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Impact of food and water-borne diseases on European population health

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Composite health measures are increasingly applied in studies aiming at describing the burden of diseases, and food and water-borne diseases (FWDs) are no exception. The Burden of Communicable Diseases in Europe (BCoDE) is a project led and funded by the European Centre for Disease Prevention and Control (ECDC) with the purpose of encouraging and empowering public health experts in the estimation of the impact of communicable diseases expressed in Disability Adjusted Life Years (DALYs). Calculation of DALYs and a critical assessment of burden of disease outputs require a thorough consideration of a number of methodological and epidemiological decisions ranging from modelling (e.g. incidence versus prevalence), disease model parameters (e.g. risks of developing complications or death) and the data feeding the number of cases.Burden of disease studies produce useful results for public health decision-making, in particular when they aim at informing preventive strategies. For this purpose, we attributed FWDs results from the BCoDE 2015 study to different exposure routes. We discuss these in the more general perspective of generating burden of disease evidence for planning and prioritisation, including the potentials and limitations of its methodology.

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Introduction

Determining the public health impact of food and water-borne diseases (FWDs) poses a number of challenges. Attempts to estimate such burden include reporting of infections [1•,2,3], incidence and mortality [4]. However, severity, duration and mortality related to FWDs vary widely; therefore, a more coherent and consistent approach is needed to enable comparison between the overall impact of diseases. Disability-adjusted life years (DALYs), a summary measure of population health developed by the Global Burden of Disease (GBD) study [5], match these requirements and are increasingly utilised to inform evidence-based health policy decision making [6,7,8,9,10,11•].

In 2006, the European Centre for Disease Prevention and Control (ECDC) commissioned a pilot estimation of seven selected infectious diseases (IDs) in order to explore the interest in and feasibility of a burden of infectious disease study and to layout its methodology [12,13]. Based on this pilot investigation, the Burden of Communicable Diseases in Europe (BCoDE) project was launched. Funded by an ECDC grant and implemented in collaboration with a European Consortium led by the Dutch National Institute for Public Health and the Environment (RIVM), the project included European experts from academic centres and national health institutes.

A consistent methodology for calculating the burden of infectious diseases expressed in DALYs, pathogen and incidence-based, was developed [14,15]. Results of the burden of selected FWDs on European Union and European Economic Area (EU/EEA) Member States, amongst others, were recently presented at the 2015 European Public Health Conference [16] and represent the findings of the BCoDE 2015 study [17]. Using the BCoDE 2015 study as a reference point, we provide an overview of, and a comparison with other methodological frameworks and options for burden of disease studies. With the purpose of informing risk assessment, we attributed the FWD disease-specific DALYs stemming from BCoDE 2015 to different exposure routes as an example illustrating how burden of disease outputs help inform public health planning and decision-making. Finally, we discuss how findings of burden of disease studies compare and how these are useful in providing scientifically sound information to risk managers and their decision making process.

Methodologies for estimating burden of foodborne and waterborne diseases

DALY is a composite metric quantifying the health losses measured in years. It was first developed as a composite health measure by the Global Burden of Disease project within the World health Organization (WHO) [18] and has evolved in time [5]. DALYs are calculated by adding years of life lost due to premature mortality (YLL) and years of life lived with a disability (YLD), associated with a specific disease. The former is based on the number of deaths associated with a disease, where deaths are stratified by age and multiplied by remaining life expectancy by age at death. YLDs are the sum of all outcomes' durations multiplied by their disability weights and the number of cases experiencing that outcome. Therefore, DALYs express the impact of the acute phase of diseases and their related short and long-term outcomes.

ECDC has the objective of surveillance and providing scientific advice on a number of communicable diseases (CDs) according to Decision 1082/2013/EU of the European Parliament and of the Council [19], which are subject to mandatory notification by EU/EEA countries to The European Surveillance System (TESSy) [20]. Within the master list of all communicable diseases, a selection of diseases were integrated in the BCoDE toolkit [21•], a stand-alone software application for calculation of DALYs. The diseases were selected by an *ad hoc* working group of the ECDC Advisory Forum based on based on data availability, perceived incidence, outbreak potential and if the disease is vaccine-preventable with widely used vaccines [22].

The GBD 2010 and 2013 studies utilised prevalence data sources [23,24••] whereas the BCoDE project modified this methodology and suggested an incidence-based and pathogen-based approach [14,15]. The effect of an incidence approach is to acknowledge future sequelae of infections on top of the disabilities due to the acute phase of the disease. The incidence-based estimation of burden also sets the baseline information for estimating the impact of prevention and control interventions in a comprehensive way by accounting for the short and long-term effects of interventions [25]. The pathogen approach assigns the disease burden to a causal or associated event. In practice, symptomatic infections are linked to outcomes through a disease progression model and visually described in outcome trees such as those displayed in the BCoDE toolkit [21•]. It is important to note that, as shown by Schroeder [26], if DALYs are calculated without time discounting (see below), the choice of a prevalence versus an incidence approach has a minimal impact on the final results in a trend steady state situation [27].

Outcome tree parameters can be based on literature reviews, observed clinical outcome data, or a mix of the two. The BCoDE toolkit [21•], for example, utilises the latter approach and case fatality proportions extracted from literature reviews were age-specifically modelled according to notified deaths by age groups, through enhanced surveillance data reported to TESSy.

Disability weights quantify health losses relating to non-fatal outcomes. Several sets of disability weights are available, all based on different elicitation methods [28]. The BCoDE toolkit utilises disability weights stemming from the European disability weights study [29,30]. Other methodological choices that need to be considered include time discounting and age weighting. The BCoDE toolkit users have the option to calculate DALYs with or without time discounting, as well as choosing the annual rate. Time discounting is particularly used in economic assessments and burden of disease studies aiming at estimating the economic impact of a disease or an intervention. For the BCoDE 2015 study, time discounting was not included as the purpose of the study was to estimate the impact of infectious diseases on the health of European citizens and not on its economy. In that sense, it was considered that there were no particular reasons why future health effects should be valued less: utilities associated to healthy life years were assumed not to decline over time [31]. Similar considerations are valid for age weighting, which has been suggested as a way to account for societal priorities. The BCoDE methodology proposes an approach aiming at measuring the impact of infectious diseases on health. Moreover, if societal priorities were to be measured when calculating DALYs, age weighting would provide incomplete and biased information. Therefore, it was decided to exclude age weighting from the BCoDE toolkit. In conclusion, for the BCoDE 2015 study, disabilities and healthy life were treated equally regardless of age and time.

Ranges of values reflecting variability and uncertainty can be defined within all parameters of the BCoDE toolkit. DALYs are then calculated through Monte Carlo simulations for which the number of iterations is set by the user. The resulting 95% uncertainty intervals (UI) are displayed in the results.

Choice of data sources: striking a very thin balance

When choosing the data source for determining incidence, researchers strive to balance data availability and quality with representativeness of the population under study. As a secondary objective, the BCoDE 2015 study aimed at exploring and describing the features of the ECDC surveillance system. Therefore, TESSy was chosen as the default data source. In principle, the approach consisted in exporting age-group and sex specific annual number of cases from TESSy's case-base database. EU/EEA MSs were considered according to data availability (i.e. if cases were reported to TESSy) and to

characteristics of their surveillance system (e.g. compulsory versus voluntary, comprehensive versus sentinel, national coverage). In conclusion, differences of MS reporting patterns need to be considered in light of the European heterogeneity with regards to the surveillance system, reporting qualities and epidemiological situations.

When estimating a baseline burden of disease, annual epidemiological variations are particularly relevant due to seasonality and outbreaks for example. Including several years of surveillance data and averaging these to obtain the annual number of cases, spreads the peak effect over several years. For example, the BCoDE 2015 study averaged cases notified to TESSy between 2009 and 2013 and the Dutch Burden of infectious disease study averaged reported cases between 2006 and 2013 [9].

Notification data are of good quality in Europe although as usual prone to a varying degree of underestimation. Underestimation stems from a combination of underreporting (infected individuals whose disease is misdiagnosed, misclassified or not reported to the national surveillance system) and underascertainment (infected individuals who never seek healthcare) [32]. Moreover, the nature and the extent of the under-estimation effect varies across countries and, at times, across epidemiological years [33]. For the BCoDE 2015 study, extensive literature reviews were undergone for each disease in order to estimate multipliers adjusting for under-estimation of reported data.

About 5.69 cases per 100,000 population of giardiasis were reported in the EU/EEA which were multiplied by 14 (with a range from 4 to 49) [7,34]. The hepatitis A average reporting rate of 2.78 per 100,000 population was multiplied by 4.5 (3.7–5.6) [35]. For listeriosis, a factor 1.7 (1.1–2.3) was applied to the average notification rate of 0.41 per 100,000 population [7], for shigellosis the notified cases of 1.67 per 100,000 population were multiplied by 18.3 (2.9–39.5) [7,36] and notified rates of verocytotoxigenic *Escherichia coli* (STEC/VTEC) (1.31 per 100,000 population) were multiplied by 26.68 (1.6–109.7) [7,34,37].

When notification data is scarce or unavailable, alternative methods should also be considered, such as capture–recapture studies, analysis of attack rates and serological studies. For example, underestimation of notified campylobacteriosis and salmonellosis symptomatic cases was estimated based on serological studies [1,38,39]. These sero-incidence studies have determined the rate of infection in several EU Member States, which provides important information on the circulation of the infection. For example, it was estimated that *Salmonella* cause 0.06–0.61 infections per person-year, respectively in Sweden and Spain. These findings should not be confused with symptomatic diseases. However, assuming that the disease-to-infection rate is constant across countries, sero-incidence studies are able to provide useful information. In the BCoDE 2015 study, for the estimation of symptomatic campylobacteriosis and salmonellosis sero-incidence results of three EU Member States (for *Salmonella*; two for *Campylobacter*) were anchored to community based studies performed in the same countries [38]. Each anchoring provided a conversion factor between infections and diseases, which were applied to the other countries. The range of estimated incident symptomatic cases was used to estimate the burden in DALYs.

Another example describing a situation where notification data is unavailable is the estimation of the incidence of symptomatic congenital toxoplasmosis. A literature research provided a range of 7.3–29 cases per 100,000 births to which no multiplier adjusting for under-estimation was applied.

In the BCoDE 2015 study, age-group and sex specific incident cases and, where applicable, multipliers adjusting for under-estimation of notified cases were inserted in the BCoDE toolkit. No time discounting was applied and 1000 Monte Carlo simulations were chosen. No modifications to the BCoDE toolkit outcome tree parameters were applied and estimated DALYs were exported into tables and graphs.

Ranking risks according to impact on health measured in DALYs

The BCoDE 2015 found that campylobacteriosis was the disease with the highest burden in the EU/EEA with 8.20 (UI: 6.68–10.01) DALYs per 100,000 population, followed by salmonellosis with 3.96 (UI: 3.68–4.26) and infection with Shiga toxin-producing *E. coli* (STEC) with 2.08 (UI: 2.59–3.21). These diseases represent more than 75% of the burden of the FWDs under study and it was estimated that slightly over 2000 deaths are associated with FWDs in the EU/EEA every year. Moreover, congenital infections (congenital toxoplasmosis and perinatal listeriosis), although rare, have a considerably high burden in newborn population, suggesting the need to continue and improve the existing preventive efforts in this vulnerable population.

As a composite health measure, DALY provides a comprehensive overview of the impact of diseases as it encompasses the relative disabilities and mortality, sustained both during the acute phase and related to the short and long-term complications of diseases. These are the reasons underlying the European Food Safety Authority's (EFSA) recommendation on using the BCoDE toolkit, and the BCoDE methodological approach, as part of the risk ranking toolbox for the Panel on Biological Hazards (BIOHAZ) [40•], in particular as a top-down method to rank pathogens.

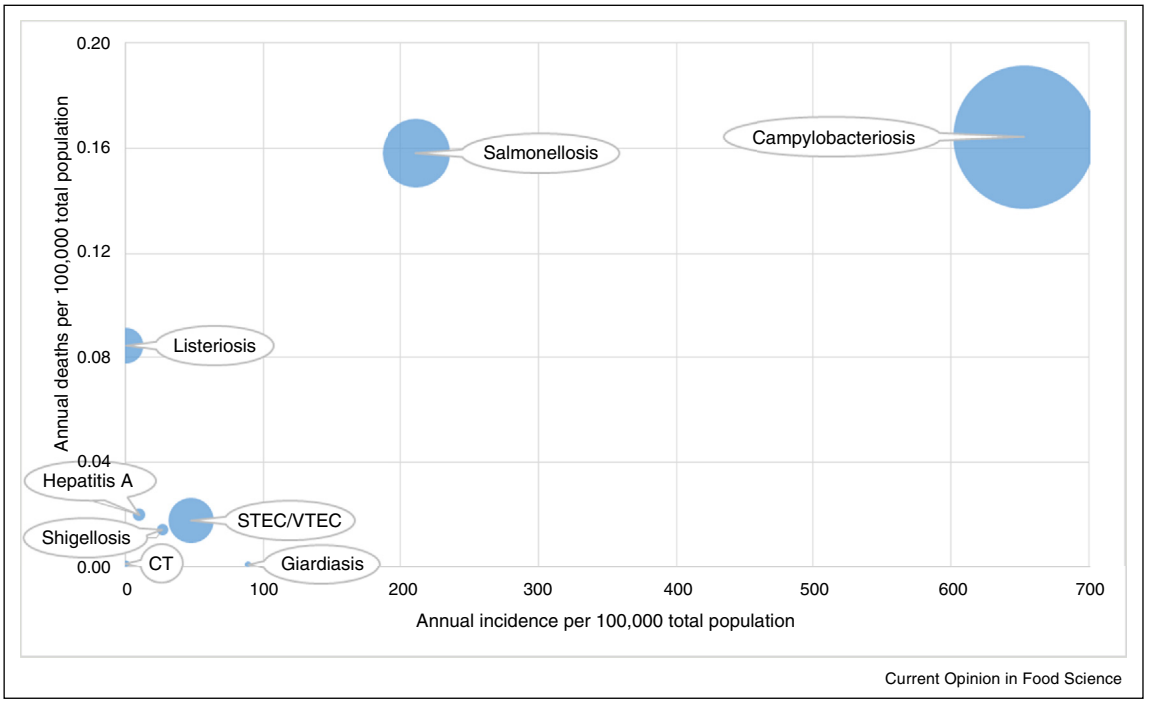
The bubble chart in Figure 1 illustrates how the resulting DALYs per 100,000 for each disease relate to their incidence and estimated deaths. For example, the high burden of campylobacteriosis is a result of both high incidence and number of associated deaths. The burden of listeriosis is mainly due to its mortality, as opposed to giardiasis. This bubble chart shows more clearly that the choice of indicator affects very much the final ranking of diseases and the ensuing interpretation of the impact on population health.

Several burden of disease studies have estimated DALYs for FWDs at the national level [41,42] and comparing the same FWD across different countries [43]. Studies with a similar methodology to the BCoDE 2015 study include the Ontario Burden of Infectious Disease Study (ONBOIDS) [44] and the World Health Organization (WHO) Foodborne Disease Burden Epidemiology Reference Group (FERG) [45••,46]. Whilst comparing the same diseases, the former found an overall burden of 3.28 DALYs per 100,000 population in contrast to our finding of 18.76. Estimated incidence was similar in both studies (475–832 cases per 100,000 population in BCoDE 2015 versus 726 in ONBOIDS), as well as risks of developing complications. However, the ONBOIDS study estimated 0.33 annual deaths attributable to *Campylobacter* enteritis, resulting in a case fatality proportion (CFP) of 0.0004% while BCoDE 2015 was set a CFP of 0.001–0.05%. As an effect, YLLs for campylobacteriosis was higher in the BCoDE 2015 study, representing 40% of the total burden against 15% in ONBOIDS. In terms of ranking, however, campylobacteriosis and salmonellosis consistently ranked as the foodborne diseases with the highest burden.

A global study of FWDs, the WHO FERG endeavour, offers results of burden of pathogens in different WHO subregions [45••,47•]. For comparison with our findings we considered EUR A region and found a higher burden of all comparable FWDs from the FERG study compared to BCoDE 2015: 26.62 (UI: 22.03–40.80) versus 19.14 (UI: 16.20–22.67) DALYs per 100,000 population. Main differences, both in terms of ranking and DALY per 100,000, are related to non-typhoidal *Salmonella enterica* (ranked first in the FERG study with 12 (UI: 7–18) DALYs per 100,000 population) and to Shiga toxin-producing *E. coli* (ranked 5th with 0.6 (95% UI: 0.2–1) DALYs per 100,000 population).

Incidence of STEC is similar across the two studies which both apply a set of multiplication factors adjusting for underestimation to notification data [48]: FERG applied the factor of 36 (with a range of 7.4–106.8) [49] whereas BCoDE 2015 chose the factor of 26.68 (with a range of

Figure 1



From BCoDE 2015: bubble chart plotting the DALYs per 100,000 (diameter of bubble) with incidence per 100,000 total population and estimated deaths per 100,000 total population from the BCoDE toolkit disease models. (CT = congenital toxoplasmosis; vCJD is not visible given the low burden).

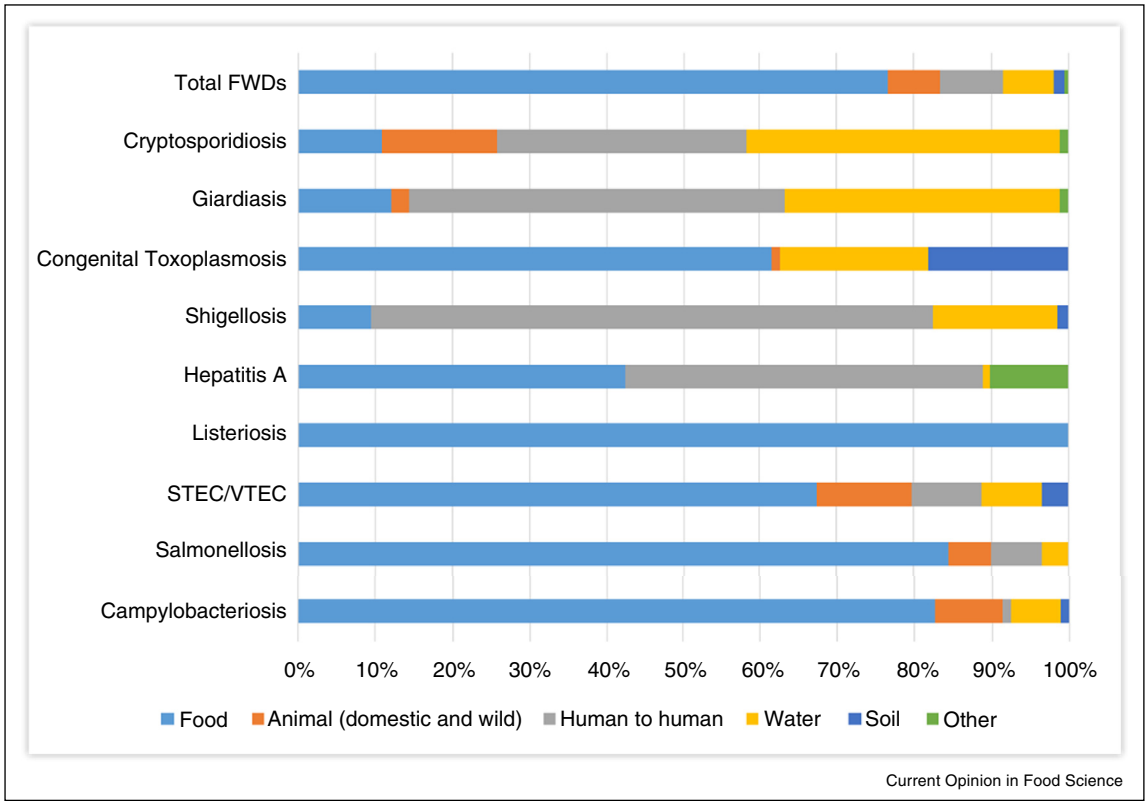
1.6–109.7) [7,34,37]. Moreover, the FERG study used the regional incidence of STEC incidence in the EUR A region of 47.1 cases per 100,000 population, not very dissimilar to our finding of 35 cases per 100,000 population. When comparing the STEC disease model (outcome tree) of BCoDE present in the ECDC BCoDE toolkit software application [21•] with that of the FERG study, they appear to include the same outcomes, except renal transplantation present in BCoDE. However, risk of developing haemolytic uraemic syndrome (HUS) and end-stage renal disease (ESRD) is higher in BCoDE 2015 than in the FERG study (age dependent interval of 0.94–1.25% [21•] against 0.03–0.8% [49] for HUS and 2.9–10.5% [21•] against 3% (ranging from 0% to 30%) [49] for ESRD, respectively).

Differences in the salmonellosis results between the two studies seem more complex and possibly related to a combination of three factors. The FERG study inputted a higher incidence (301.5 per 100,000 population versus 216 per 100,000 population in BCoDE 2015 study), a higher proportion of moderate diarrhoea (25% against 15% [44], respectively) and a higher disability weight applied to the diarrhoeal event (0.202 taken from GBD 2010 against 0.149 applied in BCoDE 2015). Moreover, one substantial difference, which might explain the higher burden in FERG study, is related to choices concerning the CFP. The ECDC BCoDE mortality per 100,000 upper range is lower (0.17 against 0.40 DALYs per 100,000 population) although median values are the same (0.16 against 0.15 DALYs per 100,000 population). However, the BCoDE disease model applied an age-group re-distribution of the CFP (stemming from enhanced surveillance information from TESSy) where nearly 70% of the deaths occur in people older than 70 years, resulting in lower YLLs from death associated to salmonellosis.

Attribution of infection to exposure routes

Attribution of the BCoDE 2015 FWDs to different exposure pathways was based on a recent global elicitation study, funded by the World Health Organization (WHO), within the framework of the Foodborne Disease Burden Epidemiology Reference Group (FERG) [50•]. Major transmission routes were through food, animal contact (domestic and wild), human to human transmission, water, soil or other. For the present study, we only considered median values and 95% uncertainty intervals

Figure 2



Percentage of DALYs from the BCoDE 2015 study attributed to different exposure routes according to WHO FERG expert elicitation (subregion EUR-A).

results for WHO subregion EUR A (European Region, Stratum A).

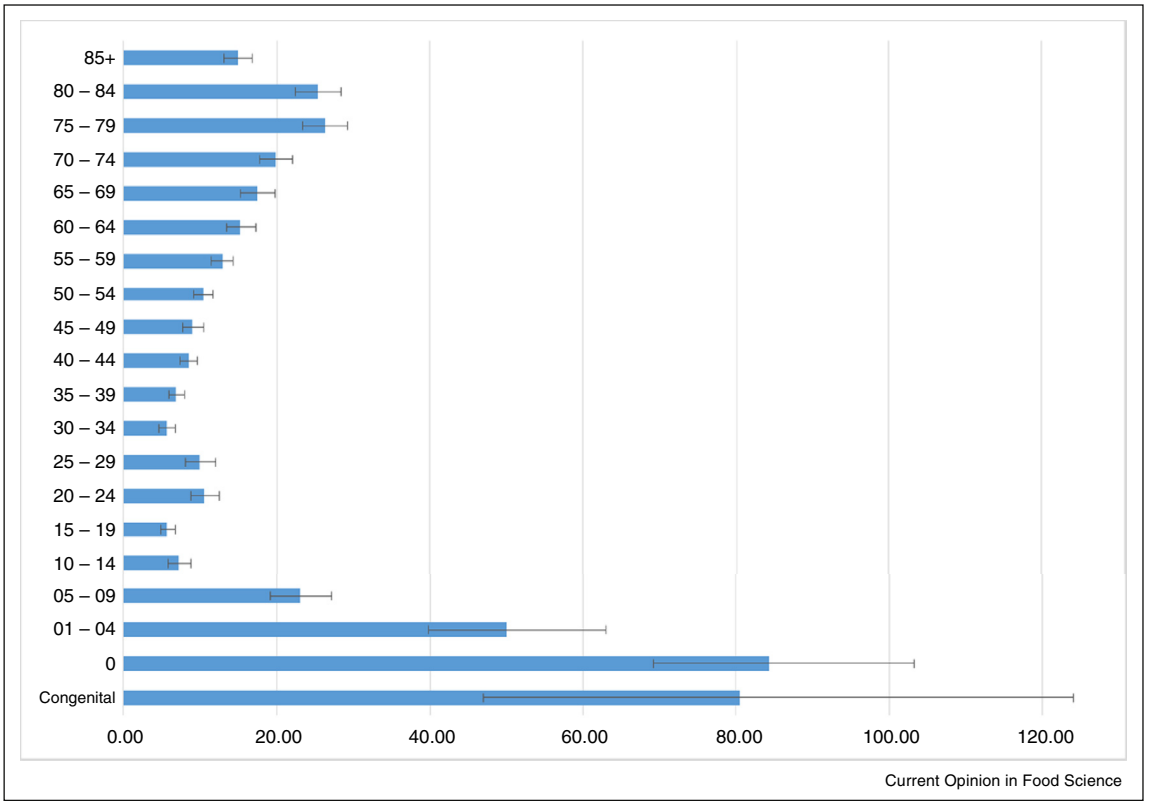
Figure 2 presents the attribution of the burden of FWDs to different exposure groups. As expected, estimation of DALYs by different exposure routes shows that most of the burden was attributed to food as the main cause of transmission, 77% (uncertainty ranging from 40% to 100%), suggesting the need to strengthen efforts to control and prevent FWDs through interventions in the food chain. For example, campylobacteriosis is the most commonly reported FWD and its trend has been increasing in the past years [3,4]. Recent studies also show that in some European countries up to 80% of the population are infected with *Campylobacter* every year, although not all develop a symptomatic disease [2]. EFSA has estimated that 50–80% of human *Campylobacter* infections can be attributed to the chicken as a reservoir, warranting appropriate prevention measures to be applied along the poultry food chain [51]. In 2012, EFSA has published options for interventions at poultry meat inspection with the aim to reduce the public health risk for *Campylobacter*, *Salmonella* and ESBL/AmpC gene-carrying bacteria [52].

This information is potentially useful for improving prevention strategies in EU/EEA countries, especially in light of the planned further work on specific food sources/categories (personal communication, Tine Hald). However, the FERG study did not specifically explore the differential exposures according to age groups. Figure 3 clearly illustrates that young children under 5 years of age are the age group at highest risk for FWD. Infection pathways in this age category might differ, which might undermine the effectiveness of interventions aiming at preventive efforts.

Burden of disease studies for planning and prioritisation

Estimation of incidence, involving critical assessments of data quality and degrees of under-estimation of reported surveillance data, is a crucial factor in the calculation of burden of disease in DALYs. Likewise, assumptions and decisions underlying the choice of incidence to input in the disease models are decisive in the interpretation of the results. As discussed above, all parameters of the disease models will also play a fundamental role in the DALY results, along with modelling decisions. These assumptions have to be accounted for when interpreting

Figure 3



Age group specific burden of food and water-borne diseases from BCoDE 2015 study: 2009–2013 DALYs per 100,000 stratum specific population (median and 95% uncertainty intervals).

and communicating outcomes from burden of disease studies, in particular for planning and prioritisation purposes during which communication of limitations and uncertainties become a complex but necessary task.

For this reason, integrative methods of risk ranking and prioritisation are highly recommended. Examples undertaken from National Health Authorities include prioritisation exercises for surveillance purposes in Germany and Sweden [53•,54]. Both studies report that infections from *Campylobacter* spp., *Salmonella* spp. and Shiga-toxin producing *E. coli* should be placed in the highest priority group. This is consistent with our findings, which ranked the diseases resulting from those infections as those with the highest burden. Moreover, listeriosis was consistently ranked as being in the high priority group. The remaining infections move between high and medium priority group depending on the study.

ECDC continues working on risk ranking methodologies [55•] and is developing a framework for emerging threats impact assessment based on multi-criteria decision analysis (MCDA) methodologies [56,57]. The underlying rationale is that quantitative methods alone, such as burden of disease outputs in DALYs, do not fully encompass all unknowns, uncertainties, variability and other 'softer' criteria such as public perception. On the other hand, MCDA risk ranking methods are subject to a certain degree of subjectivity, which may bias results.

DALY estimates of disease burden provide valuable information to be taken into account during public health decision-making for prevention strategies. Efforts aiming at improving surveillance data availability and quality will increase the precision and reliability of DALY estimates, and of infectious disease modelling efforts in general. Finally, DALYs can be one of the key inputs in comprehensive tools for risk ranking such as multi-criteria decision analysis.

Author contributions

AC wrote the first draft of the manuscript. All authors helped conceive the opinion and contributed to writing the manuscript.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.cofs.2016.06.002.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

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The authors developed a mathematical model allowing calculation of the annual incidence of Salmonella infections based on the decay of antibodies present in the serum. The model was applied to samples representing the general population in 13 countries of the European Union. Ten-fold variations were found across countries and no correlation with official notification data from national surveillance systems was established.

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This article presents an overview of the application of disability-adjusted life years (DALYs) in health economics and in particular for the economic assessment of infectious disease interventions. Economic methodologies applied to DALYs have increased in the past 10 years, although most studies were conducted in low-income countries. However, many studies analysed in the systematic review did not fully adhere to the recommended methodologies, ultimately undermining comparability across studies.

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The Burden of Communicable Disease in Europe (BCoDE) project, ran by the European Centre for Disease Prevention and Control (ECDC) produced a stand-alone software application, with a user-friendly interface and an embedded tutorial, which allows calculation of disability-adjusted life years (DALYs) for a selection of 32 communicable diseases and six healthcare-associated infections. Calculations are based on inputted incidence data from the user and disease models built in the application. Outputs include graphs, bubble charts and tables.

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The Global Burden of Disease Study 2013 (GBD 2013) generated global summary measures of population health, including results of health loss due to food-borne and water-borne diseases, allowing for comparative epidemiological analysis across countries and time. Although DALYs for infectious diseases have decreased, healthcare needs have not and variations around burden of disease are not necessarily associated with socio-demographic status.

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Part of a collection related to the World Health Organization (WHO) Foodborne Disease Burden Epidemiology Reference Group (FERG), this article illustrates the global burden of foodborne diseases measured in disability-adjusted life years (DALYs). Most frequent causes of foodborne diseases are norovirus, *Campylobacter* spp. and non-typhoidal *Salmonella enterica*, children bearing the majority of DALYs. WHO regional results are also available, European regions being amongst those with the lowest burden. In Europe, *Toxoplasma gondii* and *Listeria monocytogenes* also generate a high burden. Ranking of diseases according to their burden on population health is valuable information for prioritization and planning public health interventions.

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Also part of the WHO FERG effort, this article provides detailed information on the global and WHO regional annual number of cases, number of deaths and DALYs for foodborne diseases. Estimates were based on disease models encompassing all outcomes related to specific foodborne infections. Systematic literature reviews were performed in order to inform the disease models; these reviews are valuable for other researchers looking into modelling of infectious diseases. Moreover, age specific results are also illustrated.

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Cross-border infectious disease outbreaks pose a threat to European citizen's health and require prioritisation of the relevant pathogens. This review of the literature illustrates a range of methods used for prioritisation and ranking of threats purposes. Methodologies described, including strengths and limitations, are bibliometric index, the Delphi technique, multi-criteria decision analysis (MCDA), qualitative algorithms, and questionnaires. A common approach to risk ranking methodologies were: identifying diseases for ranking, identifying assessment criteria, weighting criteria, scoring diseases against criteria, and producing a ranked list of diseases.

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