al. (2000)	New Zealand	1999	AGE	DHC; DNHC; PL_H and intangible costs (death)	NZ $40 million	NZ $533
Roberts et al. (2003)	United Kingdom	1993–1995	AGE	DHC; DNHC; PL_H	£70 million	£315
van den Brandhof et al. (2004)	Netherlands	1999	AGE	DHC; DNHC; PL_F	€9.2 million	€103
Mangen et al. (2005)	The Netherlands	2000	AGE; GBS; ReA; IBS	DHC; DNHC; PL_F	€21 million	€233
Gellynck et al. (2008)	Belgium	2004	AGE; GBS; ReA; IBD	DHC; DNHC; PL_F	€27 million	€495
Scharff et al. (2009)	Ohio, USA		AGE; GBS	DHC; PL_H and intangible cost (morbidity and death)	US $217 million	US $3411
Lake et al. (2010)	New Zealand	2006	AGE; GBS; ReA; IBD	DHC; DNHC; PL_H	NZ $134 million	NZ $600
Ruzante et al. (2010)	Canada, associated with chicken consumption	2006	AGE; GBS	DHC; PL_H and intangible costs (death)	CAN $80 million	CAN $512
Collier et al. (2012)	USA	2007	AGE (only hospitalized cases)	DHC (including copayments by patients)	US $118 million	US $8915
Scharff (2012)	USA	2010	AGE; GBS	DHC; PL_H and intangible cost (morbidity and death)	US $1.56 billion	US $1846
Mangen et al. (2015)	Netherlands	2011	AGE; GBS; ReA; IBD; IBS	DHC; DNHC; PL_F	€82 million	€757
Tam and O'Brien (2016)	United Kingdom	2008–2009	AGE; GBS	DHC; DNHC	£51 million	£90

Abbreviations: AGE, acute gastro-enteritis; GBS, Guillain–Barré syndrome; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; ReA, reactive arthritis; DHC, direct healthcare costs; DNHC, direct nonhealthcare costs, also called patient costs; PL_H, productivity losses using the human capital approach; PL_F, productivity losses using the friction cost approach

When monetarizing intangible costs, most studies used national values for a statistical life (Todd, 1989; Buzby et al., 1997; Scott et al., 2000; Scharff et al., 2009; Scharff, 2012; Lake et al., 2010; Ruzante et al., 2010). Scharff et al. (2009); Scharff (2012) further made an estimate for intangible costs by monetarizing QALYs

considered for the period needed to replace a sick, invalid, or deceased worker, the so-called friction period that depends on the situation on the labor market, and places a zero value on individuals outside of the labor market, that is, children, retirees, and the elderly (Koopmanschap and van Ineveld, 1992).

A further complicating fact when comparing cost studies is that some studies considered both the financial impact of the disease (e.g., medical costs, patient expenses and productivity losses), and intangible costs for suffering, bad health, and premature death. Intangible costs are monetarized by using revealed or stated preferences of willingness-to-pay (WTP) (Drummond et al., 2015). WTP measures what individuals would be willing to pay to obtain health improvements, or to avoid adverse health states (Krupnick, 2004; Drummond et al., 2015). WTP can be measured by evaluating the trade-offs people actually make (revealed preferences), or by presenting people with hypothetical choices (stated preferences) (Krupnick, 2004; Drummond et al., 2015). This method is based on the trade-offs that individuals must make between health and other goods and is consistent, therefore, with the theoretical foundation of welfare economics (Drummond et al., 2015). Such trade-offs between money and fatality risks serve to estimate the value of a statistical life (Viscusi and Aldy, 2003).

Another attempt to monetarize intangible costs such as bad health and premature death was done by Scharff et al. (2009), who proposed an enhanced COI model that incorporated a value for pain and suffering. This value was calculated by monetizing losses in quality-adjusted life years (QALYs). QALY losses are roughly similar to DALYs, and are based in part on functional disability, pain, and suffering. The monetization of QALY losses was based on the assumption that one QALY is worth the value of a statistical life year. When applied to the entire USA, the enhanced COI model resulted in an estimated *Campylobacter* COI of US $8141/case, or US $6.9 billion in total, significantly higher than the estimates of the basic COI model that only considered financial impact (US $1846/case, or US $1.56 billion in total) (Scharff, 2012).

2.3.2 INDUSTRY AND GOVERNMENT COSTS

Even though COI appears to be the dominant approach for estimating the economic impact of foodborne diseases, there are various other economic losses beyond those resulting from human illness (Buzby and Roberts, 2009). Indeed, surveillance and other regulatory activities in place to monitor, prevent, and control foodborne diseases incur cost to the society.

Incidental foodborne disease outbreaks are not just associated with a peak in human illnesses, and thus a peak in COIs, they result in additional economic consequences due to costs of investigation, law suits, and loss of business by the food company (e.g., due to recalls, loss of consumer trust, or trade restrictions) (Todd, 1989). Sheerin et al. (2014), for example, estimated that a waterborne outbreak of campylobacteriosis in Darfield, New Zealand, imposed an additional NZ $95,000 to the District Council, due to additional staff time, and a commissioned investigation report.

To tackle the New Zealand *Campylobacter* epidemic, new *Campylobacter* compliance standards were imposed to the industry in 2007. Industry costs of capital investment were estimated at NZ $2 million, while increased operating costs, including purchase of chemicals and maintenance costs, were determined to be NZ $0.88 million. The new compliance program required the regulator to undertake and continue oversight of its implementation, imposing an additional annual cost on the government of NZ $0.89 million (Duncan, 2014).

Further indications on potential industry and government costs are available from cost-effectiveness studies (Havelaar et al., 2007; Elliott et al., 2012; Lake et al., 2013). The CARMA (Campylobacter Risk Management and Assessment) project aimed to assess the cost–utility of different potential *Campylobacter* intervention measures in The Netherlands. Estimates were generated of the presumed direct intervention costs and number of *Campylobacter* gastroenteritis cases averted, allowing for the calculation of cost–utility ratios (Havelaar et al., 2007). Thus, the cost of improved farm hygiene was estimated at €8–63 million, and the costs of information campaigns, for example, to stimulate hygienic kitchen behavior, or to promote home freezing of poultry, were estimated at €1 million/year. Scheduled decontamination of carcasses by dipping in lactic acid would cost €5 million, and avert 9200 *Campylobacter* cases, resulting in a cost of €28,000/DALY averted—which was found to be the most beneficial cost–utility ratio. Irradiation, probably the most effective intervention, was considered to be too expensive and therefore not cost-effective. Not considered in these estimates were potential indirect effects due to considered interventions, for example, the nonacceptance by the consumer, the loss of market shares as not being able to sell on time. The consequence would be lower selling prices (i.e., lower income for the industry) and consequently less cost-effective interventions.

Finally, for zoonotic foodborne diseases, livestock production losses due to clinical or subclinical infection may further add to the economic burden. Poultry infected with *Campylobacter*, however, are generally neither sick, nor are their growth and reproduction abilities affected (Mangen et al., 2007). Implementing farm-level interventions to control *Campylobacter* would thus result in a net rise of production costs equal to the direct intervention cost. This skewed situation might impede program uptake, and would call for governments to intervene, as the guardian of food safety.

2.4 CONCLUDING REMARKS

Several studies have focused on producing DALY and cost estimates associated with foodborne *Campylobacter* infections. From a methodological standpoint, approaches and data characteristics used for the estimates differed in both fields, making direct comparisons difficult. Alignment of approaches and methodologies would be an important future step. Nevertheless, the importance of *Campylobacter* in the foodborne disease burden was consistently shown in these studies, warranting continuing efforts the reduce food contamination by this pathogen.

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