WHO ESTIMATES OF THE GLOBAL BURDEN OF FOODBORNE DISEASES

FOODBORNE DISEASE BURDEN EPIDEMIOLOGY REFERENCE GROUP 2007-2015

World Health Organization

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This report is a compilation of the main reports of the task forces of the Reference Group. Numerous persons contributed to or read the manuscript and provided comments, including several units in WHO headquarters and Regional Offices. The text was then edited to introduce conformity in language and style.

FOREWORD

Foodborne diseases have been an issue for all societies since the beginning of humanity. The types, severity and impacts of these illnesses have changed through the ages and are still diverse across regions, countries and communities.

Yet there are some challenges common to all countries. Only a fraction of the people who become sick from food they have eaten seek medical care. Only a fraction of those cases are recognized as having been caused by a hazard in food, treated accordingly, reported to public health authorities and recorded in official disease statistics. Certain chronic diseases, such as cancer, kidney or liver failure, that result from contaminated food appear long after the ingestion of food and the causal link is never made for each case. This points to some of the challenges inherent in measuring the burden of foodborne diseases and the toll they take on lives and economies.

Up to now, the global burden of illness and deaths caused by foodborne disease has never been quantified. In order to fill this data vacuum, the World Health Organization (WHO), together with its partners, launched in 2006 the Initiative to Estimate the Global Burden of Foodborne Diseases. After an initial consultation, WHO in 2007 established a Foodborne Disease Burden Epidemiology Reference Group (FERG) to lead the initiative.

The objective of the initiative was not limited to providing estimates on the global burden of foodborne diseases for a defined list of causative agents of microbial, parasitic and chemical origin. The initiative also aimed at strengthening the capacity of countries to conduct assessments of the burden of foodborne disease, and encouraging them to use burden of foodborne disease estimates for cost-effectiveness analyses of prevention, intervention and control measures including implementation of food safety standards in an effort to improve national food safety systems.

Six taskforces were established under FERG, focusing on groups of hazards or aspects of the methodology. These taskforces commissioned systematic reviews and other studies to provide the data from which to calculate the burden estimates.

This report is an outcome of a decade of work by WHO, key partners and a number of dedicated individuals. Some additional findings, which cannot be integrated into this report, will be published and user-friendly online tools made available separately.

This report and related tools should enable governments and other stakeholders to draw public attention to this often under-estimated problem and mobilize political will and resources to combat foodborne diseases.

Kazuaki Miyagishima
Director
Department of Food Safety
and Zoonoses

EXECUTIVE SUMMARY

Foodborne diseases are an important cause of morbidity and mortality, and a significant impediment to socio-economic development worldwide, but the full extent and burden of unsafe food, and especially the burden arising from chemical and parasitic contaminants, has been unknown. Precise information on the burden of foodborne diseases can adequately inform policy-makers and help to allocate appropriate resources for food safety control and intervention efforts.

This report, resulting from the WHO Initiative to Estimate the Global Burden of Foodborne Diseases and prepared by the WHO Foodborne Disease Burden Epidemiology Reference Group (FERG), provides the first estimates of global foodborne disease incidence, mortality, and disease burden in terms of Disability Adjusted Life Years (DALYs). For the global estimates, thirty-one foodborne hazards causing 32 diseases are included, being 11 diarrhoeal disease agents (1 virus, 7 bacteria, 3 protozoa), 7 invasive infectious disease agents (1 virus, 5 bacteria, 1 protozoon), 10 helminths and 3 chemicals.

Together, the 31 global hazards caused 600 (95% uncertainty interval [UI] 420–960) million foodborne illnesses and 420,000 (95% UI 310,000–600,000) deaths in 2010. The most frequent causes of foodborne illness were diarrhoeal disease agents, particularly norovirus and *Campylobacter* spp. Foodborne diarrhoeal disease agents caused 230,000 (95% UI 160,000–320,000) deaths, particularly non-typhoidal *Salmonella enterica* (NTS, which causes diarrhoeal and invasive disease). Other major causes of foodborne deaths were *Salmonella* Typhi, *Taenia solium*, hepatitis A virus, and aflatoxin. The global burden of foodborne disease by these 31 hazards was 33 (95% UI 25–46) million DALYs in 2010; 40% of the foodborne disease burden was among children under 5 years of age. Worldwide, 18 (95% UI 12–25) million DALYs were attributed to foodborne diarrhoeal disease agents, particularly NTS and enteropathogenic *Escherichia coli* (EPEC). Other foodborne hazards with a substantial contribution to the global burden included *Salmonella* Typhi and *Taenia solium*.

Foodborne burden estimates are also reported for a further 4 bacterial and 1 chemical hazards, but only for some subregions; a global estimate was not feasible.

There were considerable differences in the burden of foodborne disease among subregions delimited on the basis of child and adult mortality. The highest burden per population was observed in Africa (AFR) (AFR D and AFR E subregions), followed by South-East Asia (SEAR) (SEAR B and SEAR D) subregions and the Eastern Mediterranean (EMR) D subregion. Diarrhoeal disease agents were the leading cause of foodborne disease burden in most subregions. NTS was an important burden in all subregions, particularly in Africa. Other main diarrhoeal causes of foodborne disease burden were EPEC, enterotoxigenic *E. coli* (ETEC) and *Vibrio cholerae* in low-income subregions, and *Campylobacter* spp. in high-income subregions. The burden of aflatoxin was high in the AFR D, Western Pacific (WPR) B and SEAR D subregions. In the SEAR subregions there was a considerable burden of *Salmonella* Typhi. The burden of *Opisthorchis* spp. was concentrated in the SEAR B subregion, where the seafood-borne trematodes *Paragonimus* spp. and *Clonorchis sinensis* were also important. In the Americas (AMR) B and D subregions, *Taenia solium* and *Toxoplasma gondii* contributed

significantly to the foodborne disease burden. The global burden of foodborne diseases is considerable, with marked regional variations. The burden of foodborne diseases is borne by individuals of all ages, but particularly by children under 5 years of age, and by persons living in low-income subregions of the world.

These estimates are conservative; further studies are needed to address the data gaps and limitations of this study.

In addition to providing global and regional estimates, the Initiative sought to promote actions at a national level. This involved capacity building through national foodborne disease burden studies, and encouraging the use of burden information in setting evidence-informed policies. A suite of tools and resources were created to facilitate national studies of the foodborne burden of disease, and pilot studies were conducted in four countries (Albania, Japan, Thailand and Uganda). Data gaps were the major hurdle in estimating the foodborne disease burden in these national studies, and the global and regional estimates provided by FERG offer an interim solution, until improved surveillance and laboratory capacity is developed.

Despite the data gaps and limitations of these initial estimates, it is apparent that the global burden of foodborne disease is considerable, and affects individuals of all ages, but particularly children under 5 years of age and persons living in low-income subregions of the world. All stakeholders can contribute to improvements in food safety throughout the food chain by incorporating these estimates into policy development at national, regional and international levels.

1 INTRODUCTION

INTRODUCTION

1.1 Motivation: the importance of food safety

Safer food saves lives. With every bite one eats, one is potentially exposed to illness from either microbiological or chemical contamination. Billions of people are at risk and millions fall ill every year; many die as a result of consuming unsafe food.

Concerns about food safety have skyrocketed in more affluent societies. However, the real tragedy of foodborne diseases is played out in the developing world. Unsafe water used for the cleaning and processing of food; poor food-production processes and food-handling (including inappropriate use of agricultural chemicals); the absence of adequate food storage infrastructure; and inadequate or poorly enforced regulatory standards–these all contribute to a high risk environment. Moreover, as a country's economy develops, the agricultural landscape changes. Intensive animal husbandry practices are put in place to maximize production, resulting in the increased prevalence of pathogens in flocks and herds. The tropical climate of many developing countries favours the proliferation of pests and naturally occurring toxins, and the risk of contracting parasitic diseases, including worm infestations.

While exposed to more hazardous environments, people in developing countries often have difficulty coping with foodborne disease. For many living at or below the poverty line, foodborne illness perpetuates the cycle of poverty. The symptoms of foodborne diseases range from mild and self-limiting (nausea, vomiting and diarrhoea) to debilitating and life-threatening (such as kidney and liver failure, brain and neural disorders, paralysis and potentially cancers), leading to long periods of absenteeism and premature death.

Foodborne pathogens take advantage of weak immune systems. Infants and young children, pregnant women, the elderly as well as those immuno-compromised, are particularly at risk of contracting and dying from common food-related diseases. Malnourished infants and children are especially exposed to foodborne hazards and are at higher risk of developing serious forms of foodborne diarrhoeal diseases; these infections in turn exacerbate malnutrition thus leading to a vicious circle of debilitation and mortality. Those who survive may suffer from delayed physical and mental development, depriving them of the opportunity to reach their full potential in society.

Beyond the individual level, foodborne diseases affect economic development, particularly challenging the tourist, agricultural and food (export) industries. Developing countries' access to food export markets will depend on their capacity to meet the international regulatory requirements determined by the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS) of the World Trade Organization (WTO). Unsafe exports can lead to significant economic losses.

1.2 The value of foodborne disease burden estimates

Foodborne diseases (FBD) are an important cause of morbidity and mortality worldwide but the full extent and cost of unsafe food, and especially the burden arising from chemical and parasitic contaminants in food, is still unknown. Detailed data on the economic costs of foodborne diseases in developing countries are largely missing.

Despite the growing international awareness of foodborne diseases as a significant risk to health and socio-

economic development, food safety remains marginalized. A major obstacle to adequately addressing food safety concerns is the lack of accurate data on the full extent and cost of foodborne diseases, which would enable policy-makers to set public health priorities and allocate resources. Epidemiological data on foodborne diseases remain scarce, particularly in the developing world. Even the most visible foodborne outbreaks often go unrecognized, unreported or uninvestigated, and may only be visible if connected to major public health or economic impact. Precise information on the burden of FBD is needed to adequately inform policy-makers and allocate appropriate resources for food safety control and intervention efforts.

In order to fill this data vacuum, the World Health Organization (WHO) Department of Food Safety, Zoonoses and Foodborne Diseases (FOS) together with its partners launched the Initiative to Estimate the Global Burden of Foodborne Diseases. The primary goal of the Initiative is:

To enable policy-makers and other stakeholders to set appropriate, evidence-based priorities in the area of food safety.

1.3 Purpose and audience

This report is a supplement to the scientific papers published in journals from the Public Library of Science (PLOS), which cover the estimates generated by the WHO Initiative to Estimate the Global Burden of Foodborne Diseases. In addition to collating the results, this report is intended to provide background and context on the project itself, as well as examining particular scientific issues in more detail. As such, it provides a comprehensive source of information on the Initiative.

1.4 Scope

This report covers:

- history of the project;
- participants;
- scientific work commissioned by the project;
- overview of approach to estimating burden of foodborne disease;
- methods, results, discussion, using a hazards-based approach;
- outputs, implications and context of results; and
- future plans.

1.5 History and structure

In September 2006, FOS launched the Initiative to Estimate the Global Burden of Foodborne Diseases at an international consultation attended by over 50 international experts. This consultation provided the strategic framework for the assessment of FBD burden, and mandated WHO to establish a Foodborne Disease Burden Epidemiology Reference Group (FERG) to engage in:

- assembling, appraising and reporting on currently existing burden of foodborne disease estimates;
- conducting epidemiological reviews for mortality, morbidity and disability in each of the major FBDs;
- providing models for the estimation of FBD burden where data are lacking;
- developing cause and source attribution models to estimate the proportion of diseases that are foodborne, and
- developing user-friendly tools for burden of FBD studies at country level.

Following a public call for advisers in the scientific press the WHO Director-General appointed the FERG members who met for the first time in November 2007. This multi-disciplinary meeting commenced with a stakeholder consultation that informed the technical discussions of FERG. The meeting

saw the establishment of the FERG Core or Steering Group (coordinating and overseeing the burden work) as well as several thematic Task Forces (TFs) to advance the work in specific areas, including:

- Enteric Diseases Task Force (EDTF);
- Parasitic Diseases Task Force (PDTF); and,
- Chemicals and Toxins Task Force (CTTF).

Subsequently, three additional Task Forces were established to address the following topics:

- Source Attribution Task Force (SATF) (established 2008);
- Country Studies Task Force (CSTF) (established 2009), with a sub-group, the Knowledge Translation and Policy Group (KTPG) (established 2010);
- Computational Task Force (CTF) (established 2012).

As shown in Figure 1, FERG consists of a Core (or Steering) Group to coordinate and oversee the scientific work, Thematic TFs advancing the work in specific areas; and external resource and technical advisers who are invited on an *ad hoc* basis to provide specific expertise.

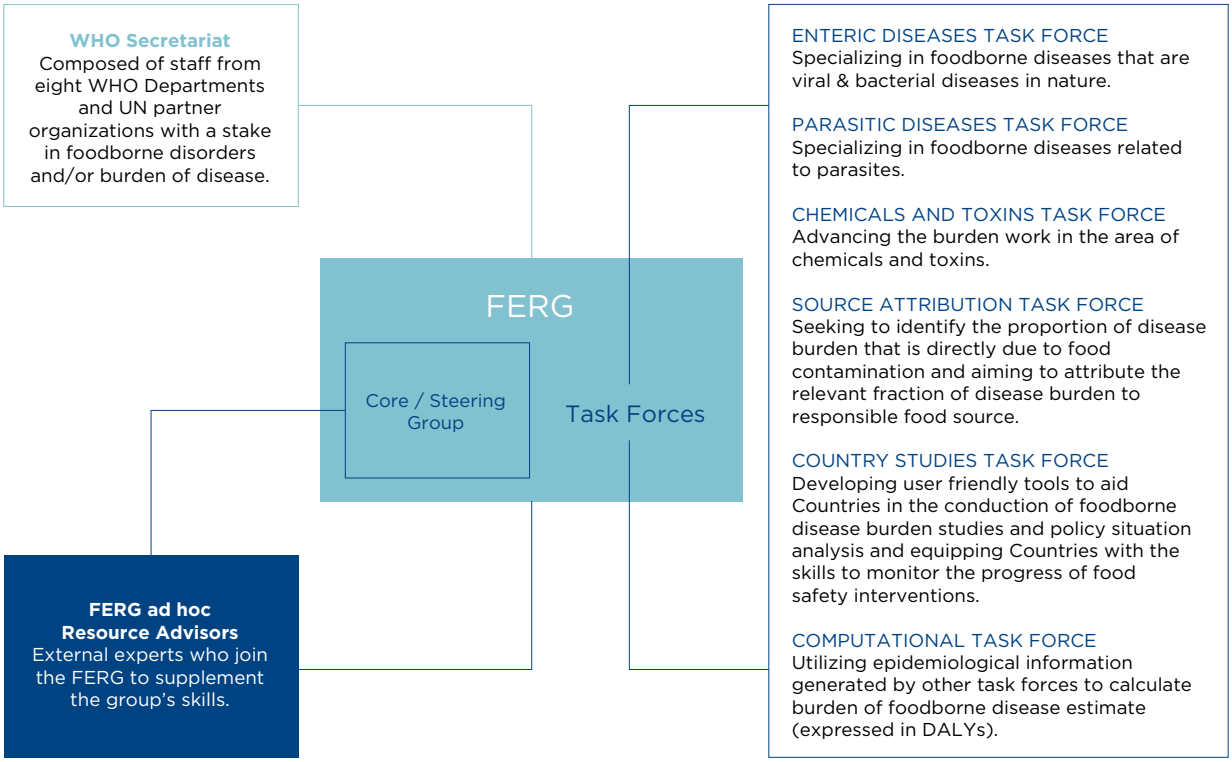
1.6 Objectives

The first report from the Initiative, published in 2008, described the following objectives[1]:

- To strengthen the capacity of countries in conducting burden of foodborne disease assessments and to increase the number of countries who have undertaken a burden of foodborne disease study.
- To provide estimates on the global burden of foodborne diseases according to age, sex and regions for a defined list of causative agents of microbial, parasitic and chemical origin.
- To increase awareness and commitment among Member States for the implementation of food safety standards.
- To encourage countries to use burden of foodborne disease estimates for cost-effective analyses of prevention, intervention and control measures.

[1] http://www.who.int/foodsafety/foodborne_disease/Summary_Doc.pdf?ua=1 Accessed 9 July 2014

Figure 1. Structure of the initiative to estimate the global burden of foodborne diseases



To meet these goals and objectives, the Initiative took two approaches.

- A Foodborne Disease Burden Epidemiology Reference Group (FERG) was established to assemble, appraise and report on burden of foodborne disease estimates.
- In-depth country studies to supplement the work of FERG and enable countries to conduct their own burden of disease studies.

1.7 Other relevant burden of disease estimates

Estimates for the burden of diseases considered to be at least partially foodborne have been published by a number of research groups. The most comprehensive estimates are those published by the following:

- Global Burden of Disease 2010 (GBD2010) study, undertaken by the Institute of Health, Metrics and Evaluation (IHME)[2]
- Mortality and Burden of Disease Unit of WHO[3]
- Estimated Cancer Incidence, Mortality and Prevalence 2012, published by the International Agency for Research on Cancer (GLOBOCAN)[4]

Throughout the course of the burden of foodborne disease project, FERG communicated with these groups, to share data and promote consistency of the estimates.

[2] http://www.healthdata.org/gbd Accessed 24 September 2014

[3] http://www.who.int/topics/global_burden_of_disease/en/ Accessed 24 September 2014

[4] http://globocan.iarc.fr/Default.aspx Accessed 24 September 2014

1.8 Timeline: FERG Meetings

1.8.1 Overview

- 25–27 September 2006 – Establishment of the initiative, Geneva[5]
- 26–28 November 2007 – FERG 1, Geneva[6]
- 17–21 November 2008 – FERG 2, Geneva[7] (plus Stakeholder Meeting)[8]
- 26–30 October 2009 – FERG 3, Geneva (plus Stakeholder Meeting)
- 8–12 November 2010 – FERG 4, Geneva[9]
- 7–10 November 2011 – Strategy Meeting and Commencement of Country Studies, Durrës, Albania
- 8–12 April 2013 – FERG 5, Geneva[10]
- 23–25 June 2014 – Review Meeting, Copenhagen

1.8.2 Extracts from reports of major meetings

25–27 September 2006– Establishment of the initiative, Geneva

WHO's Department of Food Safety, Zoonoses and Foodborne Diseases (FOS) launched an initiative to estimate the global burden of foodborne diseases from all major causes, including chemicals and zoonoses, at an international consultation. This was held in Geneva, Switzerland, from 25 to 27 September 2006, and was attended by over 50 experts from around the world.

The objectives of the meeting were:

- to launch an appeal for wider collaboration, with a detailed plan of action and time frame;
- to develop a strategic framework for burden of disease estimation that involved all relevant partners; and
- to propose elements of a standard protocol for conducting burden of illness studies in countries to obtain estimates.

The result of the Consultation was a draft strategic framework for the assessment of burden of foodborne diseases, which included:

- the outline of an evidence map for assimilating existing information on the burden of disease [along themes of
  - (i) acute infectious diseases,
  - (ii) chronic manifestations of infectious diseases; and
  - (iii) acute and chronic non-infectious illness]; and
- a time frame outlining the individual strategic activities in relation to the evidence framework.

In order to complete the strategic and technical framework, participants mandated WHO to establish a Foodborne Disease Burden Epidemiology Reference Group (FERG) and proposed the relevant skill mix required for this group. A number of funding agencies were identified that might be approached by WHO to enable the execution of this work. The Consultation concluded with the drafting of a Joint Statement of Support for the Initiative.

A summary document describing the initiative was published in 2008[11].

26–28 November 2007 – FERG 1, Geneva

5 http://www.who.int/foodsafety/publications/burden_sept06/en/ Accessed 21 April 2015

6 http://www.who.int/foodsafety/publications/burden_nov07/en/ Accessed 21 April 2015

7 http://www.who.int/foodsafety/publications/ferg2/en/ Accessed 21 April 2015

8 http://www.who.int/foodsafety/publications/ferg-stakeholders/en/ Accessed 21 April 2015

9 http://www.who.int/foodsafety/publications/ferg4/en/ Accessed 21 April 2015

10 http://www.who.int/foodsafety/publications/ferg5/en/ Accessed 21 April 2015

11 http://www.who.int/foodsafety/foodborne_disease/ferg/en/ accessed 21 April 2015

Following a public call for advisers in the scientific press, the Director-General of WHO appointed the FERG members, who met for the first time in November 2007. This multi-disciplinary meeting commenced with a stakeholder consultation that informed the technical discussions of FERG. The meeting saw the establishment of the FERG Core or Steering Group (coordinating and overseeing the burden of the work), as well as several thematic Task Forces (TFs) to advance the work in specific areas, including:

- parasitic diseases;
- chemicals and toxins; and
- enteric diseases.

In their respective areas, the TFs provided: (1) priority lists of causative agents for which burden assessments should be conducted; (2) developed concrete and very detailed work plans to commission the individual burden work; and (3) agreed on the logistic and technical steps to be taken by FERG over the next year.

17–21 November 2008 – FERG 2, Geneva (plus Stakeholder Meeting)

The second formal meeting of FERG in November 2008 (FERG 2) highlighted the progress made during the Initiative's first year, which included:

- an appraisal of the methods, and preliminary results of ten systematic reviews commissioned in the areas of enteric, parasitic and chemical causes of foodborne diseases, as well as mortality;
- the development of detailed new work plans for all FERG TFs for 2009, including new burden work to be commissioned;
- establishment of the FERG Source Attribution Task Force (SATF) and execution of its technical recommendations;
- agreement on the terms of reference of the new FERG Country Studies Task Force (CSTF) in 2009;
- formal evaluation of the activities, processes and outputs of the first year of FERG activities; and
- A major, multisectoral stakeholder meeting, which provided valuable input and recommendations to WHO in the areas of technical reviews, communication and policy.

26–30 October 2009 – FERG 3, Geneva (plus Stakeholder Meeting)

The Third Foodborne Diseases Stakeholder Meeting brought together international representatives from the various constituencies and sectors with an interest in ensuring food safety, be it through decision-making, research, production, consumption or advocacy. They included: WHO Member States; bilateral and multilateral donors; non-governmental organizations (NGOs); consumer groups; industry; and public and scientific media. The purpose of the meeting was to enable stakeholders to:

- actively engage with the Foodborne Disease Burden Epidemiology Reference Group (FERG) and its research;
- open new channels for multisectoral cooperation; and
- provide direct input into discussions about how to bridge the gap between evidence and policy.

8–12 November 2010 – FERG 4, Geneva

Continuing on the path taken during the previous FERG meeting, a large number of new foodborne disease morbidity, mortality and burden estimates were presented and discussed at FERG 4:

- the global burden of diarrhoeal diseases;
- the global burden of foodborne trematodiasis;

- the global burden of cystic echinococcosis;
- the global burden of neurocysticercosis;
- the global burden of aflatoxicosis; and
- the global burden of cassava cyanide ingestion.

In addition, the FERG experts appraised the progress made on the systematic reviews commissioned for other enterics, parasites and chemicals, and on the protocols to be used in the source attribution expert elicitation process and in the national FBD burden assessments and policy situation analyses. Each TF also made recommendations for new commissioned work.

The various TFs adopted their work plans for 2011 and beyond, which covered the continuation of the systematic reviews, the finalization of the pathogen priority lists, and the further strengthening of the interfaces between the different TFs. The Country Studies Task Force made the final preparations for initiating the pilot country studies in 2011. Four countries were selected for these studies: Albania, Japan, Thailand and Uganda.

July 2010 Mid-term evaluation commissioned from an external consultant

The overall verdict of this evaluation of the World Health Organization Initiative to Estimate the Global Burden of foodborne diseases was that it was making good progress. FERG experts and stakeholders considered it to be a very important Initiative and were in agreement with its goals and objectives. They recognized that information on the burden of foodborne diseases is required at country, regional and global levels in order to prioritize food safety interventions. The leadership and management of the Initiative by the WHO Secretariat was highly praised by the FERG experts, and described very favourably in comparison with other international advisory bodies in which some of the experts had been involved.

FERG experts recognized the complexity of the Initiative, and some reported that at the outset they had doubts about whether it was achievable. However, they had found that challenges had been overcome and continued to be addressed, many products were being produced and some had already been finalized. The project was being managed very energetically, and they expected successful outcomes in due course.

There was also a high satisfaction level with the guidance and direction of the FERG and Task Force Chairs. The global and regional representation of the FERG membership was valued and FERG experts reported that through their involvement, many of them had increased their own capacity. Stakeholder involvement was valued by FERG experts and by the stakeholders themselves. Continued expansion of stakeholder constituencies was also suggested by both groups.

A high quality of all outputs was considered very important by FERG experts, and should be maintained. Most FERG experts were satisfied with the outputs already produced– pathogen- and hazard-specific mortality and morbidity reports– although there was acknowledgement that there had been delays (some of which might not have been avoidable), and that there remained a lot more work to be done. The delays occurred initially and were mostly considered inevitable. They were dealt with, and FERG experts considered that the Initiative was progressing according to plan. Stakeholders were satisfied with the results presented at stakeholder meetings to date, and they looked forward to the production of more results.

The advocacy efforts of the coordinator of the Initiative were praised and considered to be very effective.

The main challenge to the Initiative was how to deal with the expansion to the scope of the Initiative. The need to plan to collect primary data, overcome methodological challenges, integrate knowledge translation and respond appropriately to the 63rd World Health Assembly (WHA) resolution on food safety– all these were part of the expanded scope of the Initiative. FERG experts were in agreement that the expansion of the scope was necessary and appropriate. Because quality must be maintained, adjustments must be made to timelines and resources. Timelines can be reviewed, but FERG experts and stakeholders stated that there was a limitation on timeline extension due to the risk of loss of momentum, and there was also the need to fulfil Member State and donor expectations for initial estimation of the global burden of foodborne diseases. Therefore, increasing the Initiative's human and financial resources was the most appropriate change that could be made.

FERG experts were concerned about a major threat to the Initiative, namely the dependence of the Initiative and its success on such a small number of key personnel in the WHO Secretariat. These few key people were considered excellent in terms of technical expertise, enthusiasm, energy, dedication and motivation, and much of the success so far was ascribed to these qualities. FERG experts were concerned that if there were any changes to personnel, the Initiative would be very vulnerable and could fail. They were concerned about sustainability and lack of a 'safety net', and therefore requested an expanded team at the Secretariat, with more of the existing skills. FERG experts requested that high level senior management at WHO reiterate their support for the Initiative through providing the necessary resources to ensure the success of the Initiative and the considerable investment that had been made.

7–10 November 2011– Strategy Meeting and Commencement of Country Studies, Durrës, Albania

1.8.3 Strategic revisions

In view of the increased complexity of the WHO FERG Initiative, as well as the changed environment in which the Initiative was operating, the WHO Secretariat convened a meeting with the objectives of:

- updating the Initiative's strategic framework, its milestones and timelines;
- redefining the technical scope of the Initiative, including the selection of priority areas for foodborne disease burden estimation;
- identifying key activities and resource needs for implementation; and
- updating FERG processes, roles and responsibilities.

1.8.4 Key decisions

- **Scope of technical work:** The thematic TF chairs, in consultation with their TFs, established a shortened list of pathogens and hazards for which they intended to deliver incidence and mortality estimates by the end of 2012.
- **Methodological decisions:** A range of important technical and methodological issues linked to the estimation of foodborne disease burden were discussed at the meeting in Albania, and actions agreed upon in order to ensure accuracy, utility and compatibility with other existing health metric indicatives.
- **New FERG Computational Task Force:** Continuing in this vein, a new Computational Task Force

(CTF) to work on the mathematical modelling to calculate DALYs would be established. The TF was currently set to be operational by the end of February 2012.

- **Source attribution expert elicitation:** An expert elicitation would be conducted in 2012 to determine what proportion of the burden of each hazard was foodborne, and which were the major foods associated with transmission. A list of hazards that would be included in the expert elicitation was established.

1.8.5 Country-level involvement

The 'kick-off' meeting of the FERG pilot country studies marked a major milestone for the work of the Initiative in fostering national studies of the burden of foodborne disease. For the first time, representatives of the FERG pilot countries met to present progress on the implementation of a national foodborne disease burden study. They also learnt about study tools that FERG had developed, as well as the future technical support that would be provided by FERG.

The pilot countries during the kick-off meeting:

- drafted pilot country study work plans outlining the way forward;
- provided recommendations and input to align FERG procedures and tools for national foodborne disease burden estimation and food safety policy situation analyses specific to country requirements; and
- delivered feedback and agreed on processes to communicate between participating countries, and between the countries and FERG Secretariat.

8–12 April 2013 – FERG 5, Geneva

There was a very clear path towards the end goal of publishing the estimates of burden of foodborne disease, completing the pilot studies and finishing the country tools. Each TF had outlined its priority activities for the coming year and WHO would use these to solicit the funding required to complete the FERG project.

The hazard TFs– EDTF, PDTF and CTTF– completed the technical review of the systematic reviews; reviewed and revised the final outcome trees; and made plans for completion for each hazard.

SATF finalized the expert elicitation protocol for: chemicals and toxins (inorganic arsenic, lead, cadmium and dioxins); for parasitic diseases (*Entamoeba histolytica*, *Cryptosporidium* spp., *Giardia* spp., *Echinococcus granulosus*, *Toxoplasma gondii*, *Echinococcus multilocularis* and *Ascaris* spp.); and for enteric diseases (diarrhoeal diseases [non-typhoidal *Salmonella* spp., *Campylobacter* spp., Shiga-toxin producing, enteropathogenic and enterotoxigenic *E. coli*, norovirus, *Shigella* spp., *Vibrio cholerae*], typhoid, brucellosis and hepatitis A).

The methodology and elicitation instrument were agreed with each of the hazard TFs. This expert elicitation would be the first time that the methodology had been applied at a global level for food safety and would involve disease experts from all six WHO regions. The logistics of such an enormous task were also mapped out and agreed during the meeting.

CTF (established October 2012) was able to agree on the disease models for the majority of the pathogens, as well as meeting individually with each TF to advance the DALY calculations. The database was revised, methods for imputation of missing data were advanced, and disability weights (DWs) were mapped to all outcomes.

CSTF and KTPG agreed the aims, objectives and outline for the joint

country study workshop, initiated the development of the communications strategy for the global and regional FERG results, and reviewed the situational analysis document and the outcome of the commissioned work.

23–25 June 2014– Strategy Meeting, Copenhagen

This working meeting involved detailed discussions of burden estimation across all the TFs. Progress was enhanced greatly by the attendance by Dr Colin Mathers, the Coordinator of the Mortality and Burden of Disease Unit in the Health System and Innovation Cluster at WHO, Geneva. This enabled the FERG estimation approaches to be harmonized with those used by the WHO unit.

1.9 Task Force Meetings

Only face-to-face meetings are listed. In addition to these meetings, numerous teleconferences were held by each TF. For the meetings marked*, finalized or draft meeting reports are available.

EDTF

7 - 9 June 2009 – Rome*
14 - 18 July 2010 – Tunis, Tunisia

CTTF

14 - 16 July 2009 – Geneva*
14 - 18 July 2010 – Tunis, Tunisia

PDTF

7 - 9 June 2009 – Rome*
14 - 18 July 2010 – Tunis, Tunisia

SATF

28 - 30 April 2008 – Kuala Lumpur, Malaysia*
20 - 22 April 2010 – Atlanta, USA*
14 - 18 July 2010 – Tunis, Tunisia

CTF

2 - 4 October 2012 – Establishment meeting, Antwerp, Belgium*
April 2013 – Sunday pre-meeting at FERG 5 Geneva, Switzerland
2 August 2013 – Data imputation meeting. RIVM, Bilthoven, The Netherlands
31 January 2014 – DALY calculation & Disability Weights meeting, Brussels
February 2014 – Data imputation meeting, Antwerp, Belgium

CSTF

10 - 12 June 2009 – Rome, Italy*
18 - 20 March 2010 – Atlanta, USA*
7 - 10 November 2011 – Kick off meeting (Albania, Japan, Thailand), Durrës, Albania
4 - 6 March 2012 – Kick off meeting (Uganda), Kampala, Uganda

1.10 Participants

See Appendix 1.

1.11 Declarations of Interest

All experts and resource advisers invited to participate in FERG meetings completed beforehand the WHO standard form for Declaration of Interests. At the start of each meeting, all participants were asked to confirm their interests, and to provide any additional information relevant to the subject matter of the meeting. All declared interests were assessed by the WHO Secretariat to ensure the neutrality and unbiasedness of the work.

2 COMMISSIONED WORK

COMMISSIONED WORK

Each TF commissioned specific pieces of work to provide scientific evidence on which to base estimates. Most of these were systematic reviews, either of available data on diseases, or reviews of methodology. The majority of commissioned work resulted in published papers, as listed below. Some of these publications were part funded by FERG, while others were generated as "in kind" contributions by the authors.

2.1 Enteric Diseases Task Force

The EDTF commissioned the following systematic reviews:

2.1.1 *Brucella* spp.

- Dean, A.S., Crump, L., Greter, H., Hattendorf, J., Schelling, E. & Zinsstag, J. 2012. Clinical manifestations of human brucellosis: a systematic review and meta-analysis. *PLOS Neglected Tropical Diseases,* 6(12): Art. e1929. Available at http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0001929 Accessed 2015-10-16.
- Dean, A.S., Crump, L., Greter, H., Schelling, E. & Zinsstag, J. 2012. Global burden of human brucellosis: a systematic review of disease frequency. *PLOS Neglected Tropical Diseases,* 6(10): Art e1865. Available at http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0001865 Accessed 2015-10-16.

2.1.2 Diarrhoeal disease

- Fischer Walker, C.L., Sack, D. & Black, R.E. 2010. aetiology of diarrhoea in older children, adolescents and adults: a systematic review. *PLOS Neglected Tropical Diseases,* 4(8): Art e768. Available at http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0000768 Accessed 2015-10-16.
- Fischer Walker, C.L., & Black, R.E. 2010. Diarrhoea morbidity and mortality in older children, adolescents, and adults. *Epidemiology and Infection,* 138(9): 1215–1226. Available at http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=7849267&fileId=S0950268810000592 Accessed 2015-10-16.
- Pires, S.M., Fischer Walker, C.L., Lanata, C.F., Devleesschauwer, B., Hall, A., Kirk, M.D., Duarte, A.S.R., Black, R.E., & Angulo, F.J. Aetiology-specific estimates of the global and regional incidence and mortality of diarrhoeal diseases commonly transmitted through food. *PLOS ONE*, vol 10, iss 12, DOI: 10.1371/journal.pone.0142927

2.1.3 *Mycobacterium bovis*

- Muller, B., Durr, S., Alonso, S., Hattendorf, J., Laisse, C.J., Parsons, S.D., van Helden, P.D. & Zinsstag, J. 2013. Zoonotic Mycobacterium bovis-induced tuberculosis in humans. *Emerging Infectious Diseases,* 19(6): 899–908. Available at: http://wwwnc.cdc.gov/eid/article/19/6/12-0543_article
- Durr, S., Muller, B., Alonso, S., Hattendorf, J., Laisse, C.J., van Helden, P.D. & Zinsstag, J. 2013. Differences in primary sites of infection between zoonotic and human tuberculosis: results from a worldwide systematic review. *PLOS Neglected Tropical Diseases,* 7(8): Art e2399. Available at http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0002399 Accessed 2015-10-16.

2.1.4 Shiga toxin-producing *Escherichia coli*

- Majowicz, S.E., Scallan, E., Jones-Bitton, A., Sargeant, J.M., Stapleton, J., Angulo, F.J., Yeung, D.H. & Kirk, M.D. 2014 Global incidence of human Shiga toxin-producing *Escherichia coli* infections and deaths: a systematic review and

knowledge synthesis. *Foodborne Pathogens and Disease,* 11(6): 447– 455. Available at http://online.liebertpub.com/doi/full/10.1089/fpd.2013.1704 Accessed 2015-10-17.

2.1.5 Norovirus

- Ahmed, S.M., Hall, A.J., Robinson, A.E., Verhoef, L., Premkumar, P., Parashar, U.D., Koopmans, M. & Lopman, B.A. 2014. Global prevalence of norovirus in cases of gastroenteritis: a systematic review and meta-analysis. *Lancet Infectious Diseases,* 14(8): 725– 730. Available at http://www.sciencedirect.com/science/article/pii/S1473309914707674 Accessed 2015-10-17.
- Verhoef, L., Hewitt, J., Barclay, L., Ahmed, S.M., Lake, R., Hall, A.J., Lopman, B., Kroneman, A., Vennema, H., Vinje, J. & Koopmans, M. 2015. Norovirus genotype profiles associated with foodborne transmission, 1999– 2012. *Emerging Infectious Diseases,* 45: 95– 99. Available at: http://wwwnc.cdc.gov/eid/article/21/4/14-1073_article

2.1.6 Invasive non-typhoidal *Salmonella enterica*

- Ao, T.T., Feasey, N.A., Gordon, M.A., Keddy, K.H., Angulo, F.J. & Crump, J.A. 2015. Global burden of invasive non-typhoidal *Salmonella* disease, 2010. *Emerging Infectious Diseases,* 21(6): 941– 949.
- Crump, J.A. & Kirk, M.D. Estimating the burden of febrile illnesses. *PLOS Neglected Tropical Diseases,* (in press).

2.1.7 *Listeria monocytogenes*

- Maertens de Noordhout, C., Devleesschauwer, B., Angulo, F.J., Verbeke, G., Haagsma, J., Kirk, M., Havelaar, A. & Speybroeck, N. 2014. The global burden of listeriosis: a systematic review and meta-analysis. *Lancet Infectious Diseases,* 14(11): 1073– 1082. Available at http://www.sciencedirect.com/science/article/pii/S1473309914708709 Accessed 2015-10-17.

2.2 Parasitic Diseases Task Force

PDTF commissioned the following systematic reviews:

2.2.1 *Taenia solium*

- Carabin, H., Ndimubanzi, P.C., Budke, C.M., Nguyen, H., Qian, Y., Cowan, L.D., Stoner, J.A., Rainwater, E. & Dickey, M. 2011. Clinical manifestations associated with neurocysticercosis: a systematic review. *PLOS Neglected Tropical Diseases,* 5(5): Art e1152. Available at http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0001152 Accessed 2015-10-17.
- Ndimubanzi, P.C., Carabin, H., Budke, C.M., Nguyen, H., Qian, Y.J., Rainwater, E., Dickey, M., Reynolds, S. & Stoner, J.A. 2010. A systematic review of the frequency of neurocysticercosis with a focus on people with epilepsy. *PLOS Neglected Tropical Diseases,* 4(11): Art e870. Available at http://www.plosntds.org/article/info:doi/10.1371/journal.pntd.0000870 Accessed 2015-10-17.

2.2.2 Trematodes (includes *Echinostoma* spp., *Fasciolopsis buski, Heterophyes* spp. and *Metagonimus* spp.)

- Furst, T., Keiser, J. & Utzinger, J. 2012. Global burden of human food-borne trematodiasis: a systematic review and meta-analysis. *Lancet Infectious Diseases,* 12(3): 210– 221. Available at http://www.thelancet.com/journals/laninf/article/PIIS1473– 3099(11)70294–8/fulltext Accessed 2015-10-17.

2.2.3 *Echinococcus multilocularis*

- Torgerson, P.R., Keller, K., Magnotta, M. & Ragland, N. 2010. The global burden of alveolar echinococcosis. *PLOS Neglected Tropical Diseases*, 4: e722. Available at http://www.plosntds.org/article/info:doi/10.1371/journal.pntd.0000722 Accessed 2015-10-17.

2.2.4 *Trichinella* spp.

- Devleesschauwer B, Praet N, Speybroeck N, Torgerson P R, Haagsma J A, De Smet K, Murrell K D, Pozio E and Dorny P (2014) The low global burden of trichinellosis: evidence and implications. *International Journal of Parasitology,* 45(2-3): 95– 99. Available at http://www.sciencedirect.com/science/article/pii/S0020751914001374 Accessed 2015-10-17.
- Murrell, K.D. & Pozio, E. 2011. Worldwide occurrence and impact of human trichinellosis, 1986– 2009. *Emerging Infectious Diseases,* 17(12): 2194– 2202.

2.2.5 *Toxoplasma gondii*

- Torgerson, P.R. & Mastroiacovo, P. 2013. The global burden of congenital toxoplasmosis: a systematic review. *Bulletin of the World Health Organization,* 91(7): 501– 508. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3699792/ Accessed 2015-10-17.

2.3 Chemicals and Toxins Task Force

CTTF commissioned several systematic reviews and reports.

2.3.1 Aflatoxins

- Khlangwiset, P., Shephard, G.S. & Wu, F. 2011. Aflatoxins and growth impairment: A review. *Critical Reviews in Toxicology,* 41(9): 740– 755. Available at http://informahealthcare.com/doi/abs/10.3109/10408444.2011.575766 Accessed 2015-10-17.
- Wu, F. 2010. Global Burden of aflatoxin-induced disease: Final Report for the World Health Organization (WHO) Foodborne Disease Burden Epidemiology Reference Group (FERG) Chemical Task Force. Department of Environmental and Occupational Health, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA, USA.
- Liu, Y. & Wu, F. 2010. Global burden of aflatoxin-induced hepatocellular carcinoma: a risk assessment. *Environmental Health Perspectives,* 118(6): 818– 824. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2898859/ Accessed 2015-10-17.
- Liu, Y., Chang, C.C., Marsh, G.M. & Wu, F. 2012. Population attributable risk of aflatoxin-related liver cancer: systematic review and meta-analysis. *European Journal of Cancer,* 48(14): 2125– 2136. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3374897/ Accessed 2015-10-17.

2.3.2 Arsenic

- Oberoi, S., Barchowsky, A. & Wu, F. 2014. The global burden of disease for skin, lung, and bladder cancer caused by arsenic in food. *Cancer Epidemiology Biomarkers and Prevention,* 23(7): 1187– 1194. Abstract available at http://cebp.aacrjournals.org/content/23/7/1187.abstract Accessed 2015-10-17.

2.3.3 Cassava cyanide

- Cliff, J. 2011. Incidence and prevalence estimates of cassava-cyanide induced diseases. Report for the FERG Chemicals and Toxins Task Force. Universidade Eduardo Mondlane, Mozambique.

2.3.4 Peanut Allergens

- Ezendam, J. & van Loveren, H. 2012. Parameters needed to estimate the global burden of peanut allergy: Systematic literature review. *European Journal of Food Research and Review,* 2(2): 46– 48. Available at http://www.rivm.nl/en/Library/Scientific/Reports/2012/april/Parameters_needed_to_estimate_the_global_burden_of_peanut_allergy_Systematic_literature_review Accessed 2015-10-17.

2.3.5 Dioxins

- Zeilmaker, M.J., Devleesschauwer, B., Mengelers, M.J.B., Hoekstra, J., Brandon, E.F.A. & Bokkers, B.G.H. The disease burden of dioxins: A global perspective. *RIVM Report* National Institute for Public Health and the Environment (RIVM), Netherlands.

2.4 Source Attribution Task Force

SATF commissioned the following papers:

- Pires, S.M. 2013. Assessing the applicability of currently available methods for attributing foodborne disease to sources, including food and food commodities. *Foodborne Pathogens and Disease,* 10(3): 206– 213.
- Pires, S.M., Evers, E.G., van Pelt, W., Ayers, T., Scallan, E., Angulo, F.J., Havelaar, A. & Hald, T. and the Med-Vet-Net Workpackage 28 team. 2009. Attributing the human disease burden of foodborne infections to specific sources. *Foodborne Pathogens and Disease,* 6(4): 417– 424.
- Hoffman, S., Aspinall, W., Cooke, R., Cawthorne, A., Corrigan, T., Havelaar, A., Gibb, H., Torgerson, P., Kirk, M., Angulo, F, Lake R, Speybroeck N, Devleesschauwer B, Hald T. 2015 Perspective: Research synthesis methods in an age of globalized risks: lesson from the global burden of foodborne disease expert elicitation. *Risk Analysis* DOI: 10.1111/risa.12385
- Aspinall, WP., Cooke, RM., Havelaar, AH., Hoffman, S., Hald, T. 2015. Science-based global attribution of foodborne diseases: Findings of WHO expert elcitiation. *PLOS ONE.* (in press).

2.5 Computational Task Force

- McDonald, S.A., Devleesschauwer, B., Speybroeck, N., Hens, N., Praet, N., Torgerson, P.R., Havelaar, A.H., Wu, F., Tremblay, M., Amene, E.W. & Döpfer, D. 2015. Data-driven methods for imputing national-level incidence in global burden of disease studies. *Bulletin of the World Health Organization,* 93(4): 228– 236 doi: http://dx.doi.org/10.2471/BLT.14.139972

The following two papers were not commissioned by the Computational Task Force, but several of the authors were TF members, and the papers are relevant to the Initiative estimates.

- Devleesschauwer, B., Havelaar, A.H., Maertens de Noordhout, C., Haagsma, J.A., Praet, N., Dorny, P., Duchateau, L., Torgerson, P.R., Van Oyen, H. & Speybroeck, N. 2014. Calculating disability-adjusted life years to quantify burden of disease. *International Journal of Public Health,* 59(3): 565– 569.
- Devleesschauwer, B., Havelaar, A.H., Maertens de Noordhout, C., Haagsma, J.A., Praet, N., Dorny, P., Duchateau, L., Torgerson, P.R., Van Oyen, H. & Speybroeck, N. 2014. DALY calculation in practice: a stepwise approach. *International Journal of Public Health,* 59(3): 571– 574.

2.6 Country Studies Task Force

Two systematic reviews were commissioned:

- Polinder, S., Haagsma, J.A., Stein, C. & Havelaar, A.H. 2012. Systematic review of general burden of disease studies using disability-adjusted life years. *Population Health Metrics*, 10: Art 21. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3554436/ Accessed 2015-10-17.
- Haagsma, J.A., Polinder, S., Stein, C.E. & Havelaar, A.H. 2013. Systematic review of foodborne burden of disease studies: quality assessment of data and methodology. *International Journal of Food Microbiology*, 166(1): 34– 47. Available at http://www.sciencedirect.com/science/article/pii/S0168160513002778 Accessed 2015-10-17.

The results from one of the country studies have been published:

Kumagai, Y., Gilmour, S., Ota, E., Momose, Y., Onishi, T., Bilano, V.L.F., Kasuga, F., Sekizaki, T. & Shibuya, K. 2015. Estimating the burden of foodborne diseases in Japan. Bulletin of the World Health Organization, 93(8): 540–549.

The preparation of material to augment the resources developed by the CSTF was commissioned from Sandy Campbell (Knowledge Translation Consultant, New Mexico, USA). The results of that work have been included in the Situation analysis, knowledge translation and risk communication guidance manual, one of the tools and resources developed by the CSTF.

2.7 Other relevant publications

The following articles were written by FERG members and WHO staff:

- Stein, C., Kuchenmuller, T., Hendrickx, S., Pruss-Ustun, A., Wolfson, L., Engels, D. & Schlundt, J. 2007. The Global Burden of Disease assessments – WHO is responsible? *PLOS Neglected Tropical Diseases*, 1: Art e161. Available at http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0000161 Accessed 2015-10-17.
- Havelaar, A.H., Cawthorne, A., Angulo, F., Bellinger, D., Corrigan, T., Cravioto, A., Gibb, H., Hald, T., Ehiri, J., Kirk, M., Lake, R., Praet, N., Speybroeck, N., de Silva, N., Stein, C., Torgerson, P. & Kuchenmüller, T. 2013. WHO Initiative to Estimate the Global Burden of foodborne diseases. *Lancet*, 381(Suppl. 2): S59.
- Hird, S., Stein, C., Kuchenmüller, T. & Green, R. 2009. Meeting report: Second annual meeting of the World Health Organization Initiative to estimate the global burden of foodborne diseases. *International Journal of Food Microbiology*, 133: 210– 212.
- Kuchenmüller, T., Hird, S., Stein, C., Kramarz, P., Nanda, A. & Havelaar, A.H. 2009. Estimating the global burden of foodborne diseases – a collaborative effort. *Eurosurveillance*, 14(18): 1– 4. Available at http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19195 Accessed 2015-10-17.
- Lake, R.J., Havelaar, A.H. & Kuchenmüller, T. 2013. New research on estimating the global burden of foodborne disease. pp. 260– 271, *in:* J. Sofos (ed.). *Advances in microbial food safety*. Vol. 1. Woodhead Publishing, Oxford, UK.
- Lake, R.J., Stein, C.E. & Havelaar, A.H. 2014. Estimating the burden of foodborne disease.. pp. 73– 79, *in:* Y. Motarjemi (ed.). *Encyclopedia of Food Safety*. Vol. 1. Academic Press, Waltham, MA, USA.
- Kuchenmulller, T., Abela-Ridder, B., Corrigan, T. & Tritscher, A. 2013. World Health Organization Initiative to Estimate the Global Burden of foodborne diseases. *Revue Scientifique et Technique-Office International des Epizooties*, 32(2): 459– 467.

3 OVERVIEW OF THE SCIENTIFIC APPROACH

OVERVIEW OF THE SCIENTIFIC APPROACH

3.1 The DALY metric

As mentioned in the report from the initial consultation, the Initiative was encouraged to use summary measures of public health as the metric for the burden of FBD. The disability adjusted life year (DALY) metric was chosen for the following reasons:

- It is an established WHO metric with international application; and
- It is consistent with the Global Burden of Disease project.

The DALY is calculated by adding the number of years of life lost to mortality (YLL) and the number of years lived with disability due to morbidity (YLD):

DALY = YLL + YLD

The YLL due to a specific disease in a specified population is calculated by the summation of all fatal cases (n) due to the health outcomes (l) of that specific disease, each case multiplied by the expected individual life span (e) at the age of death.

$$YLL = \sum_{l} n_l \times e_l$$

YLD is calculated by accumulation over all health outcomes (l), the product of the number of cases (n), the duration of the illness (t) and the severity weight (w) of a specific disease. It should be noted that the calculation for YLL implicitly includes a severity weight factor. The severity weight or disability weight (DW) factors are in the range zero to one, with the severity weight for death being equal to one.

$$YLD = \sum_{l} n_l \times t_l \times w_l$$

DALYs may be calculated using a **prevalence** approach which estimates the current burden of disease in a population, considering previous events. However, the more common approach is to use **incidence**, i.e. both current and future health outcomes are included. Future outcomes include sequelae and mortality resulting from the initial disease within a defined time period.

To define life expectancy for the calculation of YLL life expectancy tables for the population being studied may be used. Alternatively, life expectancy that reflects an ideal of human potential may be used.

3.2 Overarching methodology decisions by FERG in relation to DALY estimates

3.2.1 Hazard-based approach

The burden of disease estimation is hazard-based because:

- it allows a complete estimate of the burden of disease due a specific hazard;
- it includes all related sequelae; and
- measures to address foodborne diseases are often hazard specific.

3.2.2 Incidence-based approach

DALYs, and more specifically their YLD component, may be calculated from an incidence or a prevalence perspective. While incidence-based YLDs are defined as the product of the number of incident cases and the duration and disability weight (DW) of the concerned health state, prevalence-based YLDs are defined as the product of the number of prevalent cases and the corresponding DW [1,6]. In the incidence-based approach, all health outcomes, including those in future years, are assigned to the initial event (e.g., exposure to a certain hazard). This approach therefore reflects the future burden of disease resulting from current events. In the prevalence-based approach, on the other hand, the health status of a population is assessed at a specific point in time, and prevalent

diseases are attributed to initial events that happened in the past. This approach therefore reflects the current burden of disease resulting from previous events. For burden of FBD studies, the incidence-based YLD approach was deemed the most appropriate approach, because (1) this approach is more sensitive to current epidemiological trends [2]; (2) is more consistent with the hazard-based approach, since it has the point of infection (or primary health effect from exposure) as starting point for the calculations; and (3) is consistent with the estimation of YLLs, which by definition follows an incidence-based approach, as mortality can be seen as the incidence of death [3]. Nevertheless, the prevalence- and incidence-based approaches yield similar overall results if the epidemiology of disabilities and the population age-structure are constant over time [2]. However, burden estimates for specific age groups will always differ between the prevalence- and incidence-based approaches, because the former assigns the burden to the age at which the burden is experienced, while the latter assigns the burden to the age of disease onset [4].

Using the incidence for the burden estimations is important for diseases having a long period between exposure and appearance of clinical signs. An incidence-based approach for the burden estimations fits better with a hazard-based approach. However, incidence figures are not always available. For example, in the case of peanut [*Arachis hypogaea*] allergy, only prevalence figures are available. When only prevalence figures are available, incidence can be estimated based on the prevalence figures and on the duration of the disease.

Regions

Several options were available for reporting on a regional basis (14 subregions based on child and adult mortality, as described by Ezzati *et al.* [5]; 21 GBD regions [6]; and 13 GEMS Cluster Diet Regions[1]). The subregions based on mortality were chosen.[2] Countries grouped into each of the 14 subregions are listed in Appendix 2.

Reference year

The reference year for the calculation of absolute numbers was 2010.

Attribution

The choice of a method to attribute a proportion of disease incidence to foodborne transmission was a major decision for the project. The rationale for choosing a global expert elicitation process was developed after consideration of alternatives, as described below.

Estimating the burden of FBD is complicated because most of the hazards causing foodborne disease are not transmitted solely by food. The relative impact of each route differs depending on the epidemiology of the disease causing microorganism (bacteria, virus or parasite) or chemical hazards. Other factors such as the geographical region, season and food consumption patterns also influence the role of different exposures routes [7, 8]. The estimation of the burden of FBD, therefore, requires

[1] http://www.who.int/foodsafety/chem/gems/en/index1.html Accessed 23 July 2014

[2] The subregions are defined on the on the basis of child and adult mortality, as described by Ezzati *et al.* [5] Stratum A = very low child and adult mortality; Stratum B = low child mortality and very low adult mortality; Stratum C = low child mortality and high adult mortality; Stratum D = high child and adult mortality; and Stratum E = high child mortality and very high adult mortality. The use of the term 'subregion' here and throughout the text does not identify an official grouping of WHO Member States, and the "subregions" are not related to the six official WHO regions.

a delineation of the major transmission routes, including contaminated food, water, soil, air or contact with infected animals or humans. Previous efforts to quantify the contribution of specific sources (including types of foods) and transmission routes have been gathered under the term 'source attribution' or 'human illness attribution' [9, 10]. The applicability of available methods for source attribution of FBD at the global level was recently assessed by Pires [7].

Source attribution is an important tool for identifying and prioritizing effective interventions to prevent and control FBD [11]. The need for reliable source attribution estimates has prompted a growing body of research focusing on attribution, particularly for infectious agents [7, 10, 12, 13]. However, comprehensive attribution studies based on surveillance data and/or food monitoring and exposure data are still limited in scope, and to date have been performed for a few hazards only, or in a limited number of countries [14– 26].

In addition, existing studies have focused mainly on identifying specific food sources or animal reservoirs, whereas other potential transmission routes are often not quantified due to lack of data, or neglected due to the complexity of attribution models. Many studies, often designed as randomized controlled intervention trials, have been conducted to assess the importance of water, particularly for the transmission of diarrhoeal diseases (reviewed by [27] and [28]). However, other transmission routes, such as soil, air and direct contact with infected humans or animals, are generally not considered in those studies. Thus, for most countries, and at the global level, relevant studies and data for quantifying attribution of potential FBD to the major transmission routes do not exist.

In such situations, structured elicitation of scientific judgment may be used [7, 29]. When data are not available, or undertaking primary research is not feasible, a structured elicitation offers a transparent and mathematically rigorous way of evaluating and enumerating uncertainty distributions, from the judgments of many individual researchers, for quantifying risk models. Within food safety, the approach has been applied to provide national estimates for the proportion of illnesses attributable to food for specific infectious diseases [30– 37], or to inform modelling of foodborne disease risk assessment models by estimating specific model parameters and their uncertainty [38, 39].

4 HAZARD-SPECIFIC METHODOLOGY

HAZARD-SPECIFIC METHODOLOGY

The following material is derived from, and in some parts repeated verbatim from, text in the suite of papers in which the FERG results have been published.[1] These primary outputs are listed below, and have been collated in a dedicated PLOS collection entitled "The World Health Organization Estimates of the Global Burden of Foodborne Diseases", which can be accessed at the website: http://collections.plos.org/ferg-2015. We acknowledge the PLOS for permission to incorporate this material into this report. In addition to the series of published papers, the estimates of foodborne disease burden have been made available as an on-line tool which will be accessible via the WHO FERG web page.[2]

Havelaar, A.H., Kirk, M.D., Torgerson, P.R., Gibb, H.J., Hald, T., Lake, R.J., Praet, N., Angulo, F.J., Bellinger, D.C., de Silva, N.R., Gargouri, N., Speybroeck, N., Cawthorne, A., Mathers, C., Stein, C., Devleesschauwer, B. on behalf of the World Health Organization Foodborne Disease Burden Epidemiology Reference Group. 2015. World Health Organization global estimates and regional comparisons of the burden of foodborne disease, 2010. PLOS Medicine, DOI: 10.1371/journal.pmed.1001923

Kirk, M.D., Pires, S.M., Black, R.E., Caipo, M., Crump, J.A., Devleesschauwer, B., Döpfer, D., Fazil, A., Fischer-Walker, C.L., Hald, T., Hall, A.J., Keddy, K.H., Lake, R., Lanata, C.F., Torgerson, P.R., Havelaar, A.H. & Angulo, F.J. 2015. World Health Organization estimates of the global and regional disease burden of 22 foodborne bacterial, protozoal and viral diseases, 2010: A data synthesis *PLOS Medicine,* DOI:10.1371/journal.pmed.1001921

Torgerson, P.R., Devleesschauwer, B., Praet, N., Speybroeck, N., Willingham, A.L., Kasuga, F., Rokni, M.B., Zhou, X.-N., Fèvre, E.M., Sripa, B., Furst, T., Budke, C.M., Carabin, H., Kirk, M.D., Angulo, F.J., Havelaar, A. & de Silva, N. 2015. World Health Organization estimates of the global and regional disease burden of 11 foodborne parasitic diseases, 2010: a data synthesis. *PLOS Medicine,* DOI:10.1371/journal pmed.1001920

Gibb, H., Devleesschauwer, B., Bellinger, D., Bolger, P.M., Zeilmaker, M., Barchowsky, A., Oberoi, S., Wu, F., Ezendam, J., Zang, J., Carrington, C., Cliff, J., Verger, P., Pitt, J., Adegoke, G., Afshari, R., Baines, J., Bokkers, B., Mengelers, M., van Loveren, H., Rainis, H., O'Leary, K. & Liu, Y. 2015. World Health Organization estimates of the global and regional disease burden of four foodborne chemicals and toxins, 2010: a data synthesis. *F1000 Research.*

Hald, T., Aspinall, W., Devleesschauwer, B., Cooke, R., Corrigan, T., Havelaar, A., Gibb, H., Torgerson, P., Kirk, M., Angulo, F.J., Lake, R., Speybroeck, N. & Hoffmann, S. 2015. World Health Organization estimates of the relative contributions of food to the burden of disease due to selected foodborne hazards: a structured expert elicitation. *PLOS ONE*. in press.

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4.1 Hazard Selection

At the first meeting after the establishment of FERG, each hazard-based TF compiled a comprehensive universal list of foodborne hazards that could be addressed (see Appendix 3). Pragmatic decisions were then made about specific hazards for further work, based on the knowledge of TF members and applying the following criteria:

- Availability of data to estimate incidence; and
- Likely magnitude of foodborne component of burden of disease.

Each of the three papers from the hazard-based TFs (EDTF, PDTF and CTTF) includes supplementary material discussing the sources and methodology for the parameters used to estimate: incidence, clinical outcomes, duration, DW, mortality, age and sex distribution. The full details have been combined in Appendix 4. The material below explains the rationale for the sources and methods.

Burden of foodborne disease estimates were prepared for the 40 foodborne hazards causing 41 diseases shown in Figure 2.

The following methodology section describes the inputs and processes used to generate DALY estimates. This material is broadly structured as follows:

- estimation of incidence (or population attributable fraction);
- health states and disability weights;
- attribution of foodborne transmission; and
- computation.

Figure 2. Hazards for which burden of foodborne disease estimates were prepared by FERG, grouped according to TF. Hazards in grey boxes were addressed by individual TFs but were not included in the global overview. Hazards in blue boxes are pending.

PDTF	CTTF	EDTF (HAZARDS CAUSING HEALTH EFFECTS OTHER THAN ENTERIC DISEASE)	EDTF (HAZARDS CAUSING ENTERIC DISEASE)
***Ascaris* spp.**	Aflatoxin	*Brucella spp.*	*Bacillus cereus*[1]
Echinococcus multilocularis	Arsenic	*Clostridium botulinum*[3]	*Campylobacter spp.*[2]
Echinococcus granulosus	Cadmium	*Hepatitis A* virus	*Cryptosporidium spp*
Clonorchis sinensis	Cassava cyanide	*Listeria spp.*	*Clostridium perfringens*[1]
***Fasciola* spp.**	Dioxin	*Mycobacterium bovis*	*Entamoeba histolytica*
Intestinal flukes[4]	Lead	*Salmonella enterica (invasive infections) non-typhoidal*	Enteropathogenic *E. coli* (EPEC)
***Opisthorchis* spp.**	Methyl mercury	*Salmonella enterica Paratyphi A*	Enterotoxigenic *E. coli* (ETEC)
***Paragonimus* spp.**	Peanut allergens[5]	*Salmonella enterica Typhi*	*Giardia* spp.
Taenia solium			Norovirus
Toxoplasma gondii[6]			*Salmonella enterica* (non-invasive infections) non-typhoidal
***Trichinella* spp.**			*Shigella* spp.
			Shiga toxin-producing *E. coli* (STEC)
			Staphylococcus aureus[1]
			Vibrio cholerae

Note that salmonellosis and invasive salmonellosis are counted as a single hazard causing two diseases.

Notes: (1) 61 EUR and other subregion A (low mortality) countries only. (2) Includes Guillain-Barré Syndrome cases and deaths. (3) 61 EUR and other subregion A (low mortality) countries only, excluding WPR countries. (4) Includes selected species of the families Echinostomatidae, Fasciolidae, Gymnophallidae, Heterophyidae, Nanophyetidae, Neodiplostomidae and Plagiorchiidae (depending on data availability). (5) Only the burden for AMR A, EUR A and WPR A was assessed. (6) Separate estimates for congenital and acquired toxoplasmosis.

4.2 Enteric Hazards

The overall aim of the EDTF was to provide estimates of disease incidence and mortality (by age, sex and country or region) for diarrhoeal and other illnesses due to bacteria and viruses, by all causes and by selected aetiological agents, and including sequelae. Despite its name, the EDTF was not exclusively concerned with hazards causing enteric disease.

The initial list of hazards considered by EDTF is given in Appendix 3. From this list, entero-aggerative *Escherichia coli*, *Vibrio parahaemolyticus*, *V. vulnificus* and *Yersinia* spp. were excluded on the basis that there were insufficient data for global estimation and they were infrequent causes of foodborne disease.

During the course of the project, it was identified that burden estimates for three parasitic hazards (*Giardia* spp., *Cryptosporidium* spp. and *Entamoeba histolytica*) should be included with the hazards addressed by EDTF, given that that the primary disease caused by these organisms was diarrhoea, and the approach taken to estimate the burden of these hazards was applicable.

As shown in Figure 2, there were 21 hazards causing 22 diseases for which final burden estimates were prepared by EDTF. Of these diseases, four are distinct manifestations of *Salmonella enterica*

infection: invasive infections due to *S. enterica* serotype Typhi (*S.* Typhi); invasive infections due to *S.* serotype Paratyphi A (*S.* Paratyphi A); invasive infections due to non-typhoidal *S. enterica* (iNTS); and diarrhoeal disease due to non-typhoidal *S. enterica*.

Diarrhoea is a dominant feature for 14 of these diseases – ten caused by bacteria, three by protozoa, and one by a virus. One or more extra-intestinal manifestations, including bacteraemia, hepatitis and meningitis, are the dominant feature for the other eight diseases – seven caused by bacteria and one caused by a virus.

4.2.1 Estimating cases, sequelae and deaths for diarrhoeal diseases

For diarrhoeal diseases caused by *Campylobacter* spp., *Cryptosporidium* spp., *Entamoeba histolytica*, ETEC, EPEC, *Giardia* spp., norovirus, non-typhoidal *Salmonella* spp. and *Shigella* spp., because national estimates of foodborne diseases were only available from a limited number of countries, two approaches were used depending on the level of development of the country. The approaches have been described by a key accompanying publication [40].

The first approach, based on national estimates of the incidence of foodborne diseases, was applied to the 61 countries in low-mortality (EUR and other subregion A) countries [41– 49]. For countries with national estimates of incidence and mortality, these data were used. The median and associated uncertainty intervals for diarrhoeal diseases for the subregion were used to estimate incidence and mortality of diarrhoeal diseases for other countries within these subregions without national data [40].

The second approach was applied to the remaining 133 countries worldwide. For this approach, the WHO Child Health Epidemiology Reference Group (CHERG) method was modified to estimate diarrhoeal incidence and mortality for all age groups [50]. First, the overall incidence of diarrhoea from all causes (i.e. the "envelope" of diarrhoeal incidence) was estimated for 2010 by combining estimates of diarrhoeal incidence for children <5 years of age and persons ≥5 years of age [51, 52]. The overall diarrhoeal mortality (i.e. the envelope for diarrhoeal deaths) derived by WHO for 2010 was used.[3] An aetiological proportion for each disease by region was derived from systematic reviews of stool sample isolation or detection proportions from inpatient, outpatient and community-based studies of persons with diarrhoea. Following the CHERG standard approach, developed because there is limited information on pathogens among people who have died, it was assumed that the distribution of pathogens observed among inpatients hospitalized with severe diarrhoea represented the pathogen prevalence among diarrhoeal deaths [50]. To derive aetiological proportions for children <5 years of age, it was assumed that the distribution of pathogens in outpatient and community studies represented the pathogen prevalence among diarrhoeal episodes for those who did not die. The same assumption was made for persons ≥5 years of age but due to sparseness of data, inpatient studies were also included. For some pathogens it was assumed that different aetiological agents, such as *Shigella* spp., NTS and *Campylobacter* spp. had similar clinical profiles.

Initial estimates for the 61 countries in low-mortality (EUR and other subregion A) countries had been prepared using this second "CHERG approach". However, it was recognized that for

[3] http://www.who.int/gho/en/ Accessed 6 June 2014

these developed countries this would overestimate incidence of diseases, in comparison with published estimates from the national studies available.

Estimates for cholera were based on the incidence among populations at risk for cholera in endemic and non-endemic countries [53]. The case fatality ratio (CFR) for cholera was 1% in WPR subregion B; 1% in SEAR B (except 1.5% in Bangladesh); 1.3% in EMR B; 3% in SEAR D; 3.2% in EMR D; and 3.8% in AFR [53]. For all other countries, it was assumed cholera occurred only among international travellers and did not result in deaths. In this instance, the median incidence from non-endemic countries with available data for cholera was applied.

Shiga-toxin producing *E. coli* (STEC) infection incidence and mortality were based on a systematic review [54]. Sequelae, more common with O157 infections, were haemolytic uraemic syndrome (HUS) and end-stage renal disease (ESRD). Based on review, it was estimated 0.8% of O157 infections and 0.03% of infections caused by other serotypes result in HUS, and 3% of HUS cases result in ESRD. It was further estimated that the CFR for HUS was 3.7%; for ESRD the CFR was 20% in the 35 subregion A countries; and 100% in other countries.

For the incidence and mortality of foodborne intoxications caused by *Bacillus cereus*, *Clostridium perfringens* and *Staphylococcus aureus,* data from national studies conducted in low-mortality countries were used. The median incidence from national studies was applied to the 61 countries in EUR and other subregion A countries. The burden due to these three foodborne intoxications in high- and middle-mortality countries was not estimated due to the absence of data on diseases caused by these pathogens in these countries. The median CFR from national studies was 0.003% for *C. perfringens* and 0.0025% for *S. aureus*; there were no *B. cereus* deaths.

It was considered that 31% of Guillain-Barré Syndrome (GBS) cases globally were associated with antecedent *Campylobacter* infection and that the CFR for GBS was 4.1% [55, 56].

Assignment of aetiology of diarrhoeal diseases when using the CHERG approach for middle- and high mortality countries was refined by adding in an aetiological proportion for pathogens not associated with foodborne transmission (rotavirus, astrovirus, coronavirus) and for unspecified diarrhoeal agents (pathogens that are possibly foodborne but with insufficient data for estimation, and unknown agents not yet discovered).

In our study, norovirus resulted in the largest number of cases of foodborne diseases and overall burden, highlighting the global importance of this agent. However, the disease model we used in the 135 middle- and high-mortality counties included only norovirus infections that resulted in a diarrhoeal illness. If we also included estimates for norovirus infections that resulted in vomiting without diarrhoea, there would be an estimated additional 163 million norovirus cases in these countries [57].

4.2.2 Estimating cases and sequelae of, and deaths due to, extra-intestinal diseases

For diseases caused by hepatitis A virus, *Brucella* spp., *Listeria monocytogenes*, *Mycobacterium bovis*, iNTS, *S.* Paratyphi A and *S.* Typhi, a variety of approaches were used, depending on availability of data.

Institute of Health Metrics and Evaluation (IHME) Global Burden of Disease 2010

(GDB2010) data were used to estimate the burden of disease for typhoid, paratyphoid and hepatitis A [58]. IHME provided country-specific, age-standardized prevalence data for typhoid and paratyphoid fever. These data were converted to incidence by dividing by duration, and partitioned into typhoid and paratyphoid assuming a 1.0 to 0.23 ratio [59]. Country-specific hepatitis A mortality data, stratified by age and sex, were converted to incidence assuming a CFR of 0.2%.

Rates of iNTS are highly correlated with HIV prevalence and malaria risk [60]. To estimate iNTS incidence globally, age-specific estimates of incidence from a systematic review [60] were used to construct a random effect log linear model using covariates of country-specific HIV and malaria deaths, and the log of Gross Domestic Product. As data were sparse, incidence for all ages was predicted, which was converted to age-specific incidence based on age profiles for iNTS cases in low and high incidence settings [60]. From this, iNTS incidence was predicted among persons not infected with HIV [61, 62]. To estimate deaths, it was assumed that the CFR for iNTS in non-HIV infected individuals was a uniform distribution with a range 5– 20% in sub-region B-E countries and range 3.9– 6.6% in sub-region A countries [63].

Estimates for *M. bovis* infections were based on a systematic review where the proportion of human tuberculosis (TB) infections due to *M. bovis* ranged from 0.3% in AMR to 2.8% in AFR [64]. Fifty-one countries were identified that were free from *M. bovis* in cattle, based on European Union certification and the World Animal Health Information System (WAHIS) of World Organization for Animal Health.[4] All countries in a region except those free from *M. bovis* in cattle were assumed to have the same proportion of human TB infections due to *M. bovis*. To account for internationally acquired infections, all countries free of *M. bovis* in cattle were assigned the lowest observed proportion of human TB infections due to *M. bovis* (0.3%). To derive estimates of human *M. bovis* incidence, WHO country-specific human TB incidences were multiplied by the estimate of the proportion of human TB infections that were due to *M. bovis* [65]. To estimate mortality associated with *M. bovis* that accounted for HIV co-morbidity estimates were used of mortality due to human TB in HIV-negative persons (WHO data). Mortality data were adjusted by assuming that the CFR for *M. bovis* was 20% lower than human TB, as *M. bovis* infections are more likely to be extrapulmonary [66].

To estimate the incidence and mortality for brucellosis a systematic review was updated and included additional data on 32 countries that were considered *Brucella*-free in livestock (free of *B. abortus* in cattle and *B. melitensis* in sheep and goats) [67]. Incidence data were imputed to countries without estimates using a Bayesian log-normal random effects model, except for countries that were *Brucella*-free in livestock [68]. To account for internationally acquired infections, all countries that were *Brucella*-free in livestock were assigned the median incidence of human brucellosis reported from these countries. The CFR for brucellosis was 0.5%, and 40% of cases resulted in chronic infections, and 10% of cases in males resulted in orchitis [69].

The incidence and mortality for listeriosis were estimated using a systematic review that is described elsewhere [70]. In accordance with standard burden of disease practice, stillbirths were excluded

[4] OIE – www.oie.int/wahis

in our baseline burden estimates. The CFR was 14.9% for perinatal cases and 25.9% for other cases.

Incidence and mortality data for botulism were only available from countries in Europe and North America. The estimation was limited to the 55 countries in EUR and AMR subregion A, which was based on the median incidence derived from countries with national estimates of botulism. It was estimated that 35% of botulism cases were severe and that the CFR of severe botulism was 15%.

4.3 Parasitic Hazards

At the first formal meeting of FERG, the PDTF initially reviewed all parasitic diseases that could be potentially transmitted by food (Appendix 3) with 14 parasitic diseases selected as high priority. The selection criteria of these 14 diseases was based on: proportion of foodborne transmission; severity of illness and/or sequelae; frequency of illness and/or sequelae causes; global relevance; particular regional relevance; propensity to cause outbreaks; and availability of existing evidence to derive burden estimates (see meeting reports from FERG 1 and 2).

Three intestinal protozoa genera – *Cryptosporidium, Entamoeba* and *Giardia* – were considered a priority, as they were likely to result in a high disease burden, and the frequency of citations for these parasites had been markedly increasing between 1990 and 2008. For methodological reasons, the burden of the three priority intestinal protozoa that cause diarrhoeal disease was estimated by the EDTF as described above. *Toxoplasma gondii* was also considered to be of high priority because of the potential serious sequelae. *Cyclospora* was also initially considered, but a decision was made to target resources to the other intestinal protozoa, as citation frequency had remained constant over the same period.

Foodborne trematodes of high priority were *Fasciola* spp., *Clonorchis* spp., *Opisthorchis* spp., *Paragonimus* spp. and intestinal trematodes such as *Fasciolopsis buski, Heterophyes* spp. and *Metagonimus* spp. Three cestode species were considered important: *Echinococcus granulosus, E. multilocularis* and *Taenia solium*. The cestode *Taenia saginata* was considered likely to have a very low burden for human health because of the lack of serious sequelae resulting from intestinal taeniosis, and hence was excluded from the priority list. Foodborne Chagas disease was also considered for possible inclusion at the second FERG meeting, but resources were not available to commission work on the foodborne transmission of a primarily vector-borne disease. Finally the nematode species believed to have high impact were Anisakidae, *Ascaris* spp. and *Trichinella* spp. Disease caused by the Anisakidae was later considered to be an uncommon foodborne disease and was subsequently removed from the priority list.

The incidence of each of the parasitic diseases was estimated where possible. For cysticercosis, the burden was estimated from a proportion of the prevalent epilepsy cases, i.e. the number of actual cases of disease, as further detailed below. Those incident cases with sequelae (or diseased individuals) were assigned years of life lost (YLLs) if fatal, or years lived with disability (YLDs) with a DW that depended on the severity of the disease. For some diseases, such as toxoplasmosis, many of the incident cases do not have sequelae (i.e. they are sub clinical). Such cases were given a DW of zero.

Systematic reviews were undertaken to estimate the incidence, sequelae and

mortality due to these diseases [71– 77]. Where possible, public health records describing numbers of cases presenting for treatment were reviewed. These data were only available for some diseases in some countries. In others surveillance data were used (for example laboratory data on sero-conversion rates in the population).

For congenital toxoplasmosis (CT) a systematic search of nine major databases for published and unpublished sources was conducted, alongside direct contact with the authors of source materials. Searches were country specific. To be included, studies had to report on the incidence of CT, on positivity to *Toxoplasma*-specific IgM in infants and pregnant women (including sero-conversion results) or on positivity to *Toxoplasma*-specific IgG in the general population. Various modelling techniques were used, depending on the country-specific data available, to estimate the CT incidence and burden in each country. Reports of children born with CT, IgM serology of infants and pregnant women, and age-stratified sero-prevalence in women and the general population, combined with fertility rates of specific age groups, were used to directly estimate the incidence of CT, or the data was used to input into models that were able to generate CT incidences from IgM-sero-positive rates in children or pregnant women, or from the IgG-sero conversion rates in women, combined with age-specific fertility rates. These data were then synthesized into an estimate of the global incidence of CT and of the global burden of CT in disability-adjusted life years (DALYs). Further details of the methodology, inclusion criteria, PRISMA statement and the modelling techniques used are given in [76]. Data on sero-prevalence were also used to estimate the incidence of acquired toxoplasmosis. Thus changes in sero-prevalence between age of T and T+1 can be used to estimate incidence.

Incidence estimates and clinical sequelae, for diseases caused by foodborne trematodes, were mainly based on the results of two review articles [77, 78]. Incidence rates for countries without reported national prevalence were imputed, but only where there were reports of at least one autochthonous human infection, by using a hierarchical random-effects model and incidence information from other countries as input data [79]. In highly endemic zones, adult subjects either maintain the parasites acquired when young or can be newly infected as the consequence of inhabiting a zone of high infection risk. This suggests that, in those areas, the majority of infected adults should be chronically infected. However, acute lesions by repetitive infections are frequently superimposed on chronic disease [80]. Therefore, it is reasonable to assume that such overlapping series of repeat infections result in life-long sequelae. Thus the incidence of trematode infection was estimated from the numbers of new cases in each age cohort.

To estimate the incidence of alveolar echinococcosis (AE), due to infection with the larval stage of *Echinococcus multilocularis*, literature searches were undertaken in any relevant databases that could be accessed. These data sources were synthesized to obtain estimates of the incidences of AE in countries where *E. multilocularis* was known to be endemic. Further details of the strategy to obtain the data, together with the methodology to estimate incidences from the data, are described in the report from FERG 2. For cystic echinococcosis (CE), due to infection with the larval stage of *E. granulosus*, the results of a systematic review [73] and other databases were used.

T. solium neurocysticercosis (NCC) is known to cause epilepsy and other neurological sequelae [73]. A meta-analysis revealed that brain lesions due to NCC are present in approximately 29.0% (95% UI 22.9%– 35.5%) of people with epilepsy in populations living in *T. solium* endemic areas in settings with poor sanitation and pig management practices, and where pork is consumed [74]. Consequently, the incidence, prevalence, mortality and burden of disease due to epilepsy (including both idiopathic and secondary) used in the Global Burden of Disease Study 2010 (GBD2010) [58, 81– 83] were used to estimate the burden of epilepsy-associated NCC.

Once the population at risk was known, 29% of the burden of epilepsy from GBD2010 was applied to that population to estimate the burden of epilepsy attributable to NCC. Although NCC can show many other neurological and psychiatric symptoms [81], in the absence of available consistent data on these other sequelae, only the burden of NCC-associated epilepsy was estimated in this study.

In the case of NCC, prevalence-based YLDs were used. However, in the absence of evidence of strong temporal trends in incidence, this is a reasonable approximation for incidence-based YLDs.

Data on the global prevalence of human ascariosis, stratified by age, gender and country, were provided by the Institute for Health Metrics and Evaluation (IHME). Based on these data and using the life expectancy of the parasite (approximately 1 year), the equivalent incident cases were estimated from the prevalence data. The sequelae proposed in GBD2010 [82], were used in this study.

To assess the global incidence and clinical effects of human trichinellosis, outbreak reports were analysed. Searches of six international databases yielded 494 reports, of which 261 were selected for data extraction after applying strict relevance and reliability criteria. From 1986 to 2009, there were 65 818 cases reported from 41 countries, with 42 deaths. The apparent annual incidence of and mortality caused by trichinellosis was calculated by dividing the average number of cases and deaths in this 24-year period by the 1997 mid-year population. Due to the important variability in reporting of the disease, the apparent incidence and mortality rates per billion persons per year were adjusted to account for under-reporting of the cases due to under-ascertainment, medical misclassification, and/or absence of effective surveillance systems. The data analysis focused on incidence, age and sex of patients, major clinical aspects including sequelae, and meat sources of infection. Full details of the search criteria, data sources and analysis are described in [71]. The global burden of trichinellosis was subsequently estimated, which is described elsewhere [84], where full details of the methodology are given.

Of the 12 PDTF hazards (including congenital and acquired *Toxoplasma gondii* as separate entities), two hazards did not need imputation. For epilepsy due to *Taenia solium*, we applied the GBD2010 burden envelopes [81]. For trichinellosis, the regional estimates generated by Devleesschauwer *et al.* [84] were applied. For the 10 remaining hazards, the total number of countries with missing data ranged from 5 to 90 (out of 194 countries included). Among the 194 countries included, the number of hazards for which no data were available ranged from 0 to 6 (out of 10 hazards). For the five most populous countries in the world, the number of hazards with no data were 0 (China), 6 (India), 3 (United

States of America), 2 (Indonesia) and 3 (Brazil).

4.4 Chemicals and toxins

At its first meeting, the CTTF identified groups of chemicals and toxins that are of highest priority in estimating the burden of foodborne disease (Appendix 3). The hazards were ranked on: (1) the severity of potential health effects; (2) the prevalence of exposure; and (3) the availability of data to make burden estimates. After considerable discussion, the final list of chemicals and toxins for which the CTTF believed that burdens could be estimated were aflatoxin[5], cyanide in cassava, peanut allergen, dioxin and dioxin-like compounds[6], methylmercury, lead, arsenic and cadmium. Only the results for aflatoxin, cyanide in cassava, peanut allergen, and dioxin are presented here. The results for the metals will be provided in a subsequent publication.

For each of the four chemicals, a systematic literature review was conducted. It was concluded that burden estimates could be developed for: (1) cyanide in cassava, and associated *konzo* syndrome; (2) peanut (*Arachis hypogaea*) allergy; (3) aflatoxin and hepatocellular carcinoma (HCC); (4) dioxin and hypothyroidy; and (5) dioxin and decrease in sperm count.

4.4.1 Cyanide in cassava

Cassava is an important staple for over 800 million people in approximately 80 countries, mostly in sub-Saharan Africa but also in Asia, the Pacific, and South America [85]. Cassava tubers contain a varying quantity of cyanogenic glucosides, which protect the root against attack by animals and insects. Appropriate processing before consumption can reduce cyanogenic glucoside content of cassava. High dietary cyanide exposure occurs when high-cyanogenic cassava and insufficient processing combine, usually in a context of food shortage. Cyanide in cassava is associated with acute cyanide poisoning and several diseases, including *konzo* [86]. Worldwide reports exist of acute poisoning from cyanide in cassava [86], but the data are inadequate to make burden estimates. The data are sufficient, however, to make burden estimates of *konzo*. *Konzo* is an irreversible spastic paraparesis of sudden onset, associated with the consumption of bitter cassava [87, 88] and a low protein intake [89]. It is a disease of extreme poverty. *Konzo* mostly occurs in epidemics, but sporadic cases are also reported. The case definition includes the following criteria: (1) a visible, symmetrically spastic abnormality of gait while walking and/or running; (2) a history of abrupt onset (less than one week), followed by a non-progressive course in a formerly healthy person; and (3) bilaterally exaggerated knee and/or ankle jerks without signs of disease in the spine [89, 90].

Because *konzo* mostly affects remote rural areas where health infrastructure is poor or non-existent, many cases remain undiagnosed or unreported, so the true burden of disease remains unknown. No cases have been reported from urban areas. A total of 2376 *konzo* cases have been reported in 5 countries in Africa (Cameroon, Central African Republic, Democratic Republic of Congo (DRC), Mozambique, and United Republic of Tanzania) [86], corresponding to 149 cases per year for 122 million people. Dividing the average annual number of cases for each country by the corresponding country population produces an observed incidence ranging from 0.043 to 0.179 per 100 000. The

[5] The term, "aflatoxin," refers to all aflatoxins.

[6] The term, “dioxin,” refers to dioxins and dioxin-like PCBs.

degree of underestimation is difficult to determine as *konzo* occurs in rural areas, often under conditions of war, and the disease is not notifiable. The only reported calculation of underestimation was that of Tylleskar [91] in the DRC in 1994, when he estimated that at least twice as many cases may have occurred as those reported. The underestimation in the DRC is likely to be much greater more recently, due to war and displacement. It was therefore decided to account for the uncertainty in the underreporting by applying an expansion factor ranging uniformly from 1 to 10 to the observed cases. The mean annual incidence rate was therefore estimated as 0.9/100 000 (0.04 to 1.8/100 000). This estimate of the burden of *konzo* is restricted to the 5 African countries described above, and Angola. The decision to include Angola is based on a report to the World Congress on Neurology suggesting that cases have occurred in that country [92]. Although cassava consumption occurs in tropical areas throughout the world, the term *konzo* has only been used to describe cases in Africa. The incidence of *konzo* in other countries in Africa and other parts of the world is assumed to be zero.

The age of onset and gender distribution of these cases was assumed to be that observed by Tylleskar [90]. The *konzo* case-fatality ratio is approximately 21% based on four studies [90, 93– 95]. The age and gender distribution of fatal cases was assumed to be that of Tshala-Katumbay [93].

The onset of paraparesis in *konzo* is abrupt, usually within minutes or hours, with occasional progression during the first days of the illness. After that time, the paraparesis is non-progressive and permanent. As a result, duration is defined as lifelong for non-fatal cases. For fatal cases, it was assumed that death occurred one to seven years after onset, with a most likely value of three years after onset, following Banea *et al.* [94] and Tylleskar *et al.* [96].

There is no DW specifically for *konzo*. WHO defined three severity levels for *konzo*: (1) Mild = able to walk without support; (2) Moderate = uses one or two sticks or crutches to walk; and (3) Severe = not able to walk [89]. The GBD2010 DWs for mild, moderate, and severe motor impairment are 0.012, 0.076 and 0.377, respectively [82]. The distribution of *konzo* severity among 753 patients from nine different studies were mild (63%), moderate (27%) and severe (10%) [91, 93, 94, 96– 101]. This distribution and the DWs described above were used to assign a disability weight of 0.065 to *konzo*.

4.4.2 Peanut allergen

Prevalence data on peanut [*Arachis hypogaea*] allergy were used to make estimates of incidence, since allergy occurs early in life (<5 years) and is believed to be lifelong [102– 106]. All peanut allergy cases are assumed to be the result of eating peanuts or peanut products. In western countries, the prevalence of clinical peanut allergy in children is 0 to 1.8% of the population [102], corresponding to incidence rates of 0 to 22.6 per 100 000. Limited data exist on the mortality rate of peanut-induced anaphylaxis, but the majority of studies found similar rates, ranging from 0 to 0.006 deaths per 100 000 person-years [102]. Incidence was estimated only for the A level (high income) subregions; too few data exist to make estimates for other subregions [102]. Several studies have reported that 63– 66% of cases are male [102], but given the uncertainty in this number, the gender distribution was assumed to be equal for the burden of disease calculations. No DW exists for peanut allergy. Mullins *et al.* [103] reported that

52% of cases referred to a specialist allergy medical practice in Australia suffered from mild symptoms (skin and subcutaneous tissue involvement only), 42% from moderate symptoms (features suggestive of respiratory, cardiovascular or gastrointestinal involvement), and 6% from severe symptoms (cyanosis, hypotension, confusion, collapse, loss of consciousness, incontinence).
The DW for peanut allergy was assigned as a weighted average accounting for this severity distribution. GBD2010 DWs [82] for the health states defined in the category "Asthma: controlled" (DW=0.009) are considered applicable for mild and moderate cases (94%), and "Generic uncomplicated disease: anxiety about the diagnosis" (DW=0.054) for severe cases (6%), because anxiety is known to affect Quality of Life in food allergic patients [107], leading to a severity-weighted DW of 0.012 for clinically relevant peanut allergy. Unlike other childhood allergies, such as cow's milk and egg allergy, peanut allergy rarely resolves [108, 109].

4.4.3 Aflatoxin

Aflatoxins are secondary metabolites of the fungi *Aspergillus flavus* and *A. parasiticus*, and less frequently other *Aspergillus* species such as *A. nomius* [110]. These species are prevalent in food crops – particularly maize, peanuts (groundnuts), oilseeds and tree nuts – in tropical and subtropical regions worldwide [110]. It is believed that all aflatoxin exposure results from food consumption. A multiplicative model was assumed for the effects of aflatoxin exposure and hepatitis B virus (HBV) infection on hepatocellular carcinoma. Aflatoxin exposure by country is that described by Liu and Wu [110]. To account for differences in background rates between the study population from which the cancer potency factor was derived [111] and global populations, the population attributable fractions (PAFs) by country were estimated, and applied to HCC incidence and mortality based on information from WHO [112, 113].
A Bayesian log-normal random effects model [79] was used to extrapolate available PAFs to countries without data. Age-specific incidence estimates were derived from a study in China comparing age-specific incidence of HCC in Qidong, a city in China with high aflatoxin exposure, and Beijing, a city with low aflatoxin exposure [114]. The YLD and YLL envelopes for HCC available from WHO were multiplied by the proportion of the burden due to aflatoxin. Thus no DW was directly involved in the calculation.

4.4.4 Dioxin

Dioxins are mainly by-products of industrial processes, but can also result from natural phenomena, such as volcanic eruptions and forest fires. More than 90% of human exposure is through food, mainly meat and dairy products, fish and shellfish [115]. Due to the bio-accumulating and lipophilic characteristics of dioxins, daily dietary exposure leads to accumulation of these compounds in human body fat. In adults this accumulation is thought to reach a constant level (i.e. a steady state). Consequently, the dioxin body burden, rather than the daily exposure, is taken as the dose metric for chronic toxicity risk and the assessment of dioxins [116– 121]. In this context the dioxin concentration in breast milk fat directly reflects the concentration in body fat [121– 124].

Many national authorities have programmes in place to monitor dioxin in the food supply and breast milk [124– 126]. Dioxin-induced pre-natal and post-natal hypothyroidy and pre-natally induced reduced sperm production have been found to be the most sensitive

non-cancer toxic endpoints for dioxins. Estimates for dioxin-induced pre-natal and post-natal hypothyroidy and reduced fertility due to disturbed sperm formation were based on an exposure assessment, toxicity assessment and the comparison of both assessments [127, 128]. The exposure assessment is based on breast milk concentrations of dioxin from 50 countries [129]. The toxicity assessment utilizes the benchmark dose (BMD) approach [130– 132] in which the dose response of post-natal total thyroxine (TT; decrease of TT4 in adult blood), pre-natal thyroid stimulating hormone (TSH; increase in TSH in neonatal blood), and sperm production (reduced concentration of sperm cells) is analysed. The toxicity and exposure assessments are compared to derive the transgression of a dioxin-induced decrease in TT4, decrease in sperm cell count and increase in TSH across a physiological threshold indicating a disease status (i.e. incidence of hypothyroidy or impaired fertility). Additional details of these assessments may be found in Zeilmaker *et al.* [133]. The BMD analysis was performed on studies that served as the starting point for the derivation of a Tolerable Weekly Intake (TWI) [117– 120] or Reference Dose for dioxin (RfD) [121].

In a study of a mother-child cohort, Baccarelli *et al.* determined the relationship between maternal plasma dioxin concentration and TSH level [134]. A BMD analysis of these data resulted in a population distribution of the maternal body burden of dioxin corresponding to an increased TSH level of 5 µU/mL in offspring, a level not to be exceeded in 3% of newborns in iodine-replete populations [135].

Following administration of an acute oral dose to pregnant Long Evans rats on day 15 of gestation, Gray *et al.* measured the reduction in cauda epididymis sperm count in male offspring [136]. The resulting dose response data were used to calculate a BMD lower confidence limit (BMDL) and upper confidence limit (BMDU) dioxin body burden for various levels of reduction in sperm count. A WHO reference cut-off value for impaired fertility of 20 ×106 sperm cells/mL was used to link toxicity (sperm count reduction) to a disease status (impaired fertility) (i.e. the calculation of the probability of a male being born with dioxin-impaired fertility) [137].

A BMD analysis of a National Toxicology Program (NTP) two-year feeding study in rats was used to make estimates of dioxin-induced thyroid toxicity. The NTP study administered 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) [138] and 2,3,4,7,8–pentachlorodibenzofuran [139] for periods of 14, 31 and 53 weeks. The concentrations were converted to Toxic Equivalent Quotients [140] to enable a combined analysis of both congeners. BMDL and BMDU body burdens for reduction in TT4 were calculated for each of the exposure periods. A distribution of TT4 in human blood has been reported by Aoki *et al.* [135]. The 5th percentile of this distribution (65 nmol/L) was used as the cut-off for overt clinical hypothyroidism in adults.

The results of the BMD analyses and the breast milk concentrations for 50 countries were compared, taking account of possible differences between experimental animals and humans and among individual humans [127, 128]. This comparison provided country-specific estimates of the incidence of dioxin induced pre-natal and post-natal hypothyroidy and impaired fertility. The estimates were extrapolated to other countries for which no breast milk concentrations were available, by means of Bayesian random effects modelling [79].

4.5 Outcomes and disability weights

DALYs incorporate the severity of health states through the DW, reflecting the corresponding relative reduction in healthy life on a scale from zero to one. Table 1 lists the DWs used for the health states associated with each hazard. Further details are given in Appendix 5 – Structuring of the health states into disease models for computation, and Appendix 6 – Sources and derivation of DWs.

DWs for several health states have been derived for the GBD studies and for various national burden of disease studies [141]. To ensure comparability, the CTF adopted the DWs that were used for WHO's Global Health Estimates [4]. These DWs were based on those derived for the GBD 2010 study [82], but with an alternative value for primary infertility (i.e. 0.056 instead of 0.011). The latter revision was motiviated by an analysis showing that the GBD 2010 weights undervalued the health states associated with fertility [4]. For dioxin-induced hypothyroidy, the GBD2013 DW for hypothyroidy was adopted, as this health state was not included in the GBD2010 DW study [142].

Several FBDs present with unique clinical signs, for which no DWs have been derived. Acute trichinellosis, for instance, typically presents with myalgia and facial oedema, for which no specific DWs are available [84]. When DWs were missing, proxy health states were selected by a medical expert and DW expert in the CTF and confirmed by disease experts in the hazard-specific TFs.
In other instances, DWs were available for severity levels that were not explicitly considered in the disease models.
For diarrhoea, for instance, DWs were available for mild, moderate and severe diarrhoea, although the disease models only included diarrhoea as such. In those cases, weighted averages were calculated based on published reviews of severity distributions, avoiding an over- or under-estimation of YLDs that would occur if only one DW would have been selected.

Table 1. FERG hazards, causally related health states and corresponding disability weights (DWs). Details on the derivation of the DWs are provided in Appendix 4.

HAZARD	HEALTH STATE	DW
DIARRHOEAL DISEASE AGENTS		
Norovirus	Diarrhoeal disease	0.074
Campylobacter spp.	Diarrhoeal disease	0.101
	Guillain-Barré syndrome	0.445
Enteropathogenic *E. coli*	Diarrhoeal disease	0.074
Enterotoxigenic *E. coli*	Diarrhoeal disease	0.074
Shiga toxin-producing *E. coli*	Diarrhoeal disease	0.091
	Haemolytic uraemic syndrome	0.210
	End-stage renal disease	0.573
Non-typhoidal *S. enterica*	Diarrhoeal disease	0.101
	Invasive salmonellosis	0.210
Shigella spp.	Diarrhoeal disease	0.101
Vibrio cholerae	Diarrhoeal disease	0.194
Cryptosporidium spp.	Diarrhoeal disease	0.074
Entamoeba histolytica	Diarrhoeal disease	0.074
Giardia spp.	Diarrhoeal disease	0.074
INVASIVE INFECTIOUS DISEASE AGENTS		
Hepatitis A virus	Hepatitis	0.108
Brucella spp.	Acute brucellosis	0.108
	Chronic brucellosis	0.079
	Orchitis	0.097
Listeria monocytogenes, perinatal	Sepsis	0.210
	Central nervous system infection	0.426
	Neurological sequelae	0.292
Listeria monocytogenes, acquired	Sepsis	0.210
	Central nervous system infection	0.426
	Neurological sequelae	0.292
Mycobacterium bovis	Tuberculosis	0.331
Salmonella Paratyphi	Paratyphoid fever	0.210
	Liver abscesses and cysts	0.254
Salmonella Typhi	Typhoid fever	0.210
	Liver abscesses and cysts	0.254
Toxoplasma gondii, congenital	Intracranial calcification	0.010
	Hydrocephalus	0.360
	Chorioretinitis, early in life	0.033
	Chorioretinitis, later in life	0.033
	CNS abnormalities	0.360
Toxoplasma gondii, acquired	Chorioretinitis, mild	0.004
	Chorioretinitis, moderate	0.033
	Chorioretinitis, severe	0.191
	Acute illness	0.053
	Post-acute illness	0.254
ENTERIC INTOXICATIONS		
Bacillus cereus [1]	Acute intoxication	0.061
Clostridium botulinum [1]	Moderate/mild botulism	0.198
	Severe botulism	0.445

HAZARD	HEALTH STATE	DW
Clostridium perfringens (1)	Acute intoxication	0.061
Staphylococcus aureus (1)	Acute intoxication	0.061
CESTODES		
Echinococcus granulosus, cases seeking treatment	Pulmonary cystic echinococcosis	0.192
	Hepatic cystic echinococcosis	0.123
	CNS cystic echinococcosis	0.221
Echinococcus granulosus, cases not seeking treatment	Pulmonary cystic echinococcosis	0.015
	Hepatic cystic echinococcosis	0.012
	CNS cystic echinococcosis	0.054
Echinococcus multilocularis	Alveolar echinococcosis	0.123
Taenia solium	Epilepsy: treated, seizure free	0.072
	Epilepsy: treated, with recent seizures	0.319
	Epilepsy: severe	0.657
	Epilepsy: untreated	0.420
NEMATODES		
Ascaris spp.	Ascariasis infestation	0.030
	Mild abdominopelvic problems due to ascariasis	0.012
	Severe wasting due to ascariasis	0.127
Trichinella spp.	Acute clinical trichinellosis	0.637
Trematodes		
Clonorchis sinensis	Abdominopelvic problems due to heavy clonorchiosis	0.123
Fasciola spp.	Abdominopelvic problems due to heavy fasciolosis	0.123
Intestinal flukes (2)	Abdominopelvic problems due to heavy intestinal fluke infections	0.123
Opisthorchis spp.	Abdominopelvic problems due to heavy opisthorchiosis	0.123
Paragonimus spp.	Central nervous system problems due to heavy paragonimosis	0.420
	Pulmonary problems due to heavy paragonimosis	0.132
ORGANIC POLLUTANTS		
Dioxin	Infertility	0.056
	Hypothyroidy due to pre-natal exposure	0.019
	Hypothyroidy due to post-natal exposure	0.019
TOXINS AND ALLERGENS		
Aflatoxin	Hepatocellular carcinoma: diagnosis and primary therapy	0.294
	Hepatocellular carcinoma: metastatic	0.484
	Hepatocellular carcinoma: terminal phase with medication	0.508
	Hepatocellular carcinoma: terminal phase without medication	0.519
Cyanide in cassava	*Konzo*	0.065
Peanut allergens (1)	Living with peanut-induced allergy	0.012

Notes: (1) Excluded from global burden assessments. (2) Includes *Echinostoma* spp., *Fasciolopsis buski*, *Heterophyes* spp., *Metagonimus* spp. and other foodborne intestinal trematode species.

4.6 Attribution

Overall, the study was designed to provide estimates of the proportion of illness acquired through different major routes of exposure. Major exposure routes considered were: food, environmental (water, soil, air), human-to-human transmission, direct animal contact, and a variety of potential lead exposure sources. Exposure route attribution estimates were developed for 19 individual hazards for each of the fourteen subregions (Table 2). Three hazard-based TFs within FERG (EDTF, PDTF and CTTF) identified, from their prioritized lists of hazards, those to be included in the expert elicitation.

Certain hazards were considered 100% foodborne, i.e. *Listeria monocytogenes*, *Mycobacterium bovis*, all foodborne trematodes, *Taenia solium*, *Trichinella* spp., cyanide in cassava and peanut allergens. For aflatoxin, inorganic arsenic, cadmium, dioxin and methyl mercury, CTTF determined that adequate data on foodborne exposure existed to allow use of a risk assessment approach for estimating the foodborne disease burden, thus negating the need for attribution. The remaining hazards were included in the structured expert elicitation (Table 1).

Fish-borne trematodes and *Trichinella* spp. were assumed to be 100% foodborne, based on the nature of their life cycle. In addition, *Fasciola* spp. were assumed to be 100% foodborne, although there may be small opportunities for waterborne transmission [77, 143]. *Taenia solium* cysticercosis was assumed to be 100% foodborne, but indirectly. In other words, the *T. solium* life cycle cannot persist without foodborne transmission of the parasite between pigs and humans. Humans become infected by the adult stage of *T. solium* by eating pork, resulting in intestinal taeniosis. However individuals who have *T. solium* taeniosis infect themselves or others by eggs excreted in their faeces, which are then ingested, often through food contamination, resulting in cysticercosis. In the complete absence of pork consumption, there would be no *T. solium* taeniosis and hence no cysticercosis.

The regions selected for this study were based on mortality. Six general regions: Africa (AFR), the Americas (AMR), the Eastern Mediterranean (EMR), Europe (EUR), South-East Asia (SEAR) and the Western Pacific (WP) were then divided into subregions on the basis of child and adult mortality, where Stratum A = very low child and adult mortality; Stratum B = low child mortality and very low adult mortality; Stratum C = low child mortality and high adult mortality; Stratum D = high child and adult mortality; and Stratum E = high child mortality and very high adult mortality [5, 144].

4.6.1 Identification of experts

An iterative peer nomination process based on a social network sampling technique called “snowball sampling” was used to identify a pool of potential expert participants for this study. The first points of contact were identified through FERG members and other networks (e.g. Global Foodborne Infections Network – GFN; Global Environment Monitoring System – GEMS; International Network of Food Safety Authorities – INFOSAN; Joint FAO/WHO Expert meeting on Microbial Risk Assessment – JEMRA; Joint FAO/WHO Expert Committee on Food Additives – JECFA; European Food Safety Authority – EFSA scientific panels; and WHO regional food safety advisors). These persons were asked to use their professional networks and recognized expertise in relevant areas to nominate additional experts. Since the purpose of this process was to identify an adequately large pool of appropriate experts, rather than to identify the entire expert network, the process of referral continued until an adequate size pool was identified to fill panels of typically 8 to 12 experts per panel.

Table 2. Foodborne hazards, and structure of the expert panels.

HAZARD GROUPS	HAZARDS	PANEL STRUCTURE[a]	NO. OF PANELS
DIARRHEAL DISEASE			
Bacteria	*Campylobacter* spp., enteropathogenic *Escherischia coli* (EPEC), enterotoxigenic *E. coli* (ETEC), Shiga-toxin producing *E. coli* (STEC), non-typhoidal *Salmonella* spp., *Shigella* spp., *Vibrio cholerae*	Sub regional	7
Virus	Norovirus	Sub regional	1
Intestinal protozoa	*Cryptosporidium* spp., *Entamoeba histolytica, Giardia* spp.	Global	3
OTHER INFECTIOUS DISEASE			
Bacteria	*Brucella* spp., *Salmonella* Typhi	Global Sub regional	2
Virus	Hepatitis A virus	Global	1
Protozoa	*Toxoplasma gondii*	Global	1
Helminths	*Ascaris* spp., *Echinococcus granulosus*, *Echinococcus multilocularis*	Global	3
CHEMICALS			
Lead		Global	1
Total			**19**

[a] Experts on a global panel were asked to provide estimates for all 14 sub regions, whereas experts on a sub-regional panel could choose a set of sub regions depending on their expertise.

4.6.2 Selection of experts

In collaboration with the FERG hazard-based TFs, SATF defined a set of criteria for inclusion of experts. These criteria considered each expert's background (education, and current and past positions), years of experience within the field, and geographic coverage of expert within the panel. The WHO invited nominated experts to participate, and the experts were asked to complete a declaration of interests (DOI), and an expert sheet providing information on their research/working area, highest education, current position, geographical experience, and years of experience. The experts were asked also to indicate for which panel(s) they believed themselves to be best suited for. The experts were not offered any compensation for their participation. The chairs of the three hazard-based TFs and the SATF reviewed the expert's information and CVs, and a final selection was made. FERG TF chairs and members of the SATF were not eligible for the study. DOIs were evaluated by WHO.

Given the broad nature of the attribution task, care was taken to include a suitably wide range of scientific backgrounds and professional experience, and to ensure adequate geographical representation. Frequently, expert elicitations use publication record as the measure of recognized expertise [145]. However, for this study, restricting expert selection to choices based solely on publication records would have eliminated important groups of experts, in particular public-health field workers and food-safety professionals in developing countries.

4.6.3 Expert panels

The panels for *Brucella* spp., hepatitis A virus, parasitic diseases including intestinal protozoa, and lead were structured as global panels, meaning that all experts in those panels were asked to provide estimates for all fourteen subregions.
The panels for the eight bacterial and viral pathogens and *Salmonella* Typhi were structured as subregional panels. The experts on subregional panels were free to decide the subregions for which they provided their judgments. Experts participating in panels addressing more than one hazard could also choose to provide estimates only for those hazards for which they felt they had adequate expertise.

4.6.4 Analytical method

The study used Cooke's [145– 147] "Classical Model" for expert elicitation. This approach uses "calibration" or "seed" questions to develop performance weights used in aggregating experts' judgments. The paradigmatic seed question is one for which the true value is not known at the time the experts answer the question, but will be known or is expected to become known *post hoc*. So the experts are not expected to know these values, but should be able to capture a majority of them reliably by defining suitable credible intervals.

Analysis of the experts' performance on the seed variables has two main purposes: 1), to evaluate the expert's *statistical accuracy* when assigning values to probability outcomes against the seed values (i.e. how reliably the expert's credible interval responses capture the true values of the seed variables, statistically), and 2), to evaluate the expert's *informativeness* when providing uncertainty distributions over the seed variables (i.e. how concentrated (narrow) are the distributions provided). Experts are thus scored with regard to statistical accuracy (calibration score) and informativeness (information score). The statistical accuracy is measured as the p-value at which one would falsely reject the hypothesis that the expert's probability assessments were statistically accurate, and informativeness is measured as Shannon relative information with respect to a user-supplied background measure. Informativeness scores are not absolute, but relative to a set of experts assessing the same variables. The calculated calibration and information scores are used to aggregate experts' judgments on target variables. The same measures can be applied to any combination of the experts' assessments to implement criteria for aggregating the assessments.

The Cooke Classical Model provides a rigorous, quantitative means for estimating model parameters and their uncertainties and is the only elicitation procedure that has objective empirical control on expert scoring. Moreover, it allows formal optimization of aggregated uncertainty distributions in terms of statistical accuracy and informativeness [146]. The expert judgment processing software EXCALIBUR (http://www.lighttwist.net/wp/excalibur) also allows direct comparison of the results that would be obtained from unweighted aggregation of expert judgments versus those produced by weighted linear pooling (or other combination schemes).

4.6.5 Seed questions

It is not always possible to develop seed questions that are in the paradigmatic form of asking about a future event or measurement that has not been made, but could be made, in principle. The essential feature of a viable seed question is that the expert is not expected to know the exact value but, if they are a subject-

matter expert, should be able to define a narrow uncertainty range that captures the value. Therefore, an alternative is to ask about selected data or values in the topic domain, about which the expert will not have perfect knowledge, nor access to realization values at the time they are answering the seed questions, but for which the values are known to the analyst. Such "retrospective" questions are frequently used in expert elicitations applying the Cooke Classical Model (see e.g. [31, 148]).

In the present case, the seed questions formulated were a mixture of retrospective and prospective seed variables. It is possible that expert uncertainty judgments vary by subject matter domain. In this study, the possibility of such biases relevant to foodborne illness source attribution was of concern. Therefore, the seed questions were designed to focus on questions that are substantively related to foodborne illness source attribution. Further, to account for the wide range of scientific backgrounds and experiences, seed questions covered a range of substantive topics relevant to source attribution. Five main categories of seed questions were identified for the panels on biological hazards (diarrhoeal pathogens and parasites): (1) dietary patterns and food supply; (2) under 5 years mortality rate; (3) access to improved water and sanitation; (4) disease surveillance; and (5) systematic reviews related to these and other scientific topics relevant to source attribution. For the panel on lead, questions were categorized as: (1) mean blood levels; (2) dietary exposure; and (3) dietary patterns and food supply. Examples of seed questions are presented in Table 3.

Table 3. Examples of calibration seed questions

TOPIC	HAZARD	QUESTION
Dietary patterns and food supply	All microbial hazards	Among all subregions in 2010, what was the proportion of regional vegetable supply (tonne) that was imported rather than produced domestically in the subregion with the highest such percentage?
Under 5 mortality rate	*Brucella* spp., *Echinococcus* spp., intestinal protozoa, diarrhoeal pathogens	Based on WHO estimates, think of the country in the African Region that had the largest percentage point decrease from 2000 to 2010 in all-cause <5 mortality due to diarrhoea. What was that percentage point decrease?
Disease surveillance	*Ascaris* spp., *Echinococcus* spp., intestinal protozoa, hepatitis A virus, diarrhoeal pathogens (developed subregions only)	What will be the rate per 100 000 population of laboratory-confirmed human cases of *Campylobacter*iosis in 2012 in all EU member states as reported in EFSA's annual report?
Systematic review	All microbial hazards	Fewtrell *et al.* (2005) conducted a systematic review and meta-analysis to compare the evidence of relative effectiveness of improvements in drinking water, sanitation facilities and hygiene practices in less developed countries in reducing diarrhoeal illness. The meta-analysis of 5 studies was used to estimate the relative risk of diarrhoeal illness with and without multiple interventions. What was the estimated relative risk?
Mean blood level	Lead	What was the geometric mean blood lead concentration for all participants ages 1 year and older in the 2007– 2008 U.S. NHANES survey? Please express your answer as positive micrograms per deciliter (μg/dL).

All experts comprising each panel were asked the same set of seed questions, and several sets of seed questions were used across panels. This allows some consistency checks to be performed between panels on performance and scoring outcomes. The number of questions varied from nine to twelve in total, depending on the panel. Experts were asked to provide a central judgment in terms of the median value, and a 90% credible interval for each question. Seed questions were administered by facilitators through one-to-one telephone interviews. The experts were not presented with the seed questions before the interview and they were asked to provide estimates based on their experience, knowledge and judgment, without referring to other sources of information.

4.6.6 Target questions

Target questions are the substantive questions of interest. In this study, for all identified hazards, we enquired about the percentage of all human disease cases caused by exposure through each of a number of indicated exposure routes. The point of exposure was chosen as the point of attribution, i.e. the experts were asked to distribute the disease burden on the sources that was the direct cause of human exposure. So, for example, someone with a norovirus infection might be exposed by eating food contaminated with the virus, although the food may have been contaminated by wastewater at an earlier stage.

Exposure routes varied between hazards, as indicated in Table 4. In order to reduce the time and effort burden of the elicitation on expert panelists, the hazard-based TFs decided which hazard exposure routes were relevant for present purposes. So, for example, human-to-human transmission was excluded as an exposure route for *Brucella* spp. However, the questionnaires did provide experts with an option to indicate additional routes of transmission if they disagreed with the TF's evaluation.

Experts were asked to complete a set of tables for each assigned hazard and subregion. Experts were provided with the tables at the end of the telephone interview during which the seed questions were asked, and the facilitator went through several target questions with the experts to ensure that they understood the task. For the target items (but not the seed questions), the experts were free to consult any information sources they felt appropriate in the four-week period they were given to return the target item spreadsheets.

As with the seed questions, the experts were asked to provide their 5th, 50th and 95th percentile values for each question. Technically, the median values of a joint distribution do not need to add up to 100%, but because we included a category "other", we asked about a joint distribution that logically spanned all possible exposure routes. Therefore, the experts' median values for source attribution percentages for a hazard should sum to a value close to 100%. In individual cases, where these sums were found to differ significantly (i.e. outside 100% ± 10%), the experts concerned were asked to review their responses.

4.6.7 Data analysis

Weights for individual experts were computed using the Classical Model formulation, using the EXCALIBUR software, by multiplying their calibration and informativeness scores, with the products then jointly normalized to sum to unity over all experts in the group. An expert was positively weighted only if his/her *p*-value was above a certain threshold, chosen to

optimize the combined score across all seed items. See [146, 149] for further details on the computation of expert performance weights.

The normalized experts' performance weights were used to construct the joint probability distribution complying with their assessments for individual target questions (i.e. attributable proportion of illness per pathway, subregion and hazard). In a final step, 10 000 random values from the marginal cumulative distributions were simulated using probability integral transform [34]. First, independent vectors of 10 000 random deviates from a Uniform (0,100) distribution, per exposure category within a hazard-subregion combination, were generated.

The quantiles corresponding to these random deviates were then obtained via linear interpolation. To ensure that the random attributional proportions summed to 100%, a "normalization" step was applied per iteration, in which each random value was divided by the sum of random values for each exposure pathway. The resulting 10 000 normalized random attributional proportions were then summarized by their median and a 95% uncertainty interval defined by the 2.5th and 97.5th percentiles. These final manipulations were performed in R 3.1.1 [150] using functions available in the 'FERG' package [151].

Table 4. Exposure routes included in the expert elicitation, per hazard

HAZARD	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN TO HUMAN CONTACT	WATER	SOIL	AIR	PAINT	COOKWARE, POTTERY OR GLASSWARE	TOYS	OTHER
DIARRHOEAL DISEASE										
Campylobacter spp.	x	x	x	x	x	na	N/A	N/A	N/A	x
Non-typhoid *Salmonella* spp.	x	x	x	x	x	N/A	N/A	N/A	N/A	x
Shiga toxin-producing *E. coli*	x	x	x	x	x	N/A	N/A	N/A	N/A	x
Brucella spp.	x	x	N/A	x	x	N/A	N/A	N/A	N/A	x
Shigella spp.	x	N/A	x	x	x	N/A	N/A	N/A	N/A	x
Enteropathogenic *E. coli*	x	x	x	x	N/A	N/A	N/A	N/A	N/A	x
Enterotoxigenic *E. coli*	x	x	x	x	N/A	N/A	N/A	N/A	N/A	x
Cryptosporidium spp.	x	x	x	x	N/A	N/A	N/A	N/A	N/A	x
Giardia spp.	x	x	x	x	N/A	N/A	N/A	N/A	N/A	x
Tyhoid *Salmonella* spp.	x	N/A	x	x	N/A	N/A	N/A	N/A	N/A	x
Vibrio cholerae	x	N/A	x	x	N/A	N/A	N/A	N/A	N/A	x
Entamoeba histolytica	x	N/A	x	x	N/A	N/A	N/A	N/A	N/A	x
Norovirus	x	N/A	x	x	N/A	N/A	N/A	N/A	N/A	x
Hepatitis A virus	x	N/A	x	x	N/A	N/A	N/A	N/A	N/A	x
PARASITIC DISEASE										
Toxoplasma gondii	x	x	N/A	x	x	N/A	N/A	N/A	N/A	x
Echinococcus granulosus	x	x	N/A	x	x	x	N/A	N/A	N/A	x
Echinococcus multilocularis	x	x	N/A	x	x	x	N/A	N/A	N/A	x
Ascaris spp.	x	x	x	x	x	N/A	N/A	N/A	N/A	x
CHEMICALS										
Lead	x	N/A	N/A	x	x	x	x	x	x	x

Notes: N/A = not applicable, meaning that these exposure routes were considered not possible or extremely unlikely by the respective FERG TF.

4.7 Computation

Different approaches can be taken for calculating DALYs, depending on whether the interest lies in quantifying the burden of a health outcome (such as diarrhoea), a hazard (e.g. a biological agent that may cause illness in humans such as *Salmonella enterica*), or a risk factor (e.g. an exposure that inceases the likelihood of illness such as unsafe water) [152]. Since FERG is concerned with the burden of FBDs, which are caused by a wide range of hazards (bacteria, viruses, protozoa, parasites, chemicals and toxins), a natural choice is the hazard-based approach. This approach

defines the burden of a specific foodborne hazard as that resulting from the health states, i.e. acute and chronic manifestations of disease, including death, that are causally related to the hazard transmitted through food, and which may become manifest at different time scales. This approach thus allows for a comprehensive estimate of the burden of disease due to a certain hazard, including sequelae, which may have a higher burden than acute illness alone [153– 155].

4.7.1 Disease models and epidemiological data

The starting point of the CTF workflow was the outline of disease models for each of the included hazards (as chosen by the hazard-based TFs), and the epidemiological data inputs that parameterized these disease models. To obtain this information, systematic reviews were commissioned and managed by three hazard-based TFs, i.e. the Enteric Diseases Task Force (EDTF), the Parasitic Diseases Task Force (PDTF), and the Chemicals and Toxins Task Force (CTTF).

The course of disease is characterized by various health states (e.g. acute or chronic phases; short-term or long-term sequelae), possibly having different severity levels. A disease model, also referred to as an outcome tree, is a schematic representation of the various health states associated with the concerned hazard, and the possible transitions between these states. A disease model for each hazard was defined by the members and commissioned experts of each hazard-based TF, considering relevant health outcomes identified in the respective reviews.

In the context of the CTF, disease models were defined as *computational* disease models, and not merely as *biological* disease models. While biological disease models merely reflect the natural history of disease, computational disease models also reflect the input parameters needed to calculate incidence and mortality of each of the relevant health states. As such, computational disease models are a combination of disease biology and data availability.

Computational disease models may be represented as directed acyclic graphs, defined by parent and child nodes and directed edges (arrows) defining the relationships between nodes. In the CTF framework, parent nodes were either incidence, mortality, YLD or YLL rates, while child nodes were multiplicative elements, such as proportions or ratios (reflecting, e.g. the probability of developing a specific symptom following infection, or the proportion of illnesses attributable to the concerned hazard). A specific disease model "language" was developed to denote the relationship and contribution of the different nodes. Rectangles defined parent nodes, and rounded rectangles defined child nodes. Grey nodes did not contribute directly to the DALYs, green nodes contributed YLDs, and red nodes contributed YLLs. Nodes that contributed to the incidence of the index disease were identified by a thick border. Appendix 5 gives the disease models for all 36 FERG hazards.

In general, three main approaches can be distinguished for estimating the burden due to a specific hazard in food, i.e., categorical attribution, counterfactual analysis, and risk assessment. Table 5 gives an overview of the modelling strategy applied for each included hazard. As the choice of the modelling strategy was mainly driven by the type of data available, no sensitivity analyses could be performed to triangulate different modelling approaches.

Table 5. Modelling strategies for the hazards included in the WHO global burden of foodborne disease estimates

HAZARD	BURDEN ATTRIBUTION APPROACH	DISEASE MODEL APPROACH	IMPUTATION	FOODBORNE ATTRIBUTION
DIARRHOEAL DISEASE AGENTS				
Norovirus	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Campylobacter spp.	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Enteropathogenic *E. coli*	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Enterotoxigenic *E. coli*	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Shiga toxin-producing *E. coli*	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Non-typhoidal *S. enterica*	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Shigella spp.	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Vibrio cholerae	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Cryptosporidium spp.	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Entamoeba histolytica	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
Giardia spp.	Categorical attribution	Attribution	Modified CHERG approach [40]	Expert elicitation [156]
INVASIVE INFECTIOUS DISEASE AGENTS				
Hepatitis A virus	Categorical attribution	Direct: GBD2010 [3]	N/A (1)	Expert elicitation [156]
Brucella spp.	Categorical attribution	Transition	Random effects [79, 151]	Expert elicitation [156]
Listeria monocytogenes, perinatal	Categorical attribution	Transition	Random effects [79, 151]	100%
Listeria monocytogenes, acquired	Categorical attribution	Transition	Random effects [79, 151]	100%
Mycobacterium bovis	Categorical attribution	Attribution	N/A (1)	100%
Salmonella Paratyphi	Categorical attribution	Direct: GBD2010 [3]	N/A (1)	Expert elicitation [156]
Salmonella Typhi	Categorical attribution	Direct: GBD2010 [3]	N/A (1)	Expert elicitation [156]
Toxoplasma gondii, congenital	Categorical attribution	Transition	Random effects [79, 151]	Expert elicitation [156]
Toxoplasma gondii, acquired	Categorical attribution	Transition	Random effects [79, 151]	Expert elicitation [156]
ENTERIC INTOXICATIONS				
Bacillus cereus (2)	Categorical attribution	Direct	Uniform	100%
Clostridium botulinum (2)	Categorical attribution	Direct	Uniform	100%
Clostridium perfringens (2)	Categorical attribution	Direct	Uniform	100%

HAZARD	BURDEN ATTRIBUTION APPROACH	DISEASE MODEL APPROACH	IMPUTATION	FOODBORNE ATTRIBUTION
Staphylococcus aureus (2)	Categorical attribution	Direct	Uniform	100%
CESTODES				
Echinococcus granulosus, cases seeking treatment	Categorical attribution	Transition	Random effects [79, 151]	Expert elicitation [156]
Echinococcus granulosus, cases not seeking treatment	Categorical attribution	Transition	Random effects [79, 151]	Expert elicitation [156]
Echinococcus multilocularis	Categorical attribution	Transition	Random effects [79, 151]	Expert elicitation [156]
Taenia solium	Categorical attribution	Attribution	N/A (1)	100%
NEMATODES				
Ascaris spp.	Categorical attribution	Direct: GBD2010 [3]	N/A (1)	Expert elicitation [156]
Trichinella spp.	Categorical attribution	Direct	N/A (1)	100%
TREMATODES				
Clonorchis sinensis	Categorical attribution	Direct	Random effects [79, 151]	100%
Fasciola spp.	Categorical attribution	Direct	Random effects [79, 151]	100%
Intestinal flukes (3)	Categorical attribution	Direct	Random effects [79, 151]	100%
Opisthorchis spp.	Categorical attribution	Direct	Random effects [79, 151]	100%
Paragonimus spp.	Categorical attribution	Direct	Random effects [79, 151]	100%
ORGANIC POLLUTANTS				
Dioxin	Risk assessment	Direct	Random effects [79, 151]	100%
TOXINS AND ALLERGENS				
Aflatoxin	Counterfactual analysis	Attribution	Random effects [79, 151]	100%
Cyanide in cassava	Categorical attribution	Direct	Uniform	100%
Peanut allergens (2)	Categorical attribution	Direct	Uniform	100%

Notes: (1) N/A = not applicable as no imputation had to be performed because data were used that had already been imputed. (2) Excluded from global burden assessments. (3) Includes *Echinostoma* spp., *Fasciolopsis buski*, *Heterophyes* spp., *Metagonimus* spp. and other foodborne intestinal trematode species.

Categorical attribution can be used when a foodborne hazard results in an outcome (death or a specific syndrome) that is identifiable as caused by the hazard in individual cases [157]. Following the typology of Devleesschauwer et al. [152], the burden due to a specific hazard can then be calculated using an attributional model (in which the incidence of the symptom is multiplied with the attributable proportion for a given hazard) or a transitional model (in which the incidence of the hazard is multiplied with the probability of developing a given symptom). Categorical attribution was applicable for all viral, bacterial and parasitic hazards, and for cyanide in cassava and peanut allergens, and was therefore the standard method used by FERG. Appendix 5 shows the computational disease model for *Mycobacterium bovis*, which is characteristic for the attributional models. In this model, the overall incidence and mortality of tuberculosis is multiplied with the proportion attributable to *M. bovis*, resulting in the incidence and mortality of *M. bovis* tuberculosis. Appendix 5 shows the computational disease model for *Echinococcus granulosus*, which is characteristic for the transitional models. In this model, the overall incidence of infection by this parasite was multiplied with child nodes reflecting the probability of developing the concerned health states, resulting in the incidences of the specific health states.

When the hazard elevates the risk of a disease or disability outcome that occurs in the population from other causes as well, causal attribution can only be made statistically, and not on an individual basis. This is the case for many chemicals, including aflatoxin and dioxin. Aflatoxin for instance may increase the risk of hepatocellular carcinoma, but it is not possible to specify that a specific liver cancer case was caused by aflatoxin. In this situation, the standard approach for calculating the burden of environmental exposures is to use a *counterfactual analysis* in which the current disease outcomes with current exposure are compared with the disease outcomes under an alternative exposure (a min. risk exposure which could be zero, or some accepted background level) [158]. This allows calculation of a population attributable fraction (PAF) that can be applied to the all-cause burden estimates for the relevant disease outcome (the so-called burden envelope), leading to a special case of the attributional model [152]. In the context of FERG, counterfactual analysis was used to estimate the burden of aflatoxin-related hepatocellular carcinoma.

In addition to categorical attribution and counterfactual analysis, which can be considered top-down approaches, FBD burden can also be estimated by a *risk assessment* approach, which can be considered a bottom-up approach. In this approach, the incidences of the specific health states (e.g. impaired male fertility due to prenatal dioxin exposure) are estimated by combining exposure and dose-response data. The dose-response model may for instance define the probability of illness at a given exposure level, which can then be translated into an estimate of the number of incident or prevalent cases expected to occur in the exposed population [158, 191]. As this approach does not involve burden attribution, it does not necessarily ensure consistency with existing health statistics. However, risk assessment may be a valid alternative when no burden envelopes exist or when it can be demonstrated that the estimated excess risk is additive to the background risk. In the context of FERG, risk assessment was used to estimate the burden of dioxin-related hypothyroidy and impaired fertility.

4.7.2 CTF database template

A database template was developed in Excel™ [7] to collect in a standardized way the data resulting from the systematic reviews. The structure of the database was based on the disease models, with one sheet per node. Three generic sheets were defined: (1) a "RATE" sheet, for rates by country; (2) a "PROB-local" sheet, for proportions or ratios by country; and (3) a "PROB-global" sheet, for a single proportion or ratio that applied to all countries.

Each sheet consisted of four tables for entering: (1) the rate or proportion/ratio data; (2) the age distribution; (3) the sex distribution; and (4) if applicable, the duration. Using a drop-down menu, different formats could be selected for entering the input parameters, including a mean and 95% confidence interval; minimum, most likely and maximum percentiles; the shape and rate of a Gamma distribution (for rates); and the shape parameters of a Beta distribution (for proportions). Gamma and Beta distributions were chosen because their domains correspond to that of rates and proportions, respectively, and because their parameters have an intuitive interpretation (i.e., number of cases and sample size, respectively, number of positives and number of negatives). Likewise, different levels of stratification could be selected for the duration parameters (i.e. none, by age only, by sex only, by age and sex). Age distribution, sex distribution and duration were allowed to vary by country, by defining different "groups" and assigning countries to "groups".

4.7.3 Imputation

Extrapolation or imputation models may be needed when literature searches cannot provide essential epidemiological data such as incidence or mortality rates [159]. These models estimate parameters based on data of neighboring regions or other time periods. The external data used must thus be representative of the selected population, region and time. The CTF developed, tested and evaluated several possible approaches to impute missing incidence data at the country level [79]. This exercise identified several pitfalls in the use of explanatory covariates, such as the potential for overfitting and the arbitrariness in the selection of covariates. Therefore, and further motivated by a strive for parsimony and transparency, we decided to use a log-Normal random effects model as the default model for imputing missing country-level incidence data. We used the subregions as defined in Appendix 2 as the random effect or cluster variable. This model assumes that the log-transformed incidence rate in country j belonging to subregion i arises from a Normal distribution with subregion specific mean μ_i and a within-region (= between-country) variance σ_w^2. Each subregion specific mean μ_i is in turn assumed to arise from a Normal distribution with mean μ_0 and a between-region variance σ_b^2:

$$\log(\theta_{ij}) \sim Normal(\mu_i, \sigma_w^2)$$

$$\mu_i \sim Normal(\mu_0, \sigma_b^2)$$

After fitting this hierarchical random effects model to the available data, incidence values for countries with no data were imputed based on the resulting posterior predictive distributions. In other words, we represented missing incidence data by log-Normal distributions based on the fitted mean and variance parameters. For countries in a subregion where none of the countries had data, the log-incidence was imputed as multiple random draws

[7] Microsoft Corp., Redmond, Washington, USA

from a Normal distribution with mean equal to the fitted global intercept μ_0 and variance equal to the sum of the fitted between-region variance σ_b^2 and the fitted within-region variance σ_w^2 (thus imputing the log-incidence as that of a "random" country within a "random" subregion, with the uncertainty interval describing the variability between and within subregions):

$$\log(\theta_{ij}^*) \sim Normal(\mu_0, \sigma_b^2 + \sigma_w^2)$$

For countries in a subregion where at least one of the other countries had data, the log-incidence was imputed as multiple random draws from a Normal distribution with mean equal to the fitted region-specific intercept μ_i and variance equal to the fitted within-region variance σ_w^2 (thus imputing the log-incidence as that of a "random" country within the concerned subregion, with the uncertainty interval describing the variability within subregions):

$$\log(\theta_{ij}^*) \sim Normal(\mu_i, \sigma_w^2)$$

When countries were considered free from exposure through the food chain, they were excluded from the imputation model and thus did not contribute to the subregional estimates. This was the case for *Brucella* spp., as discussed in [168], and foodborne trematodes and *Echinococcus* spp., as discussed in [261]. For countries with available incidence data, no imputation was performed. The incidence data used in the probabilistic burden assessments were thus a combination of actual data and imputed estimates. No additional step had to be included to correct incidence data for potential underreporting, as this was already captured by the previous steps of the framework. Indeed, for the hazards that used an attributional model, disease envelopes were used that had already been corrected for underreporting, while for other hazards we directly drew on GBD 2010 estimates (Table 5). For the remaining hazards, either epidemiological data were used that did not need (further) correction, or the underreporting factor was included in the disease model (which was the case for *Trichinella* spp. and cyanide in cassava).

For aflatoxin, the same random effects model was used to extrapolate PAFs, but now using logit-transformed instead of log-transformed values.

The model was implemented in a Bayesian framework, using independent Normal(0, 1e5) priors for μ_0 *and* μ_i*;* a Uniform(0, 10) prior for σ_w; and a Folded-t(1) prior for σ_b, as suggested by Gelman [160]. Sensitivity analyses using Gamma priors for the variance parameters did not yield meaningful differences. The model was run in JAGS [161] through the 'rjags' package in R [162]. After a burn-in of 5000 iterations, another 5000 iterations were retained for inference. Two chains were run, and convergence was ascertained through density and trace plots, and the multivariate potential scale reduction factor (or Brooks-Gelman-Rubin diagnostic).

A crucial assumption made by this imputation model is that missing data were considered "missing at random" (MAR), meaning that missingness was independent of the unobserved data, given the observed data [163, 164]. In our case, this assumption implied that, within each subregion, countries with data provided unbiased information on those without data, and that, across subregions, subregions with data provided unbiased information on those without data. However, for five hazards (*Bacillus cereus*, *Clostridium perfringens*, *Clostridium botulinum*, *Staphylococcus aureus* and peanut allergens), only data from high-

income subregions, i.e. subregions A or B, could be retrieved. In those instances, the assumption of MAR was clearly violated, and it was decided not to extrapolate those data to the rest of the world. As a result, those hazards were excluded from the global burden of disease estimates.

Table 5 shows which imputation strategy was used for each of the included hazards. For the four intoxications, peanut allergens and cyanide in cassava, the default random effects model was not used because of the limited number of data points. Instead, the burden for each concerned country was imputed as draws from a Uniform distribution defined by the lowest and highest globally observed incidence or mortality rates. To ensure consistency with results of the Child Health Epidemiology Reference Group (CHERG), alternative imputation approaches were applied for estimating aetiological fractions for the eleven diarrhoeal agents [40, 50, 168]. For seven other hazards, no imputation had to be performed because data were used that had already been imputed. This was the case for hepatitis A virus, *Salmonella* Typhi, *Salmonella* Paratyphi, *Ascaris* spp. and *Taenia solium*, for which GBD2010 data were used, and for *Mycobacterium bovis* and *Trichinella* spp., for which other published data were used [84, 165].

4.7.4 Probabilistic burden assessment

For each hazard, incidence, mortality, YLD, YLL and DALY rates were calculated for 11 age groups (<1; 1-4; 5-14; 15-24; 25-34; 35-44; 45-54; 55-64; 65-74; 75-84; ≥85) and both sexes. When necessary, age and sex specific rates were obtained by multiplying the overall rates with outcome specific age and sex distributions. The reference year for the calculation of absolute numbers was 2010, with population estimates obtained from the 2012 revision of the United Nations World Population Prospects [166]. All estimates were generated per country, and subsequently aggregated per subregion, per region, and globally (Appendix 2).

The duration component of the YLDs is defined as the average observed duration until remission or death. For calculating YLDs when duration was lifelong, we therefore used the country-specific life expectancy (LE) [166] as duration. The time component of the YLLs, on the other hand, is defined as the ideal residual life expectancy a person would have if the world would be free from disease and provide maximal access to health care. We used the highest projected LE for 2050 as normative LE for calculating YLLs [4]. This LE table has a LE at birth of 92, higher than that of the LE tables used in the GBD studies, which were based on current death rates [1, 6]. Since even for the lowest observed death rates there are a proportion of deaths which are preventable or avertable, the highest projected LE for the year 2050 was deemed to better represent the maximum life span of an individual in good health, while acknowledging that it may still not represent the ultimate achievable human life span [166].

In line with current global burden of disease assessments, no age weighting or time discounting was applied [4, 6]. HIV infected invasive salmonellosis cases and deaths, and HIV infected *M. bovis* deaths, were excluded from the burden estimates. No further corrections were made for possible co-morbidities.

Parameter uncertainty was taken into account by performing the burden assessments in a probabilistic framework. Ten thousand Monte Carlo (parametric bootstrap) simulations of the input parameters were generated to calculate 10,000 estimates of incidence, mortality, YLD, YLL and DALY rates. These 10,000

estimates were then summarized by their median and a 95% uncertainty interval defined as the 2.5th and 97.5th percentile of the distribution of estimates. Special care was taken to deal with correlated uncertainties, for instance when the disease model included "global" probabilities (e.g., when it was assumed that the probability of developing a certain health state following infection was the same for each country). In such cases, a vector of random probabilities was simulated only once and applied to the different countries, instead of incorrectly simulating a new, independent vector of random probabilities for each country.

The structured expert elicitation using Cooke's Classical Method conducted to attribute burden to different exposure routes, providing hazards-specific estimates for each exposure route per subregion [156]. This process yielded a probabilistic estimate of the proportion foodborne, in the form of an empirical cumulative density function from which random samples could be drawn. Foodborne cases, deaths, YLDs, YLLs and DALYs were then obtained by multiplying the vectors of random values for these parameters with a vector of random values for the proportion foodborne. As before, the perfect correlation of uncertainty was dealt with by simulating only one vector of random foodborne proportions per subregion, and by applying this vector to all parameters of all countries within the concerned subregion.

RESULTS 5

RESULTS

In this section, the results of the global expert elicitation study are reported first. An overview of global and regional DALY estimates according to hazard follows. Subsequent sections report more specific hazard-based estimates, and include estimates for some hazards for which global estimates could not be derived and only regional estimates are reported (peanut allergen; toxin-producing species of bacteria).

5.1 Attribution

A total of 299 potential experts were asked by email of their interest in participating in the study. Of these154 replied positively and they were requested to forward their CV, a filled-in expert sheet and a signed declaration of interest. A total of 103 did that.
Of these, 3 were not included due to lack of experience (1) or possible conflicts of interest (2). Of the 100 experts enrolled, 78 completed interviews with facilitators and 73 returned their spreadsheets with their responses to the target questions and seed questions. The single main reason for not completing the interview and returning the spreadsheet was time constraints. All responses were reviewed (e.g. checked for missing estimates, that sums across pathways were close to 100%, and that the 5th percentile < 50th percentile < 95th percentiles), and some experts were contacted for clarification of the responses they had provided. One expert was dropped after not responding to requests for clarification. This resulted in the responses of 72 experts being included in the final dataset. Table 6 shows the distribution of experts across panels, and Figure 3 shows distribution of the experts by their geographical areas of expertise.

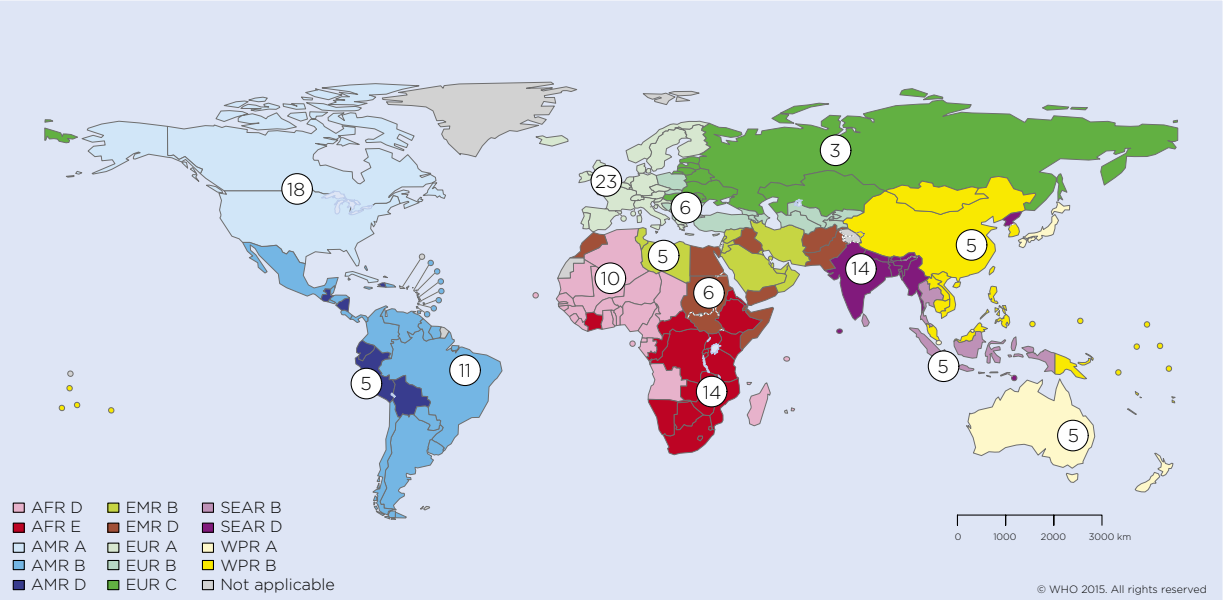
Table 6. The number of experts enrolled, interviewed and finally included in the elicitation across panels

HAZARD GROUPS		EXPERTS ENROLLED	EXPERTS INTERVIEWED	RETURNED ANSWERS
DIARRHEAL DISEASE				
Bacterial (incl. *S.* Typhi) pathogens and norovirus	Sub regional[a]	49	37	37
Intestinal protozoa	Global	12	9	9
OTHER INFECTIOUS DISEASE				
Brucella spp.	Global	10	8	7
Hepatitis A virus	Global	9	7	7
Toxoplasma gondii	Global	11	10	9
Ascaris spp.	Global	8	6	7
Echinococcus spp.	Global	7	6	6
CHEMICALS				
Lead	Global	10	9	6
Total[b]		**100**	**78**	**72**

[a] Due to the sub regional structure of these panels, the number of experts varied between 10 and 15 depending on the hazard and sub region.

[b] As several experts served on more panels, the number of experts per panel does not add up to the total number of individual experts included.

Figure 3. Geographical distribution of experts according to working experience (>3 years) per subregion. Several experts had experience in more than one subregion.



Notes: The subregions are defined on the on the basis of child and adult mortality, as described by Ezzati *et al.* [5]. Stratum A = very low child and adult mortality; Stratum B = low child mortality and very low adult mortality; Stratum C = low child mortality and high adult mortality; Stratum D = high child and adult mortality; and Stratum E = high child mortality and very high adult mortality. The use of the term 'subregion' here and throughout the text does not identify an official grouping of WHO Member States, and the "subregions" are not related to the six official WHO regions.

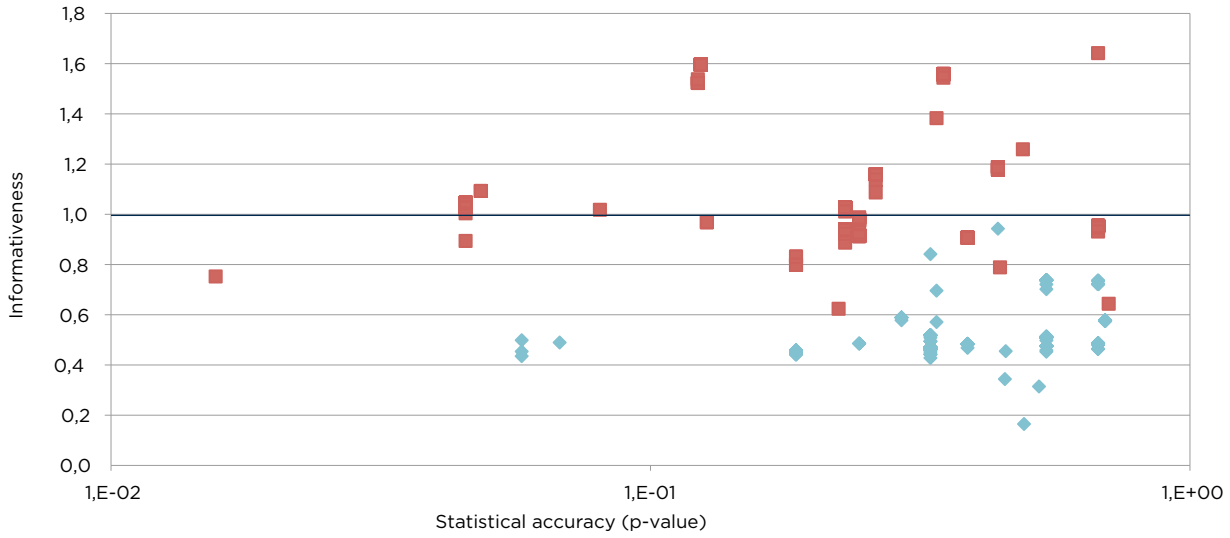
5.1.1 Expert performance

In this study, there were 115 distinct panels (i.e. panels that differed in membership or seed questions) and, overall, performance weight and equal weight combinations showed acceptable statistical accuracy. Only in the case of the panel considering lead was the *p*-value of the performance-based combination small enough to cast doubt on the usual criterion for statistical accuracy, with $p = 0.045$ (i.e. less than the 0.05 criterion). With a set of 115 panels, at least one score this low would be expected even if the performance-based combination was always statistically accurate.

Results obtained by applying equal weights pooling and performance weights pooling were compared. The equal weights solutions tended to have higher statistical accuracy than those produced by applying the performance weights. In contrast, the informativeness properties of the equal weights solutions were much lower than those provided by performance weights solutions (Figure 4). This "trade-off" between accuracy and informativeness when applying equal weights or performance weights is often seen, because the least accurate experts are typically the most informative, and their narrow 90% confidence bands often have little or no overlap. Moreover, the combined score using performance-based weights was above that of the equal weights pooling in 62% of the cases. It was therefore decided to use the performance weights combinations for constructing the joint probability distributions for the pathway attribution estimates, as long as the statistical accuracy was acceptable. It should also be noted that the weight

attributed to an expert – comprising the normalized product of their two scores – is dominated by the accuracy term, so that high informativeness cannot buy down poor accuracy. A unique feature of the present study is that a large number of experts were assessed using very similar variables, thereby allowing their informativeness scores to be compared. An in-depth analysis of the experts' performance has also been published [181].

Figure 4. Statistical accuracy versus informativeness of the experts included, when using equal weight (blue) or performance weight (red) combinations, respectively.



5.1.2 Pathway attribution results

The collective results of the performance-based weighted expert responses are shown in Appendix 7 (Table A7.1-3 for diarrhoeal disease, Table A7.4 for non-diarrhoeal parasitic disease, and Table A7.5 for lead). For most estimates there is considerable uncertainty, reflecting: (1) variations in uncertainty estimations between individual experts; (2) that, for some hazards, the values provided by experts having high performance weights in the analysis did not accord with one another; and (3) that, for some subregions or hazards, the number of contributing experts was small (<7). Thus, the broad uncertainty intervals are most likely reflecting current shortcomings in hard scientific evidence about the relative contribution to human disease from each of the transmission pathways.

Figure 5 shows the subregional estimates of the foodborne proportion for *Campylobacter* spp., non-typhoidal *Salmonella* spp., Shiga-toxin producing *Escherichia coli* (STEC), *Brucella* spp. and *Shigella* spp. For *Salmonella* spp. and *Brucella* spp., there is a clear pattern that the foodborne proportion is considered more important in the developed subregions (AMR A, EUR A and WPR A) compared with developing subregions. Although less distinct, this pattern can also be seen for *Campylobacter* spp. and STEC. For *Campylobacter* spp., *Salmonella* spp. and STEC, the foodborne transmission route was assessed by the experts to be the most important route in all subregions, followed by direct animal contact, human-to-human transmission and waterborne transmission in varying order, but generally with medians below 0.25 (Table A7.1 in Appendix 7). For *Brucella* spp., direct animal contact was considered

equally or more important than foodborne transmission in developing subregions. Human-to-human transmission was considered the most important route for *Shigella* spp. in the majority of subregions. The proportion of foodborne *Shigella* spp. infections ranged from 0.07 (95% UI 0.00– 0.46) in EUR A to 0.36 (95% UI 0.01–0.70) in WPR A (Table A7.1 in Appendix 7). Overall, foodborne transmission was assessed to be more important in South-East Asian and Western Pacific subregions than in other parts of the world. Transmission through soil or other routes was recognized by the experts to be of minor importance for these five pathogens.

Figure 6 shows the subregional estimates of the proportion foodborne for entero-pathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), *Cryptosporidium* spp. and *Giardia* spp. The estimates for EPEC are seen to follow the same pattern as described above, with the foodborne route being assessed to be more important in developed subregions. In developing subregions in the African, American and Eastern Mediterranean regions (AFR, AMR and EMR), water was identified as the most important transmission route. For ETEC, the estimated foodborne proportions were quite similar for all subregions with medians ranging from 0.33 to 0.43 (Table A7.2 in Appendix 7), but the foodborne route was only assessed by experts to be the more important route in European subregions. For *Cryptosporidium* spp. and *Giardia* spp., the foodborne proportions were also quite similar across subregions, but generally considered less important, with medians below 0.20 (Table A7.2 in Appendix 7). Human-to-human and waterborne transmission were the more important routes for these infections in all subregions.

Figure 7 shows the subregional estimates of the proportion foodborne for *Salmonella* Typhi, *Vibrio cholerae*, *Entamoeba histolytica*, norovirus, and hepatitis A virus. Overall, foodborne infections were not assessed by the experts to be the more important routes in the majority of subregions. Exceptions were hepatitis A infections, where foodborne and human-to-human transmission were evaluated equally important in most subregions, and *S.* Typhi, where foodborne and waterborne infections were assessed equally important in SEAR and WPR regions (Table A7.3 in Appendix 7). Human-to-human transmission was identified as the main exposure route for norovirus and *E. histolytica* in most subregions, whereas waterborne transmission was estimated to be the main transmission route for *V. cholerae* infections (Table A7.3 in Appendix 7).

Figure 8 shows the subregional estimates of the proportion foodborne for *Toxoplasma gondii*, *Echinococcus multilocularis*, *Echinococcus granulosus* and *Ascaris* spp. The foodborne route was assessed by the experts to be the most important transmission route for *T. gondii* and *Ascaris* spp. in most subregions, but there was a clear tendency for soil to increase in relative importance in less developed subregions (subregions D and E) (Table A7.4 in Appendix 7). Specifically for *Ascaris* spp., the foodborne route was assessed to be particularly important in developed subregions (A subregions). There was only little geographical variation between the median estimates for each of the transmission pathways for the two *Echinococcus* species. For *E. granulosus*, animal contact was clearly believed to be the most important route, with medians just over 0.50. For *E. multilocularis*, the foodborne route was considered most important, with medians ranging from 0.43 in EMR B to 0.58 in AFR D and E, AMR B and D, and SEAR B and D, but the estimates had very large uncertainty intervals (Table A7.4 in Appendix 7).

Figure 5. Subregional estimates of the proportion of foodborne illnesses caused by *Campylobacter* spp., non-typhoidal *Salmonella* spp., Shiga-toxin producing *Escherichia coli* (STEC), *Brucella* spp. and *Shigella* spp. Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles.

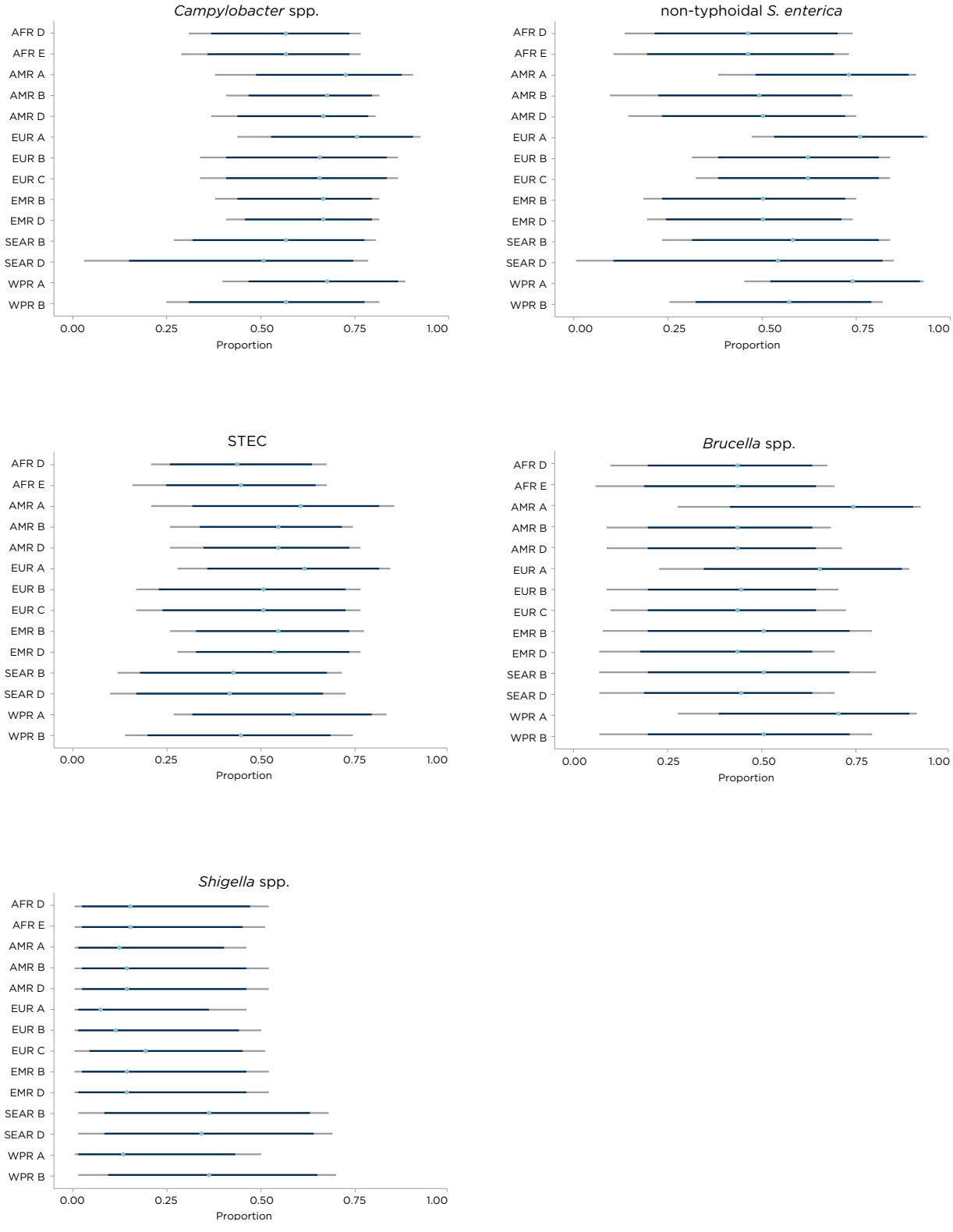
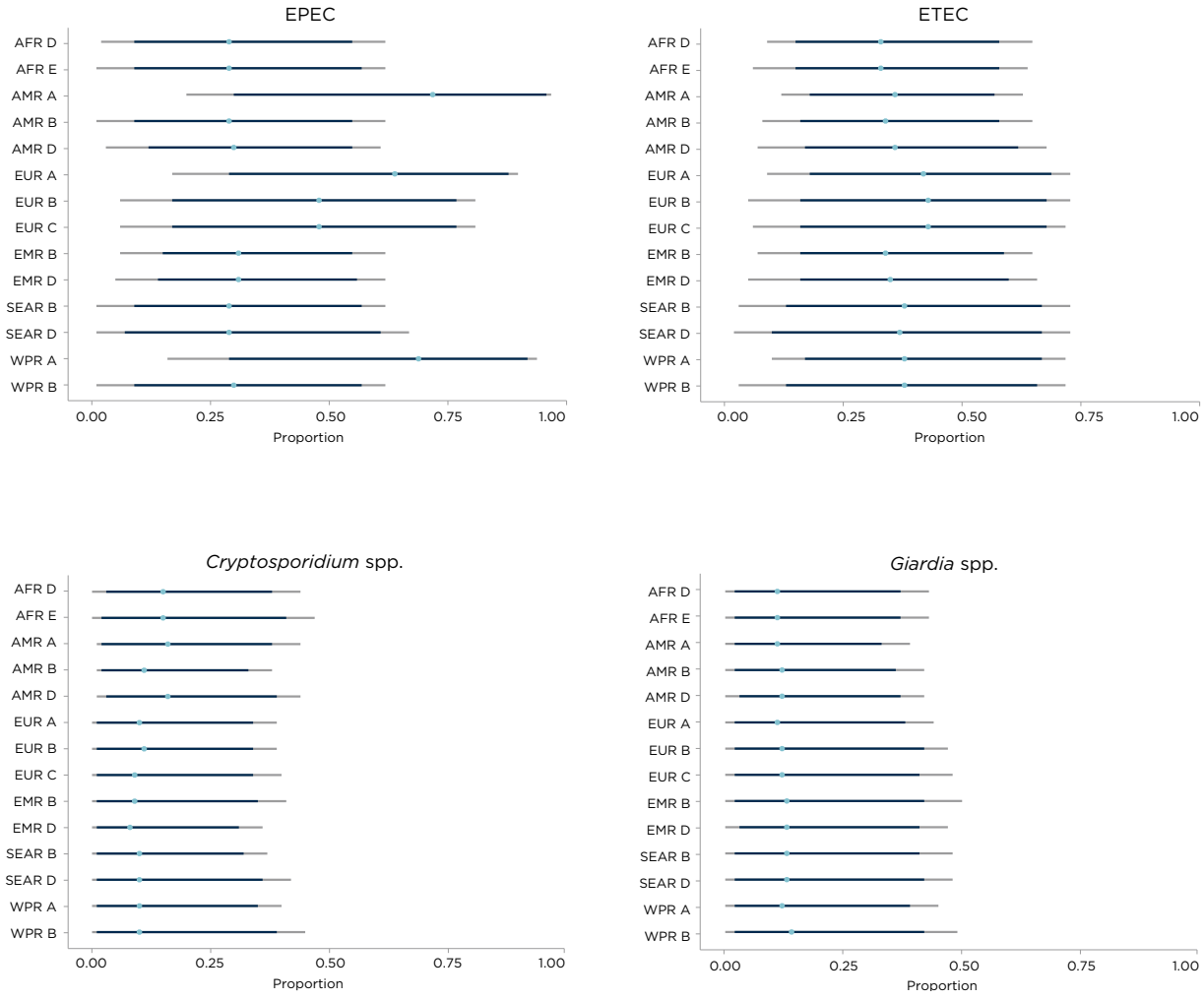
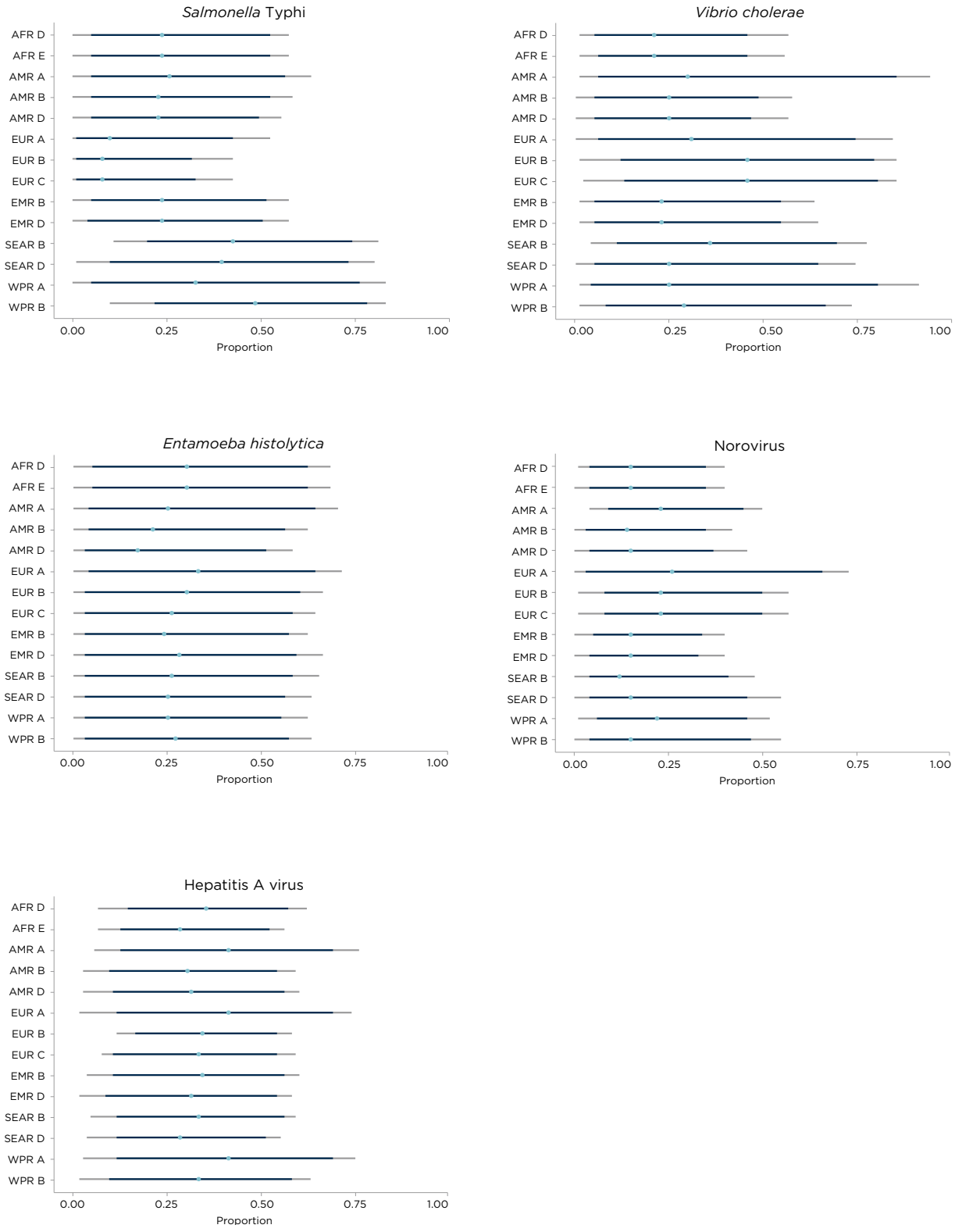


Figure 6. Subregional estimates of the proportion of foodborne illnesses caused by *enteropathogenic E.* (EPEC), *enterotoxigenic E. coli* (ETEC), *Cryptosporidium* spp. and *Giardia* spp.



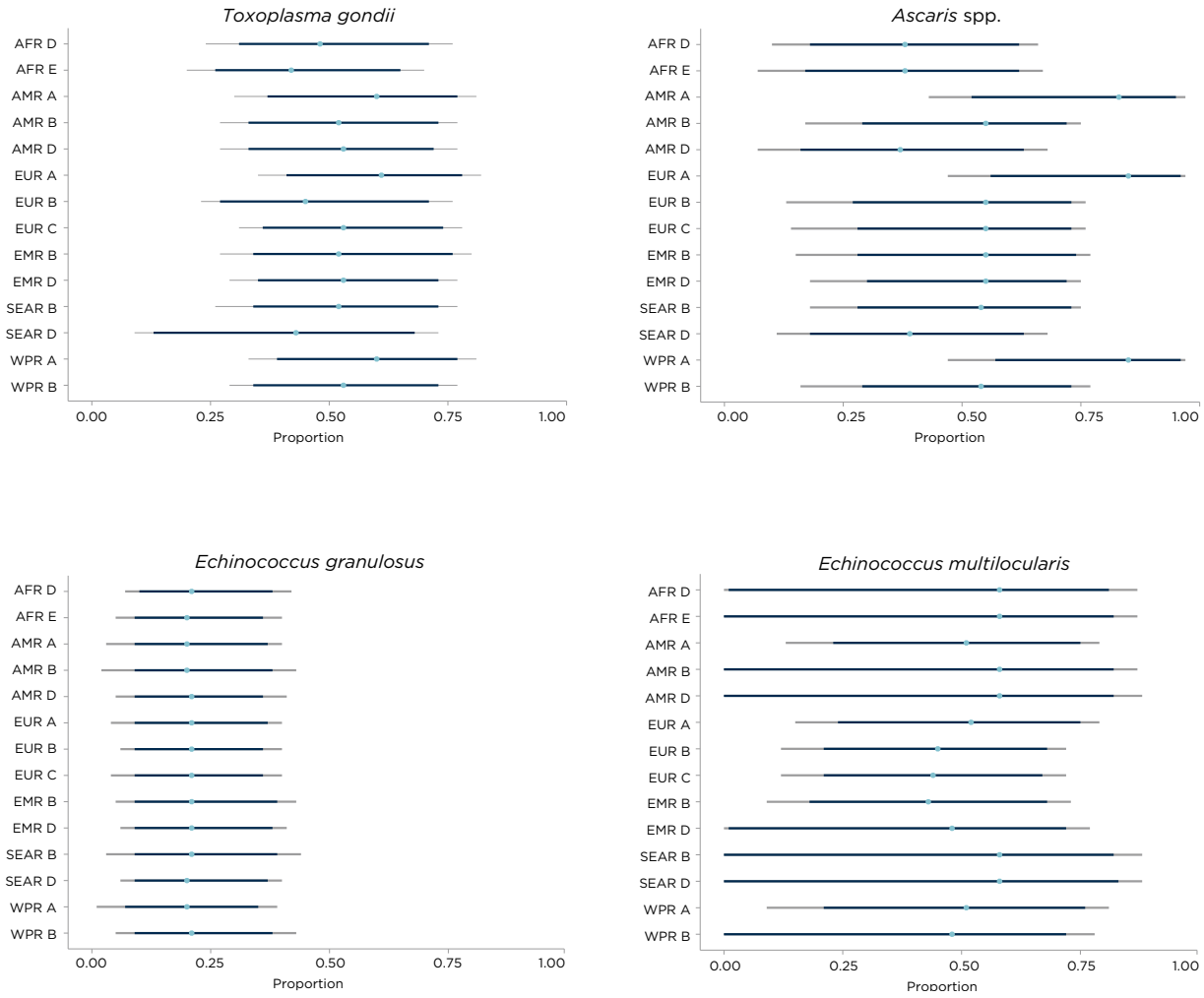
Notes: Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles.

Figure 7. Subregional estimates of the proportion of foodborne illnesses caused by typhoidal *Salmonella, Vibrio cholerae, Entamoeba histolytica,* norovirus, and hepatitis A virus.



Notes: Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles. HAV = Hepatitis A virus.

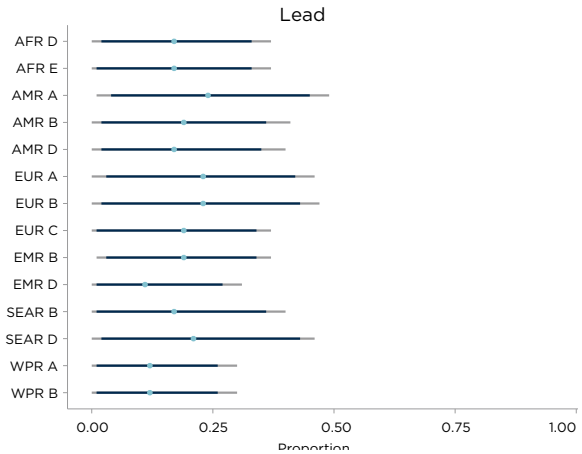
Figure 8. Subregional estimates of the proportion of foodborne illnesses caused by *Toxoplasma gondii, Echinococcus multilocularis, Echinococcus granulosus* and *Ascaris* spp.



Notes: Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles.

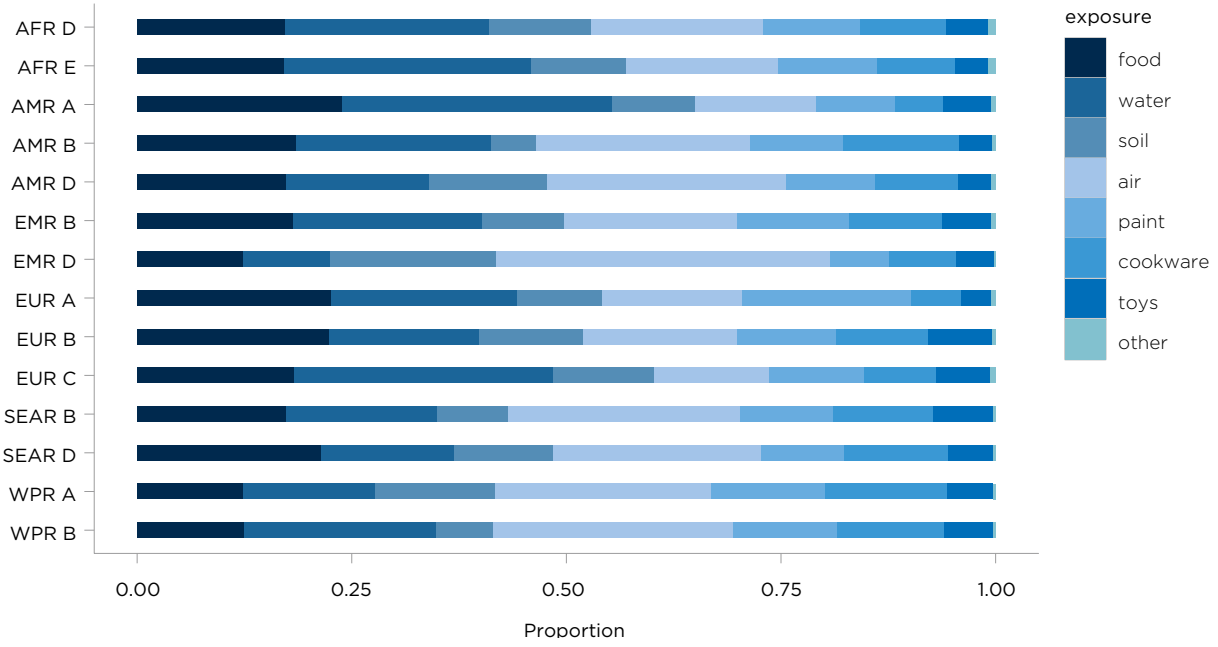
Figure 9 shows the subregional estimates of the foodborne proportion for lead exposure. Water, food and air exposure were the main transmission routes indicated by the experts with some subregional differences (Table A7.5 in Appendix 7). The foodborne route was assessed to be the most important only in two subregions in Europe. Air was assessed to be the main exposure route in seven of the 14 subregions and water in four regions. Soil, paint, cookware/pottery/glassware and toys were in comparison found to be of only minor importance in most subregions (Figure 10).

Figure 9. Subregional estimates of the proportion of disease caused by foodborne exposure to lead.



Notes: Indicated on the line plot are the 2.5th, 5th, 50th, 95th and 97.5th percentiles.

Figure 10. Subregional estimates (medians) of the proportion of disease caused by exposure to lead through eight different exposure routes.



5.2 DALY Estimates: Overview

Global disease burden

Of the approximately 600 million cases of illness caused by the 31 foodborne hazards in 2010 (see Table 7), infectious agents that cause diarrhoeal diseases accounted for the vast majority (550 million), in particular norovirus (120 million cases) and *Campylobacter* spp. (96 million cases). Among other hazards, hepatitis A virus, the helminth *Ascaris* spp. and the typhoid bacterium *Salmonella* Typhi were frequent causes of foodborne illness, causing 14, 12 and 7.6 million cases, respectively.

Foodborne diarrhoeal disease agents also caused 230,000 of the 420,000 deaths due to foodborne hazards (Table 7). Of these, non-typhoidal *S. enterica* accounted for 59,000, enteropathogenic *E. coli* (EPEC) for 37,000, norovirus for 35,000, and enterotoxigenic *E. coli* (ETEC) for 26,000 deaths. Of the 59,000 global deaths due to non-typhoidal *S. enterica*, 32,000 were in the two African subregions, and included 22,000 deaths due to invasive disease by this bacterium. The major non-diarrhoeal causes of foodborne deaths were due to *Salmonella* Typhi (52,000), the helminth *Taenia solium* (28,000) and hepatitis A virus (28,000) and aflatoxin with 20,000 (95% UI 8,000-51,000) deaths.

The global burden of FBD caused by the 31 hazards (including sequelae) in 2010 was 33 million DALYs (Table 7). Eighteen million DALYs, or 54%, of the total burden was attributed to diarrheal disease agents, particularly to non-typhoidal *S. enterica*, which was responsible for 4.0 million DALYs (Figure 11). Six diarrhoeal disease agents (norovirus, *Campylobacter* spp., EPEC, ETEC, *Vibrio cholerae* and *Shigella* spp.) each caused a foodborne burden of 1–3 million DALYs. Other foodborne hazards that contributed substantially to the global burden included *Salmonella* Typhi (3.7 million DALYs), *T. solium* (2.8 million DALYs), hepatitis A virus (1.4 million DALYs) and *Paragonimus* spp. (1.0 million DALYs). By contrast, the global burden of trichinellosis, due to the widespread nematode parasite *Trichinella*, was estimated at only 550 DALYs. For full details of results including foodborne illnesses, deaths, DALYs, YLLs and YLDs for all 31 hazards in this study, see the Supplementary Information for the overview publication [167]. The Supplementary Information also includes the results for total illnesses, deaths, DALYs, YLLs and YLDs by all exposure pathways, for all hazards that were included in the source attribution expert elicitation in Appendix 7.

Table 7. Median global number of foodborne illnesses, deaths, Years Lived with Disability (YLDs), Years of Life Lost (YLLs) and Disability Adjusted Life Years (DALYs), with 95% uncertainty intervals, 2010.

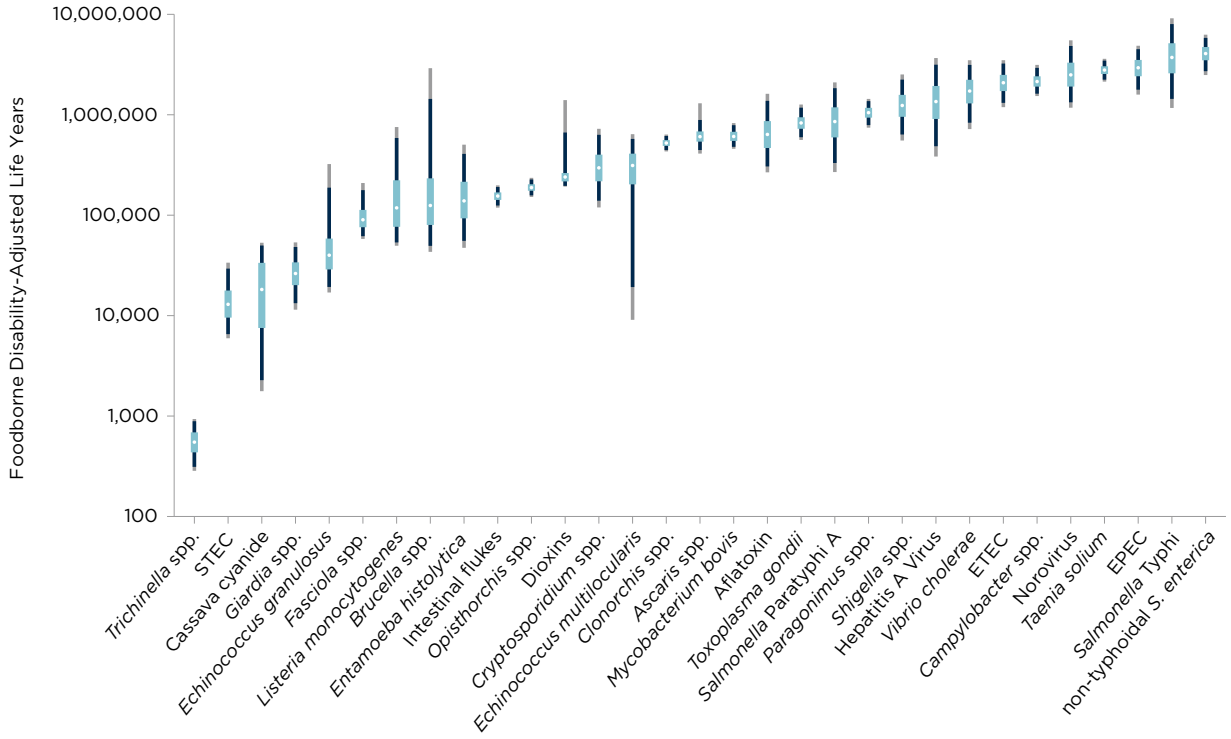
HAZARD	FOODBORNE ILLNESSES	FOODBORNE DEATHS	FOODBORNE YLDS	FOODBORNE YLLS	FOODBORNE DALYS
TOTAL	600 652 361 (417 646 804–962 834 044)	418 608 (305 128–598 419)	5 580 028 (4 780 374–8 195 314)	27 201 701 (19 655 451–38 922 210)	32 841 428 (24 809 085–46 274 735)
Diarrhoeal disease agents	548 595 679 (369 976 912–888 528 014)	230 111 (160 039–322 359)	839 463 (644 924–1 123 907)	16 821 418 (11 700 916–23 579 652)	17 659 226 (12 458 675–24 516 338)
Viruses	124 803 946 (70 311 254–251 352 877)	34 929 (15 916–79 620)	91 357 (51 047–174 130)	2 403 107 (1 102 397–5 387 672)	2 496 078 (1 175 658–5 511 092)
Norovirus	124 803 946 (70 311 254–251 352 877)	34 929 (15 916–79 620)	91 357 (51 047–174 130)	2 403 107 (1 102 397–5 387 672)	2 496 078 (1 175 658–5 511 092)
Bacteria	349 405 380 (223 127 469–590 002 559)	187 285 (131 742–254 037)	685 212 (521 848–921 335)	13 795 606 (9 688 221–18 893 580)	14 490 808 (10 303 551–19 681 271)
Campylobacter spp.	95 613 970 (51 731 379–177 239 714)	21 374 (14 604–32 584)	442 075 (322 192–587 072)	1 689 291 (1 141 055–2 652 483)	2 141 926 (1 535 985–3 137 980)
Enteropathogenic *E. coli*– EPEC	23 797 284 (10 750 919–62 931 604)	37 077 (19 957–61 262)	22 977 (9 662–66 211)	2 908 551 (1 574 520–4 833 325)	2 938 407 (1 587 757–4 865 590)
Enterotoxigenic *E. coli*– ETEC	86 502 735 (49 136 952–151 776 173)	26 170 (14 887–43 523)	70 567 (40 134–119 017)	2 011 635 (1 132 331–3 407 273)	2 084 229 (1 190 704–3 494 201)
Shiga toxin-producing *E. coli*– STEC	1 176 854 (754 108–2 523 007)	128 (55–374)	3 486 (1 741–6 996)	9 454 (4 140–27 208)	12 953 (5 951–33 664)
Non-typhoidal *S. enterica*	78 707 591 (31 843 647–211 154 682)	59 153 (36 341–89 045)	78 306 (35 961–185 179)	3 976 386 (2 410 953–6 180 921)	4 067 929 (2 486 092–6 271 290)
Shigella spp.	51 014 050 (20 405 214–118 927 631)	15 156 (6 839–30 072)	51 613 (21 184–114 267)	1 181 231 (519 372–2 445 834)	1 237 103 (554 204–2 520 126)
Vibrio cholerae	763 451 (310 910–1 567 682)	24 649 (10 304–50 042)	2 721 (1 019–6 020)	1 719 381 (718 642–3 487 195)	1 722 312 (720 029–3 491 997)
Protozoa	67 182 645 (35 794 977–120 556 797)	5 558 (2 593–11 958)	57 536 (30 526–102 608)	432 316 (195 372–960 910)	492 354 (239 400–1 034 790)
Cryptosporidium spp.	8 584 805 (3 897 252–18 531 196)	3 759 (1 520–9 115)	8 155 (3 598–17 355)	287 690 (114 012–711 990)	296 156 (119 456–724 660)
Entamoeba histolytica	28 023 571 (10 261 254–68 567 590)	1 470 (453–5 554)	20 851 (7 431–53 080)	115 740 (32 070–476 144)	138 863 (47 339–503 775)
Giardia spp.	28 236 123 (12 945 655–56 996 454)	0 (0–0)	26 270 (11 462–53 577)	0 (0–0)	26 270 (11 462–53 577)

HAZARD	FOODBORNE ILLNESSES	FOODBORNE DEATHS	FOODBORNE YLDS	FOODBORNE YLLS	FOODBORNE DALYS
Invasive infectious disease agents	35 770 163 (18 604 754–70 045 873)	117 223 (54 789–243 482)	1 098 675 (729 530–1 796 607)	6 960 656 (3 128 316–14 882 637)	8 065 581 (3 983 949–16 557 714)
Viruses	13 709 836 (3 630 847–38 524 946)	27 731 (7 169–77 320)	85 885 (22 118–250 641)	1 258 812 (325 409–3 509 844)	1 353 767 (383 684–3 672 726)
Hepatitis A virus	13 709 836 (3 630 847–38 524 946)	27 731 (7 169–77 320)	85 885 (22 118–250 641)	1 258 812 (325 409–3 509 844)	1 353 767 (383 684–3 672 726)
Bacteria	10 342 042 (3 506 116–27 627 480)	85 269 (37 573–196 544)	225 792 (108 092–604 162)	5 472 374 (2 283 968–12 803 285)	5 697 913 (2 394 245–13 384 811)
Brucella spp.	393 239 (143 815–9 099 394)	1 957 (661–45 545)	13 324 (4 095–315 952)	110 971 (37 470–2 583 081)	124 884 (43 153–2 910 416)
Listeria monocytogenes	14 169 (6 112–91 175)	3 175 (1 339–20 428)	2 255 (843–14 981)	116 109 (48 693–740 357)	118 340 (49 634–754 680)
Mycobacterium bovis	121 268 (99 852–150 239)	10 545 (7 894–14 472)	50 733 (38 441–68 052)	556 998 (417 711–761 851)	607 775 (458 364–826 115)
Salmonella Paratyphi A	1 741 120 (536 650–4 310 983)	12 069 (3 784–29 521)	26 987 (7 610–72 811)	829 136 (259 990–2 028 112)	855 730 (268 879–2 100 120)
Salmonella Typhi	7 570 087 (2 333 263–18 743 406)	52 472 (16 454–128 350)	117 334 (33 086–316 571)	3 604 940 (1 130 390–8 817 876)	3 720 565 (1 169 040–9 130 956)
Protozoa	10 280 089 (7 403 516–14 904 324)	684 (333–1 300)	763 326 (511 314–1 175 619)	62 899 (30 575–119 512)	829 071 (561 297–1 264 567)
Toxoplasma gondii	10 280 089 (7 403 516–14 904 324)	684 (333–1 300)	763 326 (511 314–1 175 619)	62 899 (30 575–119 512)	829 071 (561 297–1 264 567)
Helminths	12 928 944 (8 957 617–24 008 256)	45 226 (34 143–59 035)	3 367 987 (2 840 638–4 358 741)	2 428 929 (1 869 610–3 173 545)	5 810 589 (4 864 518–7 367 619)
Cestodes	430 864 (334 389–774 703)	36 500 (25 652–50 063)	1 220 578 (941 084–1 576 600)	1 932 154 (1 387 290–2 664 120)	3 158 826 (2 411 585–4 122 032)
Echinococcus granulosus	43 076 (25 881–371 177)	482 (150–3 974)	12 121 (5 515–99 213)	27 626 (8 577–227 715)	39 950 (16 996–322 953)
Echinococcus multilocularis	8 375 (656–17 005)	7 771 (243–15 896)	8 749 (856–22 576)	303 039 (8 102–622 954)	312 461 (9 083–640 716)
Taenia solium	370 710 (282 937–478 123)	28 114 (21 059–36 915)	1 192 236 (916 049–1 522 267)	1 586 288 (1 170 461–2 177 848)	2 788 426 (2 137 613–3 606 582)
Nematodes	12 285 286 (8 292 732–22 984 630)	1 012 (388–2 783)	518 451 (351 732–1 211 907)	80 021 (30 652–220 274)	605 738 (411 113–1 301 619)
Ascaris spp.	12 280 767 (8 287 414–22 980 491)	1 008 (384–2 781)	518 096 (351 418–1 211 691)	79 800 (30 426–220 154)	605 278 (410 668–1 301 114)
Trichinella spp.	4 472 (2 977–5 997)	4 (2–5)	342 (149–646)	210 (116–306)	550 (285–934)

HAZARD	FOODBORNE ILLNESSES	FOODBORNE DEATHS	FOODBORNE YLDS	FOODBORNE YLLS	FOODBORNE DALYS
Trematodes	218 569 (167 886–281 872)	7 533 (6 383–8 845)	1 616 785 (1 257 657–2 062 782)	403 884 (342 815–473 423)	2 024 592 (1 652 243–2 483 514)
Clonorchis sinensis	31 620 (21 515–45 059)	5 770 (4 728–6 988)	219 637 (149 514–312 718)	302 160 (247 586–366 036)	522 863 (431 520–635 232)
Fasciola spp.	10 635 (6 888–24 100)	0 (0–0)	90 041 (58 050–209 097)	0 (0–0)	90 041 (58 050–209 097)
Intestinal flukes*	18 924 (14 498–24 200)	0 (0–0)	155 165 (118 920–198 147)	0 (0–0)	155 165 (118 920–198 147)
Opisthorchis spp.	16 315 (11 273–22 860)	1 498 (1 230–1 813)	102 705 (70 849–143 938)	85 364 (70 123–103 317)	188 346 (151 906–235 431)
Paragonimus spp.	139 238 (95 610–195 078)	250 (160–371)	1 033 097 (730 118–1 423 031)	15 535 (9 971–23 035)	1 048 937 (743 700–1 438 588)
Chemicals and toxins	217 632 (172 024–1 140 463)	19 712 (8 171–51 664)	247 920 (196 490–1 410 260)	650 157 (283 769–1 617 168)	908 356 (506 112–2 714 588)
Aflatoxin	21 757 (8 967–56 776)	19 455 (7 954–51 324)	3 945 (1 551–10 667)	632 901 (265 578–1 606 493)	636 869 (267 142–1 617 081)
Cassava cyanide	1 066 (105–3 016)	227 (22–669)	2 521 (249–7 142)	15 694 (1 514–46 304)	18 203 (1 769–53 170)
Dioxin	193 447 (155 963–1 085 675)	0 (0–0)	240 056 (192 608–1 399 562)	0 (0–0)	240 056 (192 608–1 399 562)

Notes: * Includes selected species of the families Echinostomatidae, Fasciolidae, Gymnophallidae, Heterophyidae, Nanophyetidae, Neodiplostomidae and Plagiorchiidae (depending on data availability).

Figure 11. Ranking of foodborne hazards, based on Disability-Adjusted Life Years at the global level, with 95% uncertainty intervals, 2010.



Notes: White dots indicate the median burden, black boxes the inter-quartile range (50% UI), black lines the 5 and 95 percentiles (90% UI) and grey lines the 2.5 and 97.5 percentiles (95% UI). Note that the y-axis is on a logarithmic scale. Abbreviations: EPEC = Enteropathogenic *Escherichia coli*; ETEC = Enterotoxigenic *E. coli*; STEC = Shiga toxin-producing *E. coli*.

Regional differences

The studies found considerable regional differences in the burden of FBD (Table 8 and Figure 12). The highest burden per 100,000 population was observed in the two African subregions: 1,300 DALYs per 100,000 population in AFR D and 1,200 DALYs per 100,000 population in AFR E. In the South-East Asian subregions, SEAR B and SEAR D, the burden was 690 and 710 DALYs per 100,000 population, respectively, and in the Eastern Mediterranean subregion, EMR D, 570 DALYs per 100,000 population. The lowest burden was observed in the North American subregion AMR A (35 DALYs per 100,000 population), followed by the three European subregions EUR A, EUR B and EUR C, and the Western Pacific subregion WPR A (which includes Australia, New Zealand and Japan), which were all in the range of 40-50 DALYs per 100,000 population. Other subregions (AMR B and AMR D, EMR B and WPR B) had intermediate burdens, all in the range of 140-360 DALYs per 100,000 population (see Table 2 for a full list of the countries in each subregion).

The contribution of individual hazards to the burden of FBD differed markedly between subregions (Figure 12). In both African subregions, nearly 70% of the burden was due to diarrhoeal disease agents, particularly to non-typhoidal *S. enterica* (including invasive salmonellosis), EPEC, and ETEC; additionally, *V. cholerae* caused an important burden of diarrhoeal disease in the AFR E subregion, and *T. solium* caused a high burden in both African

subregions (see Table 8 for the detailed data for all hazards and all subregions). In the SEAR D and SEAR B subregions, diarrhoeal disease agents contributed approximately 50% of the total disease burden, mainly caused by a range of hazards including EPEC, norovirus, non-typhoidal *S. enterica*, ETEC and *Campylobacter* spp. In both of these subregions, there was also a considerable burden of *Salmonella* Typhi (180 DALYs per 100,000 population in SEAR B and 110 DALYs per 100,000 population in SEAR D). The burden of disease due to the fluke *Opisthorchis* spp. was almost exclusively concentrated in SEAR B (40 DALYs per 100,000 population). In EMR D, diarrhoeal disease agents were responsible for approximately 70% of the total burden of FBD, with *Campylobacter* spp. the leading cause in the region, followed by EPEC, non-typhoidal *S. enterica*, *Shigella* spp. and ETEC. Other important hazards in this region were *Salmonella* Typhi, aflatoxin and hepatitis A virus.

In the WPR B subregion, diarrhoeal disease agents accounted for approximately 14% of the FBD burden, with *Campylobacter* spp. the leading cause. In this region, the seafoodborne trematodes *Paragonimus* spp. and *Clonorchis sinensis* were important contributors to the FBD burden. In the AMR B and AMR D subregions, the contribution of diarrhoeal disease agents to the total burden was smaller than in other subregions (approximately 40% and 20%, respectively), with *Campylobacter* spp., norovirus and non-typhoidal *S. enterica* causing most burden. In the AMR B region, important causes of FBD burden were *T. solium* (25 DALYs per 100,000 population) and *T. gondii* (20 DALYs per 100,000 population). In the AMR D region, the burden of *T. solium* was particularly high at 69 DALYs per 100,000 population; the trematodes *Paragonimus* spp. and *Fasciola* spp. contributing 53 and 46 DALYs per 100,000 population, respectively to the overall disease burden.

The burden due to chemical hazards was also highly localized. Aflatoxin caused the highest burden in AFR D, WPR B and SEAR B, whereas dioxins caused the highest burden in SEAR D, EMR B and D and EUR A. The burden of cassava cyanide was limited to the AFR regions, and was similar to that of aflatoxin in AFR D.

In the three European subregions, diarrhoeal disease agents contributed to 49-68% of the total burden of FBD, with non-typhoidal *S. enterica* and *Campylobacter* spp. being the most important hazards. Other important hazards included *T. gondii* in all European subregions, *Brucella* spp. in the EUR B and *Mycobacterium bovis* in the EUR C subregions. In the WPR A region, 65% of the burden was caused by diarrhoeal disease agents, with *T. gondii* and hepatitis A virus also contributing. Finally, in the AMR A region, diarrhoeal disease agents contributed approximately 67% of the total burden, with non-typhoidal *S. enterica* and *Campylobacter* spp. the most important hazards; *T. gondii* and *L. monocytogenes* were also relatively important.

Table 8. Median rates of foodborne Disability Adjusted Life Years (DALYs) per 100 000 population, by subregion, with 95% uncertainty intervals, 2010.

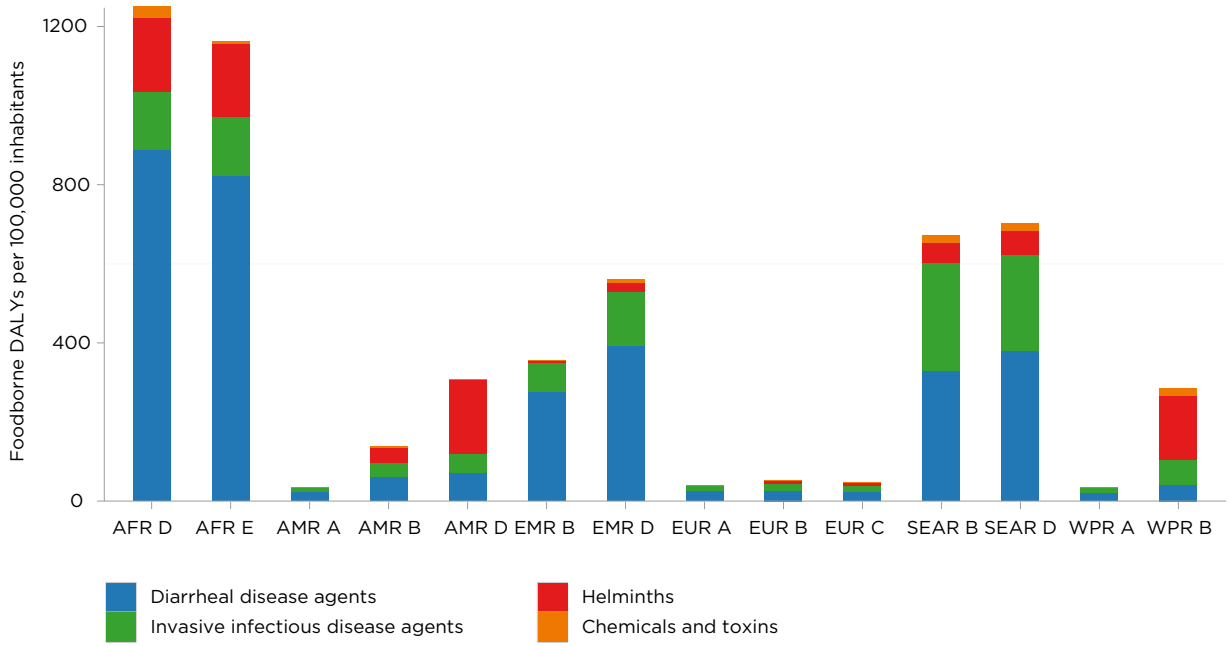
HAZARD	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B
TOTAL	1 276 (459–2263)	1 179 (726–1764)	35 (23–49)	140 (97–274)	315 (243–575)	362 (205–582)	571 (325–954)	41 (29–64)	52 (33–136)	49 (33–77)	685 (360–1291)	711 (343–1335)	36 (23–170)	293 (219–406)
Diarrhoeal disease agents	889 (196–1 731)	824 (447–1 326)	23 (13–33)	60 (36–94)	72 (40–117)	277 (153–460)	393 (217–644)	28 (17–39)	25 (14–37)	24 (13–35)	330 (154–576)	380 (159–717)	23 (14–32)	41 (21–65)
Viruses	75 (6–222)	76 (0–225)	3 (0.6–8)	12 (0–38)	13 (0–43)	28 (0.5–79)	33 (0.4–90)	4 (0–11)	3 (0.08–9)	3 (0.2–9)	55 (0–224)	69 (0.8–263)	3 (0.09–7)	4 (0–19)
Norovirus	75 (6–222)	76 (0–225)	3 (0.6–8)	12 (0–38)	13 (0–43)	28 (0.5–79)	33 (0.4–90)	4 (0–11)	3 (0.08–9)	3 (0.2–9)	55 (0–224)	69 (0.8–263)	3 (0.09–7)	4 (0–19)
Bacteria	787 (186–1 482)	712 (393–1 160)	19 (10–28)	45 (26–68)	54 (28–87)	237 (124–403)	347 (190–576)	24 (14–32)	21 (11–32)	20 (10–29)	247 (107–429)	285 (119–506)	19 (11–27)	34 (17–54)
Campylobacter spp.	71 (35–119)	70 (33–117)	9 (5–14)	15 (8–23)	15 (8–26)	75 (40–109)	97 (54–143)	10 (6–14)	8 (4–13)	8 (4–12)	37 (14–87)	33 (2–84)	9 (5–14)	10 (4–17)
Enteropathogenic *E. coli*–*EPEC*	136 (11–329)	138 (6–327)	0.006 (0.001–0.02)	7 (0.4–21)	9 (0.9–26)	46 (9–114)	60 (8–151)	0.006 (0.001–0.02)	0.004 (0–0.01)	0.004 (0–0.01)	64 (3–144)	65 (1–162)	0.006 (0.001–0.02)	5 (0.3–13)
Enterotoxigenic *E. coli*–*ETEC*	107 (26–245)	105 (17–240)	0.003 (0–0.009)	7 (1–19)	9 (2–25)	29 (6–78)	37 (5–102)	0.004 (0–0.01)	0.004 (0–0.01)	0.004 (0–0.01)	42 (3–106)	42 (2–111)	0.003 (0–0.01)	4 (0.3–11)
Shiga toxin-producing *E. coli*	0.009 (0.002–0.03)	0.08 (0.02–0.2)	0.2 (0.05–0.3)	0.4 (0.09–1)	0.5 (0.2–1)	0.2 (0.09–0.4)	0.2 (0.1–0.5)	0.6 (0.2–1)	0.07 (0.02–0.2)	0.1 (0.03–0.4)	0.2 (0.02–1)	0.2 (0.007–1)	0.4 (0.1–1)	0.01 (0.002–0.04)
Non-typhoidal *S. enterica*	338 (94–612)	193 (44–336)	9 (4–16)	11 (2–20)	14 (4–26)	50 (17–82)	67 (26–112)	12 (7–18)	12 (6–21)	11 (5–19)	59 (22–154)	58 (0–162)	9 (5–14)	9 (4–16)
Shigella spp.	37 (0–156)	37 (0–148)	0.2 (0–1)	2 (0–8)	2 (0–9)	27 (0–109)	37 (0–145)	0.09 (0–0.9)	0.1 (0–1)	0.2 (0–1)	25 (0.6–84)	25 (0.7–90)	0.2 (0–1)	4 (0.1–11)
Vibrio cholerae	70 (2–197)	143 (4–383)	0 (0–0)	0 (0–0)	0 (0–0)	0.2 (0.009–0.5)	28 (0.9–96)	0 (0–0)	0 (0–0)	0 (0–0)	2 (0.2–3)	36 (0.2–133)	0 (0–0)	0.1 (0.005–0.4)
Protozoa	20 (0–74)	21 (5–66)	0.2 (0.01–1)	2 (0.4–6)	3 (0.5–8)	6 (0.9–27)	7 (1–33)	0.2 (0–0.8)	0.2 (0–0.9)	0.2 (0–0.9)	10 (2–35)	10 (2–39)	0.2 (0–0.9)	1 (0.2–4)
Cryptosporidium spp.	12 (0–44)	12 (0–45)	0.2 (0.01–0.9)	0.7 (0.08–3)	1 (0.1–5)	3 (0–21)	3 (0–24)	0.1 (0–0.8)	0.1 (0–0.8)	0.1 (0–0.8)	6 (0–28)	6 (0–32)	0.1 (0–0.8)	0.3 (0–3)
Entamoeba histolytica	5 (0–41)	5 (0–41)	0 (0–0)	0.4 (0–2)	0.4 (0–3)	2 (0–12)	2 (0–17)	0 (0–0)	0 (0–0)	0 (0–0)	2 (0–17)	2 (0–18)	0 (0–0)	0.3 (0–1)
Giardia spp.	0.7 (0–3)	0.7 (0–3)	0.03 (0–0.1)	0.4 (0–2)	0.5 (0.01–3)	0.4 (0–2)	0.6 (0.005–2)	0.03 (0–0.1)	0.03 (0–0.1)	0.03 (0–0.1)	0.1 (0–0.9)	0.1 (0–1)	0.03 (0–0.1)	0.3 (0–1)

HAZARD	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B
Invasive infectious disease agents	146 (46–342)	147 (55–343)	10 (6–14)	38 (16–76)	49 (19–144)	73 (32–148)	137 (38–334)	10 (7–15)	19 (9–61)	16 (10–29)	272 (71–721)	244 (38–623)	10 (5–132)	65 (19–145)
Viruses	27 (4–77)	18 (3–55)	0.5 (0.07–2)	1 (0.1–4)	2 (0.2–7)	2 (0.2–5)	32 (2–102)	0.8 (0.03–2)	1 (0.2–3)	1 (0.3–4)	5 (0.6–15)	58 (6–182)	1 (0.07–3)	5 (0.3–17)
Hepatitis A virus	27 (4–77)	18 (3–55)	0.5 (0.07–2)	1 (0.1–4)	2 (0.2–7)	2 (0.2–5)	32 (2–102)	0.8 (0.03–2)	1 (0.2–3)	1 (0.3–4)	5 (0.6–15)	58 (6–182)	1 (0.07–3)	5 (0.3–17)
Bacteria	93 (31–259)	104 (40–277)	4 (2–7)	16 (4–47)	19 (5–65)	50 (16–121)	82 (22–241)	3 (3–5)	8 (3–39)	5 (3–10)	251 (59–696)	165 (27–490)	3 (1–126)	50 (12–124)
Brucella spp.	2 (0.2–53)	0.3 (0.007–18)	0.07 (0.02–0.6)	1 (0.3–16)	2 (0.2–38)	23 (3–83)	4 (0.6–68)	0.3 (0.07–1)	4 (0.7–35)	0.8 (0.07–6)	0.8 (0.004–112)	0.7 (0.003–92)	0.6 (0.02–125)	0.6 (0.09–9)
Listeria mono-cytogenes	1 (0–21)	1 (0–21)	3 (2–5)	2 (0.2–17)	1 (0–21)	1 (0–21)	1 (0–21)	3 (2–4)	0.3 (0.2–0.8)	0.6 (0.3–2)	1 (0–21)	1 (0–21)	1 (0.7–2)	1 (1–4)
Myco-bacterium bovis	25 (15–39)	34 (21–48)	0.03 (0.01–0.06)	0.4 (0.2–0.8)	2 (0.8–4)	1 (0.5–3)	13 (6–25)	0.08 (0.06–0.1)	0.6 (0.5–1)	3 (2–5)	11 (4–27)	14 (6–27)	0.1 (0.08–0.2)	3 (1–5)
Salmonella Paratyphi A	11 (0–39)	12 (0–43)	0.1 (0–0.4)	2 (0–6)	2 (0.006–7)	3 (0–12)	10 (0–36)	0.02 (0–0.1)	0.3 (0–2)	0.01 (0–0.06)	42 (7–120)	26 (0.6–80)	0.1 (0–0.5)	8 (1–22)
Salmonella Typhi	47 (0–169)	52 (0–187)	0.4 (0–2)	7 (0–27)	8 (0.03–29)	14 (0–51)	45 (0–158)	0.09 (0–0.6)	2 (0–9)	0.04 (0–0.3)	184 (32–522)	113 (3–347)	0.6 (0–2)	36 (6–95)
Protozoa	21 (8–41)	20 (9–37)	5 (2–8)	20 (9–33)	27 (10–84)	20 (10–35)	18 (9–31)	6 (3–9)	10 (5–23)	10 (5–18)	13 (6–22)	9 (2–19)	5 (3–8)	9 (4–14)
Toxoplasma gondii	21 (8–41)	20 (9–37)	5 (2–8)	20 (9–33)	27 (10–84)	20 (10–35)	18 (9–31)	6 (3–9)	10 (5–23)	10 (5–18)	13 (6–22)	9 (2–19)	5 (3–8)	9 (4–14)
Helminths	186 (125–308)	184 (141–240)	1 (0.9–4)	36 (27–134)	185 (149–229)	5 (2–15)	21 (12–40)	0.4 (0.2–1)	6 (3–27)	6 (4–15)	52 (42–64)	60 (45–80)	2 (1–3)	162 (131–202)
Cestodes	172 (112–289)	178 (136–235)	0.4 (0.3–0.6)	25 (19–34)	71 (53–95)	1 (0.2–10)	0.7 (0.1–19)	0.2 (0.05–0.5)	4 (2–25)	4 (2–12)	3 (2–5)	46 (34–61)	0.03 (0.007–0.8)	45 (25–65)
Echinococcus granulosus	0.4 (0.06–21)	0.8 (0.2–16)	0.01 (0.002–0.03)	0.3 (0.02–5)	2 (0.4–8)	0.9 (0.2–10)	0.6 (0.1–19)	0.1 (0.02–0.4)	2 (0.5–6)	0.5 (0.09–1)	0.001 (0–0.1)	0.8 (0.2–3)	0.02 (0.001–0.8)	0.3 (0.08–0.9)
Echinococcus multilocularis	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.03 (0.005–0.06)	0.005 (0–0.05)	0.03 (0.008–0.06)	2 (0.5–21)	2 (0.5–11)	0 (0–0)	0.007 (0–0.04)	0.008 (0.001–0.02)	18 (0–37)
Taenia solium	170 (110–283)	176 (134–229)	0.4 (0.3–0.6)	25 (19–32)	69 (51–91)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.9 (0.6–2)	3 (2–5)	45 (33–60)	0 (0–0)	27 (20–35)
Nematodes	13 (2–28)	5 (1–11)	0.6 (0.3–0.9)	11 (3–106)	12 (3–24)	3 (1–7)	13 (4–20)	0.04 (0.02–0.07)	1 (0.3–2)	1 (0.4–2)	8 (2–15)	13 (4–26)	0.004 (0.001–0.007)	11 (3–22)
Ascaris spp.	13 (2–28)	5 (1–11)	0.6 (0.3–0.9)	11 (3–106)	12 (3–24)	3 (1–7)	13 (4–20)	0 (0–0)	1 (0.3–2)	1 (0.3–2)	8 (2–15)	13 (4–26)	0 (0–0)	11 (3–22)
Trichinella spp.	0.001 (0–0.002)	0.001 (0–0.002)	0.009 (0.005–0.01)	0.009 (0.005–0.01)	0.009 (0.005–0.01)	0 (0–0)	0 (0–0)	0.04 (0.02–0.07)	0.04 (0.02–0.07)	0.04 (0.02–0.07)	0 (0–0.001)	0 (0–0.001)	0.004 (0.001–0.007)	0.004 (0.001–0.007)

HAZARD	AFR D	AFR E	AMR A	AMR B	AMR D	EMR B	EMR D	EUR A	EUR B	EUR C	SEAR B	SEAR D	WPR A	WPR B
Trematodes	0.06 (0.02–0.2)	0.02 (0.008–0.07)	0.2 (0.04–3)	0.1 (0.04–0.5)	101 (74–135)	0.3 (0.2–0.5)	7 (4–10)	0.2 (0.05–0.6)	0.2 (0.05–0.6)	1 (0.8–1)	40 (32–50)	0.7 (0.2–2)	2 (1–2)	106 (85–131)
Clonorchis sinensis	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.04 (0.03–0.04)	0.01 (0.003–0.04)	0.04 (0.01–0.2)	0.05 (0.01–0.2)	31 (26–38)
Fasciola spp.	0.02 (0.008–0.07)	0.01 (0.005–0.04)	0.04 (0.001–2)	0.04 (0.02–0.1)	46 (27–75)	0.2 (0.1–0.3)	7 (4–10)	0.07 (0.02–0.2)	0.06 (0.02–0.2)	0.04 (0.01–0.1)	0.02 (0.008–0.05)	0.05 (0.02–0.1)	0.07 (0.01–0.4)	0.9 (0.1–8)
Intestinal flukes*	0.01 (0.005–0.04)	0 (0–0)	0.1 (0.04–0.5)	0.06 (0.02–0.2)	0 (0–0)	0.06 (0.02–0.2)	0.08 (0.03–0.2)	0.03 (0.009–0.09)	0.05 (0.02–0.2)	0.09 (0.03–0.2)	0.2 (0.1–0.5)	0.1 (0.03–0.4)	1 (0.9–2)	9 (7–11)
Opisthorchis spp.	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.07 (0.02–0.3)	0.05 (0.01–0.3)	0.9 (0.6–1)	40 (32–50)	0.4 (0.1–1)	0 (0–0)	3 (2–4)
Paragonimus spp.	0.03 (0.008–0.08)	0.008 (0.002–0.02)	0.04 (0.004–0.6)	0.04 (0.01–0.1)	53 (38–73)	0 (0–0)	0.02 (0.008–0.07)	0 (0–0)	0 (0–0)	0.03 (0.01–0.1)	0.05 (0.008–0.5)	0.06 (0.02–0.2)	0.05 (0.02–0.2)	60 (43–83)
Chemicals and toxins	30 (8–85)	7 (3–21)	0.4 (0.2–3)	3 (0.7–16)	2 (0.09–159)	0.8 (0.3–14)	9 (4–66)	2 (1–22)	0.9 (0.4–25)	2 (2–9)	20 (4–75)	18 (13–52)	0.3 (0.06–13)	18 (3–71)
Aflatoxin	28 (7–78)	3 (1–8)	0.04 (0.006–0.2)	3 (0.6–9)	2 (0.07–137)	0.7 (0.2–3)	5 (1–17)	0.3 (0.1–0.7)	0.6 (0.3–1)	0.5 (0.2–2)	18 (3–52)	4 (0.6–15)	0.2 (0.04–0.8)	17 (3–69)
Cassava cyanide	1 (0.1–3)	3 (0.3–9)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Dioxin	0.2 (0.05–6)	0.2 (0.09–9)	0.3 (0.1–3)	0.1 (0.03–11)	0.2 (0.01–23)	0.09 (0.004–11)	3 (2–56)	2 (1–22)	0.3 (0.09–24)	2 (1–8)	0.2 (0.005–45)	14 (12–40)	0.1 (0.02–12)	0.06 (0.006–5)

Notes: * Includes selected species of the families Echinostomatidae, Fasciolidae, Gymnophallidae, Heterophyidae, Nanophyetidae, Neodiplostomidae and Plagiorchiidae (depending on data availability).

Figure 12. The global burden of foodborne disease (DALYS per 100 000 population) by hazard groups and by subregion, 2010.



The relative contribution of mortality (measured as YLL) and morbidity (measured as YLD) to the total burden of disease varied widely between hazards (Figure 13). For 18 foodborne hazards, more than 75% of the total burden was due to premature mortality (red columns in Figure 13). These mainly include hazards leading to diseases with known high case-fatality ratios (non-typhoidal *S. enterica*, EPEC, ETEC, *Shigella* spp. and *V. cholerae*, *Listeria monocytogenes*, *Salmonella* Typhi and *Salmonella* Paratyphi, *Echinococcus multilocularis* and aflatoxin). At the other extreme, more than 75% of the total burden due to morbidity (blue columns in Figure 2) were accounted for by seven foodborne hazards, of which four (*Giardia* spp., *Fasciola* spp., intestinal flukes, and dioxin) were not assumed to cause fatal illnesses.

Figure 13. Relative contribution of Years of Life Lost due to premature mortality (YLL) and Years Lived with Disability (YLD) to the global burden of 31 hazards in food, 2010.

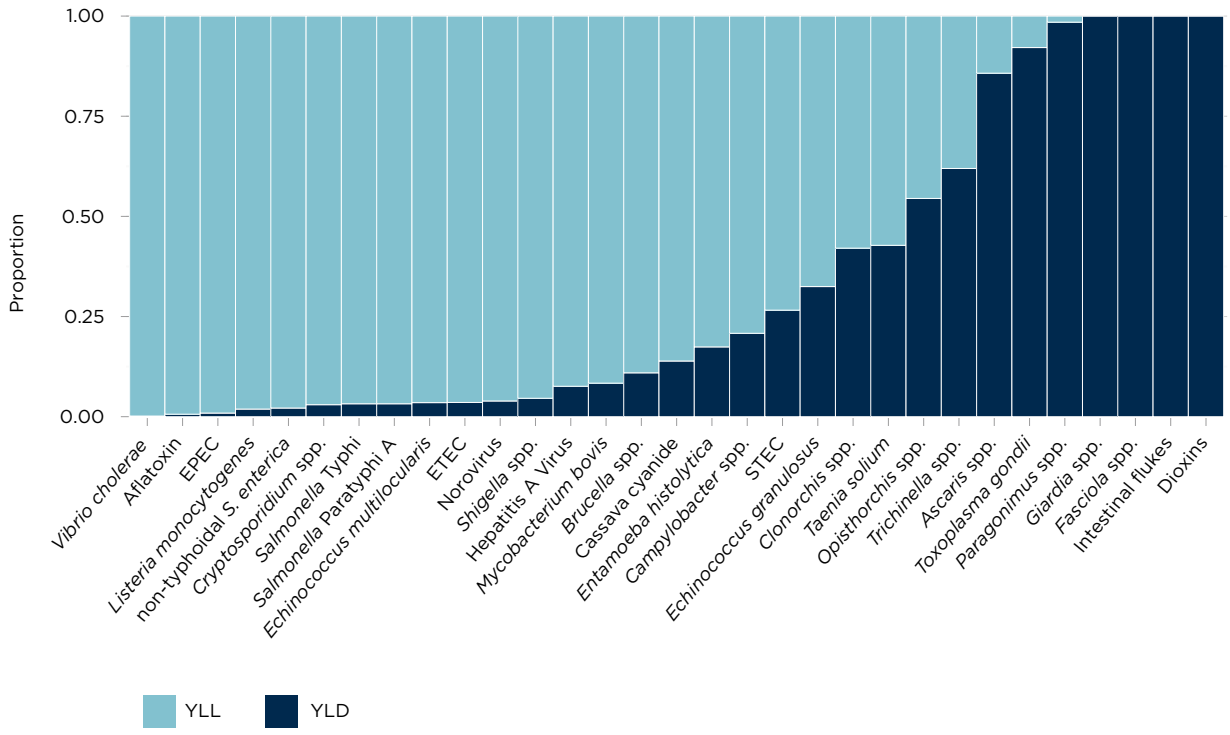
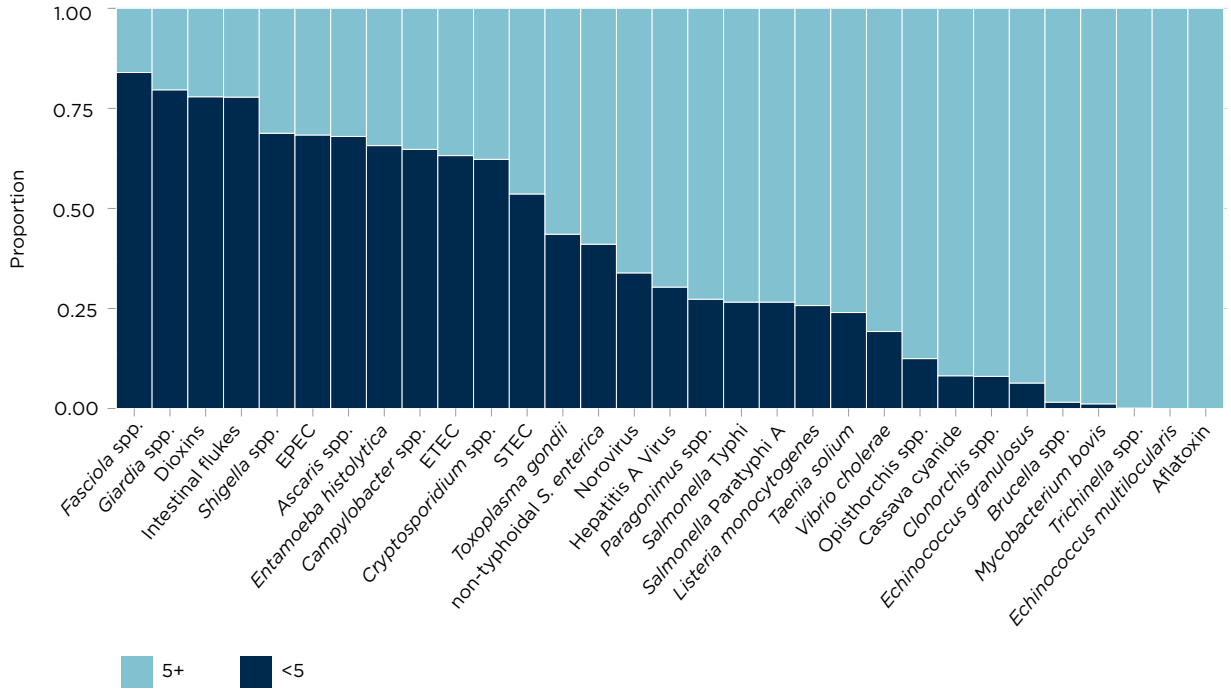


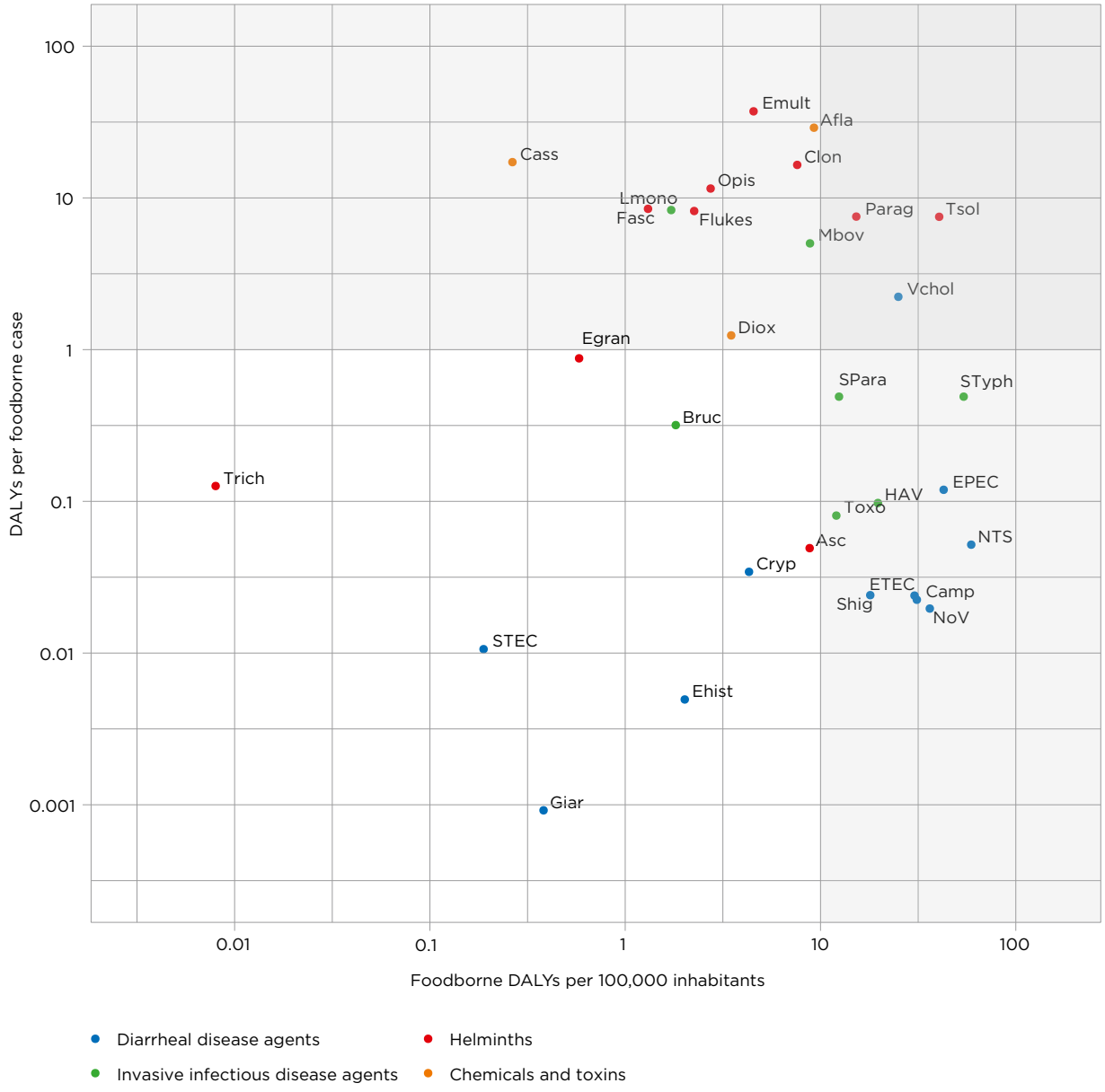
Figure 14. Age-distribution of disability adjusted life years for 31 hazards contributing to the global burden of foodborne disease, 2010.



The FERG studies show that children under five years old bear 40% of the foodborne disease burden (including, for some hazards, the life-long burden of sequelae). More than 75% of the burden of four hazards (*Fasciola* spp., *Giardia* spp., dioxins, and intestinal flukes) occurred among children under five (Figure 14). Prenatal infections accounted for 21% of the burden of *L. monocytogenes* and for 32% of the burden of *Toxoplasma gondii*. By contrast, more than 75% of the burden of 11 hazards occurred among people over five years old.

Figure 15 presents a scatterplot of the burden at individual level (DALYs per case, a measure for disease severity) and the burden at population level (foodborne DALYs per 100,000 population, also accounting for disease incidence), including uncertainty intervals. On the basis of this plot, hazards were divided by two criteria with arbitrary cut-offs as indicated by grey-shaded areas in the Figure. *V. cholerae*, *T. solium* and *Paragonimus* spp. were in the H/H category. All other diarrheal disease agents were in the H/L category, except STEC, *E. histolytica* and *Giardia* spp. (L/L). The L/L category further included *Trichinella* spp. The L/H category contained agents that are of relatively low global impact but have a high impact on affected individuals. These included different parasites, particularly *E. multilocularis*, the invasive bacteria *Brucella* spp., *L. monocytogenes* and *M. bovis*. In subregions where the burden is higher than the global average, these agents are of specific relevance to policy makers.

Figure 15. Scatterplot of the global burden of foodborne disease per 100 000 population and per incident case.



Abbreviations: NoV = Norovirus; Camp = *Campylobacter* spp.; EPEC = Enteropathogenic *Escherichia coli*; ETEC = Enterotoxigenic *E. coli*; STEC = Shiga toxin-producing *E. coli*; NTS = non-typhoidal *Salmonella enterica*; Shig = *Shigella* spp.; Vchol; *Vibrio cholerae*; Ehist = *Entamoeba histolytica*; Cryp = *Cryptosporidium* spp.; Giar = *Giardia* spp.; HAV = Hepatitis A virus; Bruc = *Brucella* spp.; Lmono = *Listeria monocytogenes*; Mbov = *Mycobacterium bovis*; SPara = *Salmonella* Paratyphi A; STyph = *Salmonella* Typhi; Toxo = *Toxoplasma gondii*; Egran = *Echinococcus granulosus*; Emult = *E. multilocularis*; Tsol = *Taenia solium*; Asc = *Ascaris* spp.; Trich = *Trichinella* spp.; Clon = *Clonorchis sinensis*; Fasc = *Fasciola* spp.; Flukes = Intestinal flukes; Opis = *Opisthorchis* spp.; Parag = *Paragonimus* spp.; Diox = Dioxin; Afla = Aflatoxin.

5.3 DALY Estimates: Enteric diseases

It was estimated that the 22 diseases in the enteric disease study caused 2.0 billion (95% UI 1.5–3.0 billion) illnesses in 2010, 39% of which (95% UI 26–53%) were in children <5 years of age. Among the 1.9 billion cases of diarrhoeal diseases, norovirus was responsible for 684 million illnesses– the largest number of cases for any pathogen (Table A8.1 in Appendix 8). The pathogens resulting in the next largest number of cases were ETEC, *Shigella* spp., *Giardia* spp., *Campylobacter* spp. and non-typhoidal *Salmonella* spp. *Campylobacter* spp. cases included almost 32 000 GBS cases. There were also 2.48 million STEC cases, which included 3610 with HUS and 253 with ESRD. Among the extra-intestinal diseases, the pathogens resulting in the most infections were hepatitis A virus, *S.* Typhi and *S.* Paratyphi A. *Brucella* spp. resulted in 0.83 million illnesses, which included almost 333 000 chronic infections and 83 300 episodes of orchitis. *L. monocytogenes* resulted in 14 200 illnesses which included 7830 cases of septicaemia, 3920 cases of meningitis, and 666 cases with neurological sequelae.

Overall, 29% (95% UI 23–36%) of all 22 diseases were estimated to be transmitted by contaminated food, equating to 582 million (95% UI 400–922 million) foodborne cases in 2010; of which 38% (95% UI 24–53%) in children <5 years of age. The pathogens resulting in the most foodborne cases were norovirus, *Campylobacter* spp., ETEC, non-typhoidal *Salmonella* spp., and *Shigella* spp. A high proportion of foodborne infections caused by *V. cholerae*, *S.* Typhi, and *S.* Paratyphi A occurred in the African region (Table A8.2 in Appendix 8). A high proportion of foodborne infections caused by EPEC, *Cryptosporidium* spp. and *Campylobacter* spp. occurred among children <5 years of age (Table A8.3 in Appendix 8) Among the 11 diarrhoeal diseases, the rate ratio of foodborne cases occurring among children <5 years of age compared with those >5 years of age was 6.44 (95% UI 3.15–12.46).

It was estimated that the 22 diseases in the enteric diseases study caused 1.09 million (95% UI 0.89–1.37 million) deaths in 2010, of which 34% (95% UI 29–38%) in children <5 years of age. Among the diarrhoeal diseases, norovirus was responsible for the most deaths. Other diarrhoeal pathogens responsible for large numbers of deaths were EPEC, *V. cholerae* and *Shigella* spp. The 37 600 deaths attributed to *Campylobacter* spp. included 1310 deaths from GBS. Among the extra-intestinal enteric diseases, the pathogens resulting in the most deaths were *S.* Typhi, hepatitis A virus, iNTS and *S.* Paratyphi A.

Overall, the 22 diseases in the enteric diseases study resulted in 351 000 (95% UI 240 000–524 000) deaths due to contaminated food in 2010; with 33% (95% UI 27–40%) in children <5 years of age. The enteric pathogens resulting in the most foodborne deaths were *S.* Typhi, EPEC, norovirus, iNTS, non-typhoidal *Salmonella* spp. and hepatitis A. The mortality rates of foodborne diseases were consistently highest in the African subregions, followed by the South Eastern Asian subregions (Table A8.2 in Appendix 8) Among the 11 diarrhoeal diseases due to contaminated food, the rate ratio of deaths in children <5 years of age compared with those >5 years of age was 8.37 (95% UI 5.90–11.4). For all 22 diseases, the rate ratio of deaths in children <5 years of age compared with those >5 years of age was 4.85 (95% UI 3.54–6.59).

It was estimated that the 22 diseases in the enteric diseases study caused 78.7 million (95% UI 65.0–97.7 million) DALYS in 2010, of which 43% (95% UI 38–48%) in children <5 years of age. The pathogens resulting in the most DALYs were norovirus, *S.* Typhi, EPEC, *V. cholerae*, ETEC, and hepatitis A (Table A8.1 in Appendix 8).

The rates of foodborne DALYs per 100 000 population are shown by hazard and by subregion in Table A8.2 in Appendix 8.

It was estimated that the 22 diseases in the enteric diseases study resulted in 25.2 million (95% UI 17.5–37.0 million) DALYs due to contaminated food; 43% (95% UI 36–50%) in children <5 years of age. Figure 17 shows the relative burden of foodborne enteric infections, if iNTS and non-typhoidal *Salmonella* spp. were grouped together. The pathogen resulting in the most foodborne DALYs was non-typhoidal *Salmonella* spp., if iNTS were included (4.07 million). Other pathogens resulting in substantial foodborne DALYs included: *S.* Typhi, EPEC, norovirus and *Campylobacter* spp. The rates of DALYs for foodborne diseases were highest in the African subregions. Overall, the 22 diseases transmitted by contaminated food resulted in 10.8 million (95% UI 7.59–15.3 million) DALYs in children <5 years of age, compared with 14.3 million (95% UI 9.42–22.5 million) DALYs in those >5 years of age.

Figure 16. The global burden of foodborne disease by subregion (DALYS per 100 000 population) caused by enteric hazards, 2010.

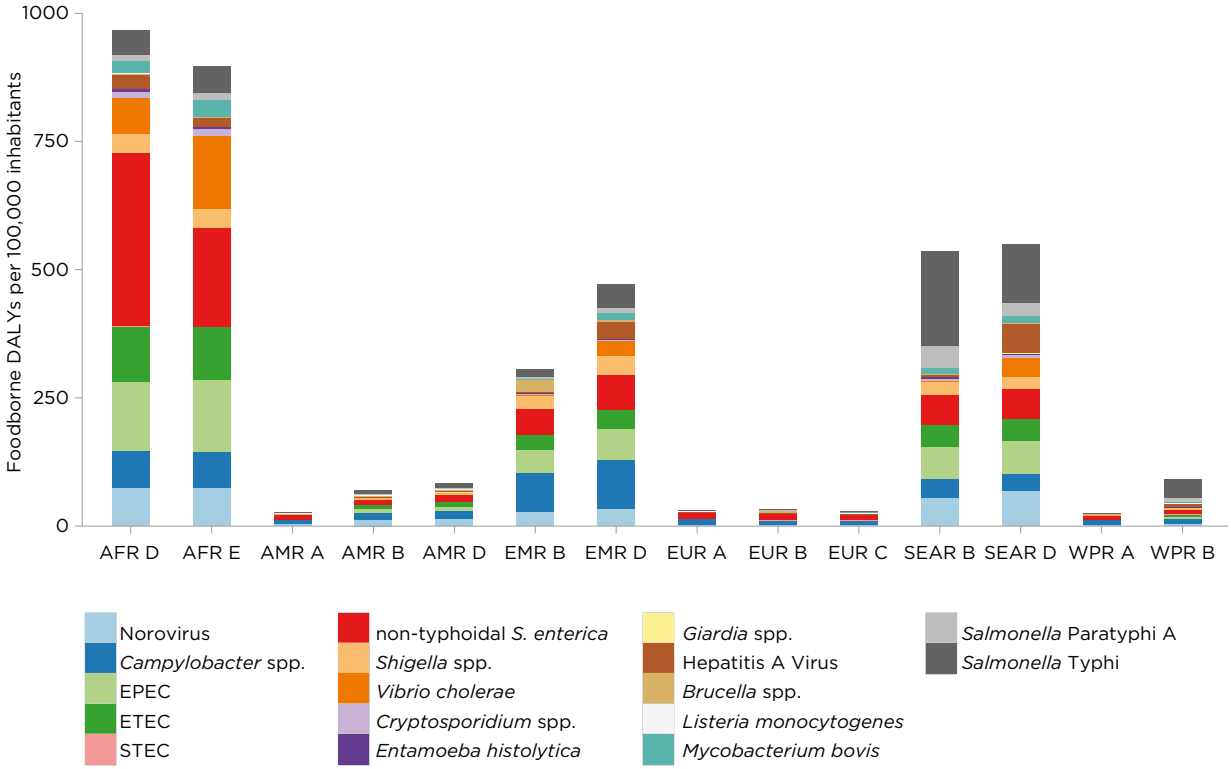
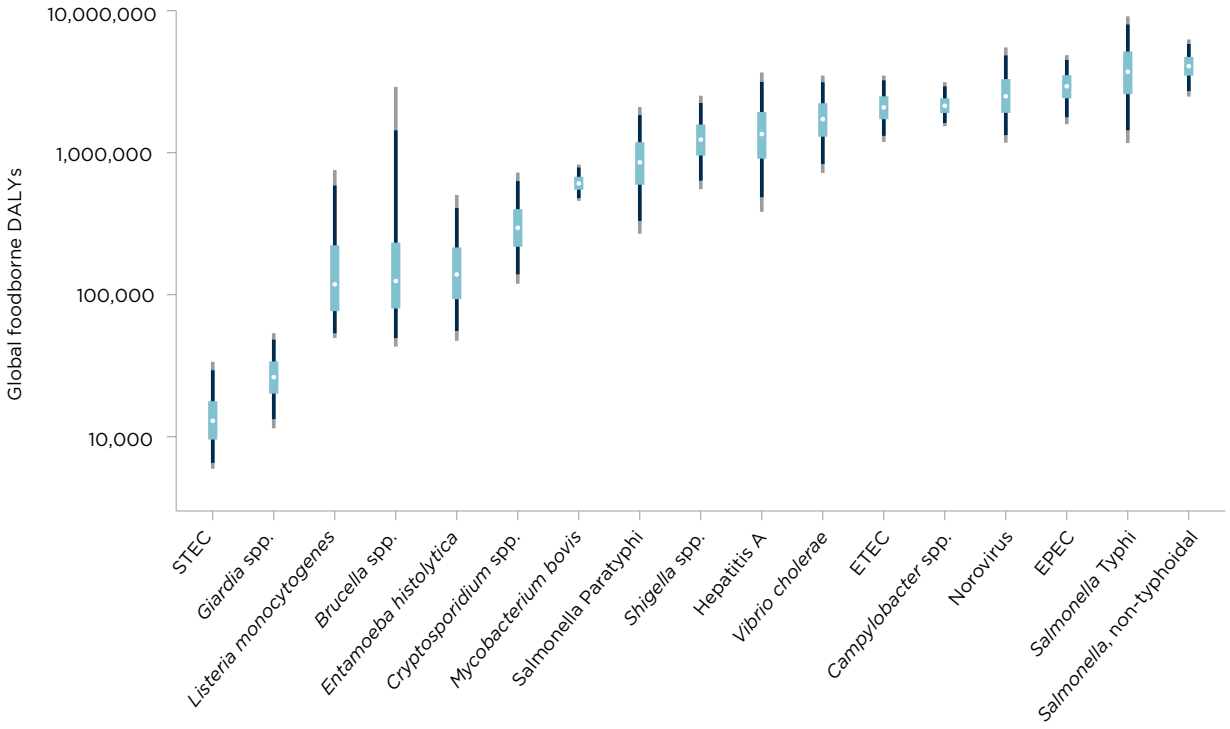


Figure 17. Disability Adjusted Life Years for each pathogen acquired from contaminated food ranked from lowest to highest with 95% Uncertainty Intervals, 2010.



Note figure is on a logarithmic scale. The figure shows the median (white dot); Inter-Quartile Range = 50% UI = 25%/75% percentiles (thick black line); 90% UI = 5%/95% percentiles (thin black line); 95% UI = 2.5%/97.5% percentiles (thin grey line). Note, four foodborne intoxications due to *Clostridium botulinum, Cl. perfringens, S. aureus*, and *Bacillus cereus* due to a lack of data for global estimation. In addition, data for non-typhoidal S*almonella enterica* infections and invasive non-typhoidal *S. enterica* have been combined.

5.4 DALY Estimates: Parasites

The parasitic diseases with the largest total number of symptomatic incident cases and symptomatic incident cases attributable to contaminated food in 2010 are acquired toxoplasmosis and ascariosis. The incidence in 2010 of each parasitic disease per 100 000 population by region are given in (Table A8.4 in Appendix 8). Also of note were the relatively few cases of human trichinellosis, with a global estimate of just 4400 cases and 4 deaths in 2010.

The number of DALYs associated with each parasite and the proportion of DALYs that were foodborne in 2010 are given in Table A8.5 in Appendix 8. In 2010 the burdens estimated to be caused by cysticercosis were 2.79 million (95% UI 2.14–3.61 million) DALYs. Foodborne trematodiasis resulted in 2.02 million (95% UI 1.65–2.48 million) DALYs. Toxoplasmosis had a burden (congenital and acquired combined) of 1.68 million (95% UI 1.24–2.45 million) DALYs, with ascariosis also resulting in 1.32 million (95% UI 1.18–2.70 million) DALYs. Echinococcosis (alveolar and cystic combined), had a burden of approximately 871 000 DALYs (CE 184 000, 95% (UI 88 100–1.59 million] DALYs; AE 688 000, 95% [UI 409 000–1.1 million] DALYs). This gives a 2010 global burden of these 11 parasitic diseases of 8.78 million (95% UI 7.62–12.5 million) DALYs, of which 6.64 million (95% UI 5.61–8.41 million) DALYs were estimated

to be foodborne. Contaminated food may be responsible for 48% (95% UI 38%–56%) of incident cases and approximately 76% (95% UI 65%–81%) of DALYs (Table 1). Stillbirths were excluded, although in the case of congenital toxoplasmosis, if counted as deaths as an alternative scenario, this would result in 4470 (95% UI 969–12 400) additional deaths and hence an addition of approximately 411 000 (95% UI 89 100–1.14 million) YLLs. Of these, approximately 2180 (95% UI 470–6090) deaths and 200 000 (95% UI 43 200–560 000) YLLs would be foodborne.

The largest global incidence rate of DALYs was found in the Western Pacific and African subregions, with 156 (95% UI 127–193) and 208 (95% UI 159–283) DALYs per 100 000, respectively, whereas the lowest was found in the European subregions, with 11 (95% UI 8–24) DALYs per 100 000 (Appendix 8 Table A8.4). However, the relative importance of the different parasitic infections varied across regions and this is clearly illustrated in Figure 18A. For example, the burden of opisthorchiosis is largely confined to SEAR subregion D, whilst cysticercosis is rarely seen in either EMR or EUR regions.

The absolute and relative foodborne burdens of these parasitic diseases, including the three enteric protozoa, are illustrated in Figure 18B. The relative proportion of the burden of each of the foodborne parasitic diseases contributed by YLLs and YLDs is illustrated in Figure 19.

Figure 18A. The relative contribution to the DALY incidence by each agent for each of the subregions. This includes enteric protozoa to complete the picture on foodborne parasitic diseases. However the detail is reported in the accompanying manuscript on foodborne enteric pathogens [168].

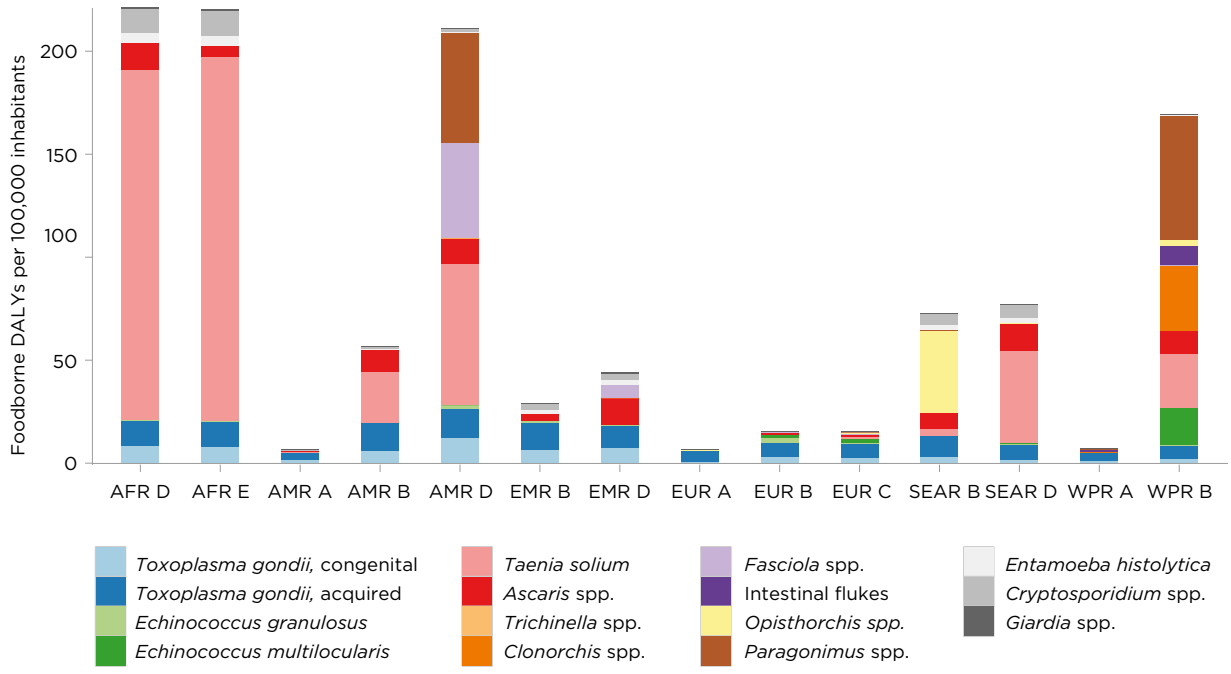


Figure 18B. Disability Adjusted Life Years for each parasite acquired from contaminated food ranked from lowest to highest with 95% Uncertainty Intervals, 2010. This includes enteric protozoa to complete the picture on foodborne parasitic diseases. However the detail is reported in the accompanying manuscript on foodborne enteric pathogens [168].

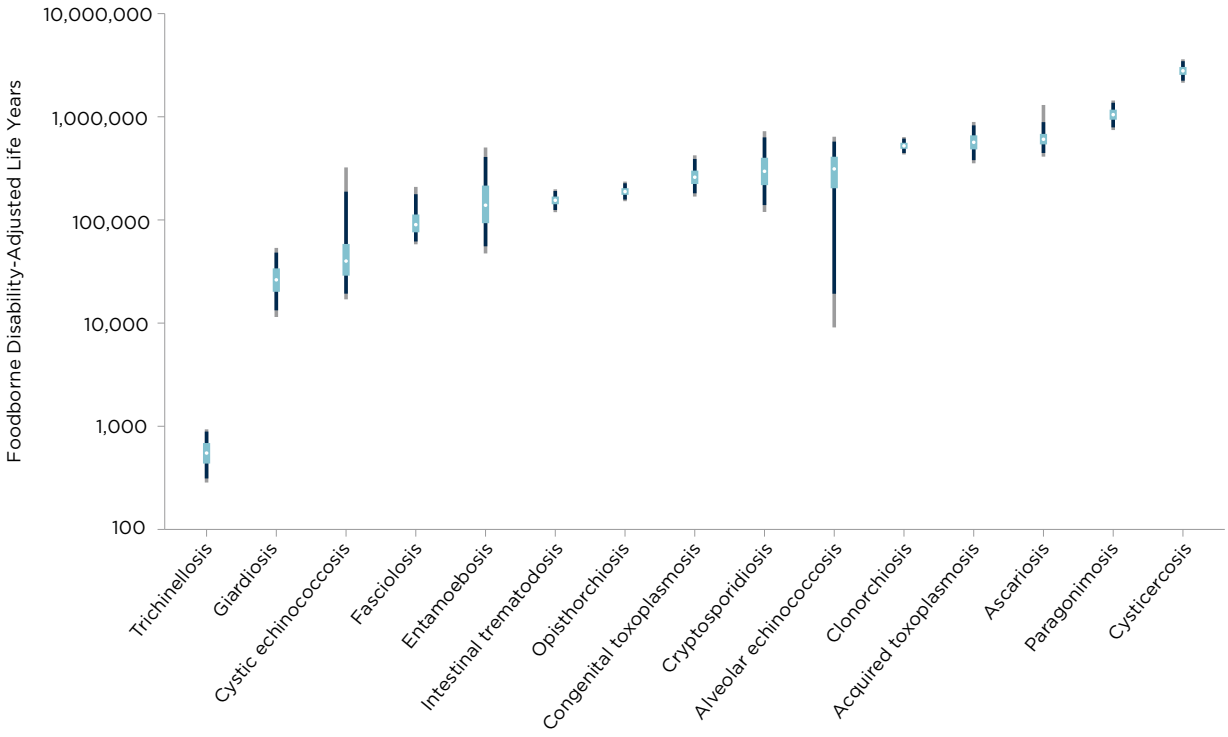
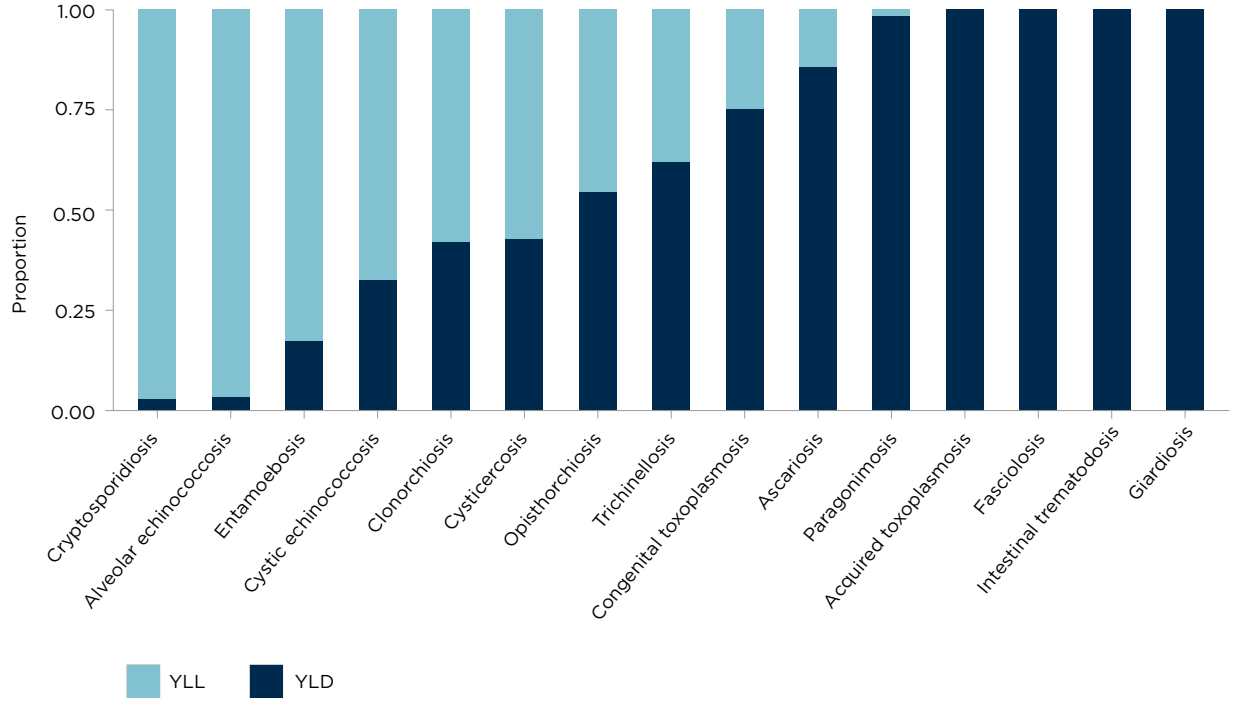


Figure 19. The relative proportion of the burden of each of the foodborne parasitic diseases contributed by YLLs and YLDs



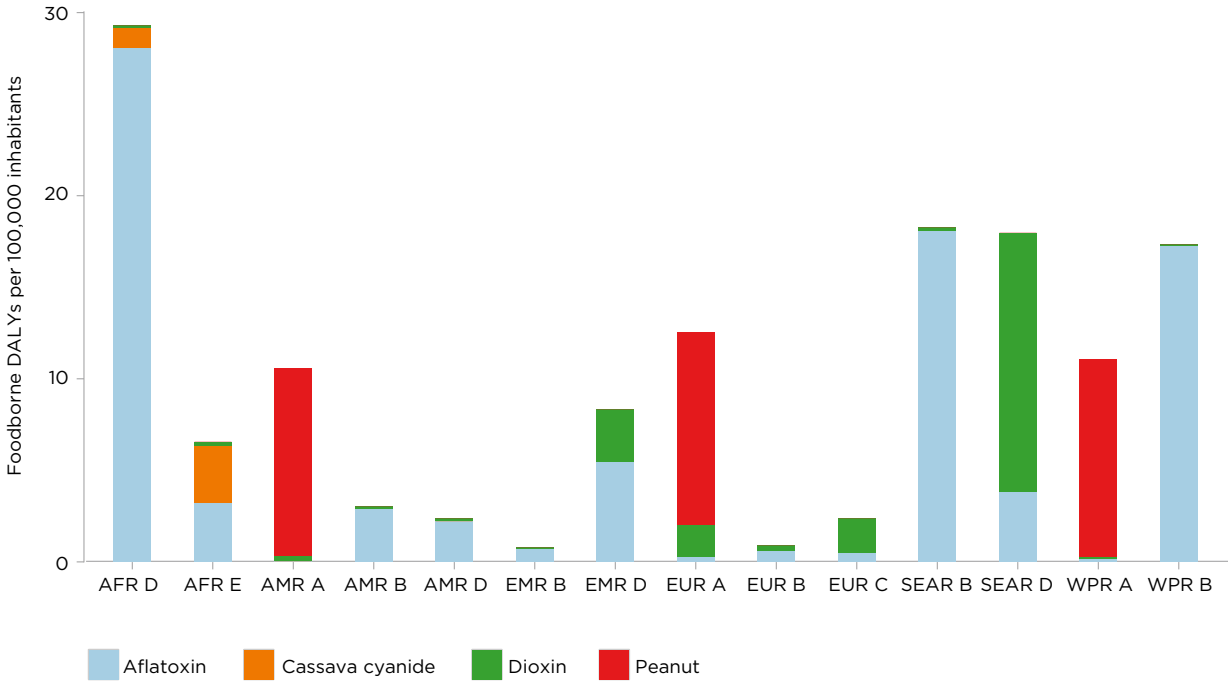
5.5 DALY Estimates: Chemicals

The analyses presented here show that four selected chemicals already have a substantial impact on the foodborne burden of disease, particularly in low- and middle-income countries. Just these four agents are estimated to be associated with 339 000 illnesses (95% UI 186 000–1 239 000); 20 000 deaths (95% UI 8 000–52 000); and 1 012 000 DALYs (95% UI 562 000–2 822 000) in 2010. These should be considered the "tip of the iceberg" in terms of foodborne chemicals and their impact on the global burden of disease. For peanut allergens, we were unable to estimate a burden for low- and middle-income countries due to data gaps. We also had to use an approximate disability weight, as there are data only on quality of life of patients with food allergy [102] and no specific data are available for peanut allergy.

The estimated number of incident cases, deaths and DALYs for each of the diseases associated with chemicals is given in Table A8.6 in Appendix 8. The chemical associated with the most number of illnesses is dioxin; however, no deaths have been reported from the presence of dioxin in the food supply. The chemical associated with the greatest number of DALYs is aflatoxin. The DALY estimates for aflatoxin and dioxin have the least uncertainty; more uncertainty is associated with the DALY estimates for peanut allergen and cyanide in cassava. The annual incidence, mortality, and DALY rate of each chemical-associated disease per 100 000 population for each of the regions is reported in Table A8.7 in Appendix 8. Peanut allergy is not reported in Table A8.7 in Appendix 8 because burden was estimated only for AMR A (United States of America, Canada and Cuba), EUR A (primarily countries in Western Europe), and WPR A (Australia, Brunei Darussalam, Japan and New Zealand) subregions. Burden estimates for cyanide in cassava are provided only for the African region (AFR) and assumed to be zero for other regions.

Figure 20 provides the DALYs per 100 000 inhabitants by global region. The regions with the highest burden per 100 000 inhabitants are the subregions in SEAR, WPR and AFR. The American Region (AMR), Eastern Mediterranean Region (EMR), and European Region (EUR) have the lowest DALYs per 100 000. Aflatoxin is the largest contributor to the burden in AFR and WPR. Dioxin makes the largest contribution in SEAR. Figure 21 contrasts the proportion of DALYs due to YLL and YLD for each of the four chemicals. Virtually all of the DALYs for aflatoxin and most of the DALYs for cyanide in cassava are due to YLL, whereas most of the DALYs for peanut allergen and all of the DALYs for dioxin are due to YLD. Figure 22 shows the uncertainty around the DALY estimates for each of the four chemicals. The chemical with the least uncertainty and the greatest number of DALYs is aflatoxin.

Figure 20. The relative contribution to the DALY incidence by each of four chemicals for each of the WHO Regions.



Notes: Peanut allergy burden was estimated only for the AMR A (United States of America, Canada and Cuba); EUR A (primarily countries in western Europe); and WPR A (Australia, Brunei Darussalam, Japan and New Zealand) subregions. Burden estimates for cyanide in cassava are provided only for the African region (AFR), and assumed to be zero for other regions.

Figure 21. The relative contributions from YLLs and YLDs for each of four chemicals.

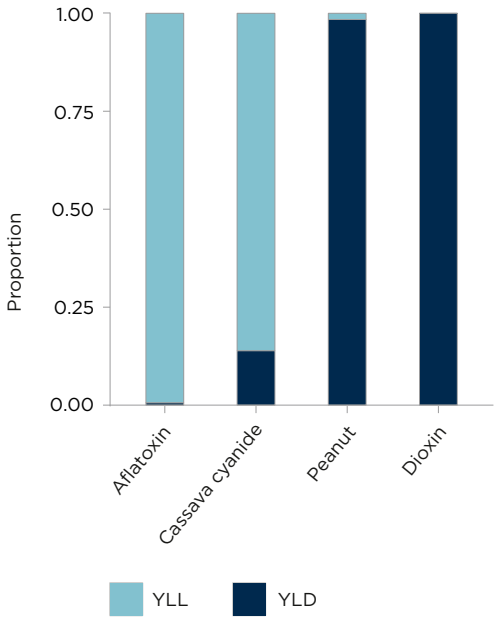
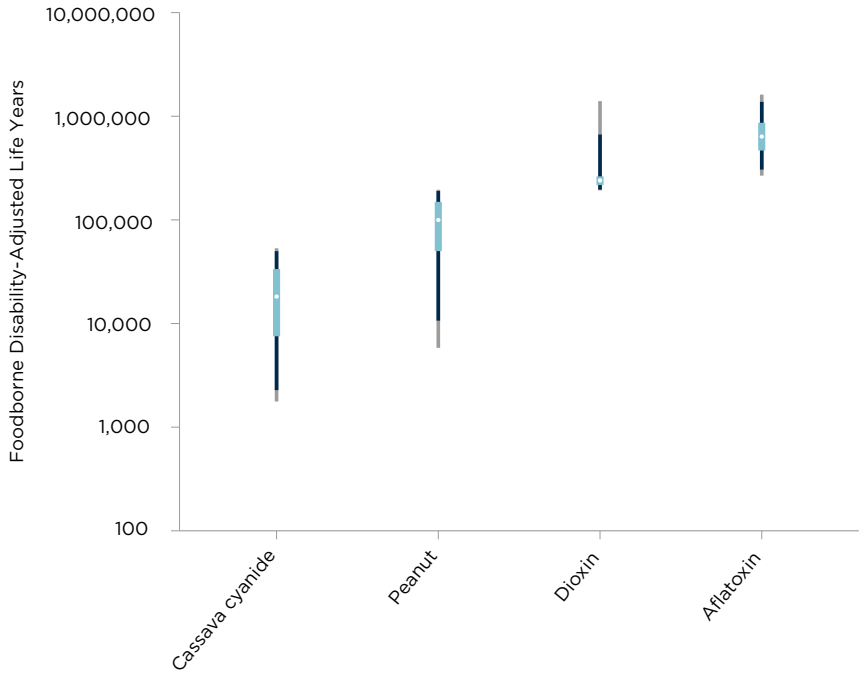


Figure 22. Disability Adjusted Life Years for each of four chemicals from contaminated food ranked, from lowest to highest, with 95% uncertainty intervals



Notes: The dot in the middle of each box represents the median, the box the 50% uncertainty interval, the dark bar the 95% uncertainty interval, and the light bar the 95% uncertainty interval.

DISCUSSION 6

DISCUSSION

This study estimates that 31 foodborne hazards resulted in 33 million DALYs in 2010, which shows the considerable public health impact of contaminated food. Importantly, children <5 years of age experienced 40% of the foodborne disease burden, despite representing only 9% of the global population. The study provides a substantial expansion of the available data on the public health impact of FBDs.

Several high-income countries have published national estimates of FBD. Estimates of food-related illnesses and deaths in the USA were estimated in the late 1990s [169] and updated to cover the period 2000–2008 [170, 171]. Similar studies are available from Australia [173], Canada [175], France [174] and the UK [172]. Some countries have extended this work to estimate DALYs, including Greece [177], the Netherlands [178], New Zealand [176] and the USA [179]. While the range of hazards covered in these studies differed from those in the FERG studies, the focus was on enteric diseases and a limited number of invasive and parasitic diseases. The FERG data, by contrast, cover numerous countries across the globe and provide a more complete picture of FBD.

Comparisons of the FERG estimate of the burden of FBD with other estimates, such as those of the Institute for Health Metrics and Evaluation's GBD 2010 study [81], must be made with care because of differences in the methodology and data used. For example, the GBD 2010 study used prevalence-based DALYS, whereas our study used incidence-based DALYs. As a consequence, the impact of sequelae such as Guillain-Barré syndrome (due to Campylobacter spp.), hemolytic uremic syndrome (due to Shiga toxin-producing E. coli) and invasive disease (due to non-typhoidal S. enterica) were attributed to the diarrheal disease agents in the FERG estimates whereas in the GBD 2010 study they were recorded in different disease categories. Furthermore, the GBD 2010 study used a different life table than FERG and more extensive mathematical modeling to account for data gaps, which smoothed the data considerably, resulting in narrower uncertainty intervals than in our study. The GBD 2010 and FERG studies used the same set of disability weights, but the FERG included some updates as recommended by WHO. Neither study applied time discounting or age-weighting in their baseline estimates.

The GBD 2010 study, which looked at all sources of disease, found that the key hazards and risk factors for disease burden were dietary risk factors (254 million DALYs), unimproved water and sanitation (211 million DALYs), HIV/AIDS (82 million DALYs), malaria (82 million DALYs), air pollution (76 million DALYs) and tuberculosis (49 million DALYs). Recently published findings from WHO[1] for 2012 were: HIV/AIDS (92million DALYs); malaria (55 million DALYs) and tuberculosis (44 million DALYs). Hence, the burden of FBD (33 million DALYs) is of a similar order of magnitude as the 'big three' infectious diseases (HIV/AIDS, malaria and tuberculosis) and air pollution, but clearly lower than the burden of dietary risk factors or unimproved water and sanitation.

The FERG estimate of 29,000 deaths due to foodborne transmission of invasive non-typhoidal *S. enterica* only included infections in non-HIV infected individuals. Ao et al. [180] estimated there were approximately 680,000 deaths due to invasive non-typhoidal salmonellosis in 2010. Of these, approximately 350,000 would be due to foodborne transmission, assuming 52% of all non-typhoidal

[1] http://apps.who.int/gho/data/node.main.DALYNUMWORLD?lang=en; accessed July 22, 2014

salmonellosis cases is transmitted by food [156]. Even though this high number of deaths among HIV infected people is not included in the FERG estimates of the burden of FBD, they would be preventable by food safety interventions.

This study is subject to several limitations, notably due to uncertainties in the data limitations on burden estimates and attribution estimates. For most hazards (25 of the 31 studied), the 95% DALY uncertainty interval (UI) ranged from one-fourth to four times the median. The uncertainty was markedly greater for *E. multilocularis* (because of uncertainty in the attribution estimates), *E. granulosus* and *L. monocytogenes* (because of uncertainties in the imputation results). In low-income countries, where the burden is highest, data availability was generally most problematic. Furthermore, in these countries, the proportions of diseases transmitted by food, water and the environment are difficult to disentangle, as contaminated water may also result in contamination of foods. Due to these limitations, it was not possible to present reliable estimates at country level, and elected to present results at subregion level.

For some hazards (e.g. *M. bovis* and *E. multilocularis*, aflatoxin and dioxin), incident illness is related to past exposures due to long incubation times of disease. For such hazards, the estimated burden reflects exposure dating back to the average incubation period of the disease rather than current exposure. For some hazards (e.g. dioxins), the impact on the child depends on the lifelong exposure of the mother.

The FERG estimates of the FBD burden are probably conservative, i.e. underestimates rather than overestimates. Limited resources and data obliged us to focus on only a subset of more than 100 hazards of potential relevance [182]. In particular, we did not include burden estimates for several chemicals (arsenic, cadmium, lead and methylmercury), because methods for estimation of the fraction of illnesses attributed to foodborne exposure to these chemicals are not readily available. Even for the hazards we have studied, it was not always possible to include all relevant disease outcomes in our estimates of burden. For example, we did not include functional bowel disorders as potential outcomes for enteric infections [183]. Inclusion of these outcomes would likely considerably increase the burden of enteric infections [184}.

Aflatoxin burden was estimated using a counterfactual approach, estimating population attributable fractions from exposure assessment estimates and cancer potency factors, and applying these to WHO estimates for incidence and mortality by hepatocellular carcinoma. Risk assessment, as used to assess the burden of dioxins [133] has been proposed as an alternative basis for estimating this particular burden, and would result in considerably higher estimates of the burden of aflatoxin [110]. Moreover, both aflatoxin and dioxin can cause other adverse health effects than the ones considered (e.g. diarrhoeal diseases [185] and aflatoxin as causes of malnutrition and stunting, dioxin and immune effects or cancer), for which data were not available to allow disease burden estimates.

A further limitation of this study is that DALYs do not quantify the full societal impact of FBD. The economic burden (cost-of-illness, losses in the agricultural and food sectors and trade impacts) is also an important factor to consider in national and international decision-making. Also, the process of food production can cause human diseases by mechanisms other than direct

transmission of pathogens through food. For example, animal husbandry is an important source of zoonotic disease agents that spread from pigs, poultry, cattle, etc., by direct contact or through the environment, and may also affect livestock health. It is increasingly necessary to consider holistically all aspects of food-related disease in a One Health Framework [186].

Despite its data gaps and assumptions, this study presents the first ever estimates of the global burden of FBD and should serve as an important resource to focus activities that will reduce this burden. A sustainable, multi-sectoral response is needed from governments and international organizations to reduce the visible and 'hidden' burden; this includes enforcement of food safety standards and effective surveillance networks at country, regional and global levels. This will require a concerted effort by all stakeholders in the food chain, from primary production to consumers. The diversity of foodborne hazards suggests the need for a multi-faceted strategy, with priorities tailored to each region. While national studies may further refine these priorities and are highly recommended, the current findings could already be a basis for developing strategies at the global, regional and national levels.

The diversity of foodborne hazards and regional differences in their importance suggest the need for consideration of these estimates at the national or even subnational level. As one of its aims, the FERG has fostered national studies of the burden of FBD, and pilot studies have been conducted in Albania, Japan, Thailand and Uganda. The tools and protocols developed by the FERG to support such national studies emphasize the collation of local data to validate its regional estimates, the consideration of local hazards that may not have been addressed at a global level, and the translation of burden estimates into food safety policy. The estimates developed by this WHO initiative will be invaluable for countries where local data gaps prevent the development of a full picture of FBD.

The considerable difference in the burden of foodborne disease between low- and high-income regions suggests that a major proportion of the current burden is avoidable. The WHO is working with governments and partners, including food producers, caterers and consumers, to reduce food contamination throughout the food chain, and particularly at the point of consumption, to levels at which the exposure to pathogens and contaminants does not pose significant risks for human health. There is, therefore, an urgent need to develop cost-effective food hygiene interventions that can be implemented in resource-poor settings. This research and development should be informed by estimates of the burden of specific food vehicles, taking all hazards into account.

General principles for strengthening food safety systems have been suggested by the WHO; they include integrating food safety into nutrition and food security policies and programs, and fostering closer collaboration between the various sectors involved (agriculture, human health, animal health, trade, tourism, etc.). The WHO recommends governments put in place risk-based food control systems and implement international food safety standards as established by the Codex Alimentarius Commission. Food handlers and consumers should handle and prepare food safely, practicing the WHO's 'Five Keys to Safer Food' and grow fruits and vegetables using the WHO's 'Five Keys to Growing Safer Fruits

and Vegetables' to decrease microbial contamination[2].

FBDs are closely linked to poverty in developing countries but they are also a global public health issue because growing international trade increases the risk of contamination in transported foods; also, migration and travel can expose populations to new hazards. Achievement of the internationally agreed Millennium Development Goals and the proposed Sustainable Development Goals, including the overarching goals of poverty reduction, achieving food security and ensuring healthy lives, will depend in part on successful reduction of the burden of FBD.

6.1 Attribution

In the attribution study, the results are presented of the first world-wide study on the contribution of contaminated food and other exposure routes to human disease caused by 18 major microbiological hazards and a chemical hazard. The study highlights the importance of the foodborne route of transmission for these hazards and– when combined with estimates of incidence, severity, duration and mortality– allows estimation of the burden of foodborne disease. Attempting to estimate foodborne transmission at the subregional level is an ambitious goal. However, this was vital given the geographically localized nature of exposure to many pathogens. The results are significant due to the global nature of the estimation, the number of experts participating, and the rigorous approach taken to assessing and including expert performance in the final estimates.

[2] http://www.who.int/campaigns/world-health-day/2015/en/

We were unable to identify epidemiological studies in the literature that delineate and quantify the importance of each transmission pathway as investigated in this study. This makes it difficult to formally validate the findings of the expert elicitation. Still, a discussion of summary findings in the context of other scientific knowledge may be of value.

The hazards can be grouped into several categories with respect to their major pathways. For *Campylobacter*, non-typhoidal *Salmonella*, STEC, *T. gondii*, and *E. multilocularis*, the foodborne route was considered the most important route in all subregions. These pathogens are all zoonotic and known to have one or more animal reservoirs. The zoonotic nature of these organisms is also reflected in experts' judgments by the identification of direct contact with animals as an important transmission route as well. Other pathogens with animal reservoirs include *E. granulosus* and *Brucella* spp., and here direct contact with animals was considered equally or more important than food as routes of transmission.

As described in the results section for several pathogens, there was a clear pattern that the experts considered the foodborne route less important in low- and middle-income subregions, where other routes (animal contact, water and soil) were believed to contribute relatively more in comparison with high-income subregions. This is consistent with data showing lower levels of access to improved water and sanitation in less developed regions compared with high-income countries. This ranking of subregions across different pathogens provides some confidence in the results, as the estimates were done independently and partly by different experts.

An expert elicitation was used to estimate source attribution parameters because of not only the lack of globally consistent data on which to base such estimates, but also a general lack of data and research on source attribution in most of the world. The generally wide uncertainty bounds provided by the expert elicitation in this study are presumed to reflect both uncertainty and variation, where uncertainty arises due to the sparseness of hard evidence data for, or the presence of conflicting evidence for, the contribution of different transmission pathways, and variation reflects the experts' beliefs concerning variations between countries within any given subregion. A study operating with smaller regions or at country level might have reduced the uncertainty due to variation.

There exist a few recent national studies that estimate the proportion of illnesses attributable to the foodborne route for specific infectious diseases [33–35, 37, 187, 188]. Table A7.6 in Appendix 7 provides the main results from these studies. Four of the six studies used some kind of formal expert elicitation, where enrolled experts were asked to provide a central estimate and their uncertainty bounds around this. The estimates published by Gkoga *et al.* [187] and Scallan *et al.* [42] were derived by the authors using a synthesis of data from different public health surveillance systems and the literature. As all six studies were conducted in developed countries, we compare the results only with the results from the relevant subregions (i.e. EUR A, AMR A and WPR A) in this study.

For the zoonotic pathogens, particularly non-typhoidal *Salmonella* spp., the estimates agree more closely and the uncertainty ranges tend to be relatively narrower than for pathogens with primarily a human reservoir (e.g. hepatitis A virus, *S.* Typhi and *V. cholerae*). Some of the differences observed may occur because we are comparing national estimates with subregional estimates, where the latter could be interpreted as a weighted average across all countries in the subregion.

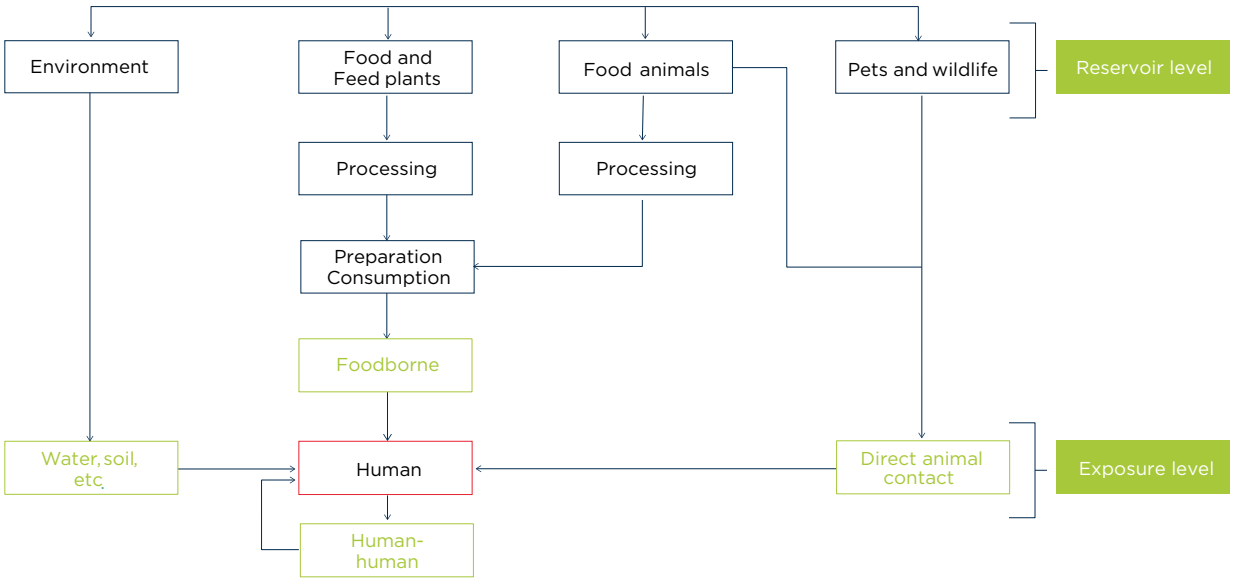
For hepatitis A, there is a strong disagreement between the national studies and this study, where the proportion foodborne is estimated to be less, but at the same level in the four national studies that investigated this pathogen. This difference cannot be readily explained, but it should be noted that there was also disagreement between the experts in this study, where three of the six experts serving on the hepatitis A virus panel provided estimates in line with those published for the national studies, whereas the remaining three experts provided considerably higher estimates. The disagreement between the experts is also reflected in the uncertainty bounds for the estimates, which are quite wide and contain the estimates from the national studies. For *S.* Typhi and *V. cholerae*, the estimates from the national studies are higher than those found in this study. One explanation could be that the national studies [35, 187, 188] were only attributing domestically acquired cases. In the study by Scallan *et al.* [42], the proportion foodborne for *S.* Typhi was estimated based on data from 17 domestic outbreaks reported in a 19–year period, where 13 outbreaks were confirmed foodborne and 4 outbreaks were of unknown origin. The same study included also only data from domestically acquired cases of *V. cholerae*, but as around 70% of all cases were estimated to be travel related, including all cases could change the proportion foodborne significantly. Infections with *S.* Typhi and *V. cholerae* are typically linked with

contaminated water sources and poor hygiene in developing regions [27], so these transmission routes are likely to be relatively more important among cases that have been travelling to these regions. This is probably what is reflected in the attribution results in this study.

The operational definition of different transmission routes, in particular the food and waterborne routes, will affect attribution estimates. Hazards transmitted by multiple routes can "change" source or vehicle during the transmission from primary source to humans, meaning that the burden of illness caused by a particular hazard attributed to a specific transmission route may vary, depending on the point-of-attribution chosen [7, 21]. The choice of point-of-attribution seems particularly critical for delineating foodborne and waterborne diseases. This is because water in itself is ingested just as a food, is used for irrigation of food plants, for washing and cleaning of food during preparation and constitutes an essential ingredient in many food products. In addition and particularly related to zoonotic diseases, the water source itself is often contaminated by an animal reservoir, including food-producing animals. Another situation relates to the consumption of water-based foods such as shellfish harvested from areas where the water is contaminated with pathogenic organisms, such as *Vibrio* spp. or enteric viruses. The burden related to the consumption of foods that have had contact with contaminated water at some stage of the production may, therefore, be attributed to either food or water depending on the point-of-attribution. It is clear that there exists no single "right" way of delineating the foodborne route from other transmission routes; however, it is critical that point of attribution be clearly defined. Definition of point-of-attribution should depend on the objective and focus of the specific study carried out, and could involve many factors, including the foodborne hazard in question, the food production systems and routines in place, the geographical occurrence of the hazard, sanitation and hygiene in the region, and consumption patterns. If point of attribution is clearly defined, then additional modelling or further research can be used to adjust attribution to exposure at other points of interest in the transmission chain. If the point of attribution is not unambiguously defined, then not only are the results of the study unclear, but it will be difficult to use them to model other relationships in the transmission chain.

FERG agreed that the point of human exposure was the most simple and understandable point-of-attribution to be used across all hazards for delineating the major transmission routes (Figure 23). FERG recognizes that for other purposes, e.g. for risk management, other points of attribution may be more appropriate (e.g. primary production, processing and retail, or preparation). Yet, the FERG's definition of point of attribution for major transmission routes directly links attribution to disease incidence, as it is the end of the transmission chain. Further modelling can then be used to work backward from exposure to identify the important points of contamination.

Figure 23. Major transmission routes of human foodborne diseases indicate two points of attribution: the reservoir level and the exposure level.



In this study, we identified potential experts through peer-nomination, for the purpose of enumerating parameter uncertainties through structured expert judgment. It is important to recognize that the goal of a structured expert judgment is not to characterize the properties of the group of experts in some sense, but to obtain uncertainty quantifications of target variable which are statistically accurate and informative. The degree to which this goal is realized is assessed objectively by referencing elicited target uncertainties to the experts' performances in judging similar, factual realizations of calibration variables in the subject matter field. This empirical validation of expert (and combined experts) uncertainty quantifications is what distinguishes formalized structured expert judgment from surveys or statistical sampling [189]. Assessment of the uncertainty judgment capabilities of experts using calibration variables has also been demonstrated to be a better predictor of expert performance compared with the usual markers of professional qualifications, such as publication records [190]. Structured expert judgment studies are, therefore, not as sensitive to selection bias and low response rates as other types of surveys. In our study, we approached 299 potential experts and ended up with a final pool of 72 (24%), which is actually a fair response rate compared with population surveys. The response rate of those that committed to participate in the study by forwarding their CV, DOI, etc. was 70%. The motives for some people declining to participate were not specifically asked for, but most of those giving a reason indicated lack of time. A few declined because they did not perceive themselves experts in the field. The reason given by the majority for not finally submitting responses to the target question, even though they had gone through the interview, was also time constraint. Although some selection bias cannot be ruled out absolutely, we do not believe that it has had major impact on the study results due to the formalized basis of the elicitation

process and objective judgment-pooling methodology.

6.2 Enteric Diseases

This study, for the first time, estimates the substantial burden of foodborne bacterial, viral and protozoal diseases in humans, particularly among children. Although children <5 years of age represent only 9% of the global population, 43% of the disease burden from contaminated food occurred in this group. Foodborne illnesses from diarrhoeal and invasive non-typhoidal *Salmonella* spp. resulted in the largest disease burden, reflecting the ubiquitous nature of *Salmonella*, the severe nature of illness, and the fact that young children are commonly infected [54]. Large human disease burdens are also imposed by foodborne infections due to norovirus and typhoid. It is important to recognize that diseases with a lower immediate burden may still warrant intervention. In particular, certain foodborne diseases may represent a larger problem in some regions. For example, the most substantial burden due to foodborne cholera occurs in African and Asian regions. Similarly, the burden of brucellosis and *M. bovis* infections were highest in the Middle Eastern and African regions.

To develop these comprehensive estimates of the disease burden of foodborne diseases, we adopted an innovative approach to incorporate the highest quality data available for each foodborne disease [40]. Due to their quality, we gave highest priority to studies with national estimates of foodborne diseases. Since studies with national estimates were only available in a few countries, we adapted the CHERG approach for estimating the disease burden of diarrhoeal diseases [50, 51]. This approach was facilitated by the availability of estimates of the envelope of diarrhoeal deaths, along with recent advances in diarrhoeal disease diagnosis, such as widespread application of polymerase chain reaction (PCR) for norovirus detection [192, 193].

In our study, norovirus resulted in the largest number of cases of foodborne diseases and overall burden, highlighting the global importance of this agent [192]. However, the disease model we used in the 135 middle- and high-mortality counties included only norovirus infections that resulted in a diarrhoeal illness. If we also included estimates for norovirus infections in these countries that resulted in vomiting without diarrhoea, there would be an estimated additional 163 million norovirus cases [194]. We also found, similar to what has been reported in national studies, that in the countries where we applied the modified CHERG approach, the aetiological cause of almost half of diarrhoeal cases and deaths remained unknown. This was probably due, in large part, to pathogens that are possibly foodborne but with insufficient data for estimation, or unknown agents not yet discovered. In this study, we focused our attention on the burden due to pathogens that were known to be transmitted by contaminated food.

When we examined the human health impact of different pathogens, various serotypes of *Salmonella enterica* resulted in the greatest foodborne burden. If we consider the combined burden attributable to *Salmonella* spp. from all invasive (including iNTS, *S.* Typhi and *S.* Paratyphi A) and diarrhoeal infections, there were an estimated 8.76 million (95% UI 5.01–15.6 million) DALYs from all transmission sources and 6.43 million (95% UI 3.08–13.2 million) DALYs from contaminated food. This highlights the significant public health importance of

Salmonella infections and the urgency of control, particularly for invasive infections in low- and middle-income settings where most of the mortality occurs [195–197].

Twelve of the diseases included in our study were also included in the GBD2010 study [6, 58, 81]. For three diseases (typhoid, paratyphoid and hepatitis A) we used GBD2010 data to derive estimates of incidence. For the other nine diarrhoeal diseases, we elected to conduct our own analysis or used updated data from commissioned systematic reviews to derive estimates. Our study builds upon the GBD2010 study by providing estimates of the proportion of each disease acquired from food; we also provide, in addition to estimates of deaths, estimates of the number of illnesses for each of the diseases [6]. Before we applied our estimate of foodborne proportions to each pathogen, our estimates of the disease burden for a few pathogens, in terms of the estimated number of deaths and DALYs, were relatively similar for diseases common to GBD2010 and FERG.

However, there were important differences in other estimates. The GBD2010 estimates of deaths due to *E. histolytica, Cryptosporidium* spp. and *Campylobacter* spp. were 10 times, 4 times and 3 times greater, respectively, than the FERG estimates [58]. The FERG estimate for DALYs for non-typhoidal *Salmonella* spp., combining diarrhoeal and invasive infections, was 4 times greater than GBD2010 [81]. The FERG estimates are relatively similar to previous global estimates of cholera, typhoid fever, salmonellosis and shigellosis [53, 54, 59, 198]. GBD2010 estimates included 'cysts and liver abscesses' as a complication of typhoid fever, which has been questioned [199]. However, we understood this categorization to be a proxy for serious typhoid fever and incorporated these data into our estimates. The CFR for each of the diseases included in our estimate are comparable to those reported in national studies. There is a continuing need for high quality studies assessing the foodborne disease burden at the national level. Our methodology for estimating the disease burden attributable to foodborne transmission could be used in future studies.

In comparing the overall burden of our findings, the diseases we included in our study resulted in 79 million DALYs in 2010. This represents approximately 3% of the 2.49 billion DALYs reported in the GBD2010 study [81]. GBD2010 estimated that approximately 25% of DALYs globally were due to deaths and disability in children <5 years of age, while we estimated that 43% of the DALYs in our study were among children <5 years of age.

There are obvious policy implications of our findings. Countries and international agencies must prioritize food safety to minimize foodborne illness, particularly among young children. The highest burden of disease due to contaminated food was in the African region, largely due to iNTS in children. In contrast to waterborne disease, the interventions for foodborne diseases are less clear and have a much weaker evidence base. For example, there are virtually no randomized studies examining the impact of interventions on reducing foodborne disease. Our results should stimulate research into prevention of foodborne illnesses and better understanding of the epidemiology of these infections.

A limitation of our estimates of the consequences for human health of foodborne diseases is that, due to data gaps, particularly in middle- and high-mortality countries, we included only a few sequelae in our estimates. We did not

include data on post-infectious sequelae, such as reactive arthritis and irritable bowel syndrome following foodborne infections. Studies of the burden of enteric pathogens in low-mortality countries highlight that excluding these sequelae under-represents the true burden of disease, but reliable data were not available from middle- and high-mortality countries [200]. Where we did include sequelae, there were insufficient data to account for age-specific effects. We also excluded stillbirths; this exclusion only affected disease burden estimates for *L. monocytogenes*.
A recent review estimated that listeriosis, which we assume is all foodborne, causes 273 stillbirths globally annually [70].

We were unable to distinguish between the effects on health from the condition under study and that of co-morbid conditions, which is common to many studies of human health. For example, salmonellosis and *M. bovis* infections may occur as HIV co-infections. If FERG included deaths among HIV-infected persons, there would have been substantial additional deaths due to invasive non-typhoidal *Salmonella* spp. deaths, some of which could presumably be averted by improvements in food safety. For some other pathogens in our estimates, such as *L. monocytogenes* and *Cryptosporidium* spp., due to a lack of reliable data we were unable to account for the excess mortality due to HIV infection.

Another important limitation of our attempt to quantify the disease burden due to foodborne disease is the inherent difficulty in estimating the proportion of illness acquired from food [7]. We relied on a structured expert elicitation study. We were unable to estimate differences in mode of transmission by age, despite this potentially being important. Expert elicitation studies can result in highly variable proportions attributed to food, depending on the nature of the experts included in elicitation studies [201, 202]. Without specific studies attributing sources of infection, it is difficult to obtain accurate estimates for foodborne transmission, but this finding regarding the need for more attribution studies is an important outcome of our study [203]. For example, the FERG expert elicitation study estimated that 18% of norovirus was foodborne, compared with 14% estimated from a recent study based on outbreak genotyping [204].

The major limitation of our study was the lack of reliable data from many regions of the world. In particular, we had the least data for some pathogens for the most populous regions of the world [50]. We tried to use the best data available and attempted to make reasoned assumptions wherever possible [205]. For some agents, such as toxin-mediated illnesses, we elected to limit our estimates to countries where diseases were endemic or where there was sufficient data. Further data on burden of enteric diseases from low- and middle-income settings, particularly high quality epidemiological data, are needed to improve our understanding of foodborne diseases [40, 205].

6.3 Parasites

In this study, we estimate for the first time the disease burden imposed by foodborne parasites. The results highlight the significant burden in low- and middle-income countries, where cycles of parasitic infection are highly specific to food sources. In addition to those detailed here, a further 357 million cases, 33 900 deaths and 2.94 million DALYs are due to enteric protozoa, of which 67.2 million cases, 5560 deaths and 492 000 DALYs are attributable to foodborne transmission (see [168] and Table 1),

completing the picture for the foodborne parasitic diseases, given data available.

We used the best evidence available combined with the natural history of the disease to obtain estimates of the incidence, mortality and sequelae of each parasitic disease. Several of the diseases were included in GBD2010 [81]. In a number of cases our estimates for the global burden of disease differ quite substantially from those of GBD2010. The estimate for echinococcosis (which combined AE and CE in one estimate) in GBD2010 is 144 000 DALYs [81]. This is less than a fifth of our combined median estimate of 871 000 DALYs. This discrepancy probably reflects different methodologies between the two studies. GBD2010 relied heavily on vital records for mortality attributed to these diseases, whereas we used an approach based on the natural history of the disease. Our choice of approach was strongly influenced by the chronic nature of these diseases, and that often only prevalence data were available. In addition, these diseases often have their highest impact in low income countries, where vital records are likely to be poor and hospital treatment unavailable. Our estimates for the global burden of CE would arguably be more consistent with an earlier estimate [206], if there had been no substantial methodological differences. The earlier report suggested a median estimate of 285 000 DALYs assuming no under-reporting, rising to 1 million DALYs where under-reporting was assumed. The earlier report also used DWs ranging from 0.2 to 0.809, depending on the severity of the disease. In the present study we used a maximum DW of 0.221, and that was only applied to the relatively small number of neurological cases.

Echinococcosis of the abdominal organs – the most common presentation – had a DW of 0.123 for treatment-seeking cases in the present study. The former study [206] also undertook age weighting and discounting, which we decided not to incorporate into this study. In addition different life tables were used. Our use of DWs was guided by GBD2010 and the results of a systematic review of the clinical manifestations of CE [75]. However, a median estimate in excess of 188 000 cases of CE per year, with the possibility of up to 1.77 million new cases, indicates a substantial burden. With a low case-fatality rate the burden in terms of DALYs is highly dependent on the DW and duration of illness. Neither of these is defined with certainty. The lack of defined DWs specific for the differing sequelae of CE must be seen as a major data gap.

When arriving at the estimates for AE, it was assumed that in excess of 90% of cases outside of Europe would be fatal. This assumption was supported by survival analyses, confirming that in the absence of aggressive treatment of this disease, including chemotherapy, most cases die [207, 208]. Our results suggest it is possible that the global burden of AE may be somewhat higher than that of CE, which may at first sight seem surprising as there are many more cases of CE globally and the parasite has a more cosmopolitan distribution. Hence, we have a median estimate of CE incidence that is ten times higher than the median estimate of AE incidence. The high case fatality ratio of AE, results in the loss of 37 DALYs per case compared with 0.98 DALYs for each case of CE. Thus the global burden of AE was driven by the large number of YLLs. For CE it was driven by the YLDs.

Our estimates for cysticercosis were higher than that of GBD2010, as a result of assigning a substantial proportion of epilepsy burden to cysticercosis, based on the results of a systematic

review [74]. Furthermore, a subsequent systematic review has largely confirmed our findings in terms of the fraction of epilepsy attributable to NCC [209]. However, our results are not inconsistent with GBD2010 [81] because we have allocated some of the burden from epilepsy to a specific aetiological agent. Nevertheless, the present estimate in this report may still underestimate the burden of cysticercosis, as there are other important clinical symptoms associated with neurocysticercosis, such as chronic headache, hydrocephalus, stroke and depressive disorders [73]. Better estimates of the role that cysticercosis plays in stroke and depressive disorders globally could considerably increase its burden estimates, since these conditions are ranked third and eleventh, respectively, in the GBD2010 [81] estimates. It is also unclear how GBD2010 arrived at their estimates for cysticercosis. If, for example, it was assumed that cysticercosis-related epilepsy can only be attributed in individuals who are serologically positive for cysticercosis, this would lead to substantive underestimates. A large proportion of cases of epilepsy attributed to cysticercosis, as shown by imaging studies, are nevertheless sero-negative. For example Montano *et al.* [210] describes 15 cases of epilepsy aetiologically confirmed as neurocysticercosis, but only 7 of these were sero-positive.

Likewise, the estimates for the burden of foodborne trematode infections may also represent underestimates. Our estimates were based on the results of an earlier study, which used estimation methods that were conservative [78]. Often, population-level information on human foodborne trematode infections were completely lacking from areas where the parasites are endemic, as indicated by substantial rates of animal infections and where human food habits suggest transmission to humans to be likely. We tried to correct for this lack of data by imputing incidence rates for all countries with at least one autochthonous human infection reported in the reviewed literature. Nevertheless, and in line with the original study [78], very conservative estimates from the imputation were accepted in an attempt to avoid inflating the burden estimates for human foodborne trematode infections based on unclear evidence.

Some diseases, such as toxoplasmosis, were not estimated in GBD2010 and will inevitably have been included in other syndromes. For example, congenital defects in GBD2010 will have incorporated the DALYs for congenital toxoplasmosis that we have estimated in the present study.

It can be argued that congenital toxoplasmosis is a vertically transmitted disease rather than foodborne. However public health measures are largely undertaken to prevent maternal (i.e. horizontal) infection, which will, as a consequence, reduce the risk of foetal infection. There is relatively little evidence that treatment to prevent vertical transmission (such as antiprotozoal treatment of acutely infected pregnant women) is effective in reducing disease burden [211].Thus it was considered a horizontally transmitted infection to the mother, although the burden of disease is suffered mostly by the foetus, following subsequent vertical transmission. Accordingly the proportion of foodborne disease suffered by the foetus is the proportion of the horizontal transmission to susceptible women that occurs through food.

With the exception of NCC, we have used an incidence approach to estimating the YLDs. This is where the YLD part of the DALY was estimated from number

of incident cases per year multiplied by the DW and duration. This is in contrast to the GBD2010 approach, which used a prevalence approach to YLDs, where YLDs were estimated by number of prevalent cases multiplied by the DW. For acute disease in generally stable epidemiological situations (i.e. no considerable shifts in the epidemiological key indicators of prevalence, incidence, duration, severity, remission and mortality) and settings with more or less stable population size, the approach makes little difference [2]. But for chronic diseases in populations that are rapidly increasing, the prevalence approach may underestimate the numbers of YLDs. Parasitic diseases are often chronic and are often of highest incidence in low income countries with increasing populations. Many parasitic diseases have durations of many years, or in the case of congenital toxoplasmosis, the sequelae are usually lifelong. Thus, as we adopted the GBD2010 data for epilepsy to estimate the burden of NCC, the YLDs will be prevalence-based. Nearly all of the burden of NCC is in low income countries, which usually have increasing populations. Therefore the cohort at the time of infection, with the burden attributed in an incidence-based approach, will be larger than earlier cohorts that are still affected by NCC but are reported in the prevalence-based approach. Accepting this limitation means that the estimates for epilepsy attributed to NCC will result in a further under-estimate of the burden of cysticercosis.

We have summarized the differences between the estimates for GBD2010 and the FERG estimates for these pathogens, including the enteric protozoa in Table 9. In addition, an issue that appears common to many hazards is that GBD2010 [9] has not published many of the search strategies used, or modelling methods to deal with data deficiencies. Until these are published we will only be able to hypothesize the reasons for some of the differences in the estimates.

The limitations in this study are similar to others in this series. There were often substantial data gaps that had to be filled by imputation and suffer from the uncertainties that surround such models. Excluding stillbirths is consistent with the approach used to estimate the burden due to enteric pathogens [168]. Congenital toxoplasmosis is the only pathogen investigated that could result in a substantial incidence of stillbirths. However, an estimate for the burden of congenital toxoplasmosis, which includes stillbirths as equivalent to neonatal deaths, has been reported as 1.2 million DALYs per annum [76]. FERG has assumed that acquired toxoplasmosis usually results in a relatively mild acute illness, with some cases suffering fatigue for a few months [212]. Although fatal cases have been recorded [213], these were assumed to be uncommon and hence zero YLLs were estimated. We have also assumed that although acquired chorioretinitis occurs following toxoplasmosis, it only occurs in a small proportion of cases (see Appendix 4). This results in approximately 1.15 million DALYs in 2010 from an estimated 20.7 million people having clinical disease following exposure to the pathogen for the first time. However, there is increasing evidence that acquired toxoplasmosis may result in a number of neurological or psychiatric diseases, such as schizophrenia and epilepsy. In GBD2010 these diseases resulted in 15.0 million and 17.4 million DALYs, respectively. From two meta-analyses [214, 215] and a large cross-sectional study conducted in China [216], it is possible to estimate that the population-attributable fraction of schizophrenia associated with seropositivity to toxoplasmosis is

approximately 9%, which on a crude level could account for approximately 1.3 million additional DALYs.

There were also some notable omissions from our study. *Taenia saginata*, which causes human taeniosis and is transmitted solely from beef, was not considered because the parasite produces very mild, unapparent clinical disease in affected humans, which would result in a DW of close to zero and hence a very low burden of human disease. However, it is accepted that this parasite generates substantial economic damage because of meat inspection and trade regulations required in many countries to detect and remove the parasite from the food chain [217]. Likewise, other cestode zoonoses, where the adult tapeworm is located in the gastrointestinal tract (e.g. *Diphyllobothrium* spp.) with few clinical signs, were also excluded. In contrast, trichinellosis was considered to be an important foodborne pathogen with potentially serious disease. However, this study has suggested that the global burden of trichinellosis is small. This is discussed elsewhere [84]. For reasons of resource limitations, we were not able to consider foodborne Chagas disease, although it was suggested as a possible priority pathogen during the second FERG meeting.

Table 9. Comparisons of the total burden of parasitic diseases (foodborne and non-foodborne) with 95% uncertainty intervals, estimated by FERG and by GBD2010 [9]

PARASITE	GBD	FERG	HYPOTHESIZED REASONS FOR DIFFERENCES BETWEEN GBD2010 AND FERG ESTIMATES
Cryptosporidium spp.	8 372000 (6 473 000–10 401 000)	2 159 331 (1 392 438–3 686 925)	Differences in DALYS estimated by GBD2010 and FERG are largely due to differences in how aetiological-specific deaths were estimated. FERG estimated aetiology specific deaths using the methodology adopted by CHERG*[35]. GBD2010 used a modelling-based approach to estimate aetiology-specific deaths, but there is no description of the GBD2010 model available to review. GBD2010 has not published the studies included, their search strategy, nor modelling methods; until these are published it is not possible to completely compare GBD2010 and FERG estimates.
Entamoeba spp. (Amoebiasis)	2 237 000 (1 728 000–2 832 000)	515 904 (222 446–1 552 466)	
Giardia spp.	Not estimated	171 100 (115 777–257 315)	
Toxoplasma gondii	Not estimated	1 684 414 (1 236 005–2 452 060)	Assumed to be included in congenital diseases and non-specific communicable diseases in GBD2010.
Echinococcus granulosus	152 000 (60 000–359 000)	183 573 (88 082–1 590 846)	GBD2010 used vital records, which are often missing in low resource countries. FERG used a natural history approach based on surveillance data. GBD2010 used prevalence-based YLDs, which will underestimate burden for a chronic disease like echinococcosis. Methods for imputation of missing data were different. GBD2010 has not published their modelling methods for missing data.
Echinococcus multilocularis		687 823 (409 190–1 106 320)	
Taenia solium	514 000 (398 000–650 000)	2 788 426 (2 137 613–3 606 582)	GBD2010 used vital records relying on a diagnosis of cysticercosis. FERG assigned a substantial proportion of the epilepsy envelope to cysticercosis in resource-poor, pork-consuming communities, based on evidence from a systematic review and meta-analysis. GBD2010 has not published their modelling methods for missing data.
Ascaris spp.	1 315 000 (713 000–2 349 000)	1 317 535 (1 182 187–2 700 572)	Only subtle differences as FERG and GBD2010 used the same source data, but FERG estimated incidence-based YLDs whereas GBD2010 used prevalence-based.
Trichinella spp	Not estimated	550 (285–934)	
Foodborne Trematodes	1 875 000 (708 000–4 837 000)	2 024 592 (1 652 243–2 483 514)	Only subtle differences as FERG and GBD2010 used the same source data, but FERG estimated incidence-based YLDs whereas GBD2010 used prevalence-based.

Notes: *Child Health Epidemiology Reference Group of the WHO/UNICEF.

However, particularly recently, the assumption that Chagas disease is primarily a vector-borne disease is being questioned [218]. For example, 70% of cases of acute Chagas disease recorded in Brazil between 2000 and 2010 were associated with food consumption [219]. As GBD2010 made an estimate of the burden of Chagas disease of 546 000 DALYs [81] there could be a significant additional burden through foodborne transmission if these data are representative. Indeed, foodborne Chagas disease may turn out to have a higher burden than the foodborne burden of some of the pathogens FERG considered, such as *Trichinella* and *Giardia* spp.

FERG was also unable to estimate the burden of foodborne cyclosporosis. This has caused outbreaks in the United States of America, such as the multi-state outbreak of 631 cases in 2013 [220]. However, the total numbers of cases over the medium to long term appears to be quite small, with a median annual incidence of 0.03 cases per 100 000 [221]. Thus any contribution to the burden of disease by this pathogen is likely to be small.

A further important limitation was relying on expert elicitation for the proportion of disease that is foodborne. This was an important issue with those parasitic diseases such as ascariosis, toxoplasmosis and echinococcosis, that can have several pathways of transmission. Expert elicitation studies can result in a highly variable proportions attributed to food. However, as data on source attribution for a number of parasites were not available, the structured elicitation undertaken offered a transparent way of evaluating and enumerating this uncertainty, and thus represents the best available source of information [156, 168].

The expert elicitation for routes of transmission estimated that a median of approximately 15% (95% UI 7–27%) of *Giardia* infections were transmitted via contaminated food. This is was higher than we expected for this enteric protozoan. For example, Scallan *et al*. [188] suggested that 7% of *Giardia* infections acquired in the United States of America were of foodborne origin. However, in contrast, a recent 40-year summary of outbreaks of giardiosis reported to the United States Centers for Disease Control and Prevention identified that 16% of 242 outbreaks were true results of foodborne transmission [222]. Both these studies suggested that the proportion of foodborne giardiosis is within the 95% uncertainty limits of our study. Furthermore, a recent report by the Food and Agriculture Organization of the United Nations (FAO) and WHO presented a multi-criteria ranking of 24 [groups of] foodborne parasites, and concluded that Giardiosis was the 11th most important foodborne parasite [223, 224], with fresh produce likely to be the vehicle of transmission. This indicates that it is accepted that this parasite has a foodborne transmission route and puts our estimates in this context.

We used epilepsy and ascaris prevalence data from GBD2010 to inform our estimates of cysticercosis and foodborne ascariosis, respectively. Therefore the accuracy of our estimates will be limited to the accuracy of the GBD2010 data from which it was derived.

Toxoplasma gondii is globally distributed, with a high proportion of the world population estimated to be seropositive. *Ascaris* spp. is the most frequently encountered human helminth, although the burden is confined to low- and middle-income countries. However, a number of diseases had very high burdens limited to distinct

geographical populations. Most of the global burden of AE is in China, and mainly on the Tibetan plateau [72]. In this highland region there are specific factors that promote transmission between wildlife, dogs and humans that are not present in other endemic areas. This results in large numbers of human cases in certain communities [225]. Such unique epidemiological conditions are not present elsewhere, even where the parasite is endemic. *Taenia solium* transmission can only be maintained where pork is consumed, pigs are left roaming, and where there is poor sanitation. Thus it is largely absent from upper-income countries and from communities where pork is not consumed, such as countries in the Middle East. Sporadic cases are occasionally reported and these are often linked to the employment of immigrants who originate from endemic countries and hence transmit the infection through poor hygienic practices [226]. Foodborne trematodes also have a limited distribution, but they cause a high burden of disease in the at-risk populations such as in South-East Asia. Trematodes have complex life cycles that include various species of molluscs. This limits their distribution to specific regions where suitable life-cycle hosts are endemic, which may be adapted to specific climatic and hydrological conditions [227]. The human disease is further limited to populations that are likely to consume the raw fish or undercooked aquatic vegetables that are the sources of transmission. Consequently, although we are reporting the global burden of these parasitic diseases, this is often borne almost completely by relatively small populations in limited geographical areas. Therefore, in such communities, these diseases have a major impact on the health of the population.

The report by FAO/WHO presented a ranking of foodborne parasites, based on multi-criteria analysis [224]. In our study, we present data on the foodborne disease burden for 13 parasites included in the FAO/WHO report. Comparing the results of the ranking from the FAO/WHO model with the results of the present study, the parasites selected by FERG had the highest rank orders in the FAO/WHO report (i.e. ranking from #1to #14), only *Trypanosoma cruzi* at rank #11 and *Cyclospora cayetanensis* at rank #13 were not assessed by FERG. *Taenia solium* was ranked #1 by both approaches and *Toxoplasma gondii* #3 by FERG and #4 by FAO/WHO. There were, however, also remarkable differences in the ranking of the individual parasites. *Paragonimus* spp. was ranked #2 by FERG, but only #14 in the FAO/WHO report, and *E. granulosus* #12 by FERG, but #2 by FAO/WHO. The disease burden of *E. multilocularis* was considerably higher than the burden of *E. granulosus* (310 000 vs. 40 000 DALYs), but nevertheless was ranked lower at #3 by FAO/WHO. The disease burden of intestinal flukes was #9 by FERG. This was higher than the #22 ranking of heterophyidae by FAO/WHO. FAO/WHO used 9 criteria for ranking, of which 6 were health-related criteria and 3 non-health criteria. This weighting of the different criteria may be responsible for the FAO/WHO report having a different ranking order for the various parasites. For example, *E. granulosus* has a global distribution and a relatively important measure in the FAO/WHO ranking. In contrast, *E. multilocularis* is only found in the northern hemisphere.

6.4 Chemicals

The assessment of the burden of disease from chemicals in food is a challenge on several levels. There are thousands of chemicals in production and many

naturally occurring toxins. How many of these chemicals and toxins make it into the food supply is unknown. The health effects of chemicals may not be observed for years following exposure (e.g. aflatoxin and liver cancer; lead and cardiovascular disease). Longitudinal studies of these effects are expensive and time-consuming. Sufficient information is available, however, to make estimates of the burden for arsenic, cadmium, methyl mercury and lead, and possibly for other chemicals and toxins (e.g. fish toxins, aristolochic acid). Other chemicals (e.g. Persistent Organic Pollutants) may not require elaborate epidemiological studies because the burden can be derived from bio-monitoring data in combination with relevant toxicity data. Estimates of the burden for these chemicals will provide a much more comprehensive understanding of the impact that chemicals in the food supply have on the burden of disease.

As the relevant disease endpoints due to foodborne chemicals may arise from different causes, various approaches are possible for estimating incidence and mortality. A "top-down" approach uses an existing estimate of morbidity or mortality of the disease endpoint by all causes (the "envelope") as a starting point. A population-attributable fraction is then calculated for the hazard under consideration, and applied to the envelope to estimate the hazard-specific incidence. This method, which is the standard in Global Burden of Disease estimations, was used for aflatoxin.

A "bottom-up" or dose-response approach uses dose-response and exposure information. The approach begins with selection of the appropriate dose-response relationship between the chemical and the particular disease. This dose-response relationship is then combined with the distribution of exposure within a population to derive an estimate of the incidence of the disease that is attributable to the exposure. A probabilistic version of this method, which is applied in chemical risk assessment, was used for dioxin [127, 128].

The two approaches would result in the same outcome if perfect data were available, and if it can be assumed that the risk of exposure to a chemical is additive to the background risk from other causes. In reality, the available data for both approaches are limited and there is insufficient information to decide conclusively whether risks are additive, multiplicative or otherwise. This may result in considerable discrepancies between results from these methods. In this study, FERG chose a "top-down" approach for aflatoxin because the cancer potency factor derived by JECFA [111] was based on a multiplicative model, and there is evidence for a high background rate in the study population underlying this estimate and the global population (see Appendix 4). Using the population-attributable fraction approach, it was estimated there were approximately 22 000 (95% UI 9 000–57 000) cases of aflatoxin-related HCC in 2010. A dose-response approach [110] estimated that, annually, 25 200–155 000 cases of HCC might be attributable to aflatoxin exposure. Even though the uncertainty intervals overlap, the differences between these two approaches are considerable. There is evidence for a high background rate in the study population underlying this estimate and the global population (see Appendix 4), which may result in over-estimation of mortality by the dose-response approach. In contrast, the global liver cancer envelope may be underestimated, particularly in Africa [228, 229], leading to underestimation of the aflatoxin-attributable incidence. Hence, there is considerable data and model uncertainty in our estimates, which should be addressed by further studies.

7 COUNTRY STUDIES

COUNTRY STUDIES

7.1 Aim and Objectives of the Task Force

The WHO initiative to estimate the global and regional burden of foodborne diseases has four stated objectives, two of which involve actions at a national level:

- To strengthen the capacity of countries in conducting burden of foodborne disease assessments, and to increase the number of countries that have undertaken a burden of foodborne disease study.
- To encourage countries to use burden of foodborne disease estimates for cost-effective analyses of prevention, intervention and control measures.

The Country Studies Task Force (CSTF) was established in 2009 to advise WHO on the initiation, conduct and completion of national burden of foodborne diseases studies.

The objectives of the Task Force were to advise WHO on:

- the development of burden of foodborne disease pilot protocols that can be used by countries to estimate their national burden of foodborne disease from enteric pathogens, parasites and chemicals and toxins;
- the development or commissioning of all relevant training materials needed to assist countries to build capacity and undertake a national burden of foodborne disease study;
- oversight of the initiation, conduct and completion of an agreed number of national foodborne disease pilot studies;
- the evaluation of the protocols after the pilot studies are completed, and on making necessary revisions; and
- oversight of the initiation, conduct and completion of 18 national burden of foodborne disease studies, 3 in each WHO region.

To specifically address the second objective above, a subgroup, the Knowledge Translation and Policy Group (KTPG), was established in 2010.

7.2 Tools and resources to facilitate national burden of foodborne disease studies

The initial activity by the CSTF was to develop of a series of tools and resources to facilitate national burden of foodborne disease studies. These were intended to promote a methodology that would be consistent with the global and regional burden estimates being developed by FERG, in particular estimating burden using the disability-adjusted life-year (DALY) metric, and strengthen capacity to develop science-based policies. These tools and resources were developed by members of the CSTF, as well as commissioned scientists, to be made available on a WHO website dedicated to the burden of foodborne disease initiative. The tools and resources included:

- reviews of existing burden -of disease studies and protocols [230, 231];
- a manual on how to conduct a national burden of foodborne disease study (adapted from the WHO manual on national burden -of disease estimation [232]);
- a hazard selection tool, including a listing of priority hazards being addressed by the WHO initiative at the global and regional levels, and guidance for identification of hazards that may be locally important;
- guidance on data collection, describing the information needed to estimate foodborne burden-of disease, and potential sources of data, such as surveillance systems, demographic databases, etc. This tool also suggests contextual information that helps to assess data quality; and a

- FERG Situation Analysis/Knowledge Translation/Risk Communication Manual (SA/KT/RC Manual).[1] The development of this resource benefited from previous burden of food- and waterborne disease studies in the Caribbean, under the auspices of the Pan American Health Organization (PAHO) [233]. A WHO Global Foodborne Infections Network capacity building workshop in July 2012 resulted in the creation of 13 issue briefs, with context-specific target audiences, and immediately implementable recommendations. The template for these issue briefs was included in the guidance manual (Dr Enrique Perez, PAHO, pers. comm.).

7.3 Pilot Studies

In 2010, WHO invited countries to express interest in conducting national burden of foodborne disease studies as a pilot process. Countries which expressed interest were sent an overview of a national burden of foodborne disease study from the FERG perspective, and a request for information relevant to the conduct of the study. Following an assessment process undertaken by the Department of Food Safety and Zoonoses (FOS) at WHO headquarters, four countries were selected for pilot studies: Albania, Japan, Thailand and Uganda. A commencement meeting for the Albanian, Japanese and Thai studies was held in November 2011, and for the Ugandan study in March 2012. The studies were supported by ongoing communication between the countries and CSTF.

[1] A situation analysis report or resource is designed to collect and summarize the contextual information concerning food safety in the country undertaking the national foodborne burden of disease study, including policies and practices, capacities, key agencies and actors in the food safety system, and to document factors that will affect the development of policies and their implementation.

7.4 Process

Each pilot country was asked to assemble a team to conduct their study. The members of these teams included representatives from government and academic institutions. Early in the process, KTPG recommended that each study team conduct a situation analysis according to the guidelines in the SA/KT/RC Manual, to describe the regulatory and economic status of food safety in the country; identify actors, policies and practices; and generally provide context for the scientific data. This analysis would also identify stakeholders who should be aware of the study, could contribute data and information, and might ultimately use the results of the study to guide decision-making.

The initial step in each study was to identify hazards in the food supply that were relevant to the pilot country. Lists of hazards and associated diseases that were considered of global and regional importance by FERG were provided; each country was able to add hazards considered important from their perspective. Available information was then collated on the incidence of diseases associated with the hazards, as well as data on the prevalence of the hazards in the food supply. These data were summarized, and then attribution of disease burden to foodborne transmission was considered, as data allowed.

KTPG sought to promote knowledge translation and risk communication throughout the development and implementation of the study. Tools for these processes, as described in the SA/KT/RC Manual, are intended to involve stakeholders from the outset so as to promote ownership, share results with stakeholders, and promote efforts to use the information for developing evidence-based policies.

Here we provide a brief overview of key data and food safety systems associated with each pilot study. As enteric disease is a common outcome of exposure to microbial foodborne hazards, there is a focus on data related to enteric disease.

7.4.1 Albania

Human health surveillance of foodborne diseases in Albania is led by the Public Health Institute within the Ministry of Health, which collates data supplied by regional departments of public health. An early warning surveillance system operates across all of Albania (similar to the system that operates in Serbia and Macedonia [234]), and the case definitions are the same as for syndromic surveillance under the International Health Regulations. Key indicators of foodborne disease are the annual rates of reported gastrointestinal illness (approximately 56 000 cases per year, approximately 2 000 cases per 100 000 population) and cases reported as food poisoning (approximately 2800 cases per year, approximately 100 cases per 100 000 population). Food poisoning cases are reported on the basis of assessment by physicians from primary health care, as well as hospitalized cases. aetiology for cases in these general disease categories is rarely investigated. Surveillance for parasitic or viral infections is not routine, apart from infection with *Entamoeba histolytica*. Cross-sectional studies of faecal samples for viral and parasitic infections have been carried out (e.g. [235, 236]).

Access to health care is limited, particularly in rural areas. A lack of awareness of entitlements, and informal payment systems, mean that 20–30% of people cannot access primary health care [237].

Another section of the Ministry of Health, the Department of Health and Environment, is responsible for general hygiene and sanitation across all businesses, including food-related businesses. The Ministry of Agriculture, Food and Consumer Protection Food Safety Directorate includes the National Food Authority (NFA), which is responsible for official control, risk assessment, and communication. Official control involves the inspection of food production hygiene, and certification of hazard analysis critical control point (HACCP)-based systems.

Data on the prevalence of hazards in the food supply are limited. Official monitoring programmes for shellfish (algal toxins and *Escherichia coli*) have been in place since 2005 to support exports to the European Union.

7.4.2 Japan

The major objectives of the Japanese country study were to assess the disease burden from major foodborne diseases in Japan and to analyse the policies on foodborne disease using the FERG framework. The study has now been published [238].

As a pilot study, three major foodborne diseases caused by *Campylobacter* spp., non-typhoid *Salmonella* spp., and enterohaemorrhagic *E. coli* (EHEC) were prioritized, based on food poisoning statistics in 2011 and an expert consultation. First, the annual incidence was estimated from reported surveillance data, adjusted for probabilities of case confirmation and physician visits. The estimated annual incidence was significantly higher than that reported in the routine surveillance data, suggesting a marked underestimation of the magnitude of foodborne diseases.

A series of systematic reviews of disabling sequelae from the three priority diseases was conducted. Subsequently, the estimated incidence

was adjusted for food-attributable proportions, which were estimated by an expert elicitation process, similar to that carried out in the Netherlands [33]. Together with the cause-of-death data from vital registration, the disease burden in terms of DALYs was estimated. In 2011, foodborne disease caused by *Campylobacter* spp., non-typhoid *Salmonella* spp. and EHEC led to an estimated 6099, 3145 and 463 DALYs in Japan, respectively. The burden from disabling sequelae was consistently higher than that due to gastroenteritis among the three major foodborne diseases. Data gaps in estimating foodborne disease burden in Japan, in particular population-based data on incidence, were also identified.

Building on the FERG framework, the policy situation analysis provided an overview of the food safety policies and systems in Japan. As a Japan-specific issue, a rigorous policy situation analysis of the management of risks associated with possible radioactive substances in food, due to the nuclear power plant accident in Fukushima after the Great East Japan Earthquake in 2011, was also completed.

7.4.3 Thailand

The Thai country study focused on the incidence of diarrhoeal disease, using data from the National Notifiable Disease Surveillance System maintained by the Bureau of Epidemiology of the Thai Ministry of Public Health. These data were supplemented by information from National Hospital Records (both in-patient and out-patient), the National Health and Welfare Survey, and community-based studies of young children. In this study, the hospital data accessed all three health insurance systems, including the universal coverage, social security, and civil servant benefit health insurance. The sharing and interoperability of all three health insurance databases contributed to data reliability and ensured entitlement to the health services covered [239].

Extrapolations from these data sources allowed an estimate of the incidence of acute diarrhoea in the community of 10–35 million illnesses in 2009 (for the National Notifiable Disease Surveillance System, acute diarrhoea is defined as at least 3 loose stools within 24 hours or any abnormal stools [e.g. watery, with mucous, or bloody]). Information on aetiology is limited, but the incidence of salmonellosis, cholera, shigellosis and *E. coli* infection were estimated from diagnoses in the National Hospital Record.

In addition, the prevalence of liver fluke infection (*Opisthorchis viverrini*, a locally important foodborne hazard transmitted via fish) and the incidence of rotavirus infection have been estimated.

Food safety regulatory activity in Thailand is led by the Bureau of Food and Water Sanitation, Department of Health, Ministry of Public Health. The popularity of street food has led to the development of a sanitation standard for vendors.

7.4.4 Uganda

The Ugandan country study established teams to separately address enteric, parasitic and chemical hazards, and source attribution [240]. A detailed situation analysis was prepared, which described the context for food safety in terms of legislation, regulatory authorities, the food supply, production and consumption. The Ugandan country study was undertaken in conjunction with a project by FAO on the use of multi-criteria decision analysis for food safety in Uganda.

Data were collated from surveillance sources (particularly the Health

Management Information System administered by the Ministry of Health, and the Central Public Health Laboratory) on acute diarrhoea (1.9 million reported outpatient cases in 2012, approximately 5700 cases per 100 000; case definition: three or more watery stools in 24 hours but not lasting for more than 14 days), cholera, dysentery, brucellosis, hepatitis E and typhoid fever. Parasitic infections are reported as worm infections or intestinal worm infections. Although such infections are very common (approximately 1.8 million outpatient infections reported annually), aetiological data are few.

The reliability of these data has improved steadily with increased access to healthcare since 2000. Uganda has undergone a number of reforms that have influenced health service delivery. Among the major reforms, conducted in the early 1990s, was the decentralized governance of districts, with attendant devolution of powers to allocate resources and deliver services, including health care. Physical access to health facilities for the population living within 5 km of a health facility increased from 49% in 2001 to 72% in 2004 [241].

Other sources of data included the Ministry of Agriculture, Animal Industry and Fisheries; the Ministry of Trade, Industry and Cooperatives; the Ministry of Water and Environment; the Ministry of Local Government and Local Authorities; and research and academic institutions.

Of the chemical hazards, the most data were available for aflatoxins, with information on the prevalence of contamination for relevant foods being available. The incidence of hepatocellular carcinoma, an important health outcome of aflatoxin exposure, is also available. Acute poisoning due to methanol in illicit alcoholic beverages is often reported. Despite cassava consumption being high in parts of Uganda, no reports of acute cyanide poisoning, *konzo* or tropical ataxic neuropathy were found.

It was important that both waterborne and foodborne transmission of diseases were included in the Ugandan study, as food safety was not considered to be independent from water safety. It was difficult to generate DALY estimates from the available data, particularly due to the shortage of community-level incidence data.

7.5 Findings and Lessons Learned

7.5.1 Data gaps

A lack of data prevented DALY calculations in several of the pilot studies. The data gaps included:

- information to assign aetiology for important syndromes such as acute gastrointestinal disease and parasitic infections;
- data on the incidence of diseases caused by some hazards, particularly chemical hazards; and
- limited outbreak and other data on which to base attribution for foodborne transmission.

7.5.2 Public and private data sources

In some countries, private hospitals provide a significant proportion of the available healthcare, and may not have the same reporting requirements as public hospitals [242]. Engagement with private hospitals and other facilities to provide a complete picture of the incidence of diseases caused by foodborne hazards may need to be specifically addressed. Data from primary producers and the food industry concerning foodborne hazards can be gathered, but economic implications, particularly for trade, mean that such data should be carefully handled and with discretion.

7.5.3 Foodborne versus waterborne disease

The separation of food and water as exposure vehicles for attribution purposes is often useful as different regulatory agencies may have responsibility for each source. However, at a community level, the differentiation between food and water may not be sensible in terms of how risks are managed. These issues should be specifically considered in a national burden study.

7.5.4 Situation analysis and knowledge translation

Social scientists, stakeholders and decision-makers need to be included in the study team from the earliest stages in order to effectively support knowledge translation and the development of science-based policies. Their involvement includes developing a situation analysis (for an example see [243]), and early and continuous efforts to recognize and incorporate knowledge translation and risk communication to audiences identified in the situation analysis. Differences in experience and perspectives can make collaboration between the social scientists and epidemiological/food safety technical participants challenging.

Knowledge translation and risk communication are usually specialist activities, and require on-going commitment and resources [244]. In order to promote uptake of research results, identified barriers and facilitators are described in the SA/KT/RC Manual.

Barriers to knowledge translation include:

- *Limitations resulting from lack of data and information.* Incomplete information, with associated caveats and uncertainty, may prevent clear conclusions being drawn for policy.
- *Differing time pressures.* Research may take months or years to complete, whereas policy-makers usually need to produce decisions in much shorter timeframes.
- *The weighting of evidence may differ.* Scientists are likely to value data and analysis most highly, whereas policy-makers may be also influenced by personal experience, anecdotal information, political and economic considerations, and other factors.

Knowledge translation can be facilitated by:

- *Strong personal relationships between researchers and policy-makers.* Face to face meetings and direct conversations can promote trust and credibility, and support formal written reports.
- *Presenting the results of research so that they address risk management questions.* Such questions are best formulated and delivered by policy-makers at the commencement of the research, but researchers should always expect to address questions of effectiveness, cost, and high risk groups.

7.6 Discussion

The pilot studies of national burdens-of-foodborne disease, initiated by WHO, have promoted the importance of such studies amongst the participating countries and disseminated internationally accepted methodology for such estimates. Few DALY estimates could be calculated, but this was not unexpected, due to data gaps. The first attempt at conducting such studies has

identified challenges in both process and information, including the recognition that data collection and analysis, development of situation analysis, and on-going knowledge translation and risk communication, require commitment of time and financial resources.

The WHO initiative has provided burden of foodborne disease estimates from global and regional perspectives. These estimates provide context and can fill many of the data gaps for individual countries undertaking foodborne burden-of disease studies. In particular, the provision of aetiology estimates for syndromic surveillance data, and attribution estimates for foodborne disease, will be particularly difficult for studies in developing countries to address individually.

The Global Burden of Disease 2010 Study (GBD2010), undertaken by IHME, Seattle, USA, covers a broad range of disease and injuries, and has published country-specific estimates for these on its website [245]. Foodborne diseases are a subset of these estimates, although estimates are typically not stratified by transmission route. National foodborne disease studies as promoted by WHO and FERG include consideration of the national context in a situation analysis (such as the existing national food control system). In addition, the WHO initiative sought to foster the knowledge translation of burden of disease data into policy through on-going cross-agency communication. Such activities are best undertaken by people from within a country.

National burden of foodborne disease studies, particularly in developing countries, now have an opportunity to fill data gaps, and assign aetiology and attribution to the incidence of foodborne diseases, using the data from the WHO initiative to augment local data. Such local data can also be used as a cross check to validate national estimates derived from regional estimates. This should allow the generation of at least preliminary burden estimates to inform national policy. The effective delivery of this information can be guided by the considerations and tools provided in the SA/KT/RC Manual. In the longer term, burden of foodborne disease information should be a fundamental component of a systematic approach to food safety, such as the risk management framework advocated by Codex [246]. Such an approach can enhance both public health and trade.

CONCLUSION 8

CONCLUSION

This report presents the first global and regional estimates of the burden of foodborne diseases. The large disease burden from food highlights the importance of food safety, particularly in Africa, South-East Asia and other more greatly affected regions. Our results indicate that some hazards, such as non-typhoidal *S. enterica,* are important causes of FBD in all regions of the world, while others – such as certain parasitic helminths and aflatoxin – are of highly focal nature resulting in high local burden.

Despite the data gaps and limitations of these initial estimates, it is apparent that the global burden of FBD is considerable, and affects individuals of all ages, but particularly children <5 years of age and persons living in low-income regions of the world. By incorporating these estimates into policy development at both national and international levels, all stakeholders can contribute to improvements in safety throughout the food chain. These results will also help to direct future research activities.

8.1 Reflections on the WHO Initiative to Estimate the Global Burden of Foodborne Diseases

When the WHO Foodborne Disease Burden Epidemiology Reference Group (FERG) first met in September 2007, they were convinced of the necessity to present estimates of the global burden of foodborne disease, but did not yet know if, and how, it could be done. They were aware of national studies on the burden of foodborne diseases, but recognized that attempting a global estimate was a daunting task. The sheer complexity of the problem was challenging: food consumption across the globe is highly diverse and the range of potential contaminants in the food supply is astounding. Yet, with the help of an army of more than a hundred scientists, specialized in their own fields, it turned out to be possible to present the first ever estimates of the global burden of foodborne disease. The process took eight years and an uncounted number of hours. All involved donated their time and experience to WHO, finding own sources of funding in addition to the limited means available and invested liberal amounts of personal time. In particular the Core Group (Task Force chairs and senior advisers) spent their time in numerous teleconferences at sometimes highly inconvenient hours, in particular for the colleagues from Australia and New Zealand. Initially annual meetings were organized, creating momentum and commitment. The global financial crisis inevitably hit FERG, and much more reliance was placed on teleconferences and other means of remote communication, slowing down the process and limiting the involvement to the Core Group mainly. Nevertheless, all FERG members and resource advisers continued to believe in and support the Initiative.

The global burden of foodborne disease was estimated in several distinct steps, building on established methods for estimating burden, as expressed in Disability Adjusted Life Years (DALYs). First, incidence of food-related diseases, including some chronic sequelae and mortality, were estimated for 31 hazards that were considered to contribute significantly to the burden, and for which sufficient data were available. The hazards included 18 enteric pathogens, 10 parasitic diseases and 3 toxic chemicals. For 5 hazards, the data were insufficient to present global estimates, and data were presented for high-income regions only. Next, information was generated on duration and severity of the incident cases of disease to produce estimates of Years Lived with Disability (YLD)

and on the number of Years of Life Lost (YLL) due to premature mortality. Many foodborne hazards are not exclusively transmitted by food, and a separate effort was set up for the attribution of exposure to different sources, including food, the environment and direct contact between humans or with animals. As many data are lacking for attribution, it was decided to apply structured expert elicitation to provide a consistent set of estimates. The global expert elicitation study involved 73 experts and 11 elicitors, and was one of the largest, if not the largest study, of this kind ever undertaken. Combining all streams of data resulted in estimates of the global burden of foodborne disease.

Unlike previously completed national burden of illness studies, FERG decided to also include chemical hazards. The inclusion of chemical hazards was particularly challenging, and it was only through determined efforts by the Chemicals and Toxins Task Force (CTTF) that several chemical hazards could be included. Whereas WHO committees such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and Joint FAO/WHO Meeting on Pesticide Residues (JMPR) typically use a risk assessment approach, a counterfactual attribution approach is commonly applied in global burden estimates of cancer, cardiovascular and other diseases. Deciding which of these approaches was most appropriate for FERG was a difficult, and as yet not fully resolved, process. As a result, burden estimates for several important chemical contaminants (methylmercury, lead, arsenic and cadmium) are expected to be presented at a later stage.

Even though all efforts were made to include the best available science in the estimates, FERG is fully aware of the limitations of the current work. Data needs for burden of illness estimates are high, and crucial information was often lacking, particularly for some of the world's most populous countries, such as China, India and Russia. FERG used statistical models and expert input to estimate some missing data. In particular, Bayesian regression modelling has been used to estimate missing disease incidence data.

Due to the limitations in data availability, FERG decided to present its estimates on a regional level, even though all calculations were made on a national level. The regional estimates are considered more robust as they build on data from several countries in most regions. Yet, the regional estimates do not reflect the diversity of risks between countries in a region, or even within a country. Maps are therefore not presented as it was considered that these would not adequately reflect regional heterogeneity.

The results of the FERG project are presented in several formats. A PLOS collection entitled "The World Health Organization Estimates of the Global Burden of Foodborne Diseases", which can be accessed at a dedicated website.[1] The website presents the key results in a series of seven peer-reviewed papers, and also provides access to a large and growing number of reviews and description of methods that have been published in different peer-reviewed journals. This large body of evidence reflects the considerable support given to FERG by the global scientific community. These papers are also accessible through a dedicated WHO website.[2] WHO has also produced this report, documenting the results and the process of estimating

[1] http://collections.plos.org/ferg-2015 accessed 2 December 2015

[2] http://www.who.int/foodsafety/areas_work/foodborne-diseases/ferg/en/ accessed 3 November 2015

the global burden of foodborne disease and an interactive website allowing stakeholders to explore the results from different perspectives.

Even though the currently presented burden of foodborne disease is substantial, it was not feasible to document the full burden, which is likely to be considerably higher. Not all relevant contaminants could be included, and for those that were included, not all relevant endpoints could be taken into account. FERG selected a shortlist of hazards at the onset, reducing a list of more than 100 contaminants to 40. Exclusions were based on initial judgments about the importance of the global or regional burden, but also on data availability. Of the 40 contaminants selected, analyses have not been completed for lead, methyl mercury, arsenic and cadmium for inclusion in this report. Of potentially relevant endpoints, only Guillain-Barré syndrome and haemolytic uraemic syndrome and invasive salmonellosis were included as outcomes for diarrhoeal diseases, but not irritable bowel syndrome or other functional bowel disorders that are increasingly linked to diarrhoeal disease in developed countries and are associated with a substantial burden. FERG estimates do not include the effects of foodborne diseases on malnutrition and development in low- and middle-income countries, and invasive salmonellosis in HIV co-morbid cases was also excluded, even though a major proportion of these infections may be foodborne. No stillbirths were included for listeriosis and toxoplasmosis, but many would be preventable by appropriate food safety interventions. The counterfactual approach for chemicals produces lower estimates than risk assessment approach (as documented for aflatoxin, see Section 6.4).

Countries who want to build their national food safety strategies are advised to combine the global estimates with national data. It is our experience that a vast amount of additional data exist but has not yet been mined because it is not available in easily accessible databases but rather in paper form. Building on such data may provide sources of validation for any estimates derived from FERG numbers. As a next step, further development of national laboratory-based surveillance programs, should be a priority.

A crucial element of the initiative, often taking a back seat during the huge effort in generating global and regional burden estimates, was therefore the promotion of foodborne burden of disease studies and capacity building in individual countries. FERG was only able to make limited progress towards this objective, in the form of pilot studies in four countries. Since some of these pilot studies encountered significant resource barriers and data shortages, it is hoped that one legacy of the initiative would be to help overcome these through local use of regional estimates. Individual countries can evaluate and apply the FERG regional burden estimates to generate national DALY-based burden data for foodborne illness prioritization. Such a process should include local data for validation where available, and be undertaken by local scientists with an awareness of the food safety context in their country. FERG has also sought to promote knowledge translation of burden of disease estimates into food safety policy at a national level.

APPENDICES

APPENDIX 1.
Formal Description of the Project and Participants

A1.1 Terms of Reference for WHO's Foodborne Disease Burden Epidemiology Reference Group (FERG)

The Foodborne Disease Burden Epidemiology Reference Group (FERG) will act as an advisory body to WHO on matters of global foodborne diseases epidemiology.

Functions:

The FERG shall have the following **functions**:

- To review epidemiological data on foodborne disease burden.
- To identify technical gaps and priorities for research activities.
- To make recommendations to WHO on the establishment of FERG TFs and other means through which scientific and technical matters are addressed.

Composition:

- FERG members shall serve in their personal capacities to represent the broad range of disciplines relevant to global foodborne disease epidemiology.
- Members of the FERG, including the Chair, shall be selected by the Director-General.
- Members of the FERG, including the Chair, shall be appointed to serve for a period of one year, and shall be eligible for re-appointment.

Operation:

The FERG shall usually meet at least twice a year. WHO shall provide any necessary scientific, technical and other support for the FERG, including for the preparation of meeting reports. FOS shall provide secretarial support.

A1.2 Foodborne Disease Burden Epidemiology Reference Group

The Foodborne Disease Burden Epidemiology Reference Group (FERG) is composed of internationally renowned experts in a broad range of disciplines relevant to global foodborne disease epidemiology. Members were appointed by the WHO Director-General, Dr Margaret Chan, following a transparent selection process.

The expert group is charged to:

- assemble, appraise and report on the current, the projected, as well as the averted burden of foodborne disease estimates;
- conduct epidemiological reviews for mortality, morbidity and disability in each of the major foodborne diseases;
- provide models for the estimation of FBD burden where data are lacking;
- develop cause attribution models to estimate the proportion of diseases that are foodborne; and, most importantly,
- use the FERG models to develop user-friendly tools for burden of foodborne disease studies at country level.

To estimate the global human health burden (expressed in Disability-Adjusted Life Years– DALYs), FERG will initially focus on microbial, parasitic, zoonotic and chemical contamination of food with an emphasis on:

- diseases whose incidence and severity is thought to be high; and
- pathogens and chemicals that are most likely to contaminate food, and that have a high degree of preventability.

A1.3 Participants

FERG Members

- Formally appointed by the WHO Director-General, following a selection procedure.
- Allocated to Core Group and TFs.
- Have full participation rights in all technical discussions.

Resource advisers

- Not formally appointed by the Director General.
- Allocated to TFs on an *ad hoc* basis (as required).
- Have full participation rights in technical discussions.

WHO Secretariat and other UN Organizations

- Have full participation rights in technical discussions.
- Allocated to TFs on an *ad hoc* basis.

Observers

- Nominated by FERG members (one per member).
- No 'formal' right of intervention in plenary.
- Participation in TFs, as appropriate.

Stakeholders

- Invited by WHO to designated sessions.
- Formal right of intervention in designated sessions.
- No participation in technical discussions to avoid conflicts of interest.

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APPENDIX 2. Subregions

SUBREGION(1) [5]	WHO MEMBER STATES
AFR D	Algeria; Angola; Benin; Burkina Faso; Cameroon; Cabo Verde; Chad; Comoros; Equatorial Guinea; Gabon; Gambia; Ghana; Guinea; Guinea-Bissau; Liberia; Madagascar; Mali; Mauritania; Mauritius; Niger; Nigeria; Sao Tome and Principe; Senegal; Seychelles; Sierra Leone; Togo.
AFR E	Botswana; Burundi; Central African Republic; Congo; Côte d'Ivoire; Democratic Republic of the Congo; Eritrea; Ethiopia; Kenya; Lesotho; Malawi; Mozambique; Namibia; Rwanda; South Africa; Swaziland; Uganda; United Republic of Tanzania; Zambia; Zimbabwe.
AMR A	Canada; Cuba; United States of America.
AMR B	Antigua and Barbuda; Argentina; Bahamas; Barbados; Belize; Brazil; Chile; Colombia; Costa Rica; Dominica; Dominican Republic; El Salvador; Grenada; Guyana; Honduras; Jamaica; Mexico; Panama; Paraguay; Saint Kitts and Nevis; Saint Lucia; Saint Vincent and the Grenadines; Suriname; Trinidad and Tobago; Uruguay; Venezuela (Bolivarian Republic of).
AMR D	Bolivia (Plurinational State of); Ecuador; Guatemala; Haiti; Nicaragua; Peru.
EMR B	Bahrain; Iran (Islamic Republic of); Jordan; Kuwait; Lebanon; Libya; Oman; Qatar; Saudi Arabia; Syrian Arab Republic; Tunisia; United Arab Emirates.
EMR D	Afghanistan; Djibouti; Egypt; Iraq; Morocco; Pakistan; Somalia; South Sudan(2); Sudan; Yemen.
EUR A	Andorra; Austria; Belgium; Croatia; Cyprus; Czech Republic; Denmark; Finland; France; Germany; Greece; Iceland; Ireland; Israel; Italy; Luxembourg; Malta; Monaco; Netherlands; Norway; Portugal; San Marino; Slovenia; Spain; Sweden; Switzerland; United Kingdom.
EUR B	Albania; Armenia; Azerbaijan; Bosnia and Herzegovina; Bulgaria; Georgia; Kyrgyzstan; Montenegro; Poland; Romania; Serbia; Slovakia; Tajikistan; The Former Yugoslav Republic of Macedonia; Turkey; Turkmenistan; Uzbekistan.
EUR C	Belarus; Estonia; Hungary; Kazakhstan; Latvia; Lithuania; Republic of Moldova; Russian Federation; Ukraine.
SEAR B	Indonesia; Sri Lanka; Thailand.
SEAR D	Bangladesh; Bhutan; Democratic People's Republic of Korea; India; Maldives; Myanmar; Nepal; Timor-Leste.
WPR A	Australia; Brunei Darussalam; Japan; New Zealand; Singapore.
WPR B	Cambodia; China; Cook Islands; Fiji; Kiribati; Lao People's Democratic Republic; Malaysia; Marshall Islands; Micronesia (Federated States of); Mongolia; Nauru; Niue; Palau; Papua New Guinea; Philippines; Republic of Korea; Samoa; Solomon Islands; Tonga; Tuvalu; Vanuatu; Viet Nam.

Notes: (1) The subregions are defined on the basis of child and adult mortality as described by Ezzati *et al.* [5]. Stratum A = very low child and adult mortality; Stratum B = low child mortality and very low adult mortality; Stratum C = low child mortality and high adult mortality; Stratum D = high child and adult mortality; and Stratum E = high child mortality and very high adult mortality. The use of the term 'subregion' here and throughout the text does not identify an official grouping of WHO Member States, and the "subregions" are not related to the six official WHO regions, which are AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WPR = Western Pacific Region.

(2) South Sudan was re-assigned to the WHO African Region in May 2013. As this study relates to time periods prior to this date, estimates for South Sudan were included in the WHO Eastern Mediterranean Region.

APPENDIX 3.
Preliminary hazards considered by each task force

At the FERG 1 meeting (26–28 November 2007), each of the hazard-based TFs considered a comprehensive list of potential foodborne hazards for the development of burden estimates. During the course of the project these lists had to be reduced, largely for practical reasons concerning the ability to generate burden estimates. For reference, the complete list is given here.

EDTF

Adenovirus
Aeromonas spp.
Astrovirus
Bacterial toxins (*B. cereus*)
Bacterial toxins (*C. perfringens*)
Bacterial toxins (*S. aureus*)
Brucella spp.
Campylobacter spp.
Clostridium botulinum
Enteroaggerative *E. coli* (EAggEC)
Entero-pathogenic *E. coli* (EPEC)
Entero-toxigenic *E. coli* (ETEC)
Enterovirus
Helicobacter pylori
Hepatitis A virus
Hepatitis E virus
Leptospira spp.
Listeria monocytogenes
Mycobacterium bovis
Non cholera Vibrios
Norovirus
Prions
Rotavirus
Salmonella (non-typhoidal) spp.
Salmonella (typhoid) spp.
Shiga-toxin producing *E. coli* (STEC)
Shigella spp.
Vibrio cholerae 01/0139
Yersinia spp.

PDTF

Ancylostoma duodenale
Angiostrongylus cantonensis
Angiostrongylus costaricensis
Anisakis simplex
Ascaris spp.
Blastocystis hominis
Capillaria philippinensis
Clonorchis sinensis
Cryptosporidium spp.
Cyclospora spp.
Dicrocoelium dendriticum
Dientamoeba fragilis
Diphyllobothrium latum
Echinococcus spp.
Echinostoma spp.
Entamoeba histolytica
Fasciola spp.
Fasciolopsis buski
Gastrodiscoides hominis
Giardia spp.
Gnathostoma spinigerum
Heterophyes heterophyes
Hymenolepis nana
Isospora belli
Linguatula serata
Metagonimus yokogawai
Nanophytes salmincola
Opisthorchis felineus
Opisthorchis viverrini
Paragonimus spp.
Sarcocystis hominis
Taenia saginata
Taenia solium
Toxocara spp.
Toxoplasma gondii
Trichinella spp.
Trichostrongylus spp.
Trichuris trichiura

CTTF

Elemental contaminants (e.g. lead, mercury, cadmium, manganese, arsenic)
Mycotoxins (e.g. aflatoxins, ochratoxins, fumonisin, trichothocenes)
Food additives (e.g. sulphites, nitrites/ nitrates, benzoic acid)
Pesticides (e.g. organophosphates, carbamates, DDT, pyrethrins)
Organic industrial pollutants (e.g. persistent organic pollutants)
Veterinary drugs/residues (e.g. antibiotics, hormones–but not antimicrobial residues)
Seafood toxins (e.g. tetrodotoxin, ciguatera, shellfish toxins, DSPs, PSPs, histamines)
Process contaminants (e.g. acrylamide, PAHs, choropropanol)
Allergens (e.g. peanuts)
Natural toxicants (e.g. cyanide in cassava, aminoglycosides)
Radionuclides and depleted uranium

APPENDIX 4.
Hazard-specific input parameter sources and methods

A4.1 Brucellosis

Incidence

There were 32 countries identified as "free of brucellosis in livestock", using 2006–2012 data reported to the World Organisation for Animal Health (OIE) [248], and a list of European countries recognized by the European Union as "officially brucellosis free" in cattle, sheep and goats in 2010 [249]. Using 2001–2004 OIE data, a previous review [250] estimated human brucellosis incidence for 9 of the countries identified as free of brucellosis in livestock. The median human brucellosis incidence from these 9 countries free of brucellosis in livestock was used as the estimated human brucellosis incidence for each of the 32 countries free of brucellosis in livestock. A FERG-commissioned systematic review was then used to screen 2385 articles [251] and a literature review for national human brucellosis incidence estimates [174, 175, 187, 188, 252, 253], to extract brucellosis national incidence estimates for 17 countries (Argentina, Canada, Chad, China, Egypt, France, Greece, Iraq, Iran, Italy, Kyrgyztan, Jordan, Mexico, Oman, Saudi Arabia, Turkey, and the United States of America). The human brucellosis incidence estimates in each of these countries were compared with human brucellosis incidence estimates in the same country in a previous review, which used 2001–2004 OIE data [250], to estimate a multiplier (mean=5.4, range 1.6–15.4) to account for under-reporting. This multiplier was used to estimate national human brucellosis incidence for countries with OIE human brucellosis data in the previous review but without national human brucellosis incidence estimates identified in the current systematic review or literature review. By multipling the human brucellosis incidence reported to OIE by the multiplier, there were 32 such countries. These steps yielded human brucellosis incidence estimates for 81 countries. The FERG Computational Task Force imputation model was then used to impute an incidence of human brucellosis in all countries with missing incidence.

Clinical Outcomes

The FERG-commissioned systematic review assisted in determining the clinical outcomes for human brucellosis [254]. These were: acute brucellosis (severe); acute brucellosis (moderate); chronic brucellosis; brucellosis orchitis; and brucellosis death. For acute brucellosis, it was assumed that 50% of cases were severe, 50% of cases were moderate, 40% of brucellosis cases resulted in chronic brucellosis, and 10% of brucellosis cases in males resulted in orchitis [254].

Duration

Acute brucellosis: duration 14 days (min. 7 days–max. 21 days). Chronic brucellosis: duration 6 months (min. 3 months– max. 24 months). Brucellosis orchitis: duration 6 months (min. 3 months–max. 24 months) [254].

Disability weight

Acute brucellosis (severe): GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Acute brucellosis (moderate): GBD2010 disability weight of 0.053 (95% UI 0.033–0.081) for infectious disease, acute episode, mild. Chronic brucellosis: GBD2010 disability weight 0.079 (95%UI 0.053–0.115) for musculoskeletal problems, legs, moderate. Brucellosis orchitis: GBD2010 disability weight of 0.097 (95% UI 0.063–0.0137) for epididymo-orchitis [82].

Mortality

Acute brucellosis and chronic brucellosis case fatality ratio 0.5% (min. CFR 0.25%–max. CFR 0.75%) [255, 256].

Age distribution

Acute brucellosis, chronic brucellosis, brucellosis orchitis and brucellosis death age distribution: 3% <15 years; 29% 15–24 years; 24% 25–34 years; 16% 35–44 years; 13% 45–54 years; 12% 55–64 years; and 3% >65 years [257].

Sex distribution

Acute brucellosis, chronic brucellosis and brucellosis deaths sex distribution: 55% male (95% UI 50%–60% male) [254]. Brucellosis orchitis: 100% male.

A4.2 Mycobacterium bovis infections

Incidence

There were 51 countries identified as "free of *Mycobacterium bovis* in cattle" using 2005–2012 data reported to OIE [248] and a list of European countries recognized by the European Union as "officially free of bovine tuberculosis" in 2010 [249]. A FERG-commissioned systematic review screened 1203 articles [258] with data from 91 countries, and estimated the median proportion of human tuberculosis cases due to *M. bovis* at the region level as 2.8% for AFR, 0.4% for EUR and 0.3% for AMR; the overall median proportion from studies in the review (1.0%) was used in the three other regions. These proportions were applied to all countries in each respective region except for the 51 countries free of *M. bovis* in cattle. The lowest observed proportion (0.3%) was assigned to the 51 countries free of *M. bovis* in cattle. Country-level human tuberculosis incidence was abstracted from the WHO Global Tuberculosis Report [165] and multiplied by population estimates and the proportion of human tuberculosis cases due to *M. bovis* to estimate human *M. bovis* cases.

Clinical Outcomes

Clinical outcomes were *M. bovis* tuberculosis and *M. bovis* death.

Duration

M. bovis tuberculosis duration was estimated using data in the 2014 WHO Global Tuberculosis Report on incidence and prevalence of human TB infections [165]; these data yielded a duration of 1.5 years in all regions except AFR, where the duration was 1 year.

Disability weight

M. bovis tuberculosis: GBD2010 disability weight of 0.331 (95% UI 0.222–0.450) for tuberculosis without HIV infection [82].

Mortality

Deaths from *M. bovis* were estimated following the same approach for estimating *M. bovis* cases after reducing the mortality by 20% due to the recognition from another FERG-commissioned review that *M. bovis* infections are more likely to result in extrapulmonary infections [259] and that extrapulmonary infections have a lower case-fatality ratio (CFR) than pulmonary tuberculosis infections; a 20% reduction in mortality was based on a review of the United States of America national surveillance data from 2009–2010, which found that the CFR for extrapulmonary tuberculosis infections was approximately 20% lower than the CFR for pulmonary tuberculosis infections. Therefore, country-level human tuberculosis mortality rates of tuberculosis among persons not infected with HIV were abstracted from the WHO Global Tuberculosis Report [165], reduced by 20%, and then multiplied by population estimates and the proportion of human tuberculosis cases due to *M. bovis* to estimate *M. bovis* deaths.

Age distribution

It was assumed that the age distribution of *M. bovis* cases and *M. bovis* deaths was the same as the age distribution of human tuberculosis cases and deaths, and therefore used the age distribution from Table 3.2 of the WHO Global Tuberculosis Report: 2% <15 years; 60% 15–44 years; 28% 45–64 years; 10% >65 years [165].

Sex distribution

It was assumed that the sex distribution of *M. bovis* cases and *M. bovis* deaths was the same as the sex distribution of human tuberculosis cases and deaths, and therefore used the sex distribution from Table 3.2 of the WHO Global Tuberculosis Report: 65% male [165].

A4.3 Typhoid

Incidence

FERG reviewed available burden of disease estimates for typhoid fever [6, 260] before selecting the IHME Global Burden of Disease 2010 (GBD2010) estimates because these estimates were published in peer-reviewed literature and were available for all countries. At the request of FERG, IHME provided GBD2010 data with country-specific, age-standardized prevalence (per 100 000 population) of "typhoid and paratyphoid fever", and "typhoid and paratyphoid liver abscesses and cysts" [6]. Assuming a steady disease state, prevalence of typhoid and paratyphoid fever was converted to incidence by dividing by duration; similarly for typhoid and paratyphoid abscesses and cysts. Typhoid fever incidence was determined using a ratio of 1.0 *Salmonella* serotype Typhi cases to 0.23 *Salmonella* serotype Paratyphi A cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997 [262]; similarly for typhoid abscesses and cysts. We used the GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) to derive a range of estimates for typhoid incidence.

Clinical Outcomes

Clinical outcomes were typhoid fever, typhoid liver abscesses and cysts, and typhoid death [6].

Duration

Typhoid fever: duration 28 days (min. 7 days–max. 42 days). Typhoid liver abscesses and cysts: duration 42 days (min. 28 days–max. 56 days). Duration was estimated based on median duration before hospitalization for typhoid fever or typhoid abscesses/cysts of 10 days, recommended treatment duration for typhoid fever of 10–14 days and for typhoid abscesses/cysts of 28–112 days, and presumed longer duration in patients with typhoid fever or typhoid abscesses/cysts who are not hospitalized [263].

Disability weight

Typhoid fever: GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Typhoid liver abscesses and cysts: GBD2010 disability weight of 0.254 (95% UI 0.170–0.355) for infectious disease, post-acute consequences, severe [82].

Mortality

GBD2010 country-specific mortality data for "typhoid and paratyphoid fevers" were obtained by sex and 20 age groups from the IHME website [58]. Typhoid mortality was determined using a ratio of 1.0 *Salmonella* serotype Typhi cases to 0.23 *Salmonella* serotype Paratyphi A cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997

[262]. The GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) were used to derive a range of estimates for paratyphoid deaths.

Age distribution

Using data from IHME, the age distribution for typhoid fever, typhoid liver abscesses and cysts, and typhoid deaths was 5% <1 year; 16% 1–4 years; 22% 5–14 years; 19% 15–24 years; 14% 25–34 years; 9% 35–44 years; 6% 45–54 years; 3% 55–64 years; 3% 65–74 years; 1% 75–84 years; and 1% >85 years [6].

Sex distribution

Using data from IHME, the sex distribution for cases of typhoid fever, and typhoid liver abscesses and cysts was 56% male, and the sex distribution for typhoid deaths was 58% male [6].

A4.4 Paratyphoid

Incidence

FERG reviewed available burden of disease estimates for typhoid and paratyphoid fever [6, 260] before selecting the IHME Global Burden of Disease 2010 (GBD2010) estimates because these estimates were published in peer-reviewed literature and were available for all countries. At the request of FERG, IHME provided GBD2010 data with country-specific, age-standardized prevalence (per 100 000 population) of "typhoid and paratyhoid fever", and "typhoid and paratyphoid liver abscesses and cysts" [6]. Assuming a steady disease state, prevalence of typhoid and paratyphoid fever was converted to incidence by dividing by duration; similarly for typhoid and paratyphoid abscesses and cysts. Paratyphoid fever incidence was determined using a ratio of 0.23 *Salmonella* serotype Paratyphi A cases to 1.0 *Salmonella* serotype Typhi cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997 [262]; similarly for paratyphoid abscesses and cysts. We used the GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) to derive a range of estimates for paratyphoid incidence.

Clinical Outcomes

Clinical outcomes were paratyphoid fever, paratyphoid liver abscesses and cysts, and paratyphoid deaths [6].

Duration

Paratyphoid fever: duration 28 days (min. 7 days–max. 42 days); paratyphoid liver abscesses and cysts: duration 42 days (min. 28 days–max. 56 days). Duration was estimated based on median duration before hospitalization for paratyphoid fever or paratyphoid abscesses and cysts of 10 days, with a recommended treatment duration for paratyphoid fever of 10–14 days and for paratyphoid abscesses and cysts of 28–112 days, and presumed longer duration in patients with paratyphoid fever or paratyphoid abscesses and cysts who are not hospitalized [263].

Disability weight

Paratyphoid fever: GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Paratyphoid liver abscesses and cysts: GBD2010 disability weight of 0.254 (95% UI 0.170–0.355) for infectious disease, post-acute consequences, severe [82].

Mortality

GBD2010 country-specific mortality data for "typhoid and paratyphoid fevers" were obtained by sex and 20 age groups

from the IHME website [58]. Paratyphoid mortality was determined using a ratio of 0.23 *Salmonella* serotype Paratyphi A cases to 1.0 *Salmonella* serotype Typhi cases observed in national laboratory-based surveillance in the United States of America and in a global survey in 1997 [262]. We used the GBD2010 range of estimates around the mean estimate of global deaths due to typhoid and paratyphoid fevers (190 242 with UI 23 786–359 075) to derive a range of estimates for paratyphoid deaths.

Age distribution

Using data from IHME, the age distribution for paratyphoid fever, paratyphoid liver abscesses and cysts, and paratyphoid deaths was 5% <1 year; 16% 1–4 years; 22% 5–14 years; 19% 15–24 years; 14% 25–34 years; 9% 35–44 years; 6% 45–54 years; 3% 55–64 years; 3% 65–74 years; 1% 75–84 years; and 1% >85 years [6].

Sex distribution

Using data from IHME, the sex distribution for cases of paratyphoid fever, and paratyphoid liver abscesses and cysts, was 56% male, and the sex distribution for paratyphoid deaths was 58% male [6].

A4.5 Hepatitis A infection

Incidence

Assuming a case-fatality ratio of 0.2% [264], the IHME Global Burden of Disease 2010 (GBD2010) country-specific data on "Hepatitis A", available on the IHME website by sex and 20 age groups [58] were converted to incidence. the GBD2010 range of estimates around the mean estimate of global deaths due to hepatitis A (102 850 with UI 51 157–228 057) to derive a range of estimates for hepatitis A incidence.

Clinical Outcomes

Clinical outcomes were acute hepatitis A (severe), acute hepatitis A (mild), and hepatitis A death. For acute hepatitis, it was assumed that 50% of cases were severe and 50% of cases were mild [264].

Duration

Acute hepatitis A: duration 21 days (min. 14 days–max. 30 days) [264].

Disability weight

Acute hepatitis A (severe): GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. Acute hepatitis A (mild): GBD2010 disability weight of 0.005 (95% UI 0.002–0.011) for infectious disease, acute episode, mild [82].

Mortality

GBD2010 country-specific mortality data for "hepatitis A" were obtained by sex and 20 age groups from the IHME website [58]. The GBD2010 range of estimates around the mean estimate of global deaths due to hepatitis A (102 850 with UI 51 157–228 057) were used to derive a range of estimates for hepatitis A deaths.

Age distribution

Using data from IHME, the age distribution for acute hepatitis A cases and hepatitis A deaths was 10% <1 year; 5% 1–4 years; 2% 5–14 years; 3% 15–24 years; 5% 25–34 years; 11% 35–44 years; 17% 45–54 years; 20% 55–64 years; 17% 65–74 years; 5% 75–84 years; and 5% >85 years [58].

Sex distribution

Using data from IHME, the sex distribution for acute hepatitis A cases and hepatitis A deaths was 57% male [58].

A4.6 Shiga toxin-producing Escherichia coli (STEC) infection

Incidence

Using a FERG-commissioned systematic review that screened 17 178 articles, and a search for national surveillance data, Shiga toxin-producing *Escherichia coli* (STEC) incidence data from 21 countries were identified. Using a hierarchical study selection process, in the subregions with prospective cohort studies or multipliers studies that estimated national STEC incidence, that STEC incidence was assigned to all countries in the subregion. In subregions with only STEC-notifiable disease data, STEC incidence for all countries in the subregion was estimated using a multipler of 36 (range 7.4–106.8) to account for under-reporting; the STEC incidence from notifiable disease data was multiplied by the multiplier to estimate the national STEC incidence. In subregions with no STEC incidence data, geographical proximity was used to extrapolate the STEC incidence to all countries in the subregion [265]. These efforts led to the following regional incidence (per 100 000 population) estimates: AFR subregions D and E 1.4; AMR subregions A and D 93.5; AMR subregion B 27.2; EMR 152.6; EUR subregion A 47.1; EUR subregion B 2.7; EUR subregion C 2.5; SEAR 66.3; WPR subregion A 44.5; and WPR subregion B 3.5.

Clinical Outcomes

Clinical outcomes of STEC infections were acute STEC diarrhoea (severe), acute STEC diarrhoea (moderate), acute STEC diarrhoea (mild), STEC haemolytic uraemic syndrome (HUS), STEC end-stage renal disease (ESRD), and STEC death. We assumed that 2% of STEC infections resulted in severe diarrhoea, 18% of STEC infections resulted in moderate diarrhoea, and 80% of STEC infections resulted in mild diarrhoea [266]. We assumed that the following percent of STEC infections were serotype O157: 36% in AMR A, AMR B, EUR and WPR A; 10% in AMR D, AFR and SEAR; and 0% in EMR. We assumed that 0.8% (min. 0.7%–max. 0.9%) of O157 STEC infections and 0.03% (min. 0.01%–max. 0.04%) of non-O157 STEC infections resulted in HUS, and the 3% (min. 0%–max. 30%) of HUS cases resulted in ESRD [265].

Duration

Acute STEC diarrhoea: duration 7 days (min. 5 days–max. 10 days) [266]. STEC haemolytic uraemia syndrome: duration 28 days (min. 14 days–max. 42 days). STEC end-stage renal disease: results in lifelong disability in countries in AMR A, EUR A and WPR A, and death in other countries [265, 267, 268].

Disability weight

Acute diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe. Acute diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate. Acute diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild. STEC haemolytic uraemic syndrome: GBD2010 disability weight 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe. STEC end-stage renal disease: GBD2010 disability weight of 0.573 (95% UI 0.397–0.749) for end-stage renal disease, on dialysis [82].

Mortality

STEC haemolytic uraemic syndrome case fatality ratio 3.7%. STEC end-stage renal disease case fatality ratio 20% in countries in AMR A, EUR A and WPR A; case fatality ratio 100% in other countries [265].

Age distribution

Acute STEC diarrhoea and STEC haemolytic uraemic syndrome age (HUS) distribution: 29% <5 years;, 20% 5–14 years; 35% 15–54 years; 16% ≥55 years. STEC end-stage renal disease (ESRD) and ESRD deaths age distribution: 41% <5 years; 18% 5–14 years; 26% 15–54 years; 15% ≥55 years. HUS deaths age distribution: 11% <1 year; 47% 1–4 years; 14% 5–14 years; 22% 15–64 years; 6% ≥65 years [267].

Sex distribution

Acute STEC diarrhoea, STEC haemolytic uraemic syndrome (HUS), STEC end-stage renal disease (ESRD), HUS deaths and ESRD deaths sex distribution: 50% male [265].

A4.7 Botulism

Incidence

Estimates of incidence were only conducted for the 61 EUR and other subregion A (low mortality) countries. Based on a literature review for articles with national estimates of foodborne diseases including botulism, we identified national estimates of the incidence of botulism from five countries: Canada [175], France [174], Georgia [269], Poland [270] and the United States of America [188]. The median botulism incidence from these five countries was from Canada, therefore the botulism incidence from Canada (0.04 per 100 000 population, with a 90% confidence interval of 0.02–0.08 per 100 000) was used as the incidence for all 55 countries in EUR and AMR A.

Clinical Outcomes

Clinical outcomes were botulism (mild to moderate), botulism (severe), and botulism death. We assumed that 35% (range 20-50%) of botulism cases resulted in severe botulism [269–271].

Duration

Botulism (mild to moderate): duration 10 days (min. 5 days–max. 20 days); botulism (severe): duration 30 days (min. 15 days–max. 180 days) [269–271].

Disability weight

- Botulism (mild to moderate): GBD2010 disability weight 0.198 (95% UI 0.137–0.278) for multiple sclerosis, mild.
- Botulism (severe): GBD2010 disability weight 0.445 (95% UI 0.303–0.593) for multiple sclerosis, moderate [82].

Mortality

Estimates of mortality were only conducted for the 55 countries in EUR and AMR A. Severe botulism case fatality ratio 15% (range 5-25%). Assume no deaths among mild to moderate botulism cases [188, 269, 270].

Age distribution

Mild to moderate botulism, severe botulism, and botulism death age distribution: mode 50 years (min. age 4 years–max. age 88 years) [269–271].

Sex distribution

Mild to moderate botulism, severe botulism, and botulism death sex distribution: 48% male [269–271].

A4.8 Clostridium perfringens intoxication

Incidence

Estimates of incidence were only conducted for the 61 EUR and other subregion A (low mortality) countries. Based on a literature review for articles with national estimates of foodborne diseases that included *Clostridium perfringens* intoxications, we identified national incidence estimates for *Clostridium perfringens* intoxications from seven countries: Australia [272], Canada [175], France [174], Netherlands [154], New Zealand [252], United Kingdom [48], and the United States of America [188]. The median *C. perfringens* intoxication incidence from these seven countries was from the United States of America, therefore the *C. perfringens* intoxication incidence from the United States of America (324.19 per 100 000 population with a 95% confidence interval of 126.14–833.44 per 100 000) was used as the *C. perfringens* intoxication incidence for all EUR and other subregion A countries.

Clinical Outcomes

Clinical outcomes were acute gastroenteritis due to *Clostridium perfringens* intoxication and death due to *C. perfringens* intoxication [273].

Duration

Acute gastroenteritis due to *Clostridium perfringens* intoxication: duration 1 day (min. 0.25 days–max. 2.5 days) [273].

Disability weight

- Acute gastroenteritis due to *Clostridium perfringens* intoxication: GBD2010 disability weight 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

Estimates of mortality were only conducted for the 61 EUR and other subregion A (low mortality) countries. National estimates of *Clostridium perfringens* intoxications cases and deaths were available from Australia [272], France [174], Netherlands [154], New Zealand [252], and the United States of America [188]; the median case fatality ratio (CFR) from these five countries was the New Zealand (0.0030% [95%CI: 0.0024%-0.0038%]), therefore the CFR from New Zealand was used as the CFR for all EUR and other subregion A countries.

Age distribution

Acute gastroenteritis and deaths due to *Clostridium perfringens* intoxication age distribution: 1% <5 years; 13% 5–14 years; 59% 15–54 years; 27% ≥55 years [273].

Sex distribution

Acute gastroenteritis and deaths due to *Clostridium perfringens* intoxication sex distribution: 63% male [273].

A4.9 Staphylococcus aureus intoxication

Incidence

Estimates of incidence were only conducted for the 61 EUR and other subregion A (low mortality) countries. Based on a literature review for articles with national estimates of foodborne diseases that included *Staphylococcus aureus* intoxication, we identified national incidence estimates for *S. aureus* intoxication from seven countries: Australia [272], Canada [175], France [174], Netherlands [154], New Zealand [252], England and Wales as a proxy for United Kingdom [172], and the United States of America [188]. The median *S. aureus* intoxication incidence

from these seven countries was from Canada, therefore the *S. aureus* intoxication incidence from the Canada (77.3 per 100 000 population with a 95% confidence interval of 50.65–118.0 per 100 000) was used as the *S. aureus* intoxication incidence for all EUR and other subregion A countries.

Clinical Outcomes

Clinical outcomes were acute gastroenteritis due to *S. aureus* intoxication and death due to *S. aureus* intoxication [273].

Duration

Acute gastroenteritis due to *S. aureus* intoxication: duration 1 day (min. 0.25 days–max. 2.5 days) [273].

Disability weight

- Acute gastroenteritis due to *S. aureus* intoxication: GBD2010 disability weight 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

Estimates of mortality were only conducted for the 61 EUR and other subregion A (low mortality) countries. National estimates of *S. aureus* intoxication cases and deaths were available from the Netherlands [154] and the United States of America [188]; the case fatality ratio (CFR) for the Netherlands was 0.0024% and for the United States of America was 0.0025%. We used the CFR from the United States of America as the CFR for all EUR and other subregion A countries with a 95% confidence interval of 0.0012%-0.0045%.

Age distribution

Acute gastroenteritis and deaths due to *S. aureus* intoxication age distribution: 5% <5 years; 19% 5–14 years; 48% 15–54 years; 28% ≥55 years [273].

Sex distribution

Acute gastroenteritis and deaths due to *S. aureus* intoxication sex distribution: 48% male [273].

A4.10 Bacillus cereus intoxication

Incidence

Estimates of incidence were only conducted for the 61 EUR and other subregion A (low mortality) countries. Based on a literature review for articles with national estimates of foodborne diseases that included Bacillus cereus intoxication, we identified national incidence estimates for Bacillus cereus intoxication from seven countries: Australia [272], Canada [175], France [174], Netherlands [154], New Zealand [252], England and Wales as a proxy for the United Kingdom [172], and the United States of America [188]. The median *B. cereus* intoxication incidence from these seven countries was for the United Kingdom (England and Wales), therefore the *B. cereus* intoxication incidence from the United Kingdom (21.4 per 100 000) was used as the *B. cereus* intoxication incidence for all EUR and other subregion A countries; because the available *B. cereus* intoxication incidence estimate from England and Wales did not include a corresponding confidence interval, the average values of the intervals from the countries with the next lowest and next highest *B. cereus* intoxication incidence were used (United States of America 5.2–49.4 and the Netherlands 11.5–67.2) for a 95% confidence interval 7.9–58.3 per 100 000.

Clinical Outcomes

Clinical outcomes were acute gastroenteritis due to *Bacillus cereus* intoxication [273].

Duration

Acute gastroenteritis due to *Bacillus cereus* intoxication: duration 1 day (min. 0.25 days–max. 2.5 days) [273].

Disability weight

- Acute gastroenteritis due to *Bacillus cereus* intoxication: GBD2010 disability weight 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

No deaths estimated.

Age distribution

Acute gastroenteritis due to *Bacillus cereus* intoxication age distribution: 3% <5 years; 14% 5–14 years; 53% 15–54 years; 30% ≥55 years [273].

Sex distribution

Acute gastroenteritis due to *Bacillus cereus* intoxication sex distribution: 50% male [273].

A4.11 Listeriosis

Incidence

Using a FERG-commissioned systematic review which screened 11 22 papers and national surveillance, listeriosis incidence data were extracted from 43 papers. National listeriosis incidence estimates were then calculated for all countries using the extracted data and imputed estimates through a multilevel random effects model [70].

Clinical Outcomes

Clinical outcomes were determined using outcome probabilities from the FERG-commissioned review and a random effects meta-regression model; for each study identified in the review, a weight was assigned reflecting the study quality. These weights were included as a fixed effect in the meta-regression model.

Clinical outcomes included perinatal and non-perinatal listeriosis; we estimated that 79.3% (min. 77.3%–max. 81.3%) of listeriosis cases were perinatal and 20.7% (min. 19.0%–max. 22.4%) were non-perinatal. Clinical outcomes among perinatal listeriosis cases were neonatal septicaemia, neonatal meningitis, neurological sequelae, stillborn, and death; stillborns were estimated but not included in the final FERG estimates of deaths and DALYS. We estimated 30.7% of perinatal listeriosis cases developed neonatal septicaemia and 15.2% (min. 13.1%–max. 17.3%) neonatal meningitis, of whom 43.8% (min. 31.8%–max. 55.8%) had neurological sequelae. Clinical outcomes among non-perinatal listeriosis cases were septicaemia, meningitis, neurological sequelae and death; it was estimated that 61.6% (min. 59.4%–max. 63.8%) of non-perinatal listeriosis cases developed septicaemia and 30.7% (min. 28.7%–max. 32.7%) meningitis, of whom 13.7% (min. 8.2%–max. 19.2%) had neurological sequelae [70].

Duration

For perinatal and non-perinatal listeriosis cases: septicaemia duration 7 days, meningitis duration 182 days, and neurological sequelae 7 years [70].

Disability weight

- For listeriosis septicaemia: GBD2010 disability weight (DW) of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe [82].
- For listeriosis meningitis: a DW of 0.426 (95% UI 0.368–0.474) derived from multiplicative methodology and expert elicitation (with bootstrap analysis for CI) using a combination of the following DWs: (1) 0.210 for infectious disease, acute episode, severe; (2) 0.126 for intellectual disability, severe; (3) average of 0.488 for epilepsy, severe and

epilepsy, treated with recent seizures; and (4) 0.76 for motor impairment, moderate.
- For listeriosis neurological sequelae: a DW of 0.292 (95% UI 0.272–0.316) derived from a multiplicative methodology and expert elicitation (with bootstrap analysis for CI) using a combination of following DWs: (1) 0.047 resulting from average of all 10 DWs involving hearing loss; (2) 0.087 resulting from average of all 5 DWs for vision loss; and (3) 0.303 resulting from average of all 4 DWs for stroke, long-term consequence [70, 82].

Mortality

Listeriosis case fatality ratios were estimated following the same approach for estimating clinical outcomes of listeriosis cases; using probabilities from the FERG-commissioned review and a random effects meta-regression model. For each study identified in the review, a weight was assigned reflecting the study quality; these weights were included as a fixed effect in the meta-regression model. The case fatality ratio for perinatal cases was 14.9% (mimimum 11.3% - max. 18.5%); 9.2% (mimimum 7.5% - max. 10.9%) resulted in neonatal deaths and 5.7% (minumum 3.8% - max. 7.6%) resulted in stillbirths; stillborns were not included in the final FERG estimates of deaths and DALYs. The case fatality ratio for non-perinatal cases was 25.9% (mimimum 23.8% - max. 29.0%).

Age distribution

The age distribution of listeriosis cases and deaths was determined from published papers during the FERG-commissioned review [70]. The age distribution for perinatal listeriosis cases and deaths was: 100% <1 month. The age distribution for non-perinatal cases and deaths was: 0% <1 year; 2% 1–4 years; 4% 5–14 years; 10% 15–34 years; 6% 35–44 years; 7% 45–54 years; 13% 55–64 years; 20% 65–74 years; 20% 75–84 years; 18% ≥85 years.

Sex distribution

The sex distribution of listeriosis cases and deaths was determined from published papers during the FERG-commissioned review [70]. The sex distribution for listeriosis cases and deaths was: 50% male.

A4.12 Non-typhoidal Salmonella infection

Incidence

The incidence of diarrhoeal non-typhoidal *Salmonella* (NTS) was estimated separately for middle and high mortality countries, and low mortality countries. For the 133 middle to high mortality countries, we used a modification of the Child Health Epidemiology Reference Group (CHERG) approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to NTS and the 10 other diarrhoeal pathogens[1] in children <5 years of age using CHERG and FERG systematic reviews of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to NTS and the other 10 diarrhoeal pathogens in persons >5 years of age

[1] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The NTS aetiological proportions were extracted from studies, and regional median NTS aetiological proportions calculated. We modified the CHERG approach by dropping regional median NTS aetiological proportion outliers that were ≥5 times greater than the global median NTS aetiological proportion, and replacing missing regional NTS aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional NTS aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional NTS incidence was applied to all countries in that subregion. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified national incidence estimates for NTS from seven countries: Australia [272], Canada [175], France [174], Netherlands [154], New Zealand [252], United Kingdom [48], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these seven countries, we used the estimated national NTS incidence (and range) for that country. For low mortality countries without a national estimate, we used the median NTS incidence from the seven national studies. The median incidence was from Australia: 301.5 per 100 000 population (which was increased by 19% to account for travellers using proxy information from New Zealand), with range 171.1–541.8.

Clinical Outcomes

Clinical outcomes were acute non-typhoidal *Salmonella* (NTS) diarrhoea (severe); acute NTS diarrhoea (moderate); acute NTS diarrhoea (mild); and NTS death. We assumed that 2% of NTS diarrhoeal cases resulted in severe diarrhoea, 25% of NTS diarrhoeal cases resulted in moderate diarrhoea, and 73% of NTS diarrhoeal cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [275]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of all non-typhoidal *Salmonella* (NTS) diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of NTS diarrhoea was 2.8 days [275].

Disability weight

- Acute non-typhoidal *Salmonella* (NTS) diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute NTS diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute NTS diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of NTS was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not

available with an uncertainity interval, we used the uncertainty range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to NTS and the other 10 diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to NTS and the other 10 diarrhoeal pathogens in persons >5 years of age, using an updated FERG systematic review of aetiology studies among inpatients [40, 274]. The NTS aetiological proportions were extracted from studies, and regional median NTS aetiological proportions calculated. We modified the CHERG approach by dropping regional median NTS aetiological proportion outliers that were >5 times greater than the global median NTS aetiological proportion, and replacing missing regional NTS aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional NTS aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional NTS mortality was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified NTS mortality estimates from five countries: Australia [272], France [174], Netherlands [154], New Zealand [252], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these five countries, we used the estimated national NTS mortality (and range) for that country. For low mortality countries without a national estimate, we used the median NTS mortality from the five national studies. The median NTS mortality was from the United States; 0.15 per 100,000 population: range 0.08 – 0.40.

Age distribution

In middle-to-high mortality countries we estimated incidence and mortality of non-typhoidal *Salmonella* (NTS) diarrhoea seperately for children <5 years of age and persons >5 years of age. In low mortality countries, the age distribution for NTS diarrhoea cases was 24% <5 years; 10% 5–14 years; 11% 15–24 years; 42% 25–64 years; and 13% >65 years [276].

Sex distribution

Salmonella sex distribution: 50% male.

A4-13 Invasive Non-typhoidal Salmonella (iNTS) infection

Incidence

Rates of iNTS are highly correlated with HIV prevalence and malaria risk [277]. To estimate iNTS incidence globally, we used age-specific estimates of incidence from a systematic review [277] to construct a random effect log linear model using covariates of country-specific HIV and malaria deaths, and the log of Gross Domestic Product. As data were sparse, we predicted incidence for all ages, which was converted to age-specific incidence based on age profiles for iNTS cases in low and high incidence settings [277]. From this, we predicted iNTS incidence among persons not infected with HIV [62, 278]. To estimate deaths, we assumed that the CFR for iNTS in non-HIV infected individuals was a

uniform distribution with a most likely value of 10% (range 5–20%) in subregion B to E countries, and a most likely value of 4.3% (range 3.9–6.6%) in subregion A countries [279].

Clinical Outcomes

Clinical outcomes were invasive *Salmonella* infection and death.

Duration

The duration of iNTS infection was assumed to be the same as the duration of typhoid which was estimated to be 28 days (min. 7 days–max. 56 days).

Disability weight

- iNTS infection: GBD2010 disability weight of 0.210 (95% UI 0.139–0.298) for infectious disease, acute episode, severe [82].

Mortality

To estimate deaths, we assumed that the CFR for iNTS in non-HIV infected individuals was a uniform distribution with a most likely value of 10% (range 5–20%) in subregion B to E countries and a most likely value of 4.3% (range 3.9–6.6%) in subregion A countries [63].

Age distribution

We assessed the age distribution of invasive NTS cases and deaths in high (Mali) and low (United States) burden settings.

Sex distribution

Salmonella sex distribution: 50% male.

A4.14 Camplyobacter infection

Incidence

The incidence of diarrhoeal *Campylobacter* was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to *Campylobacter* and the 10 other diarrhoeal pathogens[2] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40] and the aetiological proportions of diarrhoeal illnesses due to *Campylobacter* and the 10 other diarrhoeal pathogens in persons >5 years of age, using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The *Campylobacter* aetiological proportions were extracted from studies, and regional median *Campylobacter* aetiological proportions calculated. We modified the CHERG approach by dropping regional median *Campylobacter* aetiological proportion outliers that were >5 times greater than the global median *Campylobacter* aetiological proportion, and replacing missing regional *Campylobacter* aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all 11 diarrhoeal pathogens in a region equalled 1. The resultant regional *Campylobacter*

[2] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional *Campylobacter* incidence was applied to all countries in that region.

In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified national incidence estimates for *Campylobacter* from seven countries: Australia [272], Canada [175], France [174], Netherlands [154], New Zealand [252], United Kingdom [48], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these seven countries, we used the estimated national *Campylobacter* incidence (and range) for that country. For low mortality countries without a national estimate, we used the median *Campylobacter* incidence from the seven national studies. The median incidence was from Canada: 789.2 per 100 000 population (after increasing by 20% to account for travellers according to proxy infomation from the United States of America) with range of 532.3–1140.3. Using a systematic review that identified 63 papers, updated for papers published through 2013 for FERG by the author with the addition of 9 papers, the incidence of Guillain-Barre Syndrome (GBS) in all countries was estimated at 1.4 per 100 000 population (min. 1.1–max. 1.8) [55]. Based on a systematic review, we assumed that 31% (min. 28%–max. 45%) of GBS cases were due to *Campylobacter* infection [280]

Clinical Outcomes

Clinical outcomes were acute *Campylobacter* diarrhoea (severe); acute *Campylobacter* diarrhoea (moderate); acute *Campylobacter* diarrhoea (mild); Guillain-Barre Syndrome due to *Campylobacter* infection; and *Campylobacter* death. We assumed that 2% of *Campylobacter* diarrhoeal cases resulted in severe diarrhoea, 25% of *Campylobacter* diarrhoeal cases resulted in moderate diarrhoea, and 73% of *Campylobacter* diarrhoeal cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days; moderate diarrhoea was 6.4 days; and mild diarrhoea was 4.3 days [266]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of all *Campylobacter* diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of *Campylobacter* diarrhoea was 2.8 days [266]. The duration of Guillain-Barre Syndrome due to *Campylobacter* infection was assumed life-long [281].

Disability weight

- Acute *Campylobacter* diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute *Campylobacter* diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute *Campylobacter* diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild.
- Guillain-Barre Syndrome due to *Campylobacter* infection: GBD201 disability weight of 0.445 (95% UI 0.303–0.593) for multiple sclerosis, moderate [82].

Mortality

The mortality of *Campylobacter* was estimated separately for middle-to-high mortality countries, and for low mortality countries. For the 133 middle-

to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not available with an uncertainty interval, we used the uncertainty range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to *Campylobacter* and the 10 other diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to *Campylobacter* and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 282]. The *Campylobacter* aetiological proportions were extracted from studies, and regional median *Campylobacter* aetiological proportions calculated. We modified the CHERG approach by dropping regional median *Campylobacter* aetiological proportion outliers that were >5 times greater than the global median *Campylobacter* aetiological proportion, and replacing missing regional *Campylobacter* aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional *Campylobacter* aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional *Campylobacter* mortality was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified *Campylobacter* mortality estimates from five countries: Australia [272], France [174], Netherlands [154], New Zealand [252], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these five countries, we used the estimated national *Campylobacter* mortality (and range) for that country. For low mortality countries without a national estimate, we used the median *Campylobacter* mortality from the five national studies. The median Campyloacter mortality was the mean from the United States: 0.04 per 100 000 population, with a range 0–0.17). We assumed that the case fatality ratio for Gullain-Barre Syndrome due to *Campylobacter* infection was 4.1% (min. 2.4%–max. 6%) [281].

Age distribution

In middle-to-high mortality countries we estimated incidence and mortality of *Campylobacter* diarrhoea seperately for children <5 years of age and persons >5 years of age. In low mortality countries the age distribution for *Campylobacter* diarrhoea cases was 11% <5 years; 8% 5–14 years; 10% 15–24 years; 57% 25–64 years; and 14% >65 years [276]. We assumed the age distribution of *Campylobacter* Guillian-Barre Syndrome cases and deaths were the same as *Campylobacter* diarrhoea cases and deaths.

Sex distribution

Campylobacter sex distribution: 50% male.

A4.15 Norovirus infection

Incidence

The incidence of diarrhoeal norovirus and vomiting-only norovirus were

estimated separately. The incidence of diarrhoeal norovirus was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to norovirus and the 10 other diarrhoeal pathogens[3] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportions of diarrhoeal illnesses due to norovirus and the 10 other diarrhoeal pathogens in persons >5 years of age, using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]; these systematic reviews were supplemented by a FERG-commissioned norovirus systematic review [283]. The norovirus aetiological proportions were extracted from studies, and regional median norovirus aetiological proportions calculated. We modified the CHERG approach by dropping regional median norovirus aetiological proportion outliers that were >5 times greater than the global median norovirus aetiological proportion, and replacing missing regional norovirus aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional norovirus aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional norovirus incidence was applied to all countries in that region.

In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified national incidence estimates for norovirus from seven countries: Australia [272], Canada [175], France [174], Netherlands [154], New Zealand [252], United Kingdom [48], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these seven countries, we used the estimated national norovirus incidence (and range) for that country. For low mortality countries without a national estimate, we used the median norovirus incidence from the seven national studies. The median incidence was from the United States: 6978.5 per 100 000 population, with range 4 295.0–10 282.3.

To estimate the incidence of vomiting-only norovirus, based on a FERG-commissioned systematic review [57], we multiplied the incidence of diarrhoeal norovirus by 19% (min. 15%–max. 23%).

Clinical Outcomes

Clinical outcomes were acute norovirus diarrhoea (severe); acute norovirus diarrhoea (moderate); acute norovirus diarrhoea (mild); acute norovirus vomiting-only; and norovirus death. We assumed that 0.5% of norovirus diarrhoea cases resulted in severe diarrhoea, 8.5%

[3] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

of norovirus diarrhoea cases resulted in moderate diarrhoea, and 91% of norovirus diarrhoea cases resulted in mild diarrhoea.

Duration

The duration of norovirus diarrhoea was estimated to be 2 days (min. 1 day–max. 4 days). We assumed norovirus vomiting-only cases had the same duration as norovirus diarrhoea cases.

Disability weight

- Acute norovirus diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute norovirus diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute norovirus diarrhoea (mild) and acute norovirus vomiting-only: GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of norovirus was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal death from WHO; because this estimate was not available with an uncertainity interval, we used the uncertainity range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to norovirus and the other 10 diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to norovirus and the other 10 diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 274]; these systematic reviews were supplemented by a FERG-commissioned norovirus systematic review [192]. The norovirus aetiological proportions were extracted from studies, and regional median norovirus aetiological proportions calculated. We modified the CHERG approach by dropping regional median norovirus aetiological proportion outliers that were >5 times greater than the global median norovirus aetiological proportion, and replacing missing regional norovirus aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional norovirus aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional norovirus mortality was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified norovirus mortality estimates from four countries: Australia [272], Netherlands [154], New Zealand [252], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these four countries, we used the estimated national norovirus mortality (and range) for that country. For low mortality countries without a national estimate, we used the median norovirus mortality from the four national studies. The median norovirus mortality was the mean from New Zealand and the United

States: 0.18 per 100 000 with a range of 0.11– 0.28. We assumed no deaths among vomiting-only norovirus cases.

Age distribution

In middle-to-high mortality countries we estimated incidence and mortality of norovirus seperately for children <5 years of age and persons >5 years of age. In low mortality countries the age distribution for norovirus was 40% <5 years; 10% 5–14 years; 30% 15–44 years; 10% 45–64 years; and 10% >65 years [284].

Sex distribution

Norovirus sex distribution: 50% male.

A4.16 Shigellosis

Incidence

The incidence of shigellosis was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to Shigella and the 10 other diarrhoeal pathogens[4] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to Shigella and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The shigellosis aetiological proportions were extracted from studies, and regional median shigellosis aetiological proportions calculated. We modified the CHERG approach by dropping regional median shigellosis aetiological proportion outliers that were >5 times greater than the global median shigellosis aetiological proportion, and replacing missing regional shigellosis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional shigellosis aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional shigellosis incidence was applied to all countries in that region.

In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified national incidence estimates for shigellosis from five countries: Australia [272], Canada [175], France [174], New Zealand [252], and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these five countries, we used the estimated national shigellosis incidence (and range) for that country. For low mortality countries without a national estimate, we used the median shigellosis incidence from the five national studies. The median incidence was from Canada (which was increased

[4] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

by 8% to account for travellers, using proxy information from the United States of America) which was 23.6 per 100 000 population, with a range of 13.2–38.7.

Clinical Outcomes

Clinical outcomes were acute Shigella diarrhoea (severe); acute Shigella diarrhoea (moderate); acute Shigella diarrhoea (mild); and Shigella death. We assumed that 2% of Shigella cases resulted in severe diarrhoea, 25% of Shigella cases resulted in moderate diarrhoea, and 73% of Shigella cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [266]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of Shigella diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of Shigella diarrhoea was 2.8 days [266].

Disability weight

- Acute Shigella diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute Shigella diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute Shigella diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of shigellosis was estimated separately for middle-to-high mortality countries, and low mortality countries.

For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not available with an uncertainity interval, we used the uncertainity range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to Shigella and 10 other diarrhoeal pathogens[5] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to Shigella and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 274]. The shigellosis aetiological proportions were extracted from studies, and regional median shigellosis aetiological proportions calculated. We modified the CHERG approach by dropping regional median shigellosis aetiological proportion outliers that were >5 times greater than the global median shigellosis aetiological proportion, and replacing missing regional shigellosis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional shigellosis aetiological proportions were multiplied by the

[5] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

regional estimates of diarrhoea deaths, and the resultant regional shigellosis mortality was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified shigellosis mortality estimates from the United States of America [188]. This national estimate was based on national surveillance data, and expert judgment. We used the shigellosis mortality from the United States of America for all low mortality countries: 0.013 per 100,000 population with range 0.002 – 0.085.

Age distribution

In middle-to-high mortality countries we estimated incidence and mortality of *Shigella* separately for children <5 years of age and persons >5 years of age. In low mortality countries the age distribution for *Shigella* cases was 24% <5 years; 23% 5–14 years; 10% 15–24 years; 39% 25–64 years; and 4% >65 years [276].

Sex distribution

Shigella sex distribution: 50% male.

A4.17 Enterotoxigenic Escherichia coli (ETEC) infection

Incidence

The incidence of diarrhoea due to ETEC was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to ETEC and 10 other diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to ETEC and 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The ETEC aetiological proportions were extracted from studies, and regional median ETEC aetiological proportions calculated. We modified the CHERG approach by dropping regional median ETEC aetiological proportion outliers that were >5 times greater than the global median ETEC aetiological proportion, and replacing missing regional ETEC aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional ETEC aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional ETEC incidence was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), a liturature review identified a national incidence estimates for ETEC in the United States of America that was based on national surveillance data, and expert judgment [188]. We used the ETEC incidence from the United States for all low mortality countries; 13.3 per 100,000 population with range 3.9 – 34.2.

Clinical Outcomes

Clinical outcomes were acute ETEC diarrhoea (severe); acute ETEC diarrhoea (moderate); acute ETEC diarrhoea (mild); and death. We assumed that 0.5% of ETEC cases resulted in severe diarrhoea, 8.5% of ETEC cases resulted in moderate diarrhoea, and 91% of ETEC cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [266]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of ETEC diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of ETEC diarrhoea was 2.8 days [266].

Disability weight

- Acute ETEC diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute ETEC diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute ETEC diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of ETEC was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not available with an uncertainty interval, we used the uncertainty range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to ETEC and 10 other diarrhoeal pathogens[6] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to ETEC and 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 274]. The ETEC aetiological proportions were extracted from studies, and regional median ETEC aetiological proportions calculated. We modified the CHERG approach by dropping regional median ETEC aetiological proportion outliers that were >5 times greater than the global median ETEC aetiological proportion, and replacing missing regional ETEC aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant ETEC aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional ETEC mortality was applied to all countries in that region. We estimated no ETEC deaths in the 61 low mortality countries (EUR and other subregion "A" countries).

[6] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

Age distribution

In middle-to-high mortality countries we estimated incidence of diarrhoea seperately for children <5 years of age and persons >5 years of age. In low mortality countries, no information was available on the age distribution of EPEC cases; we therefore, used the age distribution for *Campylobacter* diarrhoea cases as a proxy, which was 11% <5 years; 8% 5–14 years; 10% 15–24 years; 57% 25–64 years; and 14% >65 years.

Sex distribution

ETEC sex distribution: 50% male.

A4.18 Enteropathogenic Escherichia coli (EPEC) infection

Incidence

The incidence of diarrhoea due to EPEC was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to EPEC and the 10 other diarrhoeal pathogens[7] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to EPEC and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The EPEC aetiological proportions were extracted from studies, and regional median EPEC aetiological proportions calculated. We modified the CHERG approach by dropping regional median EPEC aetiological proportion outliers that were >5 times greater than the global median EPEC aetiological proportion, and replacing missing regional EPEC aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional EPEC aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional EPEC incidence was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we adopted the assumption used in the national study in the United States of America that EPEC was as common as enterotoxigenic *E. coli* [188]. The national estimate for ETEC in the United States of America was based on national surveillance data, and expert judgment. For low mortality countries, we used the EPEC incidence from the United States of America, which was 13.33 per 100 000 population with range 4.00 – 34.24.

[7] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

Clinical Outcomes

Clinical outcomes were acute EPEC diarrhoea (severe); acute EPEC diarrhoea (moderate); acute EPEC diarrhoea (mild); and EPEC death. We assumed that 0.5% of EPEC cases resulted in severe

diarrhoea, 8.5% of EPEC cases resulted in moderate diarrhoea, and 91% of EPEC cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [188]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of EPEC diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of diarrhoea was 2.8 days [266].

Disability weight

- Acute EPEC diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute EPEC diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute EPEC diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of EPEC was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not available with an uncertainity interval, we used the uncertainity range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to EPEC and the 10 other diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to EPEC and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 274]. The EPEC aetiological proportions were extracted from studies, and regional median EPEC aetiological proportions calculated. We modified the CHERG approach by dropping regional median EPEC aetiological proportion outliers that were >5 times greater than the global median EPEC aetiological proportion, and replacing missing regional EPEC aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant EPEC aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional EPEC mortality was applied to all countries in that region. We estimated no EPEC deaths in the 61 low mortality countries (EUR and other subregion "A" countries).

Age distribution

In middle-to-high mortality countries we estimated incidence and mortality of EPEC separately for children <5 years of age and persons >5 years of age. In low mortality countries, no information was available on the age distribution of EPEC cases; we therefore used the age distribution for *Campylobacter* diarrhoea cases as a proxy, which was 11% <5 years; 8% 5–14 years; 10% 15–24 years; 57% 25–64 years; and 14% >65 years.

Sex distribution

EPEC sex distribution: 50% male.

A4.19 Cholera

Incidence

Estimates of the incidence of cholera were adapted from a published systematic review of the global burden of cholera [285] updated with 2010 population estimates. This review classified 51 countries as cholera-endemic countries based on results of the systematic review and national cholera reports in the WHO Weekly Epidemiological Record. The review then used WHO 2008 country-specific estimates of the proportion of each country's population that lacked improved sanitation [286] to estimate the proportion of the population in the cholera-endemic countries that were at risk for cholera. Then a cholera incidence was assigned to the population at risk for cholera in the cholera endemic countries based on population-based studies in India [287], Indonesia [288] and Mozambique [289]. The review also identified an additional 18 countries that reported cholera to WHO during 2000 to 2008, but were judged to be not be endemic for cholera; a country-specific cholera incidence in each of these "non-endemic" countries was estimated using the annual average number of cholera cases reported to WHO cases in each country times a multiplier of 10 to account for under-reporting. For all other countries, we used a literature review that identified national cholera incidence estimates from three countries countries: France [174], New Zealand [252] and the United States of America [188]. The cholera incidence in the United States of America was the median estimate from these three countries and was used (0.093 per 100 000 population) as the cholera incidence for all countries (other than the cholera-endemic and non-endemic countries) which did not have national incidence estimates. We used the global burden of cholera [285] range of estimates around the mean estimate of global cholera cases (2.8 million with a range of 1.4 to 4.3 million) to derive a range of estimates for cholera incidence.

Clinical Outcomes

Clinical outcomes were cholera (severe); cholera (moderate); cholera (mild); and cholera death. We assumed that 35% of cholera cases resulted in severe cholera, 40% of cholera cases resulted in moderate cholera, and 25% of cholera cases resulted in mild cholera [290, 291].

Duration

We assumed the duration of cholera was 7 days (min. 3 day–max. 10 days).

Disability weight

- Cholera (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Cholera (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Cholera (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

For 51 cholera-endemic and 18 cholera non-endemic countries, we used the case fatality ratios (CFRs) estimated in the systematic review of the global burden of cholera [285]. This review calculated a variance-weighted average cholera CFR by region; the CFR was 1% in WPR subregion B, 1% in SEAR B (except 1.5% in Bangladesh), 1.3% in EMR B, 3% in SEAR D, 3.2% in EMR D, and 3.8% in AFR. For all other countries, the literature review of national incidence estimates for cholera identified no reported deaths; therefore we assumed no cholera deaths occurred in countries (other than the cholera-endemic and non-endemic countries). We used the global burden of cholera

[285] range of estimates around the mean estimate of global cholera deaths (91 000, with a range of 28 000 to 142 000) to derive a range of estimates for cholera deaths.

Age distribution

Cholera age distribution: 15% <5 years; 25% 5–14 years; 42% 15–34 years; 15% 35–64; 3% >60 years [292, 293].

Sex distribution

Cholera sex distribution: 50% male.

A4.20 Cryptosporidiosis

Incidence

The incidence of cryptosporidiosis was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to Cryptosporidia and 10 other diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to Cryptosporidia and 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The cryptosporidiosis aetiological proportions were extracted from studies, and regional median cryptosporidiosis aetiological proportions calculated. We modified the CHERG approach by dropping regional median cryptosporidiosis aetiological proportion outliers that were >5 times greater than the global median cryptosporidiosis aetiological proportion, and replacing missing regional cryptosporidiosis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional cryptosporidiosis aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional cryptosporidiosis incidence was applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified national incidence estimates for cryptosporidiosis from six countries: Australia [272], Canada [175], Netherlands [154], New Zealand [252], United Kingdom [48] and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these six countries, we used the estimated national cryptosporidiosis incidence (and range) for that country. For low mortality countries without a national estimate, we used the median cryptosporidiosis incidence from the six national studies. The median incidence was the mean from Australia (which was increased by 19% to account for travellers, using proxy information from New Zealand) and the Netherlands, which was 128.4 per 100 000 population with a range of 50.3 – 601.6.

Clinical Outcomes

Clinical outcomes were acute cryptosporidiosis diarrhoea (severe); acute cryptosporidiosis diarrhoea (moderate); acute cryptosporidiosis diarrhoea (mild); and death. We assumed that 0.5% of cryptosporidiosis cases resulted in severe diarrhoea, 8.5% of cryptosporidiosis cases resulted in moderate diarrhoea, and 91% of cryptosporidiosis cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [266]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of cryptosporidiosis diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of diarrhoea was 2.8 days [266].

Disability weight

- Acute cryptosporidiosis diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute cryptosporidiosis diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute cryptosporidiosis diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of cryptosporidiosis was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not available with an uncertainity interval, we used the uncertainity range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) (14). We then estimated the aetiological proportions of diarrhoeal deaths due to *Cryptosporidia* and 10 other diarrhoeal pathogens[8] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to *Cryptosporidia* and 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 274]. The cryptosporidiosis aetiological proportions were extracted from studies, and regional median cryptosporidiosis aetiological proportions calculated. We modified the CHERG approach by dropping regional median cryptosporidiosis aetiological proportion outliers that were >5 times greater than the global median cryptosporidiosis aetiological proportion, and replacing missing regional cryptosporidiosis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional cryptosporidiosis aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional cryptosporidiosis mortality was

[8] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

applied to all countries in that region. In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified cryptosporidiosis mortality estimates from three countries: Netherlands [154], New Zealand [252] and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these three countries, we used the estimated national cryptosporidiosis mortality (and range) for that country. For low mortality countries without a national estimate, we used the median cryptosporidiosis mortality from the three national studies. The median cryptosporidiosis mortality was from the United States: 0.015 per 100 000 population with a range of range 0.003 – 0.080.

Age distribution

In middle-to-high mortality countries, we estimated incidence of cryptosporidiosis seperately for children <5 years of age and persons >5 years of age. In low mortality countries, the age distribution for cryptosporidiosis was 16% <5 years; 17% 5–14 years; 13% 15–24 years; 14% 25–34 years; 11% 35–44 years; 9% 45–54 years; 7% 55–64 years; 6% 65–74 years; 7% >75 years [294].

Sex distribution

Cryptosporidiosis sex distribution: 50% male.

A4.21 Giardiasis

Incidence

The incidence of giardiasis was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive "envelopes" of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to *Giardia* and the 10 other diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to *Giardia* and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The giardiasis aetiological proportions were extracted from studies, and regional median giardiasis aetiological proportions calculated. We modified the CHERG approach by dropping regional median giardiasis aetiological proportion outliers that were >5 times greater than the global median giardiasis aetiological proportion, and replacing missing regional giardiasis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional giardiasis aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional giardiasis incidence was applied to all countries in that region.

In the 61 low mortality countries (EUR and other subregion "A" countries), we used a literature review that identified

national incidence estimates for giardiasis from six countries: Australia [272], Canada [175], Netherlands [154], New Zealand [252], United Kingdom [48] and the United States of America [188]. These national estimates were based on systematic reviews, national surveillance data, and expert judgment. In these six countries, we used the estimated national giardiasis incidence (and range) for that country. For low mortality countries without a national estimate, we used the median giardiasis incidence from the six national studies. The median incidence was the mean from Canada (which was increased by 8% to account for travellers, using proxy information from the United States of America) and the United States of America, which was 384.6 per 100 000 population, with a range of 266.4–537.0.

Clinical Outcomes

Clinical outcomes were acute giardiasis diarrhoea (severe); acute giardiasis diarrhoea (moderate); acute giardiasis diarrhoea (mild); and giardiasis death. We assumed that 0.5% of giardiasis cases resulted in severe diarrhoea, 8.5% of giardiasis cases resulted in moderate diarrhoea, and 91% of giardiasis cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [266]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of giardiasis diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of diarrhoea was 2.8 days [266].

Disability weight

- Acute giardiasis diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute giardiasis diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute giardiasis diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

We estimated no giardiasis deaths.

Age distribution

In middle-to-high mortality countries, we estimated incidence of giardiasis seperately for children <5 years of age and persons >5 years of age. In low mortality countries, the age distribution for cryptosporidiosis was 20% <5 years; 17% 5–14 years; 10% 15–24 years; 11% 25–34 years; 12% 35–44 years; 12% 45–54 years; 9% 55–64 years; 5% 65–74 years; 4% >75 years [295].

Sex distribution

Giardiasis sex distribution: 50% male.

A4.22 Amoebiasis

Incidence

The incidence of diarrhoea due to amoebiasis was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. To derive “envelopes” of diarrhoea cases, for children <5 years of age we used estimates of diarrhoea incidence from a CHERG systematic review [51] and for persons >5 years of age we used a FERG-

commissioned systematic review [52]. We then estimated the aetiological proportions of diarrhoeal illnesses due to *Entamoeba histolytica* and the 10 other diarrhoeal pathogens[9] in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among outpatients and persons in the community [40], and the aetiological proportion of diarrhoeal illnesses due to *Entamoeba histolytica* and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients, outpatients and persons in the community [40, 274]. The amoebiasis aetiological proportions were extracted from studies, and regional median amoebiasis aetiological proportions calculated. We modified the CHERG approach by dropping regional median amoebiasis aetiological proportion outliers that were >5 times greater than the global median amoebiasis aetiological proportion, and replacing missing regional amoebiasis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant regional amoebiasis aetiological proportions were multiplied by the regional estimates of diarrhoea incidence, and the resultant regional amoebiasis incidence was applied to all countries in that region. We estimated no amoebiasis cases in the 61 low mortality countries (EUR and other subregion "A" countries).

[9] The 11 diarrhoeal pathogens are: non-typhoidal *Salmonella*, *Campylobacter*, *Shigella*, norovirus, enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), *Cryptosporidia*, *Giardia*, *Entamoeba histolytica*, other diarrhoeal agents not known to be foodborne (rotavirus and astrovirus), and unspecified agents.

Clinical Outcomes

Clinical outcomes were acute amoebiasis diarrhoea (severe); acute amoebiasis diarrhoea (moderate); acute amobiasis diarrhoea (mild); and amoebiasis death. We assumed that 0.5% of amoebiasis cases resulted in severe diarrhoea, 8.5% of amoebiasis cases resulted in moderate diarrhoea, and 91% of amoebiasis cases resulted in mild diarrhoea.

Duration

In children <5 years of age, duration of severe diarrhoea was 8.4 days, moderate diarrhoea was 6.4 days, and mild diarrhoea was 4.3 days [266]. Based on the assumed distribution of severe, moderate and mild diarrhoea cases, the duration of amoebiasis diarrhoea cases in children <5 years of age was estimated to be 4.9 days (min. 4.3 days–max. 8.4 days). In persons >5 years of age, the duration of diarrhoea was 2.8 days [266].

Disability weight

- Acute amoebiasis diarrhoea (severe): GBD2010 disability weight of 0.281 (95% UI 0.184–0.399) for diarrhoea, severe.
- Acute amoebiasis diarrhoea (moderate): GBD2010 disability weight of 0.202 (95% UI 0.133–0.299) for diarrhoea, moderate.
- Acute amoebiasis diarrhoea (mild): GBD2010 disability weight of 0.061 (95% UI 0.036–0.093) for diarrhoea, mild [82].

Mortality

The mortality of amoebiasis was estimated separately for middle-to-high mortality countries, and low mortality countries. For the 133 middle-to-high mortality countries, we used a modification of the CHERG approach [50]. We received envelopes of diarrhoeal deaths from WHO; because this estimate was not available with an uncertainity

interval, we used the uncertainity range from the GBD2010 estimate of diarrhoeal deaths (81.7% to 114.6% around the point estimate) [58]. We then estimated the aetiological proportions of diarrhoeal deaths due to *Entamoeba histolytica* and the 10 other diarrhoeal pathogens in children <5 years of age using a CHERG and FERG systematic review of aetiology studies among inpatients [40], and the aetiological proportions of diarrhoeal deaths due to *Entamoeba histolytica* and the 10 other diarrhoeal pathogens in persons >5 years of age using an updated FERG systematic review of aetiology studies among inpatients [40, 274]. The amoebiasis aetiological proportions were extracted from studies, and regional median amoebiasis aetiological proportions calculated. We modified the CHERG approach by dropping regional median amoebiasis aetiological proportion outliers that were >5 times greater than the global median amoebiasis aetiological proportion, and replacing missing regional amoebiasis aetiological proportions with the global median. Furthermore, for children <5 years of age, we proportionally decreased the aetiological proportions for all 11 diarrhoeal pathogens in each region so that the sum of the aetiological proportions for all diarrhoeal pathogens in a region equalled 1. The resultant amoebiasis aetiological proportions were multiplied by the regional estimates of diarrhoea deaths, and the resultant regional amobiasis mortality was applied to all countries in that region. We estimated no amoebiasis deaths in the 61 low mortality countries (EUR and other subregion "A" countries).

Age distribution

The incidence of amoebiasis diarrhoea was estimated separately for children <5 years of age and persons >5 years of age. No other information on age distribution for diarrhoea cases.

Sex distribution

Amoebiasis sex distibution: 50% male.

A4.23 Congenital Toxoplasmosis

Incidence

Full details of how estimates of congenital toxoplasmosis was estimated are available in [76] and online appendixes (available at: www.vetepi.uzh.ch/research/Diseaseburden/Burden_CT-Appendices.pdf).

Clinical Outcomes

Based on data in [296, 297], the following probabilities were assigned to clinical outcomes: neonatal death probability 0.7% (UI 0.4%–1.2%); chorioretinitis in first year of life probability 13% (UI 12%–15%); chorioretinitis later in life probability 16% (UI 5%–52%); chorioretinitis in first year of life (AMR) probability 80% (UI 70%–90%); chorioretinitis later in life (AMR) probability 10% (UI 5%–15%); intracranial calcification probability 11% (UI 7.9%–12%); hydrocephalus probability 2.0% (UI 1.0%–3.0%); CNS abnormalities 2.9% (UI 1.0%–6.0%).

Duration

Lifelong (i.e. life expectancy at birth), except chorioretinitis later in life, which has duration the same as the life expectancy at age 10 years (mean age of onset is 10 years)

Disability weight

Suitable DWs were selected from GBD2010 [82]. These were

- chorioretinitis 0.033,
- intracranial calcification 0.01,
- hydrocephalus 0.36. and
- other CNS abnormalities 0.36.

Mortality

A value of 0.7% (UI 0.4%–1.2%) was used, as these are the proportions of cases that die in the neonatal peiod. In addition, there are approximately 2.4% (2.3%–6.3%) fetal loss (stillbirths) after 24 weeks, but these were not assigned as fatal cases.

Age distribution

In AMR: 90% onset at birth, 10% at age 10 years. Other regions: 86% onset at birth, 14% at age 10 years.

Sex distribution

There is no evidence that male and female infants have different risks of having congenital toxoplasmosis. Therefore, the sex ratio at birth was used to determine the sex distribution.

A4.24 Acquired toxoplasmosis

Incidence

Generally there is an increase in sero-positivity with age, and estimates of incidence were made from age-stratified sero conversion data as the difference in prevalence between age t and age t+1. Where there were insufficient data points, a model was constructed based on the assumptions that individuals that convert remain seropositive for life and live under a constant infection pressure. In this model, the prevalence $p(t)$ at age t can be described by: $p(t) = 1-\exp(-ßt)$ where ß is the incidence. This model has been widely used for infectious diseases (see [298], for example). Incidence estimates with uncertainty limits were made using age-stratified seroconversion rates on a country by country basis, and summed over regions to derive global estimates.

Clinical Outcomes

Mild chorioretinitis p = 4.5%; moderate chorioretinitis p = 0.25%–0.69%; severe chorioretinitis 0.01%. Acute infectious disease: p = 26%; post-acute syndromes p = 2.9%. These were estimated from data in [212, 299–301], which derived from cohort and cross-sectional studies of individuals with confirmed acquired toxoplamsosis.

Duration

Eye lesions: lifelong, i.e. life expectancy at age of incident case. Acute 4 weeks; post-acute syndromes 8 weeks.

Disability weight

Mild chorioretinitis = 0.004; moderate chorioretinitis = 0.033; severe chorioretinitis = 0.191. Acute infectious disease = 0.053, post-acute syndromes = 0.254.

Mortality

None

Age distribution

Five different age distributions were used which was driven by the country-specific data.

Sex distribution

Male = 0.5

AGE DISTRIBUTION (YEARS)	<5	5-14	15-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
G1Mean	0.26	0.34	0.19	0.11	0.055	0.027	0.013	0.0057	0.0015	0.00016
G2 Mean	0.21	0.3	0.2	0.13	0.078	0.043	0.023	0.011	0.0029	0.0002
G3 Mean	0.09	0.18	0.19	0.15	0.14	0.12	0.071	0.041	0.02	0.0059
G4Mean	0.075	0.14	0.14	0.14	0.14	0.13	0.11	0.064	0.039	0.016
G5Mean	0.072	0.11	0.17	0.32	0.21	0.086	0.021	0.0049	0.00098	0.00019

A4.25 Cystic echinococcosis

Incidence

For cystic echinococcosis (CE), due to infection with the larval stage of *Echinococcus granulosus*, a systematic review was conducted to collect and synthesize data on both the frequency and clinical manifestations of CE globally [75]. In addition to information acquired via the systematic review, World Organisation for Animal Health (OIE) and European Food Safety Authority (EFSA) databases were queried to obtain officially reported numbers of human cases by country. Individual government websites and reports were also searched for relevant CE frequency data. Such data included official hospital discharge data and notified cases in countries where the disease is notifiable. Where no data are available, but the disease is believed to be endemic then the incidence was imputed.

Clinical Outcomes

Treatment-seeking: moderate abdominal pelvic problems, chronic respiratory disease moderate (chronic obstructive pulmonary disease – COPD).

CNS lesions: moderate motor and/or cognitive impairments.

Non-treatment-seeking: mild abdominal pelvic problems, mild chronic respiratory disease.

CNS: mild motor or cognitive impairments.

Duration

Lifelong for non-treatment-seeking. Median of 2 years for treated cases.

Disability weight

- Mild abdominal pelvic problems: 0.012
- Moderate abdominal pelvic problems: 0.123.
- Mild chronic respiratory disease: 0.015.
- Moderate chronic respiratory disease: 0.192.
- Mild motor or cognitive impairment: 0.054.
- Moderate motor or cognitive impairment: 0.221.

Mortality

For treatment-seeking: 2%; 1% for non-treatment-seeking.

Age distribution

AGE DISTRIBUTION (YEARS)	<5	5-14	15-24	25-34	35-44	45-54	55-64	65+
G1Mean	4.6	10.4	17.1	21.2	18.1	12.8	8.7	7.1

Sex distribution

Male = 42.8%

A4.26 Alveolar echinococcosis

Incidence

Full details of the methodology of estimating the incidence of alveolar echinococcosis (AE) can be found in [72]. In addition, this data has been updated because of subsequent reports from countries such as Kyrgyzstan [302] and Poland [303].

Clinical Outcomes

Abdominopelvic problems followed by recovery after treatment, or death.

Duration

Europe: 10 years. Other: 8 years.

Disability weight

- 0.123

Mortality

Following abdominopelvic problems: western and central Europe and north America 2–5%; eastern Europe: 10–30%; elsewhere: 100%

Age distribution

- Europe: 0–9 years, 0%; 10–19 years, 2.7%; 20–29 years, 8.8%; 30–39 years, 13.6%; 40–49 years, 18.7%; 50–59 years , 18.4%; 60–69 years, 20.6%; 70–79 years, 12.1%; 80 years and over, 5.1%.
- Eastern Europe: 0–9 years, 1.7%; 10–19 years , 5.1%; 20–29 years, 12.8%; 30–39 years, 14.5%; 40–49 years, 20.5%; 50–59 years , 17.9%; 60–69 years, 14.5%; 70–79 years, 12.0%; 80 years and over, 1.0%.
- Central Asia: 0–9 years, 2.7%; 10–19 years, 10.3%; 20–29 years, 33.3%; 30–39 years, 25.1%; 40–49 years, 14.1%; 50–59 years , 10%; 60years and over, 4.5% .
- China: 0–9 years, 1.4%; 10–19 years , 7%; 20–29 years, 10.2%; 30–39 years, 23%; 40–49 years, 24.5%; 50–59 years , 16%; 60 years and over, 17.9%.

Sex distribution

Europe: male 44%, central Asia, male 36%, China male 47%.

A4.27 Taenia solium neurocysticercosis

Incidence

Taenia solium neurocysticercosis (NCC) is known to cause epilepsy and other neurological sequelae [73]. A systematic review revealed that NCC may be responsible for approximately 29.0% (95% UI 22.9%–35.5% of the burden of epilepsy in at-risk populations in low and middle income, pork consuming societies [74]. Consequently, the number of prevalent cases of epilepsy used in the GBD2010 [58, 81–83] were utilized to estimate the prevalent cases of epilepsy-associated NCC. The total numbers of cases of idiopathic epilepsy were available by country and were corrected to the total numbers of epilepsy by dividing by 0.58 (58% of epilepsy cases being idiopathic – see appendix of [83]. Population at risk was estimated by using seven assumptions:

- (1) Countries with negligible pig populations (less than 30 000 pigs (FAO data) were assumed to have zero risk due to there being no opportunity to transmit *T. solium*. This excluded countries where the Muslim population was over 90% and a few non-Muslim countries (for example Ethiopia) where the pig population was very low.
- (2) For countries that raise pigs and have more than 80% of the population living with unimproved sanitation, population at risk was estimated as the proportion of the population that was not Muslim.
- (3) For countries that raise pigs and have less than 80% of the population living with unimproved sanitation, population at risk was estimated as the proportion of the population that was not Muslim, multiplied by the proportion of the population that lived with unimproved sanitation.
- (4) For the United States of America, it was assumed that transmission does not occur, and hence nearly all cases are in immigrants, mainly from Latin America. Thus a weighted mean of the population at risk from the entire Latin America was applied to the population of hispanic immigrants, born outside of the United States of America but now resident in the United States of America.
- (5) For the ex-Soviet states, the risk of cysticercosis was assumed to be close to zero due to lack of evidence for cysticercosis or taeniasis in public health surveillance data.
- (6) Indonesia is predominantly Muslim (87%). However, the predominantly non-Muslim provinces of Papua and

West Papua are known to be highly endemic regions for *T. solium* and hence the combined population of these provinces was used as the population at risk, with the remainder of Indonesia having zero risk.
- (7) There is no FAO data on pig populations in Sudan or South Sudan, the latter being predominantly non-Muslim and with little improved sanitation. However, extensive searches for information about pigs in Sudan revealed that the domestic pig population in both countries is negligible and hence there is virtually zero risk if cysticercosis.

Due to the absence of available data on all cysticercosis sequelae, only the frequency of NCC-associated epilepsy was estimated in this study.

Clinical Outcomes

Epilepsy-associated NCC [74]

Duration

No data.

Disability weight

- GBD2010 for epilepsy [58, 81–83]

Mortality

GBD2010 for epilepsy [58, 81–83]

Age distribution

GBD2010 for epilepsy [58, 81–83]

Sex distribution

GBD2010 for epilepsy [58, 81–83]

A4.28 Chlonorchiosis

Incidence

Incidence estimates and clinical sequelae for foodborne trematodiasis were mainly based on the results of two systematic review articles [77, 78]. The reviews identified available qualitative and quantitative information on prevalence, incidence, mortality and remission rates, sex- and age-distributions and the progression of foodborne trematodiasis into different sequelae. From these data, simplified disease models were developed and quantitative data summarized by meta-analyses. As information on incidence, remission, and duration of foodborne trematodiasis was particularly scant, zero remission was assumed and entered into the DisMod 3 software [304], together with the available prevalence and mortality estimates. DisMod 3 computed internally consistent and complete sets of sex-, age- and country-specific prevalence, incidence, remission, duration and mortality for foodborne trematodiasis and associated sequelae. However, unlike the original study, which computed incidence rates only for countries reporting national prevalence rates, and otherwise considered the incidence rate to be zero [77], the present study also imputed incidence rates for countries where no records of national prevalence or incidence rates were available, but at least one autochthonous human infection could be identified in the systematic review. Hierarchical random-effects models with incidence information from other countries as input data were applied in this additional imputation process [79].

Clinical Outcomes

Abdominal pelvic discomfort, carcinoma.

Duration

Lifelong due to low treatment coverage in affected populations, longevity of parasites in humans, high re-infection rates, supposedly high susceptibility of clinical cases, and irreversibility of pathology after several years of infection.

Disability weight

– Only for severe infections: 0.123.

Mortality

1% case fatality.

Age distribution

AGE DISTRIBUTION (YEARS)	0-1	1-4	5-9	10-14	15-19	20-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
G1Mean	5.0	8.1	11.5	13.4	22.7	12.4	13.9	8.1	2.9	1.1	0.6	0.2	0.0
G2 Mean	4.3	7.5	10.4	12.0	18.8	13.5	16.7	8.0	3.8	2.4	1.4	0.8	0.3
G3 Mean	4.1	7.2	9.1	13.0	32.9	18.6	12.9	1.6	0.3	0.1	0.1	0.1	0.1
G4Mean	6.8	8.8	11.2	12.4	23.5	12.2	13.4	7.6	2.6	0.9	0.5	0.2	0.0
G5Mean	5.1	8.2	11.4	13.2	22.6	12.5	14.0	8.0	2.9	1.1	0.6	0.3	0.1

Sex distribution

Male 65–68%.

A4.29 Fasciolosis

Incidence

Incidence estimates and clinical sequelae for foodborne trematodiasis were mainly based on the results of two systematic review articles [77, 78]. The reviews identified available qualitative and quantitative information on prevalence, incidence, mortality and remission rates, sex- and age-distributions and the progression of foodborne trematodiasis into different sequelae. From these data, simplified disease models were developed and quantitative data summarized by meta-analyses. As information on incidence, remission and duration of foodborne trematodiasis was particularly scant, zero remission was assumed, and entered into the DisMod 3 software [304], together with the available prevalence and mortality estimates. DisMod 3 computed internally consistent and complete sets of sex-, age- and country-specific prevalence, incidence, remission, duration and mortality for foodborne trematodiasis and associated sequelae. However, unlike the original study, which computed incidence rates only for countries reporting national prevalence rates and otherwise considered the incidence rate to be zero [77], the present study also imputed incidence rates for countries, where no records of national prevalence or incidence rates were available, but at least one autochthonous human infection could be identified in the systematic review. Hierarchical random-effects models with incidence information from other countries as input data were applied in this additional imputation process [79].

Clinical Outcomes

Abdominal pelvic discomfort.

Duration

Lifelong due to low treatment coverage in affected populations, longevity of parasites in humans, high re-infection rates, supposedly high susceptibility of clinical cases, and irreversibility of pathology after several years of infection

Disability weight

– 0.123

Mortality

Zero.

Age distribution

AGE DISTRIBUTION (YEARS)	0-1	1-4	5-9	10-14	15-19	20-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
G1 Mean	49.1	26.9	11.6	4.6	2.3	1.4	1.8	1.0	0.6	0.3	0.2	0.1	0.0
G2 Mean	19.5	33.1	29.5	10.4	4.3	1.4	1.0	0.4	0.2	0.1	0.0	0.0	0.0
G3 Mean	75.3	14.8	5.1	1.8	0.9	0.6	0.7	0.4	0.2	0.1	0.1	0.0	0.0
G4 Mean	21.9	52.6	16.1	1.3	0.5	0.7	1.5	1.3	1.1	0.8	0.7	0.7	0.7
G5 Mean	59.1	22.0	9.4	3.6	1.8	1.1	1.3	0.7	0.4	0.2	0.2	0.1	0.0

Sex distribution

Male = 49.5%

A4.30 Opisthorchosis

Incidence

Incidence estimates and clinical sequelae for foodborne trematodiasis were mainly based on the results of two systematic review articles [77, 78]. The reviews identified available qualitative and quantitative information on prevalence, incidence, mortality and remission rates, sex- and age-distributions and the progression of foodborne trematodiasis into different sequelae. From these data, simplified disease models were developed and quantitative data summarized by meta-analyses. As information on incidence, remission and duration of foodborne trematodiasis was particularly scant, zero remission was assumed and entered into the DisMod 3 software [304], together with the available prevalence and mortality estimates. DisMod 3 computed internally consistent and complete sets of sex-, age- and country-specific prevalence, incidence, remission, duration and mortality for foodborne trematodiasis and associated sequelae. However, unlike the original study, which computed incidence rates only for countries reporting national prevalence rates and otherwise considered the incidence rate to be zero [77], the present study also imputed incidence rates for countries, where no records of national prevalence or incidence rates, but at least one autochthonous human infection, could be identified in the systematic review. Hierarchical random-effects models with incidence information from other countries as input data were applied in this additional imputation process [79].

Clinical Outcomes

Abdominal pelvic discomfort, carcinoma.

Duration

Lifelong due to low treatment coverage in affected populations, longevity of parasites in humans, high re-infection rates, supposedly high susceptibility of clinical cases, and irreversibility of pathology after several years of infection

Disability weight

– 0.123

Mortality

Overall case fatality rate: 9.2%.

Age distribution

AGE DISTRIBUTION (YEARS)	0-1	1-4	5-9	10-14	15-19	20-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
G1 Mean	4.2	11.8	13.9	12.4	10.7	8.7	13.4	10.3	7.1	3.9	2.4	0.9	0.2
G2 Mean	4.3	13.4	15.8	15.4	12.7	8.5	10.9	8.1	5.5	2.3	2.1	0.9	0.2
G3 Mean	2.3	6.8	8.4	9.6	11.6	9.6	13.7	11.6	11.1	6.2	5.6	2.9	0.5
G4 Mean	4.2	11.7	13.8	12.4	10.7	8.7	13.4	10.3	7.2	4.0	2.4	1.0	0.2

Sex distribution

Male=55%

A4.31 Paragonimosis

Incidence

Incidence estimates and clinical sequelae for foodborne trematodiasis were mainly based on the results of two systematic review articles [77, 78]. The reviews identified available qualitative and quantitative information on prevalence, incidence, mortality and remission rates, sex- and age-distributions and the progression of foodborne trematodiasis into different sequelae. From these data, simplified disease models were developed and quantitative data summarized by meta-analyses. As information on incidence, remission and duration of foodborne trematodiasis was particularly scant, zero remission was assumed and entered into the DisMod 3 software [304], together with the available prevalence and mortality estimates. DisMod 3 computed internally consistent and complete sets of sex-, age- and country-specific prevalence, incidence, remission, duration and mortality for foodborne trematodiasis and associated sequelae. However, unlike the original study, which computed incidence rates only for countries reporting national prevalence rates and otherwise considered the incidence rate to be zero [77], the present study also imputed incidence rates for countries, where no records of national prevalence or incidence rates, but at least one autochthonous human infection, could be identified in the systematic review. Hierarchical random-effects models with incidence information from other countries as input data were applied in this additional imputation process [79].

Clinical Outcomes

Lifelong due to low treatment coverage in affected populations, longevity of parasites in humans, high re-infection rates, supposedly high susceptibility of clinical cases, and irreversibility of pathology after several years of infection.

Duration

Lifelong.

Disability weights

- Pulmonary: 0.132.
- Cerebral paragonimosis: 0.42.

Mortality

10% case fatality for cerebral cases only

Age distribution

AGE DISTRIBUTION (YEARS)	0-1	1-4	5-9	10-14	15-19	20-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
G1 Mean	8.7	11.5	12.3	10.1	9.2	6.7	12.6	12.2	7.9	4.6	2.8	1.2	0.2
G2 Mean	8.9	16.1	16.2	12.5	9.5	7.3	11.0	7.7	5.1	3.0	1.8	0.8	0.2
G3 Mean	2.6	9.0	11.4	11.5	10.9	9.8	16.5	12.5	8.1	4.2	2.4	0.9	0.2
G4 Mean	2.0	8.1	11.5	11.4	10.7	10.6	20.1	13.4	7.2	3.3	1.2	0.5	0.2
G5 Mean	8.6	11.7	12.4	10.2	9.2	6.7	12.6	12.0	7.8	4.5	2.8	1.2	0.2

Sex distribution

Male = 55.9%

A4.32 Intestinal flukes

Incidence

Incidence estimates and clinical sequelae for foodborne trematodiasis were mainly based on the results of two systematic review articles [77, 78]. The reviews identified available qualitative and quantitative information on prevalence, incidence, mortality and remission rates, sex- and age-distributions, and the progression of foodborne trematodiasis into different sequelae. From these data, simplified disease models were developed and quantitative data summarized by meta-analyses. As information on incidence, remission and duration of foodborne trematodiasis was particularly scant, zero remission was assumed and entered into the DisMod 3 software [304], together with the available prevalence and mortality estimates. DisMod 3 computed internally consistent and complete sets of sex-, age- and country-specific prevalence, incidence, remission, duration and mortality for foodborne trematodiasis and associated sequelae. However, unlike the original study, which computed incidence rates only for countries reporting national prevalence rates and otherwise considered the incidence rate to be zero [77], the present study also imputed incidence rates for countries, where no records of national prevalence or incidence rates, but at least one autochthonous human infection, could be identified in the systematic review. Hierarchical random-effects models with incidence information from other countries as input data were applied in this additional imputation process [79].

Clinical Outcomes

Abdominal pelvic discomfort.

Duration

Lifelong due to low treatment coverage in affected populations, longevity of parasites in humans, high re-infection rates, supposedly high susceptibility of clinical cases, and irreversibility of pathology after several years of infection.

Disability weight

– Heavy infections only: 0.123.

Mortality

Zero.

Age distribution

AGE DISTRIBUTION (YEARS)	0-1	1-4	5-9	10-14	15-19	20-24	25-34	35-44	45-54	55-64	65-74	75-84	85+
G1 Mean	24.4	32.7	22.1	8.3	4.3	1.9	2.5	1.8	1.0	0.5	0.3	0.2	0.0
G2 Mean	18.3	38.4	24.2	9.8	4.7	1.9	1.3	0.5	0.3	0.2	0.1	0.1	0.0
G3 Mean	70.1	10.4	6.0	2.8	1.8	1.3	2.1	1.5	1.2	1.2	0.9	0.6	0.2
G4 Mean	56.4	26.4	9.1	3.1	1.6	0.9	1.1	0.6	0.4	0.2	0.1	0.1	0.0
G5 Mean	24.8	40.8	18.6	7.7	4.5	1.7	1.0	0.4	0.2	0.1	0.1	0.1	0.0
G6 Mean	46.4	27.7	13.3	4.8	2.5	1.3	1.6	1.0	0.6	0.4	0.2	0.1	0.0

Sex distribution

Male = 55%.

A4.33 Ascaris spp.

Incidence

Age-stratified prevalence was used to estimate the burden of disease in GBD2010 [81] and these data supplied by IHME were used to estimate incidence of ascariasis. The estimated numbers of prevalent cases were available for every country and each age group.

Prevalence at age t = P(t) Prevalence at age t+1 = P(t+1) Incidence = b = proportion of population infected between t and t= t+1 P(t+1) = b*(1–P(t))–m * P(t) As proportion acquiring new infections are at a rate of b*(1–P(t)) and proportion losing infections at rate –m * P(t) Therefore incidence (proportion) of new infections is given by b=(P(t+1)+m*p(t))/1–P(t) b = proportion that are infected in time t = 1 year m = proportion that lose their infection = death rate = 1/life expectancy Approximate life expectancy of Ascaris = 1 year Therefore b=(P(t+1)+P(t))/(1–P(t)) Incidence per 100 000 per year = b *100 000 It is well known [88] that the infection pressure or incidence varies with age with ascaris. In particular children have a higher incidence. But by using this step equation all that is required is the different prevalences (proportion infected) at age t and t+1 which can be calculated from the data provided by GBD2010. Assuming the duration for ascariasis and other manifestations (mild abdominopelvic discomfort and severe wasting) are of the same duration, then this can be used to estimate the incidence of all sequelae from the stratified prevalence data. There is some evidence that ascaris induces some degree of protective immunity. But this acts to decrease the abundance of infection rather than the prevalence and so can be discounted in this exercise.

Clinical Outcomes

The clinical outcomes were death in severe cases, severe wasting, pelvic abdominal disconfort and clinical ascariasis as described in GBD2010 [82]##

Duration

Duration of each incidence case was set at a mean of 1 year

Disability weight

- For severe wasting = 0.127
- For mild abdominal pelvic discomfort = 0.012
- For clinical ascariosis = 0.296

Mortality

Incidence of mortaility due to ascariasis used the GBD2010 mortality figures. In ascaris-endemic countries this ranged from a low of 0.000095 per 100 000 per annum in Dominica to a high of 0.159 per 100 000 per annum in Equitorial Guinea. Upper-income countries had zero mortality. Globally there were 0.031 deaths per 100 000

Age distribution

Fatalities, Ascariasis and mild abdomino pelvic problems <1 year, 9%; 1–4 years, 56.7%; 5–14 years, 16%; 15–24 years, 3%; 25–34 years 2.1%; >35 years, 13.2%.

Severe wasting: <1 year, 19%; 1–4 years, 81%.

Sex distribution

Male =55.1% (fatalities), Male = 50.1% (ascaris), Male=50.2% (mild abdominal pelvic discomfort),
Male= 51% (severe wasting).

A4.34 Trichinella

Incidence

Incidence was estimated from the results of a FERG-commisioned systematic review. Full details can be found in [71]

Clinical Outcomes

In the absence of data on the probability of occurrence of the major clinical symptoms of acute trichinellosis, it was assumed, as a worst case scenario, that all patients would develop diarrhoea, facial oedema, myalgia and fever/ headache [84].

Duration

Based on the systematic review by [71], disease duration ranged from 21.5 to 70 days. These values were divided by 365 to express the duration in years.

Disability weight

Because no specific DW for acute trichinellosis is available, DWs were derived for each of the outcomes separately. The four clinical symptoms were, respectively, matched to the GBD2010 health states:

- Diarrhoea: moderate – DW = 0.202.
- Disfigurement: level 2, with itch or pain – DW = 0.187.
- Musculoskeletal problems: generalized, moderate – DW = 0.292.
- Infectious disease: acute episode, severe (DW = 0.210) [82].

These four DWs were then aggregated using the multiplicative method, which defines the aggregated DW as 1–∏i(1–DWi)=0.637 [84].

Mortality

Mortality was estimated from the results of a FERG-commisioned systematic review. Full details can be found in [71]

Age distribution

According to [71], the majority of cases were between 20 and 50 years of age, with a median of 33.1. A generalized Beta distribution was fitted to the estimates to define the full distribution of cases from age 0 to 90 years [84].

Sex distribution

According to [71], 51% of cases were male.

A4.35 Aflatoxin

Incidence

A population-attributable fraction (PAF) approach was used to estimate the incidence of aflatoxin-related hepatocellular carcinoma (HCC). We assumed a multiplicative model for the effects of aflatoxin exposure and hepatitis B virus (HBV) infection. The excess risk due to aflatoxin exposure is estimated as HCCa- = b * a for HBV-negative individuals and HCCa+ = b * h * a for HBV-positive individuals, where a = exposure to aflatoxin (ng/(kg bw * day)), b = aflatoxin cancer potency factor in HBV- individuals ((ng/(kg bw * day)-1) and h = relative risk for aflatoxin exposure in HBV+ individuals compared with HBV- individuals. We used potency factors as derived by JECFA [111]: b = 0.01 [0.002–0.03](ng/(kg bw * day)-1 and b * h = 0.30 [0.005–0.50](ng/(kg bw * day)-1. Uncertainty in the potency factors was modelled as a Gamma distribution with the most likely value as the mean and the range representing an approximate 95% confidence interval.

To account for differences in background rates between different populations, we estimated PAFs by country, and applied them to HCC incidence, based on [305]. We assumed PAFs for incidence and deaths were equal and calculated PAFs based on published studies on HCC

mortality. For the study population that was the basis of the JECFA potency estimates in Guangxi, China [306], the PAF was estimated as PAFa = ((1–p) * HCCa- + p * HCCa+)/HCC, where p = prevalence of HBV infection and HCC = total incidence of HCC by all causes. We used the HCC death rate for the Guangxi cohort, standardized to the global population (121.5 per 100 000) and calculated average exposure (607 ng/(kg bw * day) based on [[307], Table I]. HBV prevalence was 23% based on [306], resulting in PAFa = 0.383. Background death rate of HCC by all causes in the Guangxi population was calculated as HCC0,s = (HCCs–HCCa,s) / (1–ps + h * ps), with the subscript s referring to the study population; resulting in HCC0,s = 9.77 per 100 000.

To calculate attributable incidence in all countries, we estimated relative risks due to aflatoxin exposure as RRa,c = 1 + b * ac / HCC0,s, and PAFs per country as PAFa,c = (RRa,c–1) / RRa,c, with the subscript c indicating country. Attributable incidence was then calculated as HCCa,c = HCCc * PAFa,c. Aflatoxin exposure by country was based on [110], with uncertainty represented by a uniform distribution over the reported range. A Bayesian log-normal random effects model [79, 151] was used to extrapolate available PAFs to countries without data.

Clinical outcomes

Hepatocellular carcinoma.

Duration

Not applicable; population-attributable fractions as described above were directly applied to WHO YLD estimates [308].

Disability Weight

Not applicable; population-attributable fractions as described above were directly applied to WHO YLD estimates [308].

Mortality

Population-attributable fractions as described above were directly applied to WHO mortality estimates [308].

Age distribution

We compared age distributions of HCC in the populations of Beijing and Qidong from [114], and hypothesized that the main difference in HCC risk factors between these two cities is aflatoxin exposure, since every other risk factor is the same, and they are both predominantly Han (i.e. same ethnicity). Hence, the difference in age distributions was presumed to be the contribution of aflatoxin. This resulted in an average age at onset of 49.

Sex distribution

In absence of information on the sex distribution of aflatoxin-induced hepatocellular carcinoma, a 50:50 age distribution was assumed.

A4.36 Cyanide in cassava

Incidence

A total of 2376 konzo cases have been reported in 5 countries (Cameroon, Central African Republic, Democratic Republic of Congo, Mozambique and United Republic of Tanzania), corresponding to 149 cases per year for 122 million people [86]. Based on these cases and dividing the average annual number of case for each country by the corresponding country population gives an observed incidence of 0.043 to 0.179 per 100 000.

The degree of underestimation is difficult to estimate, as konzo occurs in remote rural areas, often under conditions of war, and the disease is not notifiable. The only previous calculation of underestimation was that of Tylleskar [90] in the DRC in 1994, when he estimated that there may have been at least twice as many cases as those reported. The underestimation in the DRC is now likely to be much greater, due to war and displacement. It was decided to account for the uncertainty in the underreporting by applying an expansion factor ranging from 1 to 10 to the observed cases. Therefore, the annual total of new cases would range from 149 to 1490 in the 5 countries and the mean annual incidence rate would be 0.9 per 100 000 (0.04 to 1.8 per 100 000).

We restricted our estimates of konzo disease to the 5 African countries in which the disease has been reported, together with Angola, based on a report to the World Congress on Neurology suggesting that cases have occurred in that country [92]. The incidence of konzo disease was assumed to be null in other countries around the world.

Clinical outcomes

Konzo disease is a paraparesis occurring in populations exposed to cyanogenic glycoside in a context of bitter cassava consumption associated with a low intake of protein-rich food.

Duration

The onset of paraparesis is abrupt, usually within minutes or hours, with occasional progression during the first days of the illness. After that time, the paraparesis is non-progressive and permanent. As a result, duration was defined as lifelong for non-fatal cases. For fatal cases, it was assumed that death occurred one to seven years after onset, with an average of three years after onset, following [93].

Disability Weight

No specific DW exists for konzo paraparesis. WHO [89] defined three severity levels for konzo:

1. Mild = Able to walk without support

2. Moderate = uses one or two sticks or crutches to walk

3. Severe = not being able to walk

These three severity levels can be matched with the GBD2010 health states:

- Motor impairment, mild: DW = 0.012.
- Motor impairment, moderate: DW = 0.076.
- Motor impairment, severe: DW = 0.377 [82].

Information on the distribution of konzo severity levels is available from 9 studies [86][1]. Out of a total of 753 cases, 476 (63%) were mild, 203 (27%) were moderate and 74 (10%) were severe.

The resulting weighted DW equalled 0.065.

Mortality

Information on case fatality was provided in 4 studies [94–96, 309]. Out of a total of 340 cases, 73 deaths were observed, yielding an average case fatality ratio of 21%.

Age distribution

The age and sex distribution observed by [90] was generalized to the whole konzo affected population. The age distribution for fatal cases was adapted from [309].

Sex distribution

The age and sex distribution observed by [90] was generalized to the whole konzo affected population. The sex distribution for fatal cases was adapted from [309].

A4.37 Dioxin

Incidence

Incidence rates were generated for 50 countries and specified as lower and upper bounds (hypothyroidy-postnatal & male infertility) or point estimates (hypothyroidy-prenatal). Incidence rates for the remaining 144 countries were imputed using a Bayesian log-normal random effects model [151].

Clinical outcomes

Hypothyroidy due to prenatal exposure; hypothyroidy due to postnatal exposure; or male infertility due to prenatal exposure.

Duration

Hypothyroidy was assumed to be lifelong; the male infertility impact was assumed to be present in the 20–44 age group, in accordance with [83].

Disability Weights

- Hypothyroidy due to prenatal exposure: 0.019; corresponding to GBD 2013 health state Hypothyroidy [142]. Note that no corresponding DW was available in GBD2010 or WHO Global Health Estimates (GHE).
- Hypothyroidy due to postnatal exposure: 0.019; corresponding to GBD 2013 health state Hypothyroidy [142]. Note that no corresponding DW was available in GBD2010 or WHO GHE.
- Male infertility: 0.056; corresponding to WHO GHE health state Infertility: primary [310]. Note that this is higher than the corresponding GBD2010 health state.

Mortality

No mortality was assumed.

Age distribution

Hypothyroidy due to prenatal exposure: Onset = birth.

Hypothyroidy due to postnatal exposure: Onset = 20 years.

Male infertility: Onset = 20 years.

Sex distribution

In absence of information on the sex distribution of dioxin-induced hypothyroidy, a 50:50 age distribution was assumed.

For male infertility, the entire burden was assigned to males.

A4.38 Peanut allergens

Incidence

Data on clinically confirmed peanut [*Arachis hypogaea*] allergy in children were available from six countries (Canada, Denmark, Iceland, Sweden, Turkey and UK). Average incidences ranged from 0 to 22.6 per 100 000 [102]. To reflect this uncertainty, the incidence rate of clinical peanut allergy in subregion "A" countries was modelled as a Uniform distribution ranging from 0/100 000 to 22.6/100 000. Given the lack of data, no estimates were generated for other countries.

Clinical outcomes

The symptoms of peanut allergy vary from mild to severe, from swollen lips, shortness of breath, to an anaphylactic shock, which is potentially fatal. However, because of the very short duration of acute peanut allergy, we decided not to include acute peanut allergy in the burden assessment. The considered clinical outcome was therefore living with peanut allergy and the anxiety of a possible allergic reaction.

Duration

It is assumed that peanut allergy is a lifelong disease. It is important to note that the duration of allergic symptoms is very short.

Disability Weight

Mullins *et al.* [103] reported that 52% of cases referred to a specialist allergy medical practice in Australia suffered from mild symptoms (skin and subcutaneous tissue involvement only), 42% from moderate symptoms (features suggestive of respiratory, cardiovascular or gastrointestinal involvement), and 6% from severe symptoms (cyanosis, hypotension, confusion, collapse, loss of consciousness, incontinence). We propose the DW for clinically relevant peanut allergy be a weighted average accounting for this severity distribution. GBD2010 DWs [82] for the health states "Asthma: controlled" (DW = 0.009) are considered applicable for mild and moderate cases (94%), and "Generic uncomplicated disease: anxiety about the diagnosis" (DW = 0.054) for severe cases (6%), leading to a severity-weighted DW of 0.012 for clinically relevant peanut allergy.

Mortality

The limited data on the mortality rate of peanut-induced anaphylaxis show values ranging from 0 to 0.006 deaths per 100 000 person-years [102]. To reflect this uncertainty, the mortality rate of peanut-induced anaphylaxis in subregion "A" countries was modelled as a Uniform distribution ranging from 0/100 000 to 0.006/100 000. Given the lack of data, no estimates were generated for other countries.

Age distribution

The onset of peanut allergy is early in life (median age 18–24 months, [107, 108], with continued prevalence in older age groups. All incident cases of peanut allergy were therefore assumed to develop early in life, i.e. before the age of five.

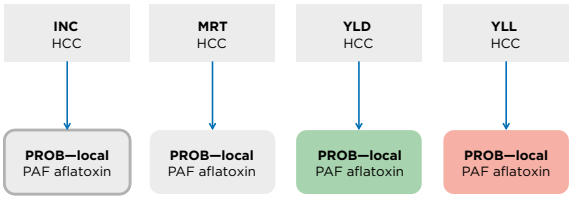
Deaths due to peanut allergen were assumed to occur at all ages, with an average age of 37 years [102][1].

Sex distribution

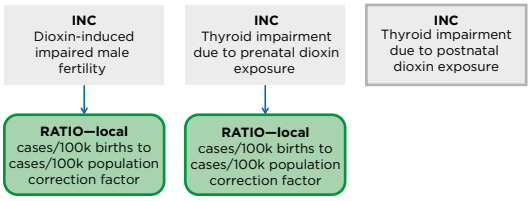
In the absence of information on the sex distribution of peanut allergy, a 50:50 age distribution was assumed.

APPENDIX 5.
Disease models

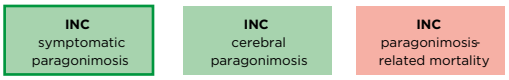
Aflatoxin
Disease Model



Dioxin
Disease Model

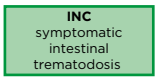


***Paragonimus* spp.**
Disease Model



***Opisthorchis* spp.**
Disease Model

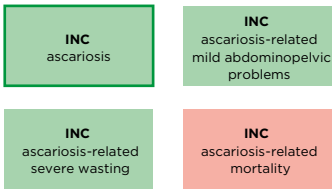
Intestinal flukes
Disease Model



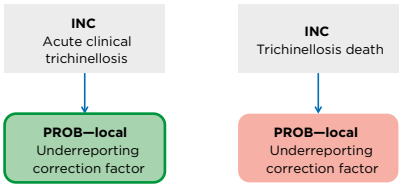
***Fasciola* spp.**
Disease Model

Clonorchis sinensis
Disease Model

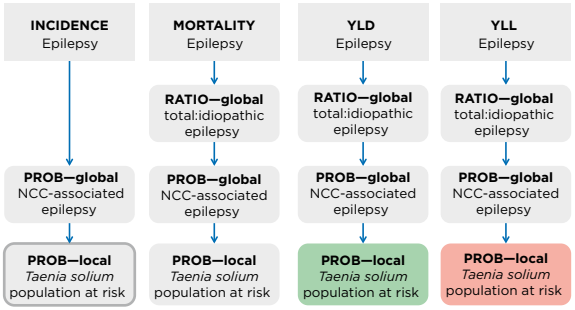
***Ascaris* spp.**
Disease Model



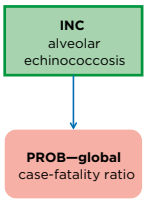
***Trichinella* spp.**
Disease Model



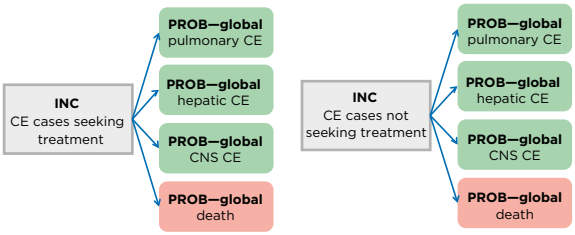
Taenia solium
Disease Model



Echinococcus multilocularis
Disease Model



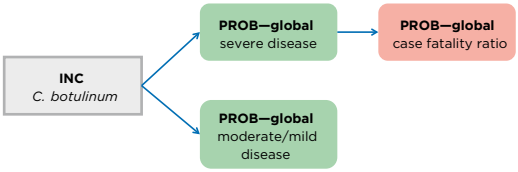
Echinococcus granulosus
Disease Model



Staphylococcus aureus
Disease Model

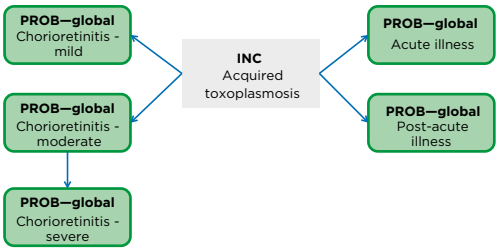
Clostridium perfringens
Disease Model

Clostridium botulinum
Disease Model

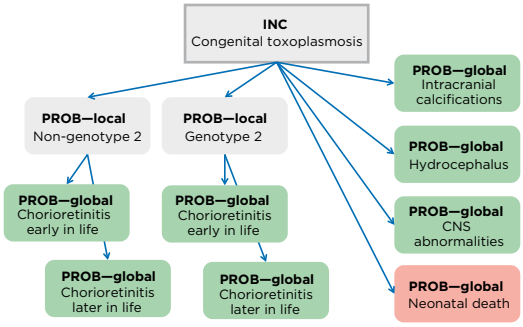


Bacillus cereus
Disease Model

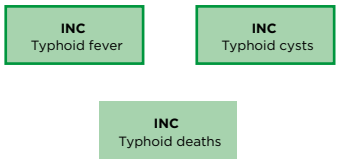
Toxoplasma gondii (acquired)
Disease Model



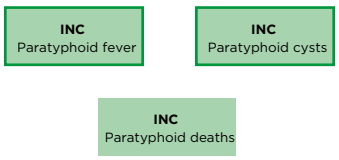
Toxoplasma gondii (congenital)
Disease Model



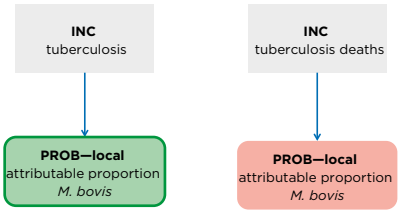
Salmonella Typhi
Disease Model



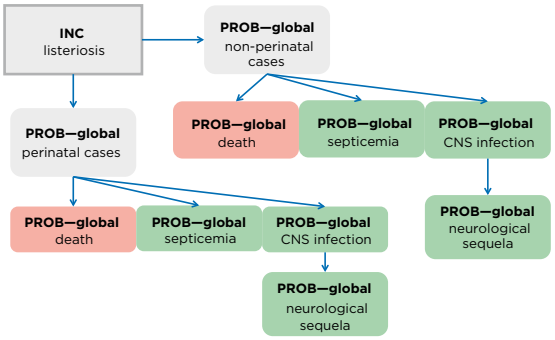
Salmonella Paratyphi
Disease Model



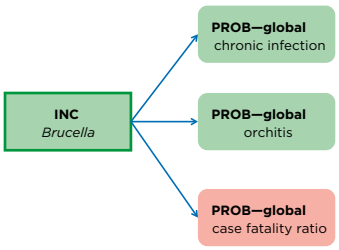
Mycobacterium bovis
Disease Model



Listeria monocytogenes
Disease Model

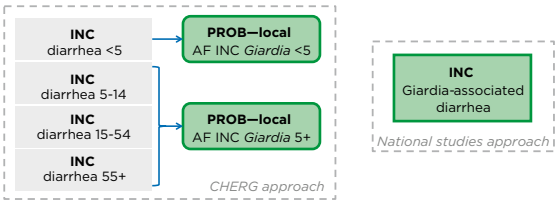


Brucella spp.
Disease Model

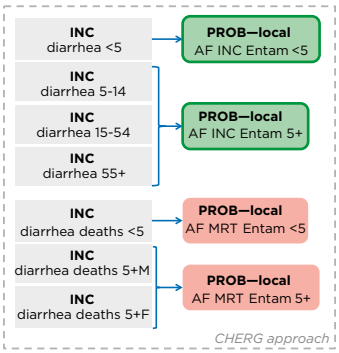


Hepatitis A virus
Disease Model

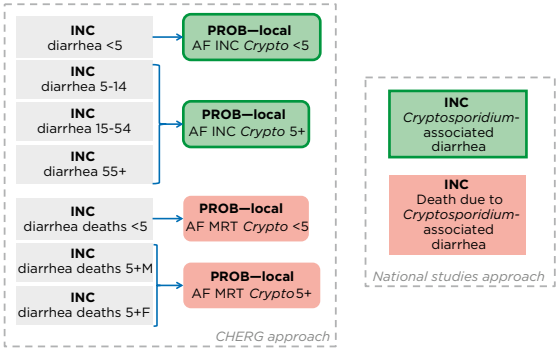
Giardia spp.
Disease Model



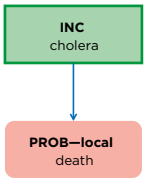
Entamoeba histolytica
Disease Model



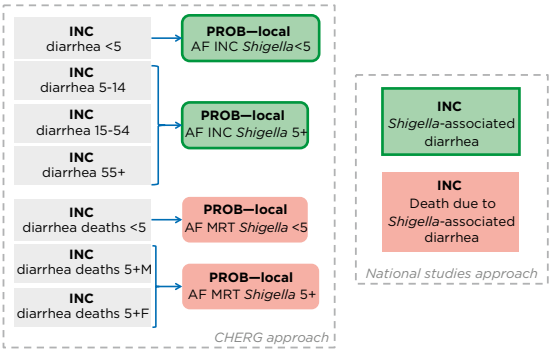
Cryptosporidium spp.
Disease Model



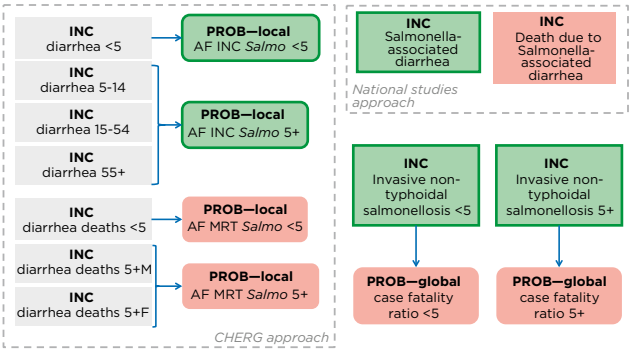
Vibrio cholerae
Disease Model



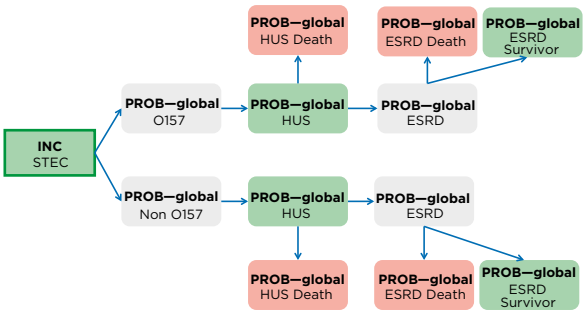
Shigella spp.
Disease Model



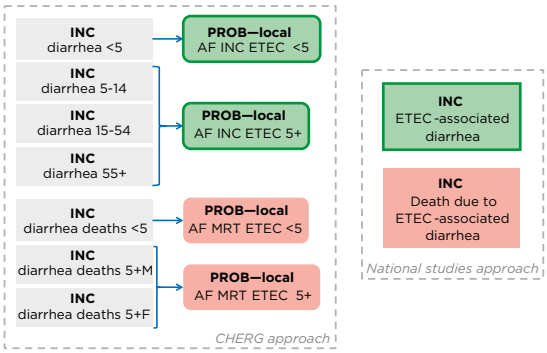
Salmonella enterica
Disease Model



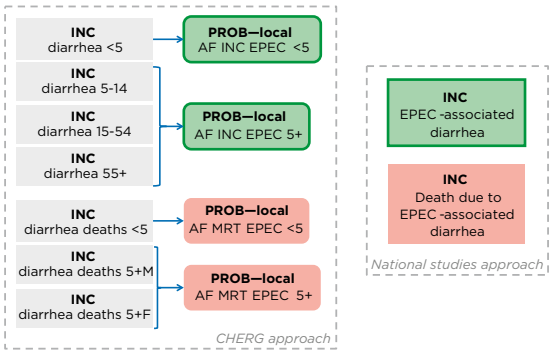
STEC
Disease Model



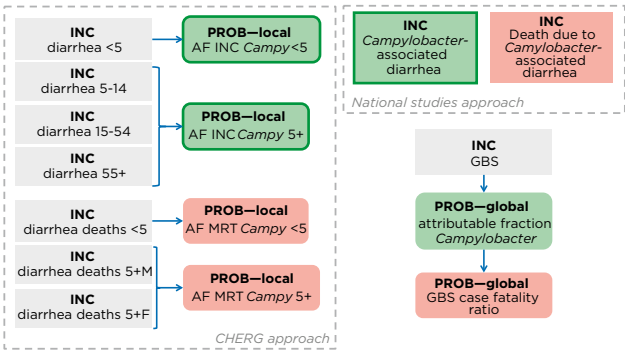
ETEC
Disease Model



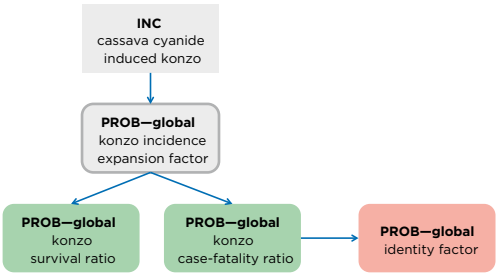
EPEC
Disease Model



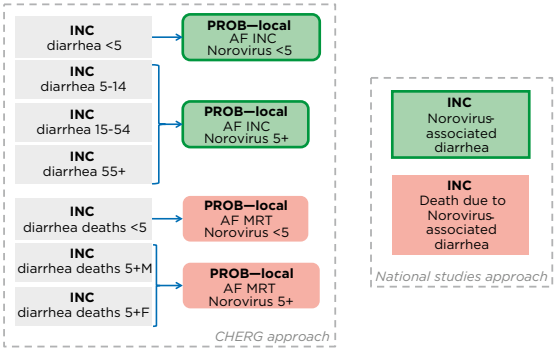
***Campylobacter* spp.**
Disease Model



Cyanide in cassava
Disease Model



Norovirus
Disease Model



Peanut allergen
Disease Model

APPENDIX 6.
Derivation of Disability Weights

Figure A6.1 FERG hazards, causally related health states and corresponding disability weights (DWs). The fourth column describes how the various DWs were derived from the Global Burden of Disease Studies (GBD) and the World Health Organization Global Health Estimates (WHO/GHE).

HAZARD	HEALTH STATE	DW	MAPPING
Diarrhoeal hazards			
Norovirus	Diarrhoeal disease	0.074	**Weighted average** of 91% *Diarrhoea: mild* (DW=0.061); 8.5% *Diarrhoea: moderate* (DW=0.202); and 0.5% *Diarrhoea: severe* (DW=0.281)
Campylobacter spp.	Diarrhoeal disease	0.101	**Weighted average** of 73% *Diarrhoea: mild* (DW=0.061); 25% *Diarrhoea: moderate* (DW=0.202); and 2% *Diarrhoea: severe* (DW=0.281)
	Guillain-Barré syndrome	0.445	**Proxy health state** of *Multiple sclerosis: moderate*
Enteropathogenic *E. coli*	Diarrhoeal disease	0.074	**Weighted average** of 91% *Diarrhoea: mild* (DW=0.061); 8.5% *Diarrhoea: moderate* (DW=0.202); and 0.5% *Diarrhoea: severe* (DW=0.281)
Enterotoxigenic *E. coli*	Diarrhoeal disease	0.074	**Weighted average** of 91% *Diarrhoea: mild* (DW=0.061); 8.5% *Diarrhoea: moderate* (DW=0.202); and 0.5% *Diarrhoea: severe* (DW=0.281)
Shiga toxin-producing *E. coli*	Diarrhoeal disease	0.091	**Weighted average** of 80% *Diarrhoea: mild* (DW=0.061); 18% *Diarrhoea: moderate* (DW=0.202); and 2% *Diarrhoea: severe* (DW=0.281)
	Haemolytic uraemic syndrome	0.210	**Proxy health state** of *Infectious disease: acute episode, severe*
	End-stage renal disease	0.573	**Mapped health state** of *End-stage renal disease: on dialysis*
Non-typhoidal *S. enterica*	Diarrhoeal disease	0.101	**Weighted average** of 73% *Diarrhoea: mild* (DW=0.061); 25% *Diarrhoea: moderate* (DW=0.202); and 2% *Diarrhoea: severe* (DW=0.281)
	Invasive salmonellosis	0.210	**Proxy health state** of *Infectious disease: acute episode, severe*
Shigella spp.	Diarrhoeal disease	0.101	**Weighted average** of 73% *Diarrhoea: mild* (DW=0.061); 25% *Diarrhoea: moderate* (DW=0.202); and 2% *Diarrhoea: severe* (DW=0.281)
Vibrio cholerae	Diarrhoeal disease	0.194	**Weighted average** of 25% *Diarrhoea: mild* (DW=0.061); 40% *Diarrhoea: moderate* (DW=0.202); and 35% *Diarrhoea: severe* (DW=0.281)
Cryptosporidium spp.	Diarrhoeal disease	0.074	**Weighted average** of 91% *Diarrhoea: mild* (DW=0.061); 8.5% *Diarrhoea: moderate* (DW=0.202); and 0.5% *Diarrhoea: severe* (DW=0.281)
Entamoeba histolytica	Diarrhoeal disease	0.074	**Weighted average** of 91% *Diarrhoea: mild* (DW=0.061); 8.5% *Diarrhoea: moderate* (DW=0.202); and 0.5% *Diarrhoea: severe* (DW=0.281)
Giardia spp.	Diarrhoeal disease	0.074	**Weighted average** of 91% *Diarrhoea: mild* (DW=0.061); 8.5% *Diarrhoea: moderate* (DW=0.202); and 0.5% *Diarrhoea: severe* (DW=0.281)

HAZARD	HEALTH STATE	DW	MAPPING
	Invasive enteric hazards		
Hepatitis A virus	Hepatitis	0.108	**Weighted average** of 50% *Infectious disease: acute episode, mild* (DW=0.005); and 50% *Infectious disease: acute episode, severe* (DW=0.210)
Brucella spp.	Acute brucellosis	0.132	**Weighted average** of 50% *Infectious disease: acute episode, moderate* (DW=0.053); and 50% *Infectious disease: acute episode, severe* (DW=0.210)
	Chronic brucellosis	0.079	**Proxy health state** of *Musculoskeletal problems: legs, moderate*
	Orchitis	0.097	**Mapped health state** of *Epididymo-orchitis*
Listeria monocytogenes, perinatal	Sepsis	0.210	**Proxy health state** of *Infectious disease: acute episode, severe*
	Central nervous system infection	0.426	**Weighted average**; see [70]
	Neurological sequelae	0.292	**Weighted average**; see [70]
Listeria monocytogenes, acquired	Sepsis	0.210	**Proxy health state** of *Infectious disease: acute episode, severe*
	Central nervous system infection	0.426	**Weighted average**; see [70] for details
	Neurological sequelae	0.292	**Weighted average**; see [70] for details
Mycobacterium bovis	Tuberculosis	0.331	**Mapped health state** of *Tuberculosis: without HIV infection*
Salmonella Paratyphi	Paratyphoid fever	0.210	**Proxy health state** of *Infectious disease: acute episode, severe*
	Liver abscesses and cysts	0.254	**Proxy health state** of *Infectious disease: post-acute consequences (fatigue, emotional lability, insomnia)*
Salmonella Typhi	Typhoid fever	0.210	**Proxy health state** of *Infectious disease: acute episode, severe*
	Liver abscesses and cysts	0.254	**Proxy health state** of *Infectious disease: post-acute consequences (fatigue, emotional lability, insomnia)*
Toxoplasma gondii, congenital	Intracranial calcification	0.010	**Proxy health state**; see [296] for details
	Hydrocephalus	0.360	**Weighted average**; see [296] for details
	Chorioretinitis, 1st year of life	0.033	**Proxy health state** of *Distance vision: moderate impairment*
	Chorioretinitis, later in life	0.033	**Proxy health state** of *Distance vision: moderate impairment*
	Central nervous system abnormalities	0.360	**Weighted average**; see [296] for details
Toxoplasma gondii, acquired	Chorioretinitis, mild	0.004	**Proxy health state** of *Distance vision: mild impairment*
	Chorioretinitis, moderate	0.033	**Proxy health state** of *Distance vision: moderate impairment*
	Chorioretinitis, severe	0.191	**Proxy health state** of *Distance vision: severe impairment*
	Acute illness	0.053	**Mapped health state** of *Infectious disease: acute episode, moderate*
	Post-acute illness	0.254	**Mapped health state** of *Infectious disease: post-acute consequences (fatigue, emotional lability, insomnia)*

HAZARD	HEALTH STATE	DW	MAPPING
	Enteric intoxications		
Bacillus cereus [1]	Acute intoxication	0.061	**Proxy health state** of *Diarrhoea: mild*
Clostridium botulinum [1]	Moderate/mild botulism	0.198	**Proxy health state** of *Multiple sclerosis: mild*
	Severe botulism	0.445	**Proxy health state** of *Multiple sclerosis: moderate*
Clostridium perfringens [1]	Acute intoxication	0.061	**Proxy health state** of *Diarrhoea: mild*
Staphylococcus aureus [1]	Acute intoxication	0.061	**Proxy health state** of *Diarrhoea: mild*
	Cestodes		
Echinococcus granulosus, cases seeking treatment	Pulmonary cystic echinococcosis	0.192	**Proxy health state** of *COPD and other chronic respiratory diseases: moderate*
	Hepatic cystic echinococcosis	0.123	**Proxy health state** of *Abdominopelvic problem: moderate*
	Central nervous system cystic echinococcosis	0.221	**Proxy health state** of *Motor plus cognitive impairments: moderate*
Echinococcus granulosus, cases not seeking treatment	Pulmonary cystic echinococcosis	0.015	**Proxy health state** of *COPD and other chronic respiratory diseases: mild*
	Hepatic cystic echinococcosis	0.012	**Proxy health state** of *Abdominopelvic problem: mild*
	Central nervous system cystic echinococcosis	0.054	**Proxy health state** of *Motor plus cognitive impairments: mild*
Echinococcus multilocularis	Alveolar echinococcosis	0.123	Proxy health state of *Abdominopelvic problem: moderate*
Taenia solium	Epilepsy: treated, seizure free	0.072	**Mapped health state** of *Epilepsy: treated, seizure free*
	Epilepsy: treated, with recent seizures	0.319	**Mapped health state** of *Epilepsy: treated, with recent seizures*
	Epilepsy: severe	0.657	**Mapped health state** of *Epilepsy: severe*
	Epilepsy: untreated	0.420	**Mapped health state** of *Epilepsy: untreated*
	Nematodes		
Ascaris spp.	Ascariasis infestation	0.030	**Mapped health state** of *Intestinal nematode infections: symptomatic*
	Mild abdominopelvic problems due to ascariasis	0.012	**Mapped health state** of *Abdominopelvic problem: mild*
	Severe wasting due to ascariasis	0.127	**Mapped health state** of *Severe wasting*
Trichinella spp.	Acute clinical trichinellosis	0.637	**Aggregate** of *Diarrhoea: moderate* (DW = 0.202); *Disfigurement: level 2, with itch or pain* (DW = 0.187); *Musculoskeletal problems: generalized, moderate* (DW = 0.292); and *Infectious disease: acute episode, severe* (DW = 0.210) [84]
	Trematodes		
Clonorchis sinensis	Abdominopelvic problems due to heavy clonorchiosis	0.123	**Proxy health state** of *Abdominopelvic problem: moderate*
Fasciola spp.	Abdominopelvic problems due to heavy fasciolosis	0.123	**Proxy health state** of *Abdominopelvic problem: moderate*
Intestinal flukes [2]	Abdominopelvic problems due to heavy intestinal fluke infections	0.123	**Proxy health state** of *Abdominopelvic problem: moderate*
Opisthorchis spp.	Abdominopelvic problems due to heavy opisthorchiosis	0.123	**Proxy health state** of *Abdominopelvic problem: moderate*

HAZARD	HEALTH STATE	DW	MAPPING
Paragonimus spp.	Central nervous system problems due to heavy paragonimosis	0.420	Proxy health state of *Epilepsy: untreated*
	Pulmonary problems due to heavy paragonimosis	0.132	Proxy health state of *Asthma: uncontrolled*
	Organic pollutants		
Dioxin	Infertility	0.056 [3]	Mapped health state of *Infertility: primary*
	Hypothyroidy due to prenatal exposure	0.019 [4]	Mapped health state of *Hypothyroidy*
	Hypothyroidy due postnatal exposure	0.019 [4]	Mapped health state of *Hypothyroidy*
	Toxins and allergens		
Aflatoxin	Hepatocellular carcinoma: diagnosis and primary therapy	0.294	Mapped health state of *Cancer: diagnosis and primary therapy*
	Hepatocellular carcinoma: metastatic	0.484	Mapped health state of *Cancer: metastatic*
	Hepatocellular carcinoma: terminal phase with medication	0.508	Mapped health state of *Cancer: terminal phase with medication*
	Hepatocellular carcinoma: terminal phase without medication	0.519	Mapped health state of *Cancer: terminal phase without medication*
Cyanide in cassava	*Konzo*	0.065	Weighted average of 63% *Motor impairment: mild* (DW=0.012); 27% *Motor impairment: moderate* (DW=0.076); and 10% *Motor impairment: severe* (DW=0.377)
Peanut [1]	Living with peanut-induced allergy	0.012	Weighted average of 94% *Asthma: controlled* (DW=0.009); and 6% *Generic uncomplicated disease: anxiety about diagnosis* (DW=0.054)

[1] Excluded from global burden assessments.

[2] Includes *Echinostoma* spp., *Fasciolopsis buski*, *Heterophyes* spp., *Metagonimus* spp. and other foodborne intestinal trematode species.

[3] Note the higher values used in WHO/GHE [310] compared with GBD2010 [82].

[4] Value taken from the GBD 2013 disability weights [142].

APPENDIX 7: Attribution – Expert Elicitation Results

Table A7.1 Subregional estimates (median and 95% uncertainty interval) of the proportion of illnesses caused by *Campylobacter* spp., non-typhoidal *Salmonella* spp., Shiga-toxin producing *Escherichia coli* (STEC), *Brucella* spp. and *Shigella* spp. through each exposure pathway.

SUBREGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN-TO-HUMAN CONTACT	WATER	SOIL	OTHER
DIARRHOEAL DISEASE						
***Campylobacter* spp.**						
AFR D	0.57 (0.31–0.77)	0.18 (0.00–0.42)	0.04 (0.00–0.22)	0.09 (0.01–0.29)	0.00 (0.00–0.12)	0.06 (0.00–0.16)
AFR E	0.57 (0.29–0.77)	0.17 (0.00–0.42)	0.04 (0.00–0.23)	0.09 (0.00–0.30)	0.00 (0.00–0.12)	0.06 (0.00–0.16)
AMR A	0.73 (0.38–0.91)	0.10 (0.00–0.37)	0.00 (0.00–0.20)	0.11 (0.00–0.32)	0.00 (0.00–0.11)	0.00 (0.00–0.02)
AMR B	0.68 (0.41–0.82)	0.11 (0.00–0.33)	0.03 (0.00–0.21)	0.08 (0.00–0.27)	0.00 (0.00–0.11)	0.06 (0.00–0.16)
AMR D	0.67 (0.37–0.81)	0.12 (0.01–0.36)	0.03 (0.00–0.21)	0.08 (0.00–0.29)	0.00 (0.00–0.15)	0.06 (0.00–0.16)
EMR B	0.67 (0.38–0.82)	0.11 (0.01–0.35)	0.03 (0.00–0.27)	0.07 (0.00–0.29)	0.00 (0.00–0.15)	0.06 (0.00–0.15)
EMR D	0.67 (0.41–0.82)	0.11 (0.00–0.34)	0.03 (0.00–0.22)	0.07 (0.00–0.27)	0.00 (0.00–0.20)	0.06 (0.00–0.15)
EUR A	0.76 (0.44–0.93)	0.08 (0.00–0.31)	0.01 (0.00–0.13)	0.06 (0.00–0.35)	0.01 (0.00–0.09)	0.00 (0.00–0.08)
EUR B	0.66 (0.34–0.87)	0.11 (0.00–0.39)	0.03 (0.00–0.21)	0.12 (0.00–0.40)	0.03 (0.00–0.13)	0.00 (0.00–0.05)
EUR C	0.66 (0.34–0.87)	0.11 (0.00–0.38)	0.03 (0.00–0.23)	0.12 (0.00–0.39)	0.03 (0.00–0.19)	0.00 (0.00–0.02)
SEAR B	0.57 (0.27–0.81)	0.13 (0.00–0.36)	0.11 (0.00–0.36)	0.05 (0.00–0.35)	0.03 (0.00–0.21)	0.02 (0.00–0.06)
SEAR D	0.51 (0.03–0.79)	0.11 (0.00–0.39)	0.11 (0.01–0.41)	0.07 (0.00–0.44)	0.03 (0.00–0.32)	0.02 (0.00–0.10)
WPR A	0.68 (0.40–0.89)	0.13 (0.00–0.33)	0.00 (0.00–0.23)	0.11 (0.00–0.32)	0.00 (0.00–0.08)	0.00 (0.00–0.01)
WPR B	0.57 (0.25–0.82)	0.17 (0.00–0.42)	0.06 (0.00–0.34)	0.05 (0.00–0.32)	0.03 (0.00–0.15)	0.02 (0.00–0.07)
Non-typhoidal *Salmonella enterica*						
AFR D	0.46 (0.13–0.74)	0.15 (0.00–0.43)	0.18 (0.00–0.48)	0.10 (0.00–0.39)	0.01 (0.00–0.13)	0.02 (0.00–0.06)
AFR E	0.46 (0.10–0.73)	0.15 (0.00–0.42)	0.18 (0.00–0.48)	0.10 (0.00–0.40)	0.01 (0.00–0.19)	0.02 (0.00–0.08)
AMR A	0.73 (0.38–0.91)	0.10 (0.00–0.39)	0.05 (0.00–0.28)	0.02 (0.00–0.22)	0.00 (0.00–0.09)	0.00 (0.00–0.05)
AMR B	0.49 (0.09–0.74)	0.19 (0.00–0.45)	0.15 (0.00–0.40)	0.09 (0.00–0.32)	0.01 (0.00–0.12)	0.02 (0.00–0.05)
AMR D	0.50 (0.14–0.75)	0.19 (0.00–0.46)	0.15 (0.00–0.39)	0.09 (0.00–0.31)	0.01 (0.00–0.12)	0.02 (0.00–0.05)
EMR B	0.50 (0.18–0.75)	0.15 (0.00–0.43)	0.15 (0.01–0.38)	0.12 (0.00–0.33)	0.01 (0.00–0.19)	0.02 (0.00–0.04)
EMR D	0.50 (0.19–0.74)	0.15 (0.00–0.43)	0.15 (0.01–0.39)	0.12 (0.00–0.32)	0.01 (0.00–0.21)	0.02 (0.00–0.05)
EUR A	0.76 (0.47–0.94)	0.05 (0.00–0.30)	0.06 (0.00–0.26)	0.03 (0.00–0.21)	0.00 (0.00–0.11)	0.00 (0.00–0.14)

SUBREGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN-TO-HUMAN CONTACT	WATER	SOIL	OTHER
EUR B	0.62 (0.31–0.84)	0.10 (0.00–0.37)	0.11 (0.01–0.32)	0.07 (0.00–0.32)	0.02 (0.00–0.12)	0.00 (0.00–0.01)
EUR C	0.62 (0.32–0.84)	0.10 (0.00–0.36)	0.10 (0.00–0.32)	0.07 (0.00–0.32)	0.02 (0.00–0.12)	0.00 (0.00–0.01)
SEAR B	0.58 (0.23–0.84)	0.06 (0.00–0.32)	0.10 (0.00–0.38)	0.11 (0.00–0.40)	0.02 (0.00–0.20)	0.00 (0.00–0.03)
SEAR D	0.54 (0.00–0.85)	0.06 (0.00–0.37)	0.10 (0.00–0.42)	0.15 (0.00–0.59)	0.02 (0.00–0.29)	0.00 (0.00–0.06)
WPR A	0.74 (0.45–0.93)	0.09 (0.00–0.31)	0.04 (0.00–0.28)	0.01 (0.00–0.22)	0.00 (0.00–0.08)	0.00 (0.00–0.04)
WPR B	0.57 (0.25–0.82)	0.10 (0.00–0.33)	0.12 (0.00–0.35)	0.08 (0.00–0.37)	0.02 (0.00–0.21)	0.00 (0.00–0.01)
Shiga toxin-producing *E. coli*						
AFR D	0.42 (0.19–0.66)	0.21 (0.04–0.46)	0.16 (0.00–0.33)	0.10 (0.00–0.30)	0.05 (0.00–0.25)	0.00 (0.00–0.03)
AFR E	0.43 (0.14–0.66)	0.21 (0.04–0.46)	0.17 (0.01–0.34)	0.10 (0.00–0.34)	0.05 (0.00–0.19)	0.00 (0.00–0.03)
AMR A	0.59 (0.19–0.84)	0.13 (0.00–0.41)	0.07 (0.00–0.32)	0.07 (0.00–0.31)	0.00 (0.00–0.13)	0.00 (0.00–0.27)
AMR B	0.53 (0.24–0.73)	0.17 (0.01–0.44)	0.11 (0.01–0.29)	0.08 (0.00–0.32)	0.04 (0.00–0.21)	0.00 (0.00–0.03)
AMR D	0.53 (0.24–0.75)	0.15 (0.00–0.43)	0.11 (0.01–0.29)	0.09 (0.00–0.32)	0.04 (0.00–0.17)	0.00 (0.00–0.03)
EMR B	0.53 (0.24–0.76)	0.15 (0.02–0.43)	0.11 (0.00–0.29)	0.10 (0.00–0.37)	0.04 (0.00–0.18)	0.00 (0.00–0.03)
EMR D	0.52 (0.26–0.75)	0.14 (0.01–0.42)	0.11 (0.01–0.30)	0.10 (0.00–0.37)	0.04 (0.00–0.17)	0.00 (0.00–0.03)
EUR A	0.60 (0.26–0.83)	0.11 (0.01–0.37)	0.08 (0.00–0.33)	0.07 (0.00–0.33)	0.03 (0.00–0.19)	0.00 (0.00–0.14)
EUR B	0.49 (0.15–0.75)	0.12 (0.00–0.42)	0.10 (0.01–0.32)	0.09 (0.00–0.38)	0.08 (0.00–0.35)	0.00 (0.00–0.01)
EUR C	0.49 (0.15–0.75)	0.12 (0.00–0.42)	0.10 (0.01–0.32)	0.09 (0.00–0.36)	0.08 (0.00–0.35)	0.00 (0.00–0.01)
SEAR B	0.41 (0.10–0.70)	0.12 (0.00–0.47)	0.07 (0.00–0.31)	0.23 (0.00–0.53)	0.06 (0.00–0.26)	0.00 (0.00–0.01)
SEAR D	0.40 (0.08–0.71)	0.13 (0.00–0.47)	0.06 (0.00–0.35)	0.23 (0.00–0.53)	0.06 (0.00–0.26)	0.00 (0.00–0.02)
WPR A	0.57 (0.25–0.82)	0.14 (0.00–0.36)	0.07 (0.00–0.35)	0.07 (0.00–0.29)	0.00 (0.00–0.16)	0.00 (0.00–0.24)
WPR B	0.43 (0.12–0.73)	0.12 (0.00–0.44)	0.07 (0.00–0.35)	0.22 (0.00–0.46)	0.06 (0.00–0.27)	0.00 (0.00–0.01)
***Brucella* spp.**						
AFR D	0.44 (0.10–0.68)	0.50 (0.26–0.81)	na	0.01 (0.00–0.08)	0.01 (0.00–0.10)	0.01 (0.00–0.06)
AFR E	0.44 (0.06–0.70)	0.50 (0.22–0.83)	na	0.01 (0.00–0.12)	0.01 (0.00–0.11)	0.01 (0.00–0.06)
AMR A	0.75 (0.28–0.93)	0.19 (0.00–0.62)	na	0.01 (0.00–0.04)	0.01 (0.00–0.09)	0.01 (0.00–0.12)
AMR B	0.44 (0.09–0.69)	0.50 (0.24–0.81)	na	0.01 (0.00–0.08)	0.01 (0.00–0.12)	0.01 (0.00–0.08)

SUBREGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN-TO-HUMAN CONTACT	WATER	SOIL	OTHER
AMR D	0.44 (0.09–0.72)	0.50 (0.18–0.81)	na	0.01 (0.00–0.12)	0.01 (0.00–0.11)	0.01 (0.00–0.06)
EMR B	0.51 (0.08–0.80)	0.43 (0.11–0.81)	na	0.01 (0.00–0.07)	0.01 (0.00–0.08)	0.01 (0.00–0.11)
EMR D	0.44 (0.07–0.70)	0.50 (0.20–0.83)	na	0.01 (0.00–0.14)	0.01 (0.00–0.15)	0.01 (0.00–0.06)
EUR A	0.66 (0.23–0.90)	0.23 (0.01–0.60)	na	0.01 (0.00–0.04)	0.01 (0.00–0.05)	0.02 (0.00–0.35)
EUR B	0.45 (0.09–0.71)	0.50 (0.20–0.81)	na	0.01 (0.00–0.07)	0.01 (0.00–0.08)	0.01 (0.00–0.06)
EUR C	0.44 (0.10–0.73)	0.50 (0.18–0.81)	na	0.01 (0.00–0.06)	0.01 (0.00–0.06)	0.01 (0.00–0.06)
SEAR B	0.51 (0.07–0.81)	0.43 (0.10–0.81)	na	0.01 (0.00–0.07)	0.01 (0.00–0.07)	0.01 (0.00–0.07)
SEAR D	0.45 (0.07–0.70)	0.50 (0.22–0.82)	na	0.01 (0.00–0.08)	0.01 (0.00–0.07)	0.01 (0.00–0.06)
WPR A	0.71 (0.28–0.92)	0.18 (0.00–0.58)	na	0.01 (0.00–0.09)	0.01 (0.00–0.26)	0.02 (0.00–0.30)
WPR B	0.51 (0.07–0.80)	0.43 (0.12–0.81)	na	0.01 (0.00–0.07)	0.01 (0.00–0.07)	0.01 (0.00–0.07)
***Shigella* spp.**						
AFR D	0.15 (0.00–0.52)	na	0.50 (0.06–0.81)	0.27 (0.03–0.62)	0.00 (0.00–0.19)	0.00 (0.00–0.13)
AFR E	0.15 (0.00–0.51)	na	0.50 (0.08–0.80)	0.26 (0.05–0.61)	0.00 (0.00–0.19)	0.00 (0.00–0.16)
AMR A	0.12 (0.00–0.46)	na	0.69 (0.33–0.93)	0.10 (0.00–0.41)	0.00 (0.00–0.21)	0.00 (0.00–0.06)
AMR B	0.14 (0.00–0.52)	na	0.51 (0.10–0.81)	0.27 (0.03–0.61)	0.00 (0.00–0.18)	0.00 (0.00–0.06)
AMR D	0.14 (0.00–0.52)	na	0.51 (0.11–0.80)	0.27 (0.02–0.60)	0.00 (0.00–0.20)	0.00 (0.00–0.02)
EMR B	0.14 (0.00–0.52)	na	0.51 (0.11–0.81)	0.28 (0.03–0.61)	0.00 (0.00–0.17)	0.00 (0.00–0.02)
EMR D	0.14 (0.00–0.52)	na	0.51 (0.11–0.81)	0.28 (0.02–0.61)	0.00 (0.00–0.18)	0.00 (0.00–0.02)
EUR A	0.07 (0.00–0.46)	na	0.54 (0.14–0.90)	0.12 (0.00–0.52)	0.01 (0.00–0.20)	0.00 (0.00–0.55)
EUR B	0.11 (0.00–0.50)	na	0.44 (0.10–0.75)	0.31 (0.04–0.60)	0.02 (0.00–0.20)	0.02 (0.00–0.21)
EUR C	0.19 (0.00–0.51)	na	0.43 (0.07–0.70)	0.26 (0.02–0.53)	0.01 (0.00–0.20)	0.05 (0.00–0.22)
SEAR B	0.36 (0.01–0.68)	na	0.30 (0.01–0.65)	0.26 (0.01–0.59)	0.04 (0.00–0.21)	0.01 (0.00–0.03)
SEAR D	0.34 (0.01–0.69)	na	0.25 (0.00–0.64)	0.29 (0.01–0.65)	0.04 (0.00–0.26)	0.01 (0.00–0.06)
WPR A	0.13 (0.00–0.50)	na	0.66 (0.25–0.91)	0.12 (0.00–0.42)	0.00 (0.00–0.22)	0.00 (0.00–0.19)
WPR B	0.36 (0.01–0.70)	na	0.28 (0.00–0.65)	0.27 (0.01–0.60)	0.04 (0.00–0.22)	0.01 (0.00–0.03)

Table A7.2 Subregional estimates (median and 95% uncertainty interval) of the proportion of Diarrhoeal Disease illnesses caused by four hazards: enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), *Cryptosporidium* spp. and *Giardia* spp. through each exposure pathway.

SUB-REGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN TO HUMAN CONTACT	WATER	OTHER
Enteropathogenic *E. coli*					
AFR D	0.29 (0.02–0.62)	0.00 (0.00–0.33)	0.16 (0.00–0.51)	0.45 (0.12–0.76)	0.00 (0.00–0.01)
AFR E	0.29 (0.01–0.62)	0.00 (0.00–0.32)	0.16 (0.00–0.51)	0.46 (0.10–0.76)	0.00 (0.00–0.01)
AMR A	0.72 (0.20–0.97)	0.00 (0.00–0.31)	0.11 (0.00–0.53)	0.00 (0.00–0.57)	0.00 (0.00–0.01)
AMR B	0.29 (0.01–0.62)	0.00 (0.00–0.34)	0.16 (0.00–0.50)	0.46 (0.12–0.76)	0.00 (0.00–0.01)
AMR D	0.30 (0.03–0.61)	0.00 (0.00–0.33)	0.15 (0.00–0.47)	0.47 (0.13–0.74)	0.00 (0.00–0.01)
EMR B	0.31 (0.06–0.62)	0.00 (0.00–0.35)	0.14 (0.00–0.44)	0.46 (0.11–0.70)	0.00 (0.00–0.01)
EMR D	0.31 (0.05–0.62)	0.00 (0.00–0.37)	0.14 (0.00–0.44)	0.45 (0.10–0.70)	0.00 (0.00–0.01)
EUR A	0.64 (0.17–0.90)	0.05 (0.00–0.38)	0.17 (0.00–0.58)	0.03 (0.00–0.31)	0.00 (0.00–0.21)
EUR B	0.48 (0.06–0.81)	0.08 (0.00–0.41)	0.26 (0.00–0.65)	0.08 (0.00–0.43)	0.00 (0.00–0.01)
EUR C	0.48 (0.06–0.81)	0.09 (0.00–0.42)	0.26 (0.00–0.65)	0.08 (0.00–0.42)	0.00 (0.00–0.02)
SEAR B	0.29 (0.01–0.62)	0.09 (0.00–0.34)	0.29 (0.01–0.62)	0.27 (0.01–0.58)	0.00 (0.00–0.02)
SEAR D	0.29 (0.01–0.67)	0.09 (0.00–0.38)	0.27 (0.00–0.65)	0.27 (0.00–0.63)	0.00 (0.00–0.05)
WPR A	0.69 (0.16–0.94)	0.00 (0.00–0.34)	0.18 (0.00–0.66)	0.00 (0.00–0.30)	0.00 (0.00–0.02)
WPR B	0.30 (0.01–0.62)	0.14 (0.00–0.40)	0.23 (0.00–0.59)	0.26 (0.02–0.55)	0.00 (0.00–0.01)
Enterotoxigenic *E. coli*					
AFR D	0.33 (0.09–0.65)	0.00 (0.00–0.33)	0.13 (0.00–0.44)	0.45 (0.12–0.71)	0.00 (0.00–0.01)
AFR E	0.33 (0.06–0.64)	0.00 (0.00–0.33)	0.13 (0.00–0.45)	0.45 (0.09–0.71)	0.00 (0.00–0.01)
AMR A	0.36 (0.12–0.63)	0.04 (0.00–0.32)	0.15 (0.00–0.37)	0.42 (0.11–0.66)	0.00 (0.00–0.19)
AMR B	0.34 (0.08–0.65)	0.00 (0.00–0.34)	0.12 (0.00–0.42)	0.46 (0.11–0.70)	0.00 (0.00–0.13)
AMR D	0.36 (0.07–0.68)	0.00 (0.00–0.32)	0.13 (0.00–0.43)	0.47 (0.10–0.72)	0.00 (0.00–0.01)
EMR B	0.34 (0.07–0.65)	0.00 (0.00–0.31)	0.13 (0.00–0.42)	0.49 (0.10–0.72)	0.00 (0.00–0.01)
EMR D	0.35 (0.05–0.66)	0.00 (0.00–0.31)	0.12 (0.00–0.41)	0.48 (0.12–0.73)	0.00 (0.00–0.01)
EUR A	0.42 (0.09–0.73)	0.05 (0.00–0.31)	0.26 (0.01–0.60)	0.18 (0.00–0.53)	0.00 (0.00–0.08)
EUR B	0.43 (0.05–0.73)	0.05 (0.00–0.34)	0.31 (0.02–0.66)	0.14 (0.00–0.47)	0.00 (0.00–0.18)
EUR C	0.43 (0.06–0.72)	0.05 (0.00–0.34)	0.31 (0.02–0.66)	0.14 (0.00–0.47)	0.00 (0.00–0.20)
SEAR B	0.38 (0.03–0.73)	0.05 (0.00–0.32)	0.09 (0.00–0.51)	0.39 (0.02–0.71)	0.00 (0.00–0.02)
SEAR D	0.37 (0.02–0.73)	0.06 (0.00–0.34)	0.09 (0.00–0.52)	0.38 (0.03–0.73)	0.00 (0.00–0.11)
WPR A	0.38 (0.10–0.72)	0.04 (0.00–0.29)	0.20 (0.00–0.53)	0.33 (0.00–0.61)	0.00 (0.00–0.01)
WPR B	0.38 (0.03–0.72)	0.04 (0.00–0.29)	0.08 (0.00–0.50)	0.39 (0.04–0.71)	0.00 (0.00–0.20)
***Cryptosporidium* spp.**					
AFR D	0.15 (0.00–0.44)	0.06 (0.00–0.27)	0.38 (0.01–0.72)	0.35 (0.01–0.68)	0.01 (0.00–0.16)
AFR E	0.15 (0.00–0.47)	0.05 (0.00–0.26)	0.36 (0.01–0.72)	0.37 (0.01–0.71)	0.01 (0.00–0.17)
AMR A	0.16 (0.01–0.44)	0.10 (0.01–0.42)	0.30 (0.03–0.64)	0.37 (0.08–0.72)	0.00 (0.00–0.09)
AMR B	0.11 (0.01–0.38)	0.20 (0.02–0.47)	0.35 (0.07–0.66)	0.26 (0.05–0.61)	0.00 (0.00–0.09)
AMR D	0.16 (0.01–0.44)	0.21 (0.03–0.49)	0.34 (0.07–0.66)	0.20 (0.03–0.59)	0.00 (0.00–0.08)
EMR B	0.09 (0.00–0.41)	0.14 (0.00–0.46)	0.31 (0.02–0.65)	0.36 (0.05–0.69)	0.01 (0.00–0.17)
EMR D	0.08 (0.00–0.36)	0.13 (0.00–0.43)	0.32 (0.01–0.66)	0.38 (0.06–0.71)	0.01 (0.00–0.17)

SUB-REGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN TO HUMAN CONTACT	WATER	OTHER
EUR A	0.10 (0.00–0.39)	0.14 (0.00–0.44)	0.30 (0.01–0.65)	0.38 (0.03–0.70)	0.01 (0.00–0.09)
EUR B	0.11 (0.00–0.39)	0.16 (0.00–0.46)	0.28 (0.01–0.64)	0.37 (0.02–0.68)	0.01 (0.00–0.08)
EUR C	0.09 (0.00–0.40)	0.15 (0.00–0.48)	0.29 (0.01–0.64)	0.36 (0.05–0.70)	0.01 (0.00–0.09)
SEAR B	0.10 (0.00–0.37)	0.13 (0.00–0.46)	0.31 (0.01–0.66)	0.38 (0.02–0.71)	0.01 (0.00–0.09)
SEAR D	0.10 (0.00–0.42)	0.13 (0.00–0.46)	0.30 (0.01–0.66)	0.37 (0.03–0.71)	0.01 (0.00–0.15)
WPR A	0.10 (0.00–0.40)	0.12 (0.00–0.46)	0.29 (0.01–0.66)	0.39 (0.03–0.72)	0.01 (0.00–0.09)
WPR B	0.10 (0.00–0.45)	0.10 (0.00–0.45)	0.29 (0.01–0.66)	0.39 (0.04–0.73)	0.01 (0.00–0.10)
			***Giardia* spp.**		
AFR D	0.11 (0.00–0.43)	0.03 (0.00–0.27)	0.43 (0.01–0.75)	0.33 (0.05–0.69)	0.02 (0.00–0.18)
AFR E	0.11 (0.00–0.43)	0.03 (0.00–0.25)	0.44 (0.04–0.75)	0.32 (0.04–0.67)	0.02 (0.00–0.19)
AMR A	0.11 (0.00–0.39)	0.14 (0.00–0.41)	0.25 (0.00–0.64)	0.42 (0.05–0.75)	0.00 (0.00–0.12)
AMR B	0.12 (0.00–0.42)	0.18 (0.00–0.47)	0.32 (0.01–0.67)	0.30 (0.04–0.65)	0.00 (0.00–0.09)
AMR D	0.12 (0.00–0.42)	0.18 (0.00–0.46)	0.36 (0.01–0.69)	0.26 (0.03–0.63)	0.00 (0.00–0.10)
EMR B	0.13 (0.00–0.50)	0.02 (0.00–0.15)	0.45 (0.03–0.77)	0.32 (0.03–0.71)	0.01 (0.00–0.19)
EMR D	0.13 (0.00–0.47)	0.02 (0.00–0.25)	0.39 (0.02–0.73)	0.35 (0.03–0.71)	0.01 (0.00–0.18)
EUR A	0.11 (0.00–0.44)	0.02 (0.00–0.15)	0.47 (0.02–0.79)	0.32 (0.03–0.72)	0.01 (0.00–0.14)
EUR B	0.12 (0.00–0.47)	0.02 (0.00–0.15)	0.44 (0.02–0.77)	0.34 (0.02–0.73)	0.01 (0.00–0.12)
EUR C	0.12 (0.00–0.48)	0.02 (0.00–0.15)	0.44 (0.02–0.77)	0.34 (0.04–0.74)	0.01 (0.00–0.13)
SEAR B	0.13 (0.00–0.48)	0.02 (0.00–0.23)	0.41 (0.02–0.74)	0.35 (0.02–0.72)	0.01 (0.00–0.17)
SEAR D	0.13 (0.00–0.48)	0.02 (0.00–0.22)	0.41 (0.02–0.76)	0.35 (0.03–0.72)	0.01 (0.00–0.16)
WPR A	0.12 (0.00–0.45)	0.02 (0.00–0.31)	0.46 (0.02–0.78)	0.29 (0.01–0.68)	0.01 (0.00–0.18)
WPR B	0.14 (0.00–0.49)	0.02 (0.00–0.29)	0.43 (0.02–0.75)	0.30 (0.03–0.69)	0.01 (0.00–0.19)

Table A7.3 Subregional estimates (median and 95% uncertainty interval) of the proportion of Diarrhoeal Disease illnesses caused by *Salmonella* Typhi, *Vibrio cholerae*, *Entamoeba histolytica*, norovirus, and hepatitis A virus through each exposure pathway.

SUBREGION	FOOD	HUMAN-TO-HUMAN CONTACT	WATER	OTHER
		***Salmonella* Typhi**		
AFR D	0.24 (0.00–0.58)	0.22 (0.00–0.54)	0.51 (0.13–0.82)	0.00 (0.00–0.09)
AFR E	0.24 (0.00–0.58)	0.22 (0.00–0.53)	0.51 (0.16–0.81)	0.00 (0.00–0.10)
AMR A	0.26 (0.00–0.64)	0.11 (0.00–0.48)	0.57 (0.14–0.87)	0.00 (0.00–0.37)
AMR B	0.23 (0.00–0.59)	0.21 (0.00–0.53)	0.52 (0.14–0.82)	0.00 (0.00–0.10)
AMR D	0.23 (0.00–0.56)	0.21 (0.00–0.52)	0.53 (0.18–0.81)	0.00 (0.00–0.09)
EMR B	0.24 (0.00–0.58)	0.21 (0.00–0.53)	0.52 (0.15–0.82)	0.00 (0.00–0.10)
EMR D	0.24 (0.00–0.58)	0.21 (0.00–0.53)	0.52 (0.15–0.83)	0.00 (0.00–0.10)
EUR A	0.10 (0.00–0.53)	0.23 (0.00–0.72)	0.41 (0.00–0.83)	0.01 (0.00–0.66)
EUR B	0.08 (0.00–0.43)	0.47 (0.16–0.78)	0.35 (0.04–0.62)	0.02 (0.00–0.21)
EUR C	0.08 (0.00–0.43)	0.47 (0.15–0.78)	0.35 (0.03–0.62)	0.02 (0.00–0.21)
SEAR B	0.43 (0.11–0.82)	0.12 (0.00–0.49)	0.40 (0.01–0.70)	0.00 (0.00–0.03)
SEAR D	0.40 (0.01–0.81)	0.13 (0.00–0.54)	0.42 (0.00–0.80)	0.00 (0.00–0.10)
WPR A	0.33 (0.00–0.84)	0.11 (0.00–0.55)	0.48 (0.00–0.86)	0.00 (0.00–0.36)
WPR B	0.49 (0.10–0.84)	0.13 (0.00–0.51)	0.33 (0.01–0.66)	0.00 (0.00–0.03)
		Vibrio cholerae		
AFR D	0.21 (0.01–0.57)	0.02 (0.00–0.31)	0.72 (0.29–0.94)	0.00 (0.00–0.03)
AFR E	0.21 (0.01–0.56)	0.02 (0.00–0.30)	0.72 (0.33–0.94)	0.00 (0.00–0.04)
AMR A	0.30 (0.01–0.95)	0.02 (0.00–0.43)	0.59 (0.00–0.93)	0.00 (0.00–0.37)
AMR B	0.25 (0.00–0.58)	0.02 (0.00–0.27)	0.70 (0.33–0.95)	0.00 (0.00–0.34)
AMR D	0.25 (0.00–0.57)	0.02 (0.00–0.29)	0.69 (0.34–0.94)	0.00 (0.00–0.29)
EMR B	0.23 (0.01–0.64)	0.02 (0.00–0.30)	0.69 (0.25–0.94)	0.00 (0.00–0.03)
EMR D	0.23 (0.01–0.65)	0.02 (0.00–0.31)	0.70 (0.23–0.94)	0.00 (0.00–0.03)
EUR A	0.31 (0.00–0.85)	0.03 (0.00–0.44)	0.44 (0.00–0.86)	0.01 (0.00–0.57)
EUR B	0.46 (0.01–0.86)	0.11 (0.00–0.47)	0.36 (0.00–0.77)	0.00 (0.00–0.36)
EUR C	0.46 (0.02–0.86)	0.11 (0.00–0.47)	0.36 (0.00–0.76)	0.00 (0.00–0.38)
SEAR B	0.36 (0.04–0.78)	0.14 (0.00–0.50)	0.45 (0.02–0.79)	0.00 (0.00–0.02)
SEAR D	0.25 (0.00–0.75)	0.08 (0.00–0.50)	0.58 (0.04–0.91)	0.00 (0.00–0.02)
WPR A	0.25 (0.01–0.92)	0.04 (0.00–0.64)	0.56 (0.00–0.93)	0.00 (0.00–0.05)
WPR B	0.29 (0.01–0.74)	0.13 (0.00–0.49)	0.51 (0.04–0.83)	0.00 (0.00–0.30)
		Norovirus		
AFR D	0.15 (0.01–0.40)	0.68 (0.37–0.89)	0.07 (0.00–0.38)	0.04 (0.00–0.23)
AFR E	0.15 (0.00–0.40)	0.68 (0.38–0.89)	0.07 (0.00–0.37)	0.04 (0.00–0.24)
AMR A	0.23 (0.04–0.50)	0.50 (0.18–0.79)	0.22 (0.00–0.49)	0.00 (0.00–0.22)
AMR B	0.14 (0.00–0.42)	0.72 (0.36–0.90)	0.06 (0.00–0.40)	0.04 (0.00–0.24)
AMR D	0.15 (0.00–0.46)	0.72 (0.36–0.89)	0.06 (0.00–0.41)	0.04 (0.00–0.23)
EMR B	0.15 (0.00–0.40)	0.72 (0.43–0.89)	0.07 (0.00–0.30)	0.04 (0.00–0.22)
EMR D	0.15 (0.00–0.40)	0.72 (0.42–0.89)	0.06 (0.00–0.32)	0.04 (0.00–0.23)
EUR A	0.26 (0.00–0.73)	0.43 (0.00–0.83)	0.17 (0.00–0.58)	0.00 (0.00–0.36)
EUR B	0.23 (0.01–0.57)	0.32 (0.02–0.67)	0.33 (0.00–0.65)	0.04 (0.00–0.34)

SUBREGION	FOOD	HUMAN-TO-HUMAN CONTACT	WATER	OTHER
EUR C	0.23 (0.01–0.57)	0.33 (0.02–0.67)	0.33 (0.01–0.63)	0.04 (0.00–0.33)
SEAR B	0.12 (0.00–0.48)	0.53 (0.13–0.83)	0.21 (0.00–0.53)	0.00 (0.00–0.42)
SEAR D	0.15 (0.00–0.55)	0.46 (0.00–0.79)	0.29 (0.00–0.72)	0.00 (0.00–0.35)
WPR A	0.22 (0.01–0.52)	0.48 (0.12–0.77)	0.22 (0.00–0.51)	0.00 (0.00–0.32)
WPR B	0.15 (0.00–0.55)	0.46 (0.00–0.79)	0.28 (0.01–0.68)	0.00 (0.00–0.34)
Hepatitis A				
AFR D	0.36 (0.07–0.63)	0.40 (0.10–0.68)	0.17 (0.00–0.49)	0.04 (0.00–0.10)
AFR E	0.29 (0.07–0.57)	0.36 (0.08–0.64)	0.30 (0.06–0.59)	0.02 (0.00–0.06)
AMR A	0.42 (0.06–0.77)	0.46 (0.04–0.78)	0.01 (0.00–0.19)	0.10 (0.00–0.32)
AMR B	0.31 (0.03–0.60)	0.46 (0.16–0.74)	0.11 (0.00–0.39)	0.09 (0.00–0.21)
AMR D	0.32 (0.03–0.61)	0.35 (0.11–0.65)	0.26 (0.04–0.57)	0.04 (0.00–0.09)
EMR B	0.35 (0.04–0.61)	0.42 (0.17–0.69)	0.15 (0.02–0.34)	0.09 (0.00–0.20)
EMR D	0.32 (0.02–0.59)	0.36 (0.11–0.66)	0.22 (0.00–0.49)	0.08 (0.00–0.23)
EUR A	0.42 (0.02–0.75)	0.46 (0.10–0.79)	0.01 (0.00–0.17)	0.10 (0.00–0.32)
EUR B	0.35 (0.12–0.59)	0.35 (0.18–0.61)	0.20 (0.01–0.36)	0.08 (0.00–0.19)
EUR C	0.34 (0.08–0.60)	0.42 (0.17–0.69)	0.14 (0.00–0.35)	0.09 (0.00–0.24)
SEAR B	0.34 (0.05–0.60)	0.35 (0.14–0.65)	0.23 (0.04–0.55)	0.04 (0.00–0.09)
SEAR D	0.29 (0.04–0.56)	0.37 (0.13–0.64)	0.29 (0.06–0.56)	0.02 (0.00–0.06)
WPR A	0.42 (0.03–0.76)	0.46 (0.10–0.79)	0.01 (0.00–0.16)	0.10 (0.00–0.29)
WPR B	0.34 (0.02–0.64)	0.36 (0.06–0.66)	0.21 (0.01–0.47)	0.08 (0.00–0.20)
Entamoeba histolytica				
AFR D	0.30 (0.00–0.68)	0.37 (0.00–0.73)	0.25 (0.00–0.63)	0.04 (0.00–0.21)
AFR E	0.30 (0.00–0.68)	0.37 (0.00–0.72)	0.24 (0.00–0.62)	0.04 (0.00–0.22)
AMR A	0.25 (0.00–0.70)	0.34 (0.00–0.76)	0.33 (0.00–0.74)	0.00 (0.00–0.19)
AMR B	0.21 (0.00–0.62)	0.38 (0.02–0.76)	0.32 (0.00–0.70)	0.00 (0.00–0.20)
AMR D	0.17 (0.00–0.58)	0.37 (0.04–0.76)	0.37 (0.01–0.73)	0.00 (0.00–0.20)
EMR B	0.24 (0.00–0.62)	0.42 (0.01–0.76)	0.24 (0.00–0.62)	0.04 (0.00–0.22)
EMR D	0.28 (0.00–0.66)	0.39 (0.00–0.75)	0.25 (0.00–0.65)	0.04 (0.00–0.22)
EUR A	0.33 (0.00–0.71)	0.49 (0.03–0.83)	0.15 (0.00–0.51)	0.01 (0.00–0.16)
EUR B	0.30 (0.00–0.66)	0.42 (0.02–0.76)	0.20 (0.00–0.59)	0.04 (0.00–0.20)
EUR C	0.26 (0.00–0.64)	0.42 (0.02–0.76)	0.23 (0.00–0.61)	0.04 (0.00–0.19)
SEAR B	0.26 (0.00–0.65)	0.38 (0.00–0.75)	0.28 (0.00–0.68)	0.04 (0.00–0.18)
SEAR D	0.25 (0.00–0.63)	0.37 (0.00–0.72)	0.29 (0.01–0.69)	0.04 (0.00–0.19)
WPR A	0.25 (0.00–0.62)	0.41 (0.00–0.74)	0.26 (0.01–0.62)	0.04 (0.00–0.25)
WPR B	0.27 (0.00–0.63)	0.41 (0.00–0.73)	0.24 (0.01–0.62)	0.05 (0.00–0.23)

Table A7.4 Subregional estimates (median and 95% uncertainty interval) of the proportion of illnesses caused by *Toxoplasma gondii*, *Echinococcus multilocularis*, *Echinococcus granulosus* and *Ascaris* spp. through each exposure pathway.

SUBREGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN-TO-HUMAN CONTACT	WATER	SOIL	AIR	OTHER
PARASITIC DISEASE							
Toxoplasma gondii							
AFR D	0.48 (0.24–0.76)	0.01 (0.00–0.20)	na	0.11 (0.00–0.37)	0.36 (0.07–0.57)	na	na
AFR E	0.42 (0.20–0.70)	0.01 (0.00–0.19)	na	0.16 (0.02–0.41)	0.38 (0.05–0.58)	na	na
AMR A	0.60 (0.30–0.81)	0.01 (0.00–0.28)	na	0.19 (0.01–0.42)	0.19 (0.00–0.46)	na	na
AMR B	0.52 (0.27–0.77)	0.01 (0.00–0.20)	na	0.23 (0.01–0.45)	0.22 (0.00–0.46)	na	na
AMR D	0.53 (0.27–0.77)	0.01 (0.00–0.21)	na	0.23 (0.02–0.44)	0.22 (0.00–0.45)	na	na
EMR B	0.52 (0.27–0.80)	0.01 (0.00–0.20)	na	0.11 (0.01–0.29)	0.34 (0.02–0.56)	na	na
EMR D	0.53 (0.29–0.77)	0.01 (0.00–0.20)	na	0.23 (0.02–0.43)	0.22 (0.00–0.42)	na	na
EUR A	0.61 (0.35–0.82)	0.01 (0.00–0.21)	na	0.19 (0.02–0.36)	0.18 (0.00–0.40)	na	na
EUR B	0.45 (0.23–0.76)	0.01 (0.00–0.20)	na	0.15 (0.02–0.35)	0.37 (0.01–0.58)	na	na
EUR C	0.53 (0.31–0.78)	0.01 (0.00–0.20)	na	0.23 (0.03–0.41)	0.22 (0.01–0.41)	na	na
SEAR B	0.52 (0.26–0.77)	0.01 (0.00–0.19)	na	0.23 (0.03–0.45)	0.22 (0.00–0.43)	na	na
SEAR D	0.43 (0.09–0.73)	0.01 (0.00–0.22)	na	0.27 (0.03–0.58)	0.26 (0.00–0.56)	na	na
WPR A	0.60 (0.33–0.81)	0.01 (0.00–0.21)	na	0.19 (0.02–0.37)	0.18 (0.00–0.43)	na	na
WPR B	0.53 (0.29–0.77)	0.01 (0.00–0.20)	na	0.23 (0.04–0.43)	0.22 (0.00–0.43)	na	na
Echinococcus granulosus							
AFR D	0.21 (0.07–0.42)	0.51 (0.25–0.72)	na	0.18 (0.01–0.34)	0.09 (0.00–0.20)	0.00 (0.00–0.06)	0.00 (0.00–0.01)
AFR E	0.20 (0.05–0.40)	0.52 (0.27–0.73)	na	0.18 (0.00–0.35)	0.09 (0.00–0.19)	0.00 (0.00–0.06)	0.00 (0.00–0.06)
AMR A	0.20 (0.03–0.40)	0.52 (0.30–0.75)	na	0.17 (0.00–0.31)	0.09 (0.00–0.20)	0.00 (0.00–0.14)	0.00 (0.00–0.01)
AMR B	0.20 (0.02–0.43)	0.52 (0.28–0.73)	na	0.18 (0.00–0.34)	0.09 (0.00–0.22)	0.00 (0.00–0.14)	0.00 (0.00–0.01)
AMR D	0.21 (0.05–0.41)	0.51 (0.29–0.72)	na	0.18 (0.01–0.35)	0.09 (0.00–0.23)	0.00 (0.00–0.13)	0.00 (0.00–0.01)
EMR B	0.21 (0.05–0.43)	0.51 (0.28–0.73)	na	0.17 (0.00–0.32)	0.09 (0.00–0.19)	0.00 (0.00–0.14)	0.00 (0.00–0.06)
EMR D	0.21 (0.06–0.41)	0.52 (0.28–0.72)	na	0.18 (0.00–0.32)	0.09 (0.00–0.18)	0.00 (0.00–0.14)	0.00 (0.00–0.01)
EUR A	0.21 (0.04–0.40)	0.51 (0.29–0.72)	na	0.18 (0.00–0.33)	0.09 (0.00–0.20)	0.00 (0.00–0.14)	0.00 (0.00–0.01)

SUBREGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN-TO-HUMAN CONTACT	WATER	SOIL	AIR	OTHER
EUR B	0.21 (0.06–0.40)	0.52 (0.27–0.73)	na	0.18 (0.00–0.33)	0.09 (0.00–0.19)	0.00 (0.00–0.15)	0.00 (0.00–0.01)
EUR C	0.21 (0.04–0.40)	0.51 (0.26–0.73)	na	0.18 (0.00–0.35)	0.09 (0.00–0.21)	0.00 (0.00–0.15)	0.00 (0.00–0.01)
SEAR B	0.21 (0.03–0.44)	0.51 (0.22–0.73)	na	0.18 (0.00–0.35)	0.09 (0.00–0.19)	0.00 (0.00–0.13)	0.00 (0.00–0.01)
SEAR D	0.20 (0.06–0.40)	0.52 (0.29–0.73)	na	0.18 (0.00–0.34)	0.09 (0.00–0.19)	0.00 (0.00–0.14)	0.00 (0.00–0.01)
WPR A	0.20 (0.01–0.39)	0.53 (0.30–0.75)	na	0.18 (0.00–0.33)	0.09 (0.00–0.20)	0.00 (0.00–0.13)	0.00 (0.00–0.01)
WPR B	0.21 (0.05–0.43)	0.51 (0.29–0.73)	na	0.17 (0.00–0.32)	0.09 (0.00–0.21)	0.00 (0.00–0.14)	0.00 (0.00–0.01)
Echinococcus multilocularis							
AFR D	0.58 (0.00–0.87)	0.02 (0.00–0.42)	na	0.20 (0.00–0.61)	0.20 (0.00–0.63)	0.00 (0.00–0.03)	0.00 (0.00–0.00)
AFR E	0.58 (0.00–0.87)	0.02 (0.00–0.41)	na	0.20 (0.00–0.62)	0.20 (0.00–0.61)	0.00 (0.00–0.03)	0.00 (0.00–0.00)
AMR A	0.51 (0.13–0.79)	0.03 (0.00–0.50)	na	0.17 (0.01–0.40)	0.16 (0.01–0.38)	0.00 (0.00–0.11)	0.00 (0.00–0.03)
AMR B	0.58 (0.00–0.87)	0.02 (0.00–0.38)	na	0.20 (0.00–0.62)	0.20 (0.00–0.61)	0.00 (0.00–0.03)	0.00 (0.00–0.00)
AMR D	0.58 (0.00–0.88)	0.02 (0.00–0.41)	na	0.19 (0.00–0.61)	0.20 (0.00–0.60)	0.00 (0.00–0.03)	0.00 (0.00–0.00)
EMR B	0.43 (0.09–0.73)	0.14 (0.00–0.55)	na	0.17 (0.00–0.42)	0.17 (0.00–0.42)	0.00 (0.00–0.06)	0.00 (0.00–0.01)
EMR D	0.48 (0.00–0.77)	0.12 (0.00–0.49)	na	0.20 (0.00–0.54)	0.20 (0.00–0.53)	0.00 (0.00–0.04)	0.00 (0.00–0.00)
EUR A	0.52 (0.15–0.79)	0.03 (0.00–0.48)	na	0.17 (0.01–0.40)	0.16 (0.00–0.39)	0.00 (0.00–0.11)	0.00 (0.00–0.03)
EUR B	0.45 (0.12–0.72)	0.13 (0.00–0.52)	na	0.18 (0.02–0.38)	0.17 (0.00–0.37)	0.00 (0.00–0.13)	0.00 (0.00–0.03)
EUR C	0.44 (0.12–0.72)	0.14 (0.00–0.53)	na	0.17 (0.01–0.38)	0.17 (0.00–0.37)	0.00 (0.00–0.12)	0.00 (0.00–0.03)
SEAR B	0.58 (0.00–0.88)	0.02 (0.00–0.41)	na	0.20 (0.00–0.61)	0.20 (0.00–0.61)	0.00 (0.00–0.03)	0.00 (0.00–0.00)
SEAR D	0.58 (0.00–0.88)	0.02 (0.00–0.37)	na	0.20 (0.00–0.62)	0.20 (0.00–0.60)	0.00 (0.00–0.05)	0.00 (0.00–0.00)
WPR A	0.51 (0.09–0.81)	0.04 (0.00–0.52)	na	0.16 (0.00–0.41)	0.16 (0.00–0.40)	0.00 (0.00–0.03)	0.00 (0.00–0.01)
WPR B	0.48 (0.00–0.78)	0.12 (0.00–0.49)	na	0.20 (0.00–0.54)	0.20 (0.00–0.54)	0.00 (0.00–0.12)	0.00 (0.00–0.03)
Ascaris spp.							
AFR D	0.38 (0.10–0.66)	0.00 (0.00–0.09)	0.00 (0.00–0.08)	0.19 (0.07–0.40)	0.39 (0.07–0.65)	na	0.00 (0.00–0.06)
AFR E	0.38 (0.07–0.67)	0.00 (0.00–0.09)	0.00 (0.00–0.09)	0.19 (0.07–0.41)	0.39 (0.05–0.65)	na	0.00 (0.00–0.06)
AMR A	0.83 (0.43–0.97)	0.00 (0.00–0.29)	0.00 (0.00–0.08)	0.05 (0.00–0.18)	0.06 (0.00–0.42)	na	0.00 (0.00–0.06)
AMR B	0.55 (0.17–0.75)	0.00 (0.00–0.13)	0.00 (0.00–0.09)	0.19 (0.06–0.40)	0.22 (0.05–0.50)	na	0.00 (0.00–0.04)

SUBREGION	FOOD	ANIMAL CONTACT (DOMESTIC AND WILD)	HUMAN-TO-HUMAN CONTACT	WATER	SOIL	AIR	OTHER
AMR D	0.37 (0.07–0.68)	0.00 (0.00–0.15)	0.00 (0.00–0.08)	0.18 (0.05–0.41)	0.41 (0.04–0.69)	na	0.00 (0.00–0.04)
EMR B	0.55 (0.15–0.77)	0.00 (0.00–0.10)	0.00 (0.00–0.07)	0.20 (0.02–0.44)	0.22 (0.02–0.51)	na	0.00 (0.00–0.06)
EMR D	0.55 (0.18–0.75)	0.00 (0.00–0.10)	0.00 (0.00–0.09)	0.20 (0.04–0.43)	0.21 (0.04–0.51)	na	0.00 (0.00–0.05)
EUR A	0.85 (0.47–0.97)	0.00 (0.00–0.25)	0.00 (0.00–0.09)	0.05 (0.00–0.18)	0.06 (0.00–0.38)	na	0.00 (0.00–0.06)
EUR B	0.55 (0.13–0.76)	0.00 (0.00–0.27)	0.00 (0.00–0.10)	0.19 (0.03–0.40)	0.22 (0.02–0.50)	na	0.00 (0.00–0.06)
EUR C	0.55 (0.14–0.76)	0.00 (0.00–0.25)	0.00 (0.00–0.12)	0.19 (0.03–0.40)	0.22 (0.04–0.50)	na	0.00 (0.00–0.05)
SEAR B	0.54 (0.18–0.75)	0.00 (0.00–0.14)	0.00 (0.00–0.08)	0.20 (0.03–0.44)	0.22 (0.01–0.52)	na	0.00 (0.00–0.05)
SEAR D	0.39 (0.11–0.68)	0.00 (0.00–0.12)	0.00 (0.00–0.07)	0.20 (0.04–0.44)	0.38 (0.04–0.65)	na	0.00 (0.00–0.06)
WPR A	0.85 (0.47–0.97)	0.00 (0.00–0.23)	0.00 (0.00–0.09)	0.05 (0.00–0.19)	0.06 (0.00–0.37)	na	0.00 (0.00–0.06)
WPR B	0.54 (0.16–0.77)	0.00 (0.00–0.24)	0.00 (0.00–0.11)	0.20 (0.02–0.43)	0.21 (0.02–0.49)	na	0.00 (0.00–0.06)

Table A7.5 Subregional estimates (median and 95% uncertainty interval) of the proportion of illnesses caused by exposure to lead through each pathway.

SUBREGION	FOOD	WATER	SOIL	AIR	PAINT	COOKWARE, POTTERY OR GLASSWARE	TOYS	OTHER
LEAD								
AFR D	0.17 (0.00–0.37)	0.22 (0.06–0.48)	0.12 (0.00–0.27)	0.20 (0.03–0.39)	0.08 (0.00–0.32)	0.09 (0.01–0.24)	0.04 (0.00–0.16)	0.00 (0.00–0.04)
AFR E	0.17 (0.00–0.37)	0.28 (0.06–0.54)	0.10 (0.00–0.28)	0.18 (0.00–0.38)	0.08 (0.00–0.33)	0.07 (0.00–0.27)	0.02 (0.00–0.17)	0.00 (0.00–0.04)
AMR A	0.24 (0.01–0.49)	0.30 (0.05–0.61)	0.09 (0.00–0.27)	0.12 (0.00–0.50)	0.04 (0.00–0.35)	0.05 (0.00–0.22)	0.05 (0.00–0.19)	0.00 (0.00–0.02)
AMR B	0.19 (0.00–0.41)	0.22 (0.04–0.46)	0.04 (0.00–0.16)	0.26 (0.00–0.51)	0.06 (0.00–0.35)	0.09 (0.01–0.38)	0.02 (0.00–0.20)	0.00 (0.00–0.02)
AMR D	0.17 (0.00–0.40)	0.14 (0.03–0.42)	0.13 (0.00–0.35)	0.29 (0.00–0.57)	0.05 (0.00–0.36)	0.04 (0.00–0.35)	0.02 (0.00–0.19)	0.00 (0.00–0.02)
EMR B	0.19 (0.01–0.37)	0.21 (0.06–0.42)	0.10 (0.00–0.22)	0.21 (0.00–0.41)	0.09 (0.00–0.36)	0.07 (0.00–0.32)	0.02 (0.00–0.23)	0.00 (0.00–0.02)
EMR D	0.11 (0.00–0.31)	0.09 (0.03–0.23)	0.07 (0.00–0.55)	0.38 (0.10–0.66)	0.04 (0.00–0.24)	0.06 (0.00–0.23)	0.02 (0.00–0.18)	0.00 (0.00–0.01)
EUR A	0.23 (0.00–0.46)	0.19 (0.05–0.47)	0.10 (0.00–0.24)	0.16 (0.00–0.37)	0.14 (0.04–0.48)	0.05 (0.00–0.20)	0.02 (0.00–0.18)	0.00 (0.00–0.02)
EUR B	0.23 (0.00–0.47)	0.16 (0.02–0.40)	0.12 (0.00–0.30)	0.18 (0.00–0.40)	0.05 (0.00–0.38)	0.09 (0.01–0.28)	0.06 (0.00–0.23)	0.00 (0.00–0.02)
EUR C	0.19 (0.00–0.37)	0.29 (0.11–0.54)	0.11 (0.00–0.30)	0.12 (0.00–0.35)	0.03 (0.00–0.39)	0.06 (0.00–0.25)	0.04 (0.00–0.22)	0.00 (0.00–0.03)
SEAR B	0.17 (0.00–0.40)	0.17 (0.02–0.38)	0.07 (0.00–0.23)	0.28 (0.00–0.54)	0.05 (0.00–0.36)	0.08 (0.00–0.33)	0.05 (0.00–0.24)	0.00 (0.00–0.01)
SEAR D	0.21 (0.00–0.46)	0.15 (0.05–0.31)	0.11 (0.00–0.27)	0.24 (0.05–0.46)	0.06 (0.00–0.30)	0.11 (0.03–0.27)	0.03 (0.00–0.23)	0.00 (0.00–0.01)
WPR A	0.12 (0.00–0.30)	0.14 (0.03–0.36)	0.14 (0.00–0.32)	0.27 (0.00–0.51)	0.09 (0.00–0.38)	0.11 (0.03–0.37)	0.03 (0.00–0.19)	0.00 (0.00–0.01)
WPR B	0.12 (0.00–0.30)	0.22 (0.06–0.45)	0.06 (0.00–0.19)	0.30 (0.00–0.53)	0.08 (0.00–0.38)	0.09 (0.00–0.36)	0.03 (0.00–0.24)	0.00 (0.00–0.01)

Table A7.6 Percent of illness acquired through the foodborne transmission route for six national studies and this study[a].

	HAVELAAR ET AL., 2008	GKOGKA ET AL., 2011	THIS STUDY	RAVEL ET AL., 2010	SCALLAN ET AL., 2011	THIS STUDY	LAKE ET AL., 2010	VALLY ET AL., 2014	THIS STUDY
Country/sub region	NL	GR	EUR A	CA	USA	AMR A	NZ	AU	WPR A
Period	2006	1996-2006	2010	2008	2010	2010	2005	2010	2010
Method	Formal expert elicitation	Derived by the authors b)	Formal expert elicitation	Formal expert elicitation	Derived by the authors b)	Formal expert elicitation	Formal expert elicitation	Formal expert elicitation	Formal expert elicitation
Only domestically acquired cases	yes	depended on the data used	no	yes	yes	no	no	yes	no
HAZARDS									
Brucella spp.	-	84 (50-100)	66 (23-90)	-	50 (40-60)	75 (28-93)	-	-	-
Campylobacter spp.	42 (16-84)	55 (30-80)	76 (44-93)	68 (54-82)	80 (73-86)	73 (38-91)	56 (26-82)	76 (70-80)	68 (40-89)
Cryptosporidium spp.	12 (0-20)	5.6 (5.6-8)	10 (0-39)	9 (3-16)	8 (6-12)	16 (1-44)	-	-	-
Entamoeba histolytica	-	50 (10-100)	33 (0-71)	-	-	-	-	-	-
Enteropathogenic *E. coli*	-	-	-	-	-	-	-	24 (10-49)	69 (16-94)
Enterotoxigenic *E. coli*	-	-	-	-	100 (99-100)c)	36 (12-63)	-	24 (10-49)	38 (10-72)
Giardia spp.	13 (0-24)	10 (5-30)	11 (0-44)	-	7 (5-10)	11 (0-39)	-	-	-
Hepatitis A	11 (0-20)	8 (5-11)	42 (2-75)	-	6 (4-16)	42 (6-77)	-	12 (7-20)	42 (3-76)
Non-typhoidal *Salmonella* spp.	55 (32-88)	95 (55-95)	76 (47-94)	80 (68-92)	94 (91-96)	73 (38-91)	60 (18-83)	71 (65-75)	74 (45-93)
Norovirus	17 (16-47)	-	26 (0-73)	31 (14-48)	26 (19-35)	23 (4-50)	39 (8-64)	17 (5-30)	22 (1-52)
Salmonella Typhi	-	80 (55-95)	10 (0-53)	-	100 (76-100)	26 (0-64)	-	-	-
Shiga toxin-producing *E. coli*	42 (21-78)	51 (40-90)	60 (26-83)	76 (60-91)	82 (75-87)	59 (19-84)	40 (6-95)	55 (30-75)	57 (25-82)
Shigella spp.	-	10 (8.2-31)	7 (0-46)	18 (7-29)	31 (23-40)	12 (0-46)	-	11 (5-20)	13 (0-50)
Toxoplasma gondii	56 (26-88)	50 (30-63)	61 (35-82)	-	50 (40-60)	60 (30-81)	-	-	-
Vibrio cholerae	-	-	-	82 (66-98)	100 (99-100)	30 (1-95)	-	-	-

[a] This table presents a measure of central tendency with its associated uncertainty bound from each study. Because studies differ in how they measure central tendency and uncertainty, we cannot label the columns with a single heading. Measures include: this study (median, 90% credibility interval (CI)); Havelaar et al., 2008 (mean, 90% CI); Gkogka et al., 2011(median, min-max); Ravel et al., 2010 (mean, 95% CI); Scallan et al., 2011 (mean, 90% CI); Lake et al., 2010 (mean, 95% CI); Valley et al., 2014 (median, 95% CI).

[b] These estimates were derived by a synthesis of data from different public health surveillance systems and the literature.

[c] Only ETEC cases reported as part of foodborne outbreaks were included in the study by Scallan et al. (2011). Consequently the proportion foodborne was per definition 100% and cannot be readily compared with the estimate in this study, which considers infections acquired from all transmission routes.

APPENDIX 8.
DATA TABLES FOR INDIVIDUAL HAZARD CLASSES: ENTERIC, PARASITIC, CHEMICAL[1]

Table A8.1 Median number of foodborne Illnesses, Deaths, and Disability Adjusted Life Years (DALYs), with 95% uncertainty intervals, 2010.

PATHOGEN	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	PROPORTION FOODBORNE (95% UI)	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYs (95% UI)
Diarrhoeal Disease	1 912 159 038 (1 413 002 730–2 849 323 016)	715 196 (603 325–846 397)	55 139 959 (46 746 114–65 120 623)	0.29 (0.22–0.36)	548 285 159 (369 733 377–888 360 956)	199 892 (136 903–286 616)	15 780 400 (11 043 288–22 251 264)
Campylobacter spp.*	166 175 078 (92 227 873–300 877 905)	37 604 (27 738–55 101)	3 733 822 (2 857 037–5 273 652)	0.58 (0.44–0.69)	95 613 970 (51 731 379–177 239 714)	21 374 (14 604–32 584)	2 141 926 (1 535 985–3 137 980)
Cryptosporidium spp.	64 003 709 (43 049 455–104 679 951)	27 553 (18 532–44 654)	2 159 331 (1 392 438–3 686 925)	0.13 (0.07–0.24)	8 584 805 (3 897 252–18 531 196)	3 759 (1 520–9 115)	296 156 (119 456–724 660)
Entamoeba histolytica	103 943 952 (47 018 659–210 632 459)	5 450 (2 194–17 127)	515 904 (222 446–1 552 466)	0.28 (0.14–0.44)	28 023 571 (10 261 254–68 567 590)	1 470 (453–5 554)	138 863 (47 339–503 775)
Enteropathogenic *E. coli*	81 082 327 (40 716 656–171 419 480)	122 760 (97 115–154 869)	9 717 390 (7 602 047–12 387 029)	0.30 (0.17–0.48)	23 797 284 (10 750 919–62 931 604)	37 077 (19 957–61 262)	2 938 407 (1 587 757–4 865 590)
Enterotoxigenic *E. coli*	240 886 759 (160 890 532–377 471 599)	73 857 (53 851–103 026)	5 887 541 (4 190 610–8 407 186)	0.36 (0.24–0.50)	86 502 735 (49 136 952–151 776 173)	26 170 (14 887–43 523)	2 084 229 (1 190 704–3 494 201)
Giardia spp.	183 842 615 (130 018 020–262 838 002)	0 (0–0)	171 100 (115 777–257 315)	0.15 (0.08–0.27)	28 236 123 (12 945 655–56 996 454)	0 (0–0)	26 270 (11 462–53 577)
Norovirus	684 850 131 (490 930 402–1 122 947 359)	212 489 (160 595–278 420)	15 105 714 (11 649 794–19 460 578)	0.18 (0.11–0.30)	124 803 946 (70 311 254–251 352 877)	34 929 (15 916–79 620)	2 496 078 (1 175 658–5 511 092)
Non-typhoidal *Salmonella enterica*,	153 097 991 (64 733 607–382 208 079)	56 969 (43 272–88 129)	4 377 930 (3 242 020–7 175 522)	0.52 (0.35–0.67)	78 439 785 (31 579 011–210 875 866)	28 693 (17 070–49 768)	2 183 146 (1 314 295–3 981 424)
Shigella spp.	190 849 501 (97 832 995–363 915 689)	65 796 (46 317–97 036)	5 407 736 (3 771 300–8 107 456)	0.27 (0.13–0.44)	51 014 050 (20 405 214–118 927 631)	15 156 (6 839–30 072)	1 237 103 (554 204–2 520 126)
Shiga toxin-producing *E. coli*	2 481 511 (1 594 572–5 376 503)	269 (111–814)	26 827 (12 089–72 204)	0.48 (0.33–0.60)	1 176 854 (754 108–2 523 007)	128 (55–374)	12 953 (5 951–33 664)
Vibrio cholerae	3 183 394 (2 211 329–4 146 250)	105 170 (78 671–126 058)	7 347 635 (5 496 431–8 804 408)	0.24 (0.10–0.46)	763 451 (310 910–1 567 682)	24 649 (10 304–50 042)	1 722 312 (720 029–3 491 997)
Intoxications	5 409 083 (2 187 762–12 929 293)	175 (70–407)	9 905 (3 993–23 527)	1.00	5 409 083 (2 187 762–12 929 293)	175 (70–407)	9 905 (3 993–23 527)
*Bacillus cereus***	256 775 (43 875–807 547)	0 (0–0)	45 (7–171)	1.00	256 775 (43 875–807 547)	0 (0–0)	45 (7–171)
*Clostridium botulinum****	475 (183–990)	24 (7–65)	1 036 (299–2 805)	1.00	475 (183–990)	24 (7–65)	1 036 (299–2 805)
*Clostridium perfringens***	3 998 164 (837 262–11 529 642)	120 (25–351)	6 963 (1 423–20 493)	1.00	3 998 164 (837 262–11 529 642)	120 (25–351)	6 963 (1 423–20 493)

PATHOGEN	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYs (95% UI)	PROPORTION FOODBORNE (95% UI)	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYs (95% UI)
*Staphylococcus aureus***	1 073 339 (658 463–1 639 524)	25 (10–55)	1 575 (702–3 244)	1.00	1 073 339 (658 463–1 639 524)	25 (10–55)	1 575 (702–3 244)
Invasive enteric diseases	77 929 723 (36 606 712–149 676 316)	371 002 (218 593–631 271)	23 070 841 (13 388 154–39 912 033)	0.34 (0.17–0.52)	25 569 838 (10 019 370–58 282 758)	146 981 (81 052–274 835)	9 107 557 (4 891 985–17 483 327)
Brucella spp.	832 633 (337 929–19 560 440)	4 145 (1 557–95 894)	264 073 (100 540–6 187 148)	0.47 (0.30–0.61)	393 239 (143 815–9 099 394)	1 957 (661–45 545)	124 884 (43 153–2 910 416)
Hepatitis A	46 864 406 (14 417 704–111 771 902)	93 961 (29 602–221 677)	4 580 758 (1 599 296–10 408 164)	0.30 (0.14–0.49)	13 709 836 (3 630 847–38 524 946)	27 731 (7 169–77 320)	1 353 767 (383 684–3 672 726)
Listeria monocytogenes	14 169 (6 112–91 175)	3 175 (1 339–20 428)	118 340 (49 634–754 680)	1.00	14 169 (6 112–91 175)	3 175 (1 339–20 428)	118 340 (49 634–754 680)
Mycobacterium bovis	121 268 (99 852–150 239)	10 545 (7 894–14 472)	607 775 (458 364–826 115)	1.00	121 268 (99 852–150 239)	10 545 (7 894–14 472)	607 775 (458 364–826 115)
invasive non-typhoidal *Salmonella enterica*	596 824 (596 824–596 824)	63 312 (38 986–94 193)	3 895 547 (2 401 034–5 790 874)	0.48 (0.28–0.64)	284 972 (167 455–384 321)	29 391 (14 948–50 463)	1 794 575 (886 443–3 107 172)
Salmonella enterica Paratyphi A	4 826 477 (1 782 796–10 323 273)	33 325 (12 309–71 278)	2 367 164 (875 236–5 066 375)	0.37 (0.19–0.58)	1 741 120 (536 650–4 310 983)	12 069 (3 784–29 521)	855 730 (268 879–2 100 120)
Salmonella enterica Typhi	20 984 683 (7 751 285–44 883 794)	144 890 (53 519–309 903)	10 292 017 (3 805 373–22 027 716)	0.37 (0.19–0.58)	7 570 087 (2 333 263–18 743 406)	52 472 (16 454–128 350)	3 720 565 (1 169 040–9 130 956)
TOTAL	2 000 626 631 (1 494 986 030–2 942 534 533)	1 092 584 (892 999–1 374 238)	78 730 084 (64 963 913–97 740 062)	0.29 (0.23–0.36)	581 902 722 (400 741 151–922 031 380)	350 686 (240 030–524 042)	25 175 035 (17 547 264–37 021 003)

Notes: * = Includes Guillain-Barré Syndrome cases and deaths; ** = 61 EUR and other subregion A (low mortality) countries only; *** 61 EUR and subregion A (low mortality) countries only, and excluding WPR A countries

[1] Note that non-typhoidal Salmonella enterica was split over diarrhoeal and invasive disease, whereas in Table 7 it was exclusively listed under diarrhoeal disease agents.

Table A8.2 Median rates of foodborne illnesses, deaths and Disability Adjusted Life Years (DALYs) per 100 000 persons, by region, with 95% uncertainty intervals, 2010.

PATHOGEN*	AFR			AMR			EMR			EUR			SEAR			WPR			GLOBAL		
	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)
Diarrhoeal Disease	9 830 (3 969–21 567)	9 (5–14)	687 (369–1 106)	7 900 (4 497–13 850)	0.5 (0.3–0.7)	44 (30–63)	16 387 (7 729–34 176)	4 (2–6)	354 (218–544)	2 483 (1 439–4 136)	0.3 (0.2–0.4)	23 (16–30)	7 074 (2 570–19 537)	5 (2–9)	363 (177–649)	6 302 (2 501–17 289)	0.3 (0.1–0.5)	33 (17–54)	7 968 (5 373–12 911)	3 (2–4)	229 (160–323)
Campylobacter spp.**	2 221 (335–8 482)	0.8 (0.4–1)	70 (41–112)	1 389 (490–3 207)	0.07 (0.04–0.1)	13 (8–18)	1 873 (488–5 608)	1 (0.6–1)	90 (56–130)	522 (363–687)	0.05 (0.03–0.09)	9 (6–13)	1 152 (200–3 372)	0.4 (0.1–0.9)	33 (9–83)	876 (359–3 855)	0.04 (0.02–0.1)	10 (4–17)	1 390 (752–2 576)	0.3 (0.2–0.5)	31 (22–46)
Cryptosporidium spp.	205 (35–813)	0.2 (0.04–0.4)	13 (3–37)	114 (32–355)	0.007 (0.002–0.02)	0.6 (0.2–2)	346 (52–1 287)	0.04 (0.004–0.2)	4 (0.4–20)	21 (4–70)	0.003 (0–0.009)	0.2 (0.03–0.6)	78 (10–474)	0.09 (0.01–0.4)	6 (0.9–29)	32 (2–170)	0.003 (0–0.03)	0.3 (0.02–3)	125 (57–269)	0.05 (0.02–0.1)	4 (2–11)
Entamoeba histolytica	796 (98–3 868)	0.05 (0.009–0.4)	5 (0.9–39)	212 (16–1 209)	0.001 (0–0.009)	0.3 (0.03–1)	737 (79–3 110)	0.02 (0.002–0.2)	2 (0.3–14)	0 (0–0)	0 (0–0)	0 (0–0)	256 (27–1 188)	0.03 (0.004–0.2)	3 (0.3–17)	229 (0–1 598)	0.001 (0–0.003)	0.3 (0–1)	407 (149–997)	0.02 (0.007–0.08)	2 (0.7–7)
Enteropathogenic *E. coli*	454 (125–1 215)	2 (0.6–3)	140 (50–282)	189 (35–730)	0.06 (0.01–0.1)	5 (1–12)	430 (116–1 222)	0.7 (0.2–2)	57 (18–131)	8 (3–16)	0 (0–0)	0.005 (0.002–0.01)	594 (62–2 775)	0.9 (0.2–2)	66 (15–146)	166 (8–395)	0.06 (0.003–0.1)	5 (0.2–12)	346 (156–915)	0.5 (0.3–0.9)	43 (23–71)
Enterotoxigenic *E. coli*	982 (312–2 480)	1 (0.6–3)	109 (46–216)	1 281 (299–3 295)	0.05 (0.01–0.1)	5 (1–12)	4 971 (1 685–10 849)	0.4 (0.1–1)	35 (11–89)	6 (2–13)	0 (0–0)	0.004 (0.001–0.01)	1 075 (229–3 521)	0.6 (0.1–1)	42 (10–104)	555 (43–2 430)	0.04 (0.003–0.1)	4 (0.3–10)	1 257 (714–2 206)	0.4 (0.2–0.6)	30 (17–51)
Giardia spp.	809 (172–2 574)	0 (0–0)	0.8 (0.2–3)	309 (62–1 249)	0 (0–0)	0.3 (0.05–1)	670 (133–2 193)	0 (0–0)	0.6 (0.1–2)	54 (16–123)	0 (0–0)	0.03 (0.009–0.1)	159 (16–903)	0 (0–0)	0.1 (0.01–0.9)	354 (8–1 519)	0 (0–0)	0.3 (0.005–1)	410 (188–828)	0 (0–0)	0.4 (0.2–0.8)
Norovirus	1 749 (491–5 060)	1 (0.3–3)	81 (24–185)	2 491 (898–6 186)	0.1 (0.04–0.3)	9 (3–23)	2 796 (744–7 376)	0.4 (0.1–1)	33 (9–76)	1 652 (630–3 294)	0.05 (0.02–0.1)	4 (1–8)	841 (113–5 631)	1 (0.2–3)	71 (15–230)	1 305 (189–6 441)	0.05 (0.004–0.2)	4 (0.4–17)	1 814 (1 022–3 653)	0.5 (0.2–1)	36 (17–80)
Non-typhoidal *Salmonella enterica*	896 (175–2 994)	1 (0.5–2)	89 (42–147)	1 002 (378–1 990)	0.1 (0.06–0.2)	7 (4–12)	1 610 (147–14 052)	0.6 (0.3–1)	54 (26–87)	186 (118–275)	0.1 (0.08–0.2)	8 (5–14)	908 (88–4 758)	0.7 (0.2–2)	49 (11–147)	898 (170–6 428)	0.02 (0.01–0.03)	2 (1–7)	1 140 (459–3 065)	0.4 (0.2–0.7)	32 (19–58)
Shigella spp.	523 (45–2 865)	0.5 (0.1–2)	43 (8–124)	278 (35–1 443)	0.02 (0.003–0.05)	1 (0.3–5)	627 (55–4 648)	0.4 (0.07–1)	38 (6–117)	3 (0.9–8)	0.003 (0–0.01)	0.2 (0.03–0.8)	1 084 (177–3 927)	0.3 (0.07–1)	25 (5–83)	689 (19–2 549)	0.04 (0.002–0.1)	4 (0.1–10)	741 (297–1 728)	0.2 (0.1–0.4)	18 (8–37)
Shiga toxin-producing *E. coli*	5 (2–9)	0 (0–0.002)	0.05 (0.02–0.1)	16 (9–30)	0.004 (0.001–0.01)	0.3 (0.1–0.9)	65 (37–97)	0.002 (0–0.004)	0.2 (0.1–0.5)	18 (9–28)	0.003 (0.001–0.006)	0.3 (0.1–0.8)	19 (2–95)	0.002 (0–0.01)	0.2 (0.02–1)	3 (2–6)	0 (0–0.001)	0.05 (0.02–0.1)	17 (11–37)	0.002 (0–0.005)	0.2 (0.09–0.5)
Vibrio cholerae	43 (13–101)	2 (0.5–4)	112 (35–252)	0.02 (0.008–0.05)	0 (0–0)	0 (0–0)	9 (0.4–28)	0.3 (0.01–1)	20 (0.7–69)	0.03 (0.01–0.06)	0 (0–0)	0 (0–0)	17 (0.7–52)	0.4 (0.007–2)	30 (0.5–109)	0.2 (0.01–0.5)	0.002 (0–0.005)	0.1 (0.005–0.3)	11 (5–23)	0.4 (0.1–0.7)	25 (10–51)
Invasive enteric diseases	425 (156–976)	5 (3–8)	307 (160–508)	31 (11–81)	0.3 (0.2–0.6)	16 (8–35)	394 (80–1 056)	2 (0.7–4)	108 (41–250)	19 (9–51)	0.2 (0.1–0.3)	10 (7–19)	872 (169–2 288)	4 (1–9)	250 (81–598)	163 (30–391)	0.9 (0.3–2)	58 (19–134)	372 (146–847)	2 (1–4)	132 (71–254)

PATHOGEN*	AFR			AMR			EMR			EUR			SEAR			WPR			GLOBAL		
	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)
Brucella spp.	3 (0.4–110)	0.02 (0.002–0.5)	1 (0.1–34)	3 (1–37)	0.01 (0.005–0.2)	0.9 (0.3–12)	33 (10–187)	0.2 (0.05–0.9)	11 (3–60)	4 (1–33)	0.02 (0.006–0.2)	1 (0.4–11)	2 (0.02–302)	0.01 (0–1)	0.8 (0.006–96)	2 (0.5–61)	0.01 (0.002–0.3)	0.6 (0.1–19)	6 (2–132)	0.03 (0.01–0.7)	2 (0.6–42)
Hepatitis A	232 (60–643)	0.5 (0.1–1)	23 (7–60)	12 (3–33)	0.02 (0.006–0.07)	1 (0.3–3)	237 (17–772)	0.5 (0.04–2)	23 (2–74)	11 (3–28)	0.02 (0.006–0.06)	1 (0.3–3)	494 (57–1 590)	1 (0.1–3)	48 (6–151)	51 (3–164)	0.1 (0.006–0.3)	5 (0.3–15)	199 (53–560)	0.4 (0.1–1)	20 (6–53)
Listeria monocytogenes	0.1 (0–2)	0.03 (0–0.6)	1 (0–21)	0.3 (0.1–1)	0.07 (0.03–0.3)	3 (1–11)	0.1 (0–2)	0.03 (0–0.6)	1 (0–21)	0.2 (0.2–0.3)	0.04 (0.03–0.06)	2 (1–2)	0.1 (0–2)	0.03 (0–0.6)	1 (0–21)	0.2 (0.1–0.4)	0.04 (0.03–0.09)	1 (1–3)	0.2 (0.09–1)	0.05 (0.02–0.3)	2 (0.7–11)
Mycobacterium bovis	7 (4–9)	0.5 (0.3–0.7)	30 (19–42)	0.1 (0.05–0.2)	0.007 (0.003–0.01)	0.4 (0.2–0.8)	1 (0.8–2)	0.2 (0.08–0.3)	9 (5–18)	0.2 (0.1–0.3)	0.02 (0.01–0.03)	0.9 (0.7–1)	2 (0.9–4)	0.2 (0.1–0.5)	13 (6–26)	0.8 (0.4–1)	0.04 (0.02–0.07)	2 (1–4)	2 (1–2)	0.2 (0.1–0.2)	9 (7–12)
Invasive non-typhoidal *Salmonella* enterica	25 (12–37)	3 (1–5)	169 (71–306)	0.7 (0.4–0.9)	0.06 (0.03–0.1)	3 (1–5)	1 (0.7–2)	0.1 (0.06–0.3)	8 (3–14)	0.8 (0.6–1)	0.07 (0.04–0.1)	3 (2–5)	2 (0.3–2)	0.2 (0.03–0.3)	9 (2–16)	1 (0.5–2)	0.1 (0.05–0.2)	6 (2–10)	4 (2–6)	0.4 (0.2–0.7)	26 (13–45)
Salmonella enterica Paratyphi A	25 (5–73)	0.2 (0.04–0.5)	12 (3–36)	2 (0.4–7)	0.02 (0.003–0.05)	1 (0.2–4)	17 (2–55)	0.1 (0.01–0.4)	9 (1–28)	0.2 (0.03–1)	0.002 (0–0.008)	0.1 (0.01–0.6)	58 (11–167)	0.4 (0.1–1)	29 (7–83)	18 (3–47)	0.1 (0.02–0.3)	8 (1–20)	25 (8–63)	0.2 (0.05–0.4)	12 (4–31)
Salmonella enterica Typhi	108 (24–317)	0.7 (0.2–2)	53 (12–155)	10 (2–32)	0.07 (0.01–0.2)	5 (0.9–16)	73 (9–240)	0.5 (0.06–2)	37 (5–122)	1 (0.1–5)	0.007 (0–0.03)	0.5 (0.05–2)	250 (50–725)	2 (0.4–5)	128 (29–361)	77 (12–203)	0.5 (0.07–1)	33 (5–87)	110 (34–272)	0.8 (0.2–2)	54 (17–133)
TOTAL	10 304 (4 279–22 108)	14 (8–21)	1 001 (562–1 543)	7 937 (4 515–13 899)	0.8 (0.5–1)	61 (40–93)	16 865 (8 051–34 712)	6 (4–9)	470 (286–728)	2 506 (1 455–4 168)	0.5 (0.3–0.6)	32 (24–45)	8 068 (3 294–20 663)	9 (4–17)	622 (306–1 145)	6 491 (2 630–17 528)	1 (0.6–2)	93 (45–175)	8 369 (5 723–13 318)	5 (3–8)	366 (255–538)

Notes: * Table does not include four foodborne intoxications caused by *Clostridium botulinum*, *Cl. perfringens*, *S. aureus*, and *Bacillus cereus* due to a lack of data for global estimation.

** Includes Guillain-Barré Syndrome cases and deaths

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Table A8.3 Median number of Illnesses, Deaths, and Disability Adjusted Life Years (DALYs) by age group, with 95% uncertainty intervals, 2010.

PATHOGEN*	AGE GROUP: <5 YEARS OF AGE			AGE GROUP: ≥5 YEARS OF AGE			RATIO <5:≥5		
	ILLNESSES	DEATHS	DALYS	ILLNESSES	DEATHS	DALYS	ILLNESSES	DEATHS	DALYS
	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	RATIO <5:≥5 (95% UI)	RATIO <5:≥5 (95% UI)	RATIO <5:≥5 (95% UI)
Diarrhoeal Disease	216 839 210 (148 937 428–309 926 253)	91 621 (62 442–132 707)	8 547 149 (5 903 945–12 254 175)	327 209 075 (179 670 939–643 705 133)	107 500 (69 907–163 979)	7 205 002 (4 790 026–10 747 526)	0.66 (0.32–1.28)	0.86 (0.60–1.16)	1.19 (0.86–1.60)
Campylobacter spp.**	47 988 357 (22 436 891–102 663 926)	13 861 (8 754–23 670)	1 383 499 (911 878–2 279 897)	42 883 268 (18 350 672–112 061 441)	7 436 (4 930–9 974)	750 578 (540 003–956 663)	1.11 (0.34–3.47)	1.91 (1.21–3.08)	1.87 (1.26–2.92)
Cryptosporidium spp.	5 986 213 (2 569 532–12 738 924)	1 989 (678–5 683)	185 057 (64 847–518 497)	2 253 036 (774 628–8 639 265)	1 673 (638–4 149)	104 794 (40 408–256 055)	2.61 (0.69–8.01)	1.23 (0.42–2.72)	1.83 (0.65–3.93)
Entamoeba histolytica	8 480 759 (1 593 697–30 849 576)	896 (90–4 852)	92 213 (15 997–444 002)	17 828 477 (5 378 578–50 963 825)	524 (218–1 110)	43 984 (20 149–85 551)	0.48 (0.08–2.38)	1.75 (0.18–8.71)	2.14 (0.38–9.49)
Enteropathogenic *E. coli*	17 312 780 (6 767 766–54 104 398)	22 156 (11 944–37 473)	2 004 543 (1 084 856–3 389 584)	5 458 601 (2 145 370–16 561 005)	14 647 (7 305–25 447)	911 012 (457 215–1 575 768)	3.20 (0.85–11.78)	1.52 (1.03–2.29)	2.21 (1.52–3.29)
Enterotoxigenic *E. coli*	38 352 806 (21 144 875–64 795 160)	14 056 (7 045–26 784)	1 303 490 (668 837–2 446 758)	46 811 878 (20 306 649–103 801 449)	11 933 (6 382–18 887)	767 975 (419 834–1 204 273)	0.82 (0.35–1.96)	1.21 (0.63–2.10)	1.74 (0.95–2.93)
Giardia spp.	18 773 028 (8 075 497–38 649 748)	0 (0–0)	20 677 (8 552–44 101)	8 693 968 (3 337 657–24 195 602)	0 (0–0)	5 016 (1 945–13 791)	2.11 (0.84–5.22)	N/A	4.04 (1.57–10.28)
Norovirus	34 582 700 (19 595 826–59 592 939)	8 992 (4 251–19 347)	844 376 (406 822–1 776 252)	89 056 582 (46 054 795–206 532 318)	25 807 (11 201–61 642)	1 638 925 (730 924–3 844 771)	0.38 (0.19–0.73)	0.35 (0.22–0.54)	0.52 (0.33–0.78)
Salmonella enterica, non-typhoidal	15 274 234 (6 514 539–41 696 874)	12 531 (6 562–30 779)	1 149 675 (609 216–2 792 992)	60 293 254 (18 488 275–189 066 838)	15 807 (8 762–21 942)	1 016 047 (576 408–1 405 079)	0.26 (0.06–1.16)	0.84 (0.44–1.83)	1.19 (0.64–2.57)
Shigella spp.	15 516 627 (5 416 319–38 620 351)	8 863 (3 250–20 925)	819 280 (309 576–1 909 450)	34 049 173 (10 186 959–95 312 884)	6 060 (2 734–11 511)	404 144 (188 009–749 866)	0.45 (0.13–1.70)	1.49 (0.60–3.26)	2.06 (0.87–4.43)
Shiga toxin-producing *E. coli*	339 905 (217 805–728 708)	63 (30–170)	6 969 (3 278–17 751)	836 948 (536 302–1 794 298)	65 (24–204)	5 989 (2 654–15 877)	0.41 (0.41–0.41)	0.96 (0.81–1.31)	1.16 (1.09–1.29)
Vibrio cholerae	114 518 (46 636–235 152)	3 697 (1 546–7 506)	331 395 (138 538–672 643)	648 933 (264 273–1 332 530)	20 952 (8 758–42 535)	1 390 973 (581 491–2 820 499)	0.18 (0.18–0.18)	0.18 (0.18–0.18)	0.24 (0.24–0.24)
Invasive enteric diseases	4 336 215 (1 675 945–9 422 681)	23 727 (11 866–45 950)	2 180 916 (1 085 765–4 219 254)	21 182 632 (8 375 340–49 059 198)	123 026 (69 306–230 318)	6 900 776 (3 799 471–13 355 093)	0.21 (0.15–0.23)	0.19 (0.14–0.22)	0.32 (0.23–0.35)
Brucella spp.	4 144 (1 527–93 225)	21 (7–463)	1 988 (687–44 999)	389 106 (142 279–9 006 169)	1 936 (654–45 081)	122 904 (42 484–2 865 643)	0.01 (0.01–0.01)	0.01 (0.01–0.01)	0.02 (0.02–0.02)

PATHOGEN*	AGE GROUP: <5 YEARS OF AGE			AGE GROUP: ≥5 YEARS OF AGE			RATIO <5:≥5		
	ILLNESSES	DEATHS	DALYS	ILLNESSES	DEATHS	DALYS	ILLNESSES	DEATHS	DALYS
	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	NUMBER (95% UI)	RATIO <5:≥5 (95% UI)	RATIO <5:≥5 (95% UI)	RATIO <5:≥5 (95% UI)
Hepatitis A	2 165 243 (573 433–6 084 381)	4 380 (1 132–12 211)	411 592 (112 767–1 130 290)	11 544 593 (3 057 415–32 440 565)	23 351 (6 036–65 109)	941 278 (269 448–2 538 627)	0.19 (0.19–0.19)	0.19 (0.19–0.19)	0.44 (0.39–0.46)
Listeria monocytogenes	1 240 (393–10 502)	330 (126–2 138)	30 750 (11 700–198 862)	12 936 (5 716–80 766)	2 851 (1 200–18 271)	87 569 (36 830–561 221)	0.10 (0.07–0.13)	0.11 (0.08–0.16)	0.34 (0.24–0.49)
Mycobacterium bovis	869 (732–1 049)	76 (58–101)	7 134 (5 477–9 496)	120 398 (99 119–149 188)	10 470 (7 836–14 372)	600 639 (452 917–816 737)	0.01 (0.01–0.01)	0.01 (0.01–0.01)	0.01 (0.01–0.01)
Salmonella enterica, invasive non-typhoidal	45 549 (25 019–62 638)	4 700 (2 268–8 188)	421 523 (203 340–733 940)	239 467 (142 115–321 539)	24 692 (12 655–42 246)	1 373 635 (684 718–2 373 326)	0.19 (0.17–0.20)	0.19 (0.17–0.20)	0.31 (0.29–0.32)
Salmonella enterica Paratyphi A	357 814 (110 286–885 942)	2 480 (778–6 067)	227 507 (71 530–557 578)	1 383 306 (426 364–3 425 041)	9 588 (3 007–23 454)	627 953 (197 302–1 541 909)	0.26 (0.26–0.26)	0.26 (0.26–0.26)	0.36 (0.36–0.36)
Salmonella enterica Typhi	1 555 715 (479 504–3 851 923)	10 783 (3 381–26 377)	989 159 (311 001–2 424 250)	6 014 372 (1 853 758–14 891 483)	41 689 (13 072–101 973)	2 730 232 (857 835–6 703 954)	0.26 (0.26–0.26)	0.26 (0.26–0.26)	0.36 (0.36–0.36)
TOTAL	221 451 463 (153 244 508–315 075 166)	116 613 (80 862–165 379)	10 831 919 (7 587 557–15 271 603)	350 711 509 (199 599 319–673 777 073)	232 916 (152 283–368 498)	14 250 088 (9 419 295–22 483 691)	0.63 (0.32–1.18)	0.50 (0.36–0.68)	0.76 (0.56–1.01)

Notes: * Table does not include four foodborne intoxications due to *Clostridium botulinum*, *Cl. perfringens*, *S. aureus* and *Bacillus cereus* due to a lack of data for global estimation. ** Includes Guillain-Barré Syndrome cases and Deaths

Table A8.4 Median rate per 100 000 of foodborne Illnesses, Deaths and Disability Adjusted Life Years (DALYs) by region, with 95% uncertainty intervals, 2010.

PATHOGEN	AFR			AMR			EMR			EUR			SEAR			WPR			GLOBAL		
	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)
Enteric protozoa#	1 995 (549–5 866)	0.2 (0.07–0.7)	21 (6–62)	733 (222–2 077)	0.009 (0.003–0.03)	1 (0.5–3)	1 989 (560–5 118)	0.07 (0.01–0.3)	7 (2–28)	77 (21–181)	0.003 (0–0.009)	0.2 (0.04–0.7)	584 (133–1 946)	0.1 (0.03–0.4)	11 (3–36)	737 (124–2 566)	0.005 (0–0.03)	1 (0.2–4)	976 (520–1 752)	0.08 (0.04–0.2)	7 (3–15)
Cryptosporidium spp.#	205 (35–813)	0.2 (0.04–0.4)	13 (3–37)	114 (32–355)	0.007 (0.002–0.02)	0.6 (0.2–2)	346 (52–1 287)	0.04 (0.004–0.2)	4 (0.4–20)	21 (4–70)	0.003 (0–0.009)	0.2 (0.03–0.6)	78 (10–474)	0.09 (0.01–0.4)	6 (0.9–29)	32 (2–170)	0.003 (0–0.03)	0.3 (0.02–3)	125 (57–269)	0.05 (0.02–0.1)	4 (2–11)
Entamoeba spp.#	796 (98–3 868)	0.05 (0.009–0.4)	5 (0.9–39)	212 (16–1 209)	0.001 (0–0.009)	0.3 (0.03–1)	737 (79–3 110)	0.02 (0.002–0.2)	2 (0.3–14)	0 (0–0)	0 (0–0)	0 (0–0)	256 (27–1 188)	0.03 (0.004–0.2)	3 (0.3–17)	229 (0–1 598)	0.001 (0–0.003)	0.3 (0–1)	407 (149–997)	0.02 (0.007–0.08)	2 (0.7–7)
Giardia spp.#	809 (172–2 574)	0 (0–0)	0.8 (0.2–3)	309 (62–1 249)	0 (0–0)	0.3 (0.05–1)	670 (133–2 193)	0 (0–0)	0.6 (0.1–2)	54 (16–123)	0 (0–0)	0.03 (0.009–0.1)	159 (16–903)	0 (0–0)	0.1 (0.01–0.9)	354 (8–1 519)	0 (0–0)	0.3 (0.005–1)	410 (188–828)	0 (0–0)	0.4 (0.2–0.8)
Invasive infectious disease	230 (133–387)	0.03 (0.01–0.05)	21 (11–36)	160 (92–263)	0.009 (0.004–0.02)	15 (9–26)	196 (119–295)	0.02 (0.009–0.04)	19 (11–30)	119 (80–189)	0.005 (0.002–0.01)	8 (5–14)	137 (56–245)	0.006 (0.002–0.01)	10 (4–19)	117 (65–177)	0.005 (0.002–0.01)	8 (4–13)	149 (108–217)	0.01 (0.005–0.02)	12 (8–18)
Toxoplasma gondii, congenital	2 (0.8–4)	0.03 (0.01–0.05)	8 (4–15)	1 (0.7–2)	0.009 (0.004–0.02)	5 (3–9)	1 (0.7–3)	0.02 (0.009–0.04)	7 (4–13)	0.3 (0.2–0.7)	0.005 (0.002–0.01)	2 (1–3)	0.4 (0.1–0.9)	0.006 (0.002–0.01)	2 (0.8–5)	0.3 (0.2–0.7)	0.005 (0.002–0.01)	2 (1–4)	0.7 (0.5–1)	0.01 (0.005–0.02)	4 (2–6)
Toxoplasma gondii, acquired	229 (132–386)	0 (0–0)	12 (6–22)	159 (92–261)	0 (0–0)	10 (5–17)	195 (118–292)	0 (0–0)	11 (6–18)	119 (79–188)	0 (0–0)	6 (4–10)	137 (55–244)	0 (0–0)	8 (3–15)	116 (65–176)	0 (0–0)	6 (3–10)	149 (107–216)	0 (0–0)	8 (5–13)
Cestodes	15 (11–37)	2 (1–3)	177 (131–247)	4 (3–7)	0.1 (0.08–0.2)	20 (15–26)	0.7 (0.3–18)	0.009 (0.002–0.2)	0.8 (0.2–17)	1 (0.5–2)	0.04 (0.02–0.2)	2 (1–10)	9 (7–13)	0.4 (0.3–0.5)	38 (28–50)	4 (3–6)	0.6 (0.2–1)	41 (23–60)	6 (5–11)	0.5 (0.4–0.7)	46 (35–60)
Echinococcus granulosus	0.7 (0.2–23)	0.007 (0.001–0.2)	0.6 (0.2–18)	0.3 (0.1–3)	0.004 (0–0.04)	0.3 (0.1–3)	0.7 (0.3–18)	0.009 (0.002–0.2)	0.7 (0.2–17)	0.8 (0.4–2)	0.009 (0.003–0.03)	0.8 (0.3–2)	0.8 (0.2–2)	0.008 (0.002–0.03)	0.6 (0.2–2)	0.3 (0.09–0.7)	0.004 (0–0.01)	0.3 (0.08–0.8)	0.6 (0.4–5)	0.007 (0.002–0.06)	0.6 (0.2–5)
Echinococcus multilocularis	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0.002)	0 (0–0.001)	0.01 (0.004–0.05)	0.07 (0.03–0.4)	0.03 (0.01–0.2)	1 (0.4–8)	0 (0–0)	0 (0–0)	0.006 (0–0.03)	0.4 (0–0.8)	0.4 (0–0.8)	16 (0–34)	0.1 (0.01–0.2)	0.1 (0.004–0.2)	5 (0.1–9)
Taenia solium	14 (11–19)	2 (1–3)	175 (129–241)	3 (3–4)	0.1 (0.08–0.1)	19 (15–25)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.002 (0.001–0.003)	0.2 (0.1–0.4)	8 (6–11)	0.4 (0.3–0.5)	37 (28–50)	4 (3–5)	0.2 (0.1–0.3)	24 (18–32)	5 (4–7)	0.4 (0.3–0.5)	41 (31–52)
Nematodes	170 (68–288)	0.02 (0.005–0.07)	9 (4–17)	130 (60–793)	0.01 (0.004–0.04)	7 (3–57)	200 (72–282)	0.02 (0.004–0.06)	10 (4–15)	8 (4–12)	0.002 (0–0.006)	0.6 (0.3–1)	255 (88–461)	0.01 (0.001–0.08)	12 (4–23)	213 (57–358)	0.01 (0.001–0.06)	10 (3–20)	179 (121–334)	0.01 (0.006–0.04)	9 (6–19)
Ascaris spp.	170 (68–288)	0.02 (0.005–0.07)	9 (4–17)	130 (60–793)	0.01 (0.003–0.04)	7 (3–57)	200 (72–282)	0.02 (0.004–0.06)	10 (4–15)	8 (4–11)	0.002 (0–0.006)	0.6 (0.3–1)	255 (88–461)	0.01 (0.001–0.08)	12 (4–23)	213 (57–358)	0.01 (0.001–0.06)	10 (3–20)	178 (120–334)	0.01 (0.006–0.04)	9 (6–19)
Trichinella spp.	0 (0–0.001)	0 (0–0)	0.001 (0–0.002)	0.06 (0.04–0.07)	0 (0–0)	0.009 (0.005–0.01)	0.002 (0–0.003)	0 (0–0)	0 (0–0)	0.4 (0.3–0.5)	0 (0–0)	0.04 (0.02–0.07)	0.002 (0–0.004)	0 (0–0)	0 (0–0.001)	0.01 (0.004–0.02)	0 (0–0)	0.004 (0.001–0.007)	0.06 (0.04–0.09)	0 (0–0)	0.008 (0.004–0.01)
Trematodes	0.006 (0.002–0.02)	0 (0–0)	0.04 (0.01–0.1)	1 (0.8–2)	0 (0–0.001)	9 (7–13)	0.6 (0.4–0.9)	0 (0–0)	5 (3–7)	0.06 (0.04–0.1)	0 (0–0)	0.4 (0.3–0.8)	0.7 (0.5–1)	0.06 (0.05–0.08)	8 (6–10)	11 (8–14)	0.4 (0.3–0.4)	97 (78–120)	3 (2–4)	0.1 (0.09–0.1)	29 (24–36)
Clonorchis sinensis	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.01 (0.008–0.01)	0.004 (0.001–0.01)	0 (0–0.001)	0.04 (0.01–0.1)	2 (1–2)	0.3 (0.3–0.4)	29 (24–35)	0.5 (0.3–0.7)	0.08 (0.07–0.1)	8 (6–9)

PATHOGEN	AFR			AMR			EMR			EUR			SEAR			WPR			GLOBAL		
	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)
Fasciola spp.	0.003 (0–0.008)	0 (0–0)	0.02 (0.007–0.06)	0.5 (0.3–0.9)	0 (0–0)	4 (2–7)	0.6 (0.4–0.8)	0 (0–0)	5 (3–7)	0.006 (0.002–0.02)	0 (0–0)	0.06 (0.02–0.2)	0.006 (0.002–0.02)	0 (0–0)	0.05 (0.02–0.1)	0.09 (0.01–0.8)	0 (0–0)	0.8 (0.1–7)	0.2 (0.1–0.4)	0 (0–0)	1 (0.8–3)
Intestinal flukes *	0 (0–0.003)	0 (0–0)	0.006 (0.002–0.02)	0.009 (0.003–0.03)	0 (0–0)	0.08 (0.02–0.3)	0.009 (0.003–0.03)	0 (0–0)	0.07 (0.03–0.2)	0.006 (0.003–0.01)	0 (0–0)	0.05 (0.02–0.1)	0.02 (0.006–0.05)	0 (0–0)	0.1 (0.05–0.4)	1 (0.8–1)	0 (0–0)	8 (6–11)	0.3 (0.2–0.4)	0 (0–0)	2 (2–3)
Opisthorchis spp.	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.05 (0.04–0.08)	0 (0–0)	0.3 (0.2–0.5)	0.6 (0.4–0.9)	0.06 (0.05–0.07)	8 (6–10)	0.2 (0.2–0.3)	0.02 (0.02–0.03)	3 (2–3)	0.2 (0.2–0.3)	0.02 (0.02–0.03)	3 (2–3)
Paragonimus spp.	0.002 (0–0.007)	0 (0–0)	0.02 (0.005–0.05)	0.6 (0.4–0.8)	0 (0–0.001)	5 (3–7)	0.002 (0–0.006)	0 (0–0)	0.02 (0.006–0.05)	0.001 (0–0.004)	0 (0–0)	0.009 (0.003–0.03)	0.008 (0.002–0.04)	0 (0–0)	0.06 (0.02–0.3)	7 (5–10)	0.01 (0.008–0.02)	55 (39–76)	2 (1–3)	0.004 (0.002–0.005)	15 (11–21)
TOTAL (excluding enteric protozoa)	418 (277–644)	2 (1–3)	208 (159–283)	293 (195–1 035)	0.1 (0.1–0.2)	51 (41–112)	398 (253–535)	0.05 (0.03–0.3)	35 (25–58)	128 (89–199)	0.05 (0.03–0.2)	11 (8–24)	404 (220–649)	0.5 (0.4–0.6)	69 (54–89)	346 (188–512)	1 (0.5–1)	156 (127–193)	337 (265–553)	0.7 (0.5–0.9)	96 (82–122)
TOTAL	2 428 (934–6 426)	2 (2–3)	232 (176–317)	1 060 (507–2 790)	0.1 (0.1–0.2)	53 (42–113)	2 390 (933–5 535)	0.1 (0.05–0.4)	44 (30–76)	210 (136–328)	0.05 (0.03–0.2)	12 (8–24)	1 007 (461–2 491)	0.6 (0.5–1)	80 (61–114)	1 089 (429–3 088)	1 (0.6–1)	158 (128–195)	1 325 (851–2 237)	0.8 (0.6–1)	104 (88–132)

Notes: * Includes selected species of the families Echinostomatidae, Fasciolidae, Gymnophallidae, Heterophyidae, Nanophyetidae, Neodiplostomidae and Plagiorchiidae (depending on data availability). # Enteric protozoa are included to complete the picture for foodborne parasitic diseases, but are reported in detail elsewhere [5].Illnesses are defined as the numbers of new cases in 2010. For *Taenia solium* this is estimated from GBD2010 [9] regional incidence data and modified as the actual number of cases of epilepsy attributed to cysticercosis. The YLD component of the DALY for cysticercosis is prevalence-based, estimated from GBD2010 data.

TableA8.5 Median number of total and foodborne Illnesses, Deaths, and Disability Adjusted Life Years (DALYs), with 95% uncertainty intervals, 2010

PATHOGEN	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	PROPORTION FOODBORNE – ILLNESSES (95% UI)	PROPORTION FOODBORNE – DALYS (95% UI)	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYS (95% UI)
Enteric protozoa	356 688 438 (251 929 267–517 872 930)	33 925 (22 933–53 614)	2 940 604 (1 978 442–4 686 855)	0.19 (0.12–0.28)	0.17 (0.09–0.29)	67 182 645 (35 794 977–120 556 797)	5 558 (2 593–11 958)	492 354 (239 400–1 034 790)
Cryptosporidium spp.#	64 003 709 (43 049 455–104 679 951)	27 553 (18 532–44 654)	2 159 331 (1 392 438–3 686 925)	0.13 (0.07–0.24)	0.14 (0.06–0.28)	8 584 805 (3 897 252–18 531 196)	3 759 (1 520–9 115)	296 156 (119 456–724 660)
Entamoeba histolytica#	103 943 952 (47 018 659–210 632 459)	5 450 (2 194–17 127)	515 904 (222 446–1 552 466)	0.28 (0.14–0.44)	0.28 (0.13–0.47)	28 023 571 (10 261 254–68 567 590)	1 470 (453–5 554)	138 863 (47 339–503 775)
Giardia spp.#	183 842 615 (130 018 020–262 838 002)	0 (0–0)	171 100 (115 777–257 315)	0.15 (0.08–0.27)	0.15 (0.07–0.27)	28 236 123 (12 945 655–56 996 454)	0 (0–0)	26 270 (11 462–53 577)
Invasive infectious disease	20 817 916 (16 337 908–29 091 701)	1 409 (701–2 620)	1 684 414 (1 236 005–2 452 060)	0.49 (0.40–0.59)	0.49 (0.40–0.59)	10 280 089 (7 403 516–14 904 324)	684 (333–1 300)	829 071 (561 297–1 264 567)
Toxoplasma gondii, congenital	98 900 (67 858–188 748)	1 409 (701–2 620)	526 515 (359 756–835 537)	0.49 (0.40–0.58)	0.49 (0.40–0.58)	48 823 (31 893–93 213)	684 (333–1 300)	259 618 (168 510–422 935)
Toxoplasma gondii, acquired	20 710 906 (16 235 987–28 955 435)	0 (0–0)	1 153 779 (772 676–1 733 114)	0.49 (0.40–0.59)	0.49 (0.39–0.59)	10 228 111 (7 351 013–14 844 411)	0 (0–0)	565 816 (354 029–891 032)
Cestodes	596 838 (482 828–2 169 206)	48 269 (36 956–70 978)	3 721 581 (2 942 173–5 416 945)	0.72 (0.35–0.79)	0.85 (0.65–0.93)	430 864 (334 389–774 703)	36 500 (25 652–50 063)	3 158 826 (2 411 585–4 122 032)
Echinococcus granulosus	188 079 (156 848–1 770 405)	2 225 (749–19 627)	183 573 (88 082–1 590 846)	0.21 (0.15–0.30)	0.21 (0.15–0.29)	43 076 (25 881–371 177)	482 (150–3 974)	39 950 (16 996–322 953)
Echinococcus multilocularis	18 451 (11 384–29 619)	17 118 (10 184–27 346)	687 823 (409 190–1 106 320)	0.47 (0.04–0.75)	0.48 (0.01–0.76)	8 375 (656–17 005)	7 771 (243–15 896)	312 461 (9 083–640 716)
Taenia solium	370 710 (282 937–478 123)	28 114 (21 059–36 915)	2 788 426 (2 137 613–3 606 582)	1.00	1.00	370 710 (282 937–478 123)	28 114 (21 059–36 915)	2 788 426 (2 137 613–3 606 582)
Nematodes	26 845 649 (25 375 461–47 940 713)	2 227 (865–5 946)	1 318 104 (1 183 025–2 701 170)	0.45 (0.31–0.59)	0.46 (0.31–0.59)	12 285 286 (8 292 732–22 984 630)	1 012 (388–2 783)	605 738 (411 113–1 301 619)
Ascaris spp.	26 840 692 (25 371 434–47 937 154)	2 224 (862–5 942)	1 317 535 (1 182 187–2 700 572)	0.45 (0.31–0.59)	0.46 (0.31–0.59)	12 280 767 (8 287 414–22 980 491)	1 008 (384–2 781)	605 278 (410 668–1 301 114)
Trichinella spp.	4 472 (2 977–5 997)	4 (2–5)	550 (285–934)	1.00	1.00	4 472 (2 977–5 997)	4 (2–5)	550 (285–934)
Trematodes	218 569 (167 886–281 872)	7 533 (6 383–8 845)	2 024 592 (1 652 243–2 483 514)	1.00	1.00	218 569 (167 886–281 872)	7 533 (6 383–8 845)	2 024 592 (1 652 243–2 483 514)
Chlonorchis sinensis	31 620 (21 515–45 059)	5 770 (4 728–6 988)	522 863 (431 520–635 232)	1.00	1.00	31 620 (21 515–45 059)	5 770 (4 728–6 988)	522 863 (431 520–635 232)
Fasciola spp.	10 635 (6 888–24 100)	0 (0–0)	90 041 (58 050–209 097)	1.00	1.00	10 635 (6 888–24 100)	0 (0–0)	90 041 (58 050–209 097)
Intestinal flukes *	18 924 (14 498–24 200)	0 (0–0)	155 165 (118 920–198 147)	1.00	1.00	18 924 (14 498–24 200)	0 (0–0)	155 165 (118 920–198 147)

PATHOGEN	ILLNESSES (95% UI)	DEATHS (95% UI)	DALYS (95% UI)	PROPORTION FOODBORNE – ILLNESSES (95% UI)	PROPORTION FOODBORNE – DALYS (95% UI)	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYS (95% UI)
Opisthorchis spp.	16 315 (11 273–22 860)	1 498 (1 230–1 813)	188 346 (151 906–235 431)	1.00	1.00	16 315 (11 273–22 860)	1 498 (1 230–1 813)	188 346 (151 906–235 431)
Paragonimus spp.	139 238 (95 610–195 078)	250 (160–371)	1 048 937 (743 700–1 438 588)	1.00	1.00	139 238 (95 610–195 078)	250 (160–371)	1 048 937 (743 700–1 438 588)
TOTAL (excluding enteric protozoa)	48 405 537 (43 376 746–79 049 913)	59 724 (48 017–83 616)	8 777 198 (7 620 016–12 511 566)	0.48 (0.38–0.56)	0.76 (0.65–0.81)	23 220 595 (18 215 499–38 081 817)	45 927 (34 763–59 933)	6 639 989 (5 611 955–8 414 684)
TOTAL	407 149 528 (301 670 420–585 323 226)	94 620 (77 140–125 670)	11 794 391 (10 164 903–15 675 990)	0.22 (0.16–0.31)	0.61 (0.52–0.67)	91 148 998 (58 576 614–153 950 104)	51 909 (40 020–66 992)	7 161 689 (6 078 248–9 074 283)

Table A8.6 Median number of foodborne Illnesses, Deaths, and Disability Adjusted Life Years (DALYs), with 95% Uncertainty Intervals, 2010

CHEMICAL	FOODBORNE ILLNESSES (95% UI)	FOODBORNE DEATHS (95% UI)	FOODBORNE DALYS (95% UI)
Aflatoxin	21 757 (8 967–56 776)	19 455 (7 954–51 324)	636 869 (267 142–1 617 081)
Cyanide in cassava	1 066 (105–3 016)	227 (22–669)	18 203 (1 769–53 170)
Dioxin	193 447 (155 963–1 085 675	0 (0–0)	240 056 (192 608–1 399 562)
Peanut allergens*	107 167 (6 262–210 093)	28 (2–56)	99 717 (5 827–195 489)
TOTAL	338 611 (185 705–1 238 725	19 736 (8 210–51 700)	1 012 362 (562 087–2 822 481)

Notes: * = Only the burdens for AMR A, EUR A and WPR A were assessed.

Table A8.7 Median rate per 100 000 foodborne (FB) Illnesses, Deaths, and Disability Adjusted Life Years (DALYs) by region, with 95% uncertainty intervals, 2010.

REGION		CHEMICAL			
		AFLATOXIN	CYANIDE IN CASSAVA	DIOXIN	TOTAL
AFR	FB Illnesses (95% UI)	0.4 (0.1–1)	0.1 (0.01–0.4)	0.2 (0.07–7)	0.7 (0.3–8)
	FB Deaths (95% UI)	0.4 (0.1–1)	0.03 (0.003–0.08)	0 (0–0)	0.4 (0.1–1)
	FB DALYs (95% UI)	15 (5–40)	2 (0.2–6)	0.2 (0.07–8)	18 (7–49)
AMR	FB Illnesses (95% UI)	0.08 (0.02–0.6)	0 (0–0)	0.2 (0.05–6)	0.2 (0.1–7)
	FB Deaths (95% UI)	0.08 (0.02–0.6)	0 (0–0)	0 (0–0)	0.08 (0.02–0.6)
	FB DALYs (95% UI)	2 (0.4–15)	0 (0–0)	0.2 (0.07–9)	2 (0.6–24)
EMR	FB Illnesses (95% UI)	0.2 (0.04–0.5)	0 (0–0)	2 (1–35)	2 (1–35)
	FB Deaths (95% UI)	0.1 (0.04–0.4)	0 (0–0)	0 (0–0)	0.1 (0.04–0.4)
	FB DALYs (95% UI)	4 (1–13)	0 (0–0)	2 (2–43)	7 (3–51)
EUR	FB Illnesses (95% UI)	0.02 (0.01–0.03)	0 (0–0)	1 (0.7–13)	1 (0.7–13)
	FB Deaths (95% UI)	0.02 (0.01–0.03)	0 (0–0)	0 (0–0)	0.02 (0.01–0.03)
	FB DALYs (95% UI)	0.5 (0.3–0.8)	0 (0–0)	1 (0.9–19)	2 (1–19)
SEAR	FB Illnesses (95% UI)	0.2 (0.08–0.6)	0 (0–0)	9 (8–32)	10 (8–32)
	FB Deaths (95% UI)	0.2 (0.08–0.5)	0 (0–0)	0 (0–0)	0.2 (0.07–0.5)
	FB DALYs (95% UI)	7 (2–17)	0 (0–0)	12 (10–41)	19 (13–54)
WPR	FB Illnesses (95% UI)	0.6 (0.1–2)	0 (0–0)	0.05 (0.005–4)	0.8 (0.1–5)
	FB Deaths (95% UI)	0.5 (0.09–2)	0 (0–0)	0 (0–0)	0.5 (0.09–2)
	FB DALYs (95% UI)	16 (3–63)	0 (0–0)	0.07 (0.007–6)	16 (3–65)
GLOBAL	FB Illnesses (95% UI)	0.3 (0.1–0.8)	0.02 (0.002–0.04)	3 (2–16)	3 (3–17)
	FB Deaths (95% UI)	0.3 (0.1–0.7)	0.003 (0–0.01)	0 (0–0)	0.3 (0.1–0.8)
	FB DALYs (95% UI)	9 (4–24)	0.3 (0.03–0.8)	3 (3–20)	13 (7–39)

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GLOSSARY

Foodborne disease

A foodborne disease (FBD) can be defined as a disease commonly transmitted through ingested food. FBDs comprise a broad group of illnesses, and may be caused by microbial pathogens, parasites, chemical contaminants and biotoxins.

Burden of disease

In the context of this Initiative, the term "burden of disease" follows the principles of the Global Burden of disease Study, and includes the quantification of morbidity, all disabling complications and mortality in a single summary measure (DALY).

DALY (disability-adjusted life year)

A health gap measure that combines the years of life lost due to premature death (YLL) and the years lived with disability (YLD) from a disease or condition, for varying degrees of severity, making time itself the common metric for death and disability. One DALY equates to one year of healthy life lost.

Food

According to the Codex Alimentarius Commission, "food means any substance, whether processed, semi-processed or raw, which is intended for human consumption, and includes drink, chewing gum and any substance which has been used in the manufacture, preparation or treatment of food but does not include cosmetics or tobacco or substances used only as drugs". The definition includes all bottled drinks.

Source attribution

Source attribution (SA) is the partitioning of the human burden of a particular disease to specific sources. With regards to foodborne diseases, SA can be conducted at various points along the food distribution chain, from the animal reservoir to the point of consumption.

ABBREVIATIONS

BMD	Benchmark Dose
BMDL	Benchmark Dose lower 5% confidence bound
BMDU	Benchmark Dose upper confidence limit
BoD	Burden of Disease
BW	Body Weight
CDC	Centers for Disease Control and Prevention [of the United States of America]
CE	Cystic Echinococcosis
CEA	Comparative Exposure Assessment
CFR	Case fatality ratio
CHERG	Child Health Epidemiology Reference Group
CI	Confidence Interval
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CRA	Comparative Risk Assessment
CSTF	Country Studies Task Force
CT	Congenital Toxoplasmosis
CTF	Computational Task Force
CTTF	Chemicals and Toxins Task Force
DALY	Disability-adjusted life year
DOI	Declaration of interests
DRC	Democratic Republic of Congo
DW	Disability Weight
EAggEC	Enteroaggerative *E. coli*
ECDC	European Centre for Disease Prevention and Control
EDTF	Enteric Disease Task Force
EFSA	European Food Safety Authority
EPEC	Enteropathogenic *Escherichia coli*
ESRD	End-stage renal disease
ETEC	Enterotoxigenic *Escherichia coli*
EU	European Union
FAO	Food and Agriculture Organization of the United Nations

FBD	Foodborne Diseases
FDA	United States Food and Drug Administration
FERG	Foodborne Disease Burden Epidemiology Reference Group
FOS	[WHO] Department of Food Safety, Zoonoses and Foodborne Diseases
GBD	Global Burden of Disease
GBD2010	Institute of Health Metrics and Evaluation Global Burden of Disease Study, 2010.
GBS	Guillain-Barré Syndrome
GEMS	Global Environment Monitoring System
GFN	Global Foodborne Infections Network
HALE	Health-Adjusted Life Expectancy
HAV	hepatitis A virus
HBV	hepatitis B virus
HCC	Hepatocellular Carcinoma
HUS	[STEC] haemolytic uraemic syndrome
IARC	International Agency for Research on Cancer
IHME	Institute of Health Metrics and Evaluation
iNTS	Invasive non-typhoid salmonellosis
JECFA	Joint FAO/WHO Expert Committee on Food Additives
KT	Knowledge Translation
KTPG	Knowledge Translation and Policy Group
LE	life expectancy
LOS	Lipo-oligosaccharides
MAR	“missing at random”
MAL-ED	Interactions of Malnutrition & Enteric Infections: Consequences for Child Health and Development
MDG	Millennium Development Goal(s)
NBD	National Burden of Disease
NCC	Neurocysticercosis
NGO	non-governmental organization
NTP	National Toxicology Program
NTS	Non-typhoidal *Salmonella enterica*

OIE	World Organisation for Animal Health
PAF	population attributable fraction
PAHO	Pan American Health Organization
PCB	Polychlorinated Biphenyl
PCR	polymerase chain reaction
PDTF	Parasitic Diseases Task Force
RfD	Reference Dose
RIVM	The Dutch National Institute for Public Health and the Environment
SA	Source attribution
SATF	Source Attribution Task Force
SPS	[Agreement on the Application of] Sanitary and Phytosanitary Measures [of the WTO]
STEC	Shiga toxin-producing *Escherichia coli*
TF	task force
TWI	Tolerable Weekly Intake
UI	uncertainty interval
UN	United Nations
UNEP	United Nations Environment Programme
UNICEF	United Nations Children's Funds
US EPA	United States Environmental Protection Agency
USA	United States of America
USDA	United States Department of Agriculture
WHA	World Health Assembly
WHO	World Health Organization
WTO	World Trade Organization
YLD	years lived with disability
YLL	years of life lost

This report presents the first global and regional estimates of the burden of foodborne diseases. The large disease burden from food highlights the importance of food safety, particularly in Africa, South-East Asia and other regions. Despite the data gaps and limitations of these initial estimates, it is apparent that the global burden of foodborne diseases is considerable, and affects individuals of all ages, particularly children <5 years of age and persons living in low-income regions of the world. By incorporating these estimates into policy development at both national and international levels, all stakeholders can contribute to improvements in safety throughout the food chain. These results will also help to direct future research activities.

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