WHO Initiative to Estimate the Global Burden of Foodborne Diseases

Fifth formal meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG)

8-12 April 2013, Geneva, Switzerland

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OF FOOD SAFETY
AND ZOONOSES

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WHO Library Cataloguing-in-Publication Data :

WHO initiative to estimate the global burden of foodborne diseases: fifth formal meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG), 8-12 April 2013, Geneva, Switzerland.

1.Food Contamination. 2.Foodborne Diseases - epidemiology. 3.Cost of Illness.
I.World Health Organization.

ISBN 978 92 4 150796 7 (NLM classification: WA 701)

Printed in Switzerland

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Acknowledgments

The Department of Food Safety and Zoonoses (FOS), World Health Organization (WHO), Geneva, Switzerland, wishes to express its sincere thanks to all those who contributed towards the success of this meeting.

First and foremost we wish to thank all participants for their valuable technical input and their collegiality during the meeting. We are particularly grateful to Dr Arie Havelaar for his outstanding chairmanship of this meeting, as well as to the Chairs of the FERG Task Forces – Dr Fred Angulo, Dr Herman Gibb, Dr Tine Hald, Dr Robin Lake and Dr Paul Torgerson, for their excellent leadership. A very special thanks goes to Juanita Haagsma for her diligent and excellent rapporteuring of the meeting as well as to Chrystelle Daffara for leading the administrative arrangements.

Acronyms and abbreviations used in this document

CDC	Centers for Disease Control and Prevention (of the USA)
CHERG	Child Health Epidemiology Reference Group
CSTF	Country Studies Task Force
CTF	Computational Task Force
CTTF	Chemicals and Toxins Task Force
DALY	disability-adjusted life year
EDTF	Enteric Disease Task Force
EFSA	European Food Safety Authority
EPEC	enteropathogenic Escherichia coli
ETEC	enterotoxigenic Escherichia coli
FBD	foodborne disease
FERG	Foodborne Disease Burden Epidemiology Reference Group
GBD	Global Burden of Disease
GEMS	Global Environment Monitoring System
GFN	Global Foodborne Infections Network
GFR	glomerular filtration rate
GUI	graphic user interface
IHME	Institute of Health Metrics and Evaluation
IQ	intelligence quotient
KTPG	Knowledge Translation and Policy Group
MAL-ED	Interactions of Malnutrition & Enteric Infections: Consequences for Child Health and Development
PDTF	Parasitic Diseases Task Force
SATF	Source Attribution Task Force
SD	standard deviation
STEC	Shiga-toxin-producing Escherichia coli
TF	task force
WHO	World Health Organization
YLD	years lived with disability
YLL	years of life lost

Declarations of Interest

All experts and resource advisers invited to participate in the meeting completed beforehand the WHO standard form for declaration of interests. At the start of the meeting, all participants were asked to confirm their interests, and to provide any additional information relevant to the subject matter of the meeting. No conflicts of interest were identified.

Definitions

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 and the years lived with disability 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.

The table below shows the main elements that are needed to arrive at burden estimates expressed in DALYs.

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”(1). The definition includes all bottled drinks.

1. Introduction

This report summarizes the discussions during the fifth meeting of the Foodborne Disease Burden Epidemiology Reference Group (FERG) on 8–12 April 2013, and related meetings, at the World Health Organization (WHO) Headquarters in Geneva, Switzerland. This was the final meeting of the entire FERG and it is envisioned that the foodborne burden of disease estimates will be released in 2015. The participants are listed in Annex 1.

Dr Kazuaki Miyagishima, Director, WHO Department of Food Safety and Zoonoses, opened the meeting. Professor Arie Havelaar reviewed the history of FERG since its inception in 2006, and outlined the aims of the current meeting (FERG5). Dr Rob Lake presented the agenda.

1.1 Objectives of the meeting

The objectives of the meeting were:

- to present the final results of the systematic reviews commissioned by the task forces on enteric diseases, parasitic diseases and chemicals and toxins;
- to develop preliminary estimates of the global and regional burden of foodborne disease (FBD), through joint discussions between the hazard task forces and the Computational Task Force (CTF); and
- to review the status of country studies and identify additional tools and training resources for situation analysis and knowledge translation.

2. Objectives and organizational structure of FERG

2.1 Objectives of FERG

FERG acts as an advisory body to WHO on global epidemiology of foodborne diseases. FERG was established in 2006, at which time foodborne disease was not included as a risk factor in the Global Burden of Diseases Study.

The objectives of FERG are to:

- assemble, appraise and report on estimates of the current, projected and averted burden of foodborne disease;
- conduct epidemiological reviews of the mortality, morbidity and disability associated with each of the major foodborne diseases;
- devise models for the estimation of FBD burden where data are lacking;
- develop source attribution models to estimate what proportion of each disease is foodborne; and, most importantly
- use the devised models to develop user-friendly tools for studies of burden of foodborne disease at country level.
- Furthermore, the initiative aims to:
- strengthen the capacity of countries to assess burden of foodborne disease and encourage countries to undertake a study of burden of foodborne disease;
- encourage countries to use burden of foodborne disease estimates to set evidence-informed policies;
- provide estimates of the global burden of foodborne diseases, according to age, sex and region, for a defined list of causative agents of microbial, parasitic, and chemical origin.

In estimating the global human health burden, expressed in disability-adjusted life years (DALYs), FERG has considered microbial, parasitic, and chemical contamination of food, and has specifically focused on diseases whose incidence and severity are thought to be high and on pathogens and chemicals that are most likely to contaminate food and that are preventable. Initially, FERG was intended to be a 5-year project, from 2007 to 2012. The current aim of FERG is to publish the estimates of the global burden of foodborne disease in 2014.

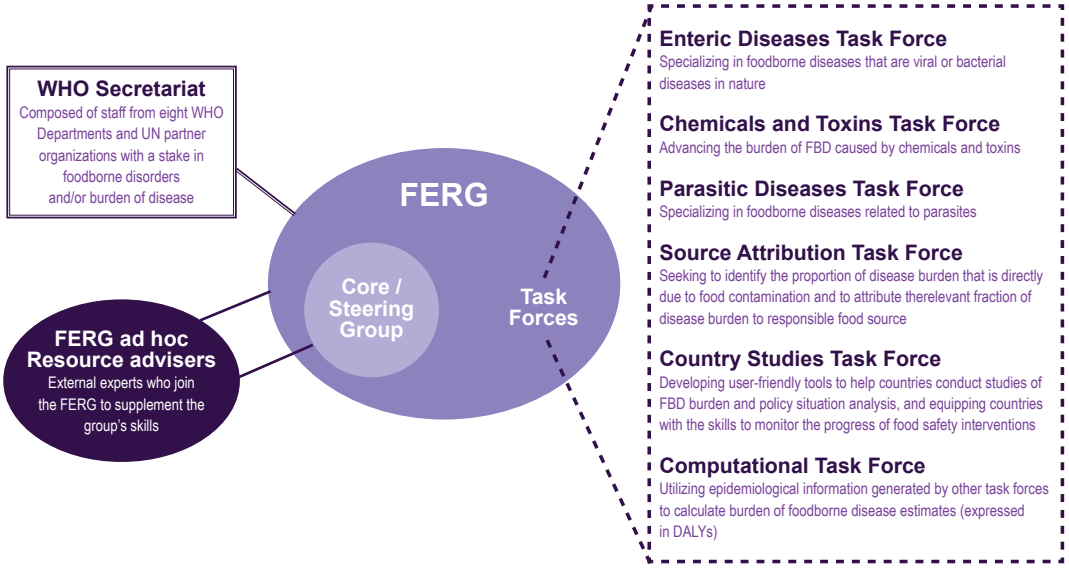
2.2 Organizational structure of FERG

FERG consists of: a Core (or Steering) Group, which coordinates and oversees the scientific work; six thematic task forces, which work in specific areas, as shown in Figure 1; and external resource and technical advisers, who are invited on an ad hoc basis to provide specific expertise.

In March 2012, the sixth task force – the Computational Task Force – was established, with the overall aim of advising and assisting WHO in converting into DALYs the results

of (a) the global epidemiological reviews of mortality, morbidity and disability associated with each of the major foodborne diseases, and (b) the epidemiological data resulting from the FERG country studies.

Figure 1. Organizational structure of FERG



3. Global Burden of Disease Study 2010

In December 2012, the results of the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) were published (2) This study estimated the burden of premature death and disability due to 291 diseases and injuries, 1160 sequelae, and 67 risk factors, for 20 age groups and both sexes, in 1990, 2005 and 2010. Estimates were produced for 187 countries and 21 regions.

The GBD 2010 estimates are not official WHO estimates, but this does not mean that they cannot be used by WHO programmes. However, the Organization has concerns about the results, particularly for the WHO priority diseases, such as human immunodeficiency virus (HIV) infection and malaria. WHO will continue to produce its own estimates for these diseases, which will be less detailed than the GBD estimates. WHO intends to produce regular updates of causes of death, with the next one expected by the end of 2013. Furthermore, WHO will continue to estimate DALYs. There is a clear consensus that the burden of disease concept and the DALY metric are useful and important for some programmes. For estimates of years lived with a disability (YLD), WHO will draw on GBD estimates, except when there is reason to believe that the estimates are not valid or improved models are available. WHO will not revise all the GBD 2010 estimates, but will revise estimates for certain diseases, particularly environmental diseases.

The estimates of WHO and GBD 2010 for total diarrhoeal disease are comparable, but there are differences in distribution by etiology. A group should be formed to discuss the reasons for the differences and consistency checks should be made if possible. The official WHO estimates should be updated by the end of 2013.

WHO has advised that DisMod-MR, the software that was used for burden of disease analysis for regional, national and subnational populations in GBD 2010, should not be used for FERG estimates, because it is undocumented and not in the public domain.

New disability weights were derived for GBD 2010. WHO considers that these disability weights are generally consistent, although those for sensory impairments are very low in comparison with previously derived disability weights. WHO recommends using the GBD 2010 disability weights, unless there is a good reason not to, e.g. if there is a discrepancy between the health states included in the epidemiological data and the health states reflected by the disability weight. There will be a follow-up of the disability weight Internet survey in 2013 to validate the GBD 2010 disability weights.

4. Enteric Disease Task Force

Initially, the Enteric Disease Task Force (EDTF) planned to estimate the burden of disease associated with 30 enteric agents. However, during the FERG meeting in Albania in 2011, it was decided to focus on 18 priority agents.

The EDTF held a meeting immediately prior to FERG5, in order to:

- discuss the status of the systematic reviews of enteric diseases;
- review, modify, simplify and reach agreement on the disease models of the agents;
- liaise with the Computational Task Force to discuss how to proceed for each of the agents;
- consult the Source Attribution Task Force to discuss the expert panels.

4.1 Diarrhoeal diseases and sequelae

The project on Interactions of Malnutrition & Enteric Infections: Consequences for Child Health and Development (MAL-ED) and the Global Enteric Multicenter Study may have additional information on the fraction of diarrhoeal cases that can be attributed to certain agents, and on the existence of other sequelae; this should be followed up (3, 4).

The EDTF decided that, with a few exceptions, diarrhoeal diseases have moderate illness as an outcome (i.e. infections would not be divided into mild, moderate and severe). The exceptions are Salmonella infection (which includes invasive infections), Shiga-toxin-producing Escherichia coli (STEC) (which includes haemolytic uraemic syndrome (HUS) and end-stage renal disease (ESRD)), and Campylobacter infection (which includes Guillain-Barré syndrome). Furthermore, the EDTF simplified the models of diarrhoeal diseases, to exclude reactive arthritis, inflammatory bowel disease and irritable bowel syndrome, because data on these outcomes are scarce, particularly in low-resource countries.

4.1.1 *Campylobacter*

The disease model of *Campylobacter* has been simplified. The health outcomes now included are diarrhoea and Guillain-Barré syndrome. In order to estimate the incidence of Guillain-Barré syndrome, an estimate of all Guillain-Barré cases will first be constructed and subsequently the number of cases due to *Campylobacter* will be estimated. A systematic review has been performed on the association between *Campylobacter* and Guillain-Barré syndrome (5). Several items of work related to this issue, including the global estimate of Guillain-Barré syndrome and the fatality rate for Guillain-Barré syndrome, will be followed up.

To estimate the burden of disease, data on duration, severity and case-fatality in low- and high-income settings are needed, as well as on residual symptoms.

4.1.2 Typhoid and paratyphoid fever

A review and critique of alternative estimates of typhoid and paratyphoid fever were presented during the meeting of the EDTF. The methods and results of three studies of typhoid or paratyphoid fever were summarized and critically reviewed : (1) Johns Hopkins University 2010 (6); (2) International Vaccine Institute 2010 (7) and (3) the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease Study 2010 (2). All the approaches had strong points and shortcomings, but on balance the GBD 2010 approach was recommended, despite the opacity of its methods. The task force agreed to adopt the GBD 2010 typhoid estimates, but will consult the WHO typhoid group to determine if they have any potential concerns. IHME will need to be contacted to provide estimates of incidence.

4.1.3 Non-invasive and invasive Salmonella infection

Invasive *Salmonella* infection has very different symptoms from non-invasive infection. After some discussion, the Task Force decided that severe acute infectious disease is a good proxy for invasive Salmonella. The EDTF decided to combine the *Salmonella* estimates from the commissioned study by Pires, which includes the estimates of the Child Health Epidemiology Reference Group (CHERG), with those generated from a systematic review on invasive salmonellosis by Crump and Ao (unpublished work). Crump has agreed to provide recommendations on appropriate disability weights and case-fatality rate for invasive salmonellosis.

There are co-morbidity issues related to invasive salmonellosis, malaria and HIV infection. It is not clear how deaths associated with this situation should be counted. Should all deaths be counted as invasive salmonella deaths? Or should there be a correction for co-morbidities by, for instance, comparing the figures with those for AIDS deaths in areas where invasive salmonellosis is less significant? This may also be an issue for other agents, and a consistent approach is needed.

Separate source attribution for invasive and non-invasive salmonellosis is not needed.

4.1.4 *Mycobacterium bovis*

To arrive at estimates for the burden of *Mycobacterium* bovis infection, the EDTF will use WHO estimates of human tuberculosis, and assume that approximately 1% (or exact value to be taken from the systematic review) of tuberculosis cases are caused by *M. bovis* and that 100% of those are foodborne. The assumption of 1% *M. bovis* infections is likely to be conservative. However, because of difficulties associated with microscopy and culture of *M. bovis*, this is appropriate at this point. The next step is to obtain a list of *M. bovis*-free countries from the World Organisation for Animal Health.

4.1.5 Brucellosis

The systematic review of brucellosis by Dean et al. (8) gives the incidence of brucellosis in various countries. These data will be transferred to the CTF for imputation. The US Centers for Disease Control and Prevention (CDC) will be consulted to explore the possibility of using alternative approaches to extrapolation to generate additional estimates and check the validity of the results produced by the CTF imputation. If the CDC project

is not feasible, colleagues from both CDC and WHO are willing to review the estimates generated by the CTF. Currently there is no disease model for brucellosis, but the EDTF will provide such a model within two months.

4.1.6 *Listeria*

A systematic review and a multilevel meta-analysis were conducted to calculate incidence of listeriosis and distribution of outcomes by WHO subregion and by age group. So far, the incidence of listeriosis has been calculated for 7 of the 14 WHO subregions and work is continuing. If estimates cannot be obtained for all WHO subregions, only well established, published national estimates will be used (e.g. from the USA, Canada and various countries in Europe). Countries with no estimates will be left out of further calculations. This fallback position will ensure that listeriosis is not completely ignored, while at the same time avoiding unjustifiable extrapolations that might detract from the message.

In the coming months the EDTF will collect information from the countries that have well established estimates for listeriosis. It will also collect less well validated data from other countries and try to extrapolate them. Furthermore, resource advisers will consult with the WHO Meningitis Group to explore if the CHERG estimates of meningitis deaths and cases can be used to estimate those associated with Listeria. The health outcomes of *Listeria* infection are septicaemia and meningitis. Meningitis may also cause residual disability, such as hearing problems and cognitive impairments. A variable case-fatality rate for meningitis will be used for developed and developing countries, and a strategy will need to be devised to ascertain these case-fatality rates. Expert elicitation is not needed for attribution of listeriosis, because it is 100% foodborne; attribution to food type will be included in the expert attribution study.

4.1.7 STEC

The STEC disease model includes diarrhoeal disease, haemolytic uraemic syndrome and end-stage renal disease. Proxy disability weights are needed for haemolytic uraemic syndrome. Data are also needed on duration, severity and case-fatality in high- and low-income settings, for both haemolytic uraemic syndrome and end-stage renal disease. For the calculation of the burden of disease due to ESRD, countries will be divided according to whether the population has good or poor access to health care. Without health care, a patient with ESRD will die. With health care, there will be a long-term impact on health-related quality of life that is difficult to assess. There are ESRD models from the Netherlands and the USA.

The probability of developing haemolytic uraemic syndrome is different for different types of STEC, and the distribution of STEC types varies by region. A systematic review of STEC has been performed, and will provide data on incidence, and the numbers of cases of acute illness, HUS, ESRD, and deaths. It is not clear how the other data will be obtained.

4.1.8 Bacterial toxins

The EDTF decided not to remove toxins from the list of hazards being considered at this point, since doing so might mean that they would be neglected in the future. The EDTF

will attempt to collect and compile all readily available incidence data on intoxications from countries and subsequently explore if the CTF imputation tool can be used. CDC will conduct a quick systematic review to compile existing incidence data on toxins. The burden of disease associated with toxins will probably be reported only for the countries that have readily available estimates.

4.1.9 Hepatitis A

Tim Nguyen (WHO) and David Rein (University of Chicago) were consulted about GBD estimates related to hepatitis A. Concerns were raised about the transparency and repeatability of the GBD estimates. The WHO Hepatitis Group is currently generating estimates using alternative approaches. FERG will use the WHO results, which are expected to be available by early June. The final results should be published by September, which will mean that the estimates can be officially used by FERG, since they will have been peer-reviewed.

4.1.10 Norovirus

A systematic review of norovirus has been conducted by Hall et al. (unpublished work). During the EDTF meeting, it was decided that the norovirus estimates will not be corrected for isolation of norovirus from control samples. During FERG5, no key additional points or issues were identified.

The EDTF proposes to commission the Danish National Food Institute (DTU Food) to estimate the global incidence and mortality of diarrhoeal diseases caused by 11 foodborne hazards (eight enteric diseases and three parasitic diseases).

The project has the following overall objectives:

- to estimate the global and regional incidence and mortality of diarrhoeal disease caused by the agents *Shigella, Campylobacter, Salmonella, enterotoxigenic E. coli* (ETEC), *enteropathogenic E. coli* (EPEC), *Vibrio cholerae*, norovirus, "unknown diarrhoeal agents", *Cryptosporidium, Giardia lamblia* and amoebae in children under 5 years of age; and
- to estimate the global and regional incidence and mortality of diarrhoeal disease caused by the same agents in the population aged 5 years and over.

To accomplish these objectives, site visits will take place at the Nutritional Research Institute in Lima, Peru, and the Johns Hopkins University in Baltimore, Maryland, USA. The work will be performed between 15 April 2013 and 1 October 2013.

The deliverables of the commissioned work are:

1. a list of studies on the etiology of diarrhoea episodes and deaths in children under five years of age;
2. a list of studies on the etiology of diarrhoea episodes and deaths in older children, adolescents and adults;
3. country-level estimates of the proportion of diarrhoea episodes and deaths caused by the 11 named foodborne hazards in children under 5 years (to be delivered to the CTF);

4. regional estimates of the proportion of diarrhoea episodes and deaths caused by the 11 named foodborne hazards in children under 5 years;
5. country-level estimates of the proportion of diarrhoea episodes and deaths caused by the 11 named foodborne hazards in the population aged 5 years and over (to be delivered to the CTF);
6. regional estimates of the proportion of diarrhoea episodes and deaths caused by the 11 named foodborne hazards in the population aged 5 years and over;
7. a list of references and extracted information on the duration of diarrhoea episodes (to be discussed by the EDTF).

4.2 Meeting between the EDTF and the CTF

A meeting was held between the EDTF and the CTF, during which the EDTF explained the five categories of calculation for the enteric agents (Table 1).

- The first category concerns typhoid, for which existing GBD estimates will be used. The GBD 2010 study calculated DALYs based on prevalence data. However, FERG will base its DALY estimates on incidence data. As a result, GBD prevalence estimates will need to be converted to incidence estimates, and the EDTF will determine the best approach to convert prevalence DALYs to incidence DALYs. Furthermore, GBD information on deaths and the age distribution of death will be used. It is expected that IHME will have information on the latter.
- The second category concerns STEC, Listeria and invasive *Salmonella*. For these agents, hierarchal models are constructed on the basis of a systematic review, to arrive at estimates for each of the 14 WHO subregions. Case-fatality ratios will be derived from the systematic reviews. The age distribution of death is also needed; the ETDF will discuss this further.
- For brucellosis, *Clostridium perfringens, C. botulinum, Bacillus cereus and Staphylococcus aureus,* systematic reviews are not available, and there are only a few data points. The available data will be shared with the CTF, to see if it is possible to impute these data. If imputation is not possible for the toxins, they may not be included in the final FERG estimates. Toxin deaths may be derived from the estimates of GBD and CHERG based on hospital patients. As regards brucellosis, countries that are free of the disease will need to be taken into account. Mortality due to brucellosis will be assessed using case-fatality ratios.
- For *Shigella*, cholera, EPEC, ETEC, *Campylobacter*, norovirus, other diarrhoeal diseases and maybe *Salmonella*, the point of departure for the calculations is the CHERG estimates for diarrhoea episodes. These estimates will be portioned out by etiology for patients aged under and over 5 years. Estimates of disease duration for these pathogens and age distribution of deaths are still needed; estimates of duration of illness will be provided by reviewers currently working on STEC, norovirus and diarrhoeal diseases.
- The fifth category concerns hepatitis A virus and *M. bovis*. For hepatitis A virus, the WHO Hepatitis Group will provide incidence and mortality estimates by region. For *M. bovis*, the WHO Tuberculosis Group will provide estimates of human tuberculosis incidence and mortality by country.

Table 1. Overview of the five approaches to calculation of DALYs for enteric agents

Category	Agent or disease	Approach to arrive at DALY estimates
1	Typhoid fever	Use existing GBD 2010 estimates and convert prevalence to incidence
2	STEC, *Listeria*, invasive *Salmonella*	Use data from systematic reviews and hierarchal modelling
3	Brucellosis, *Clostridium perfringens, C. botulinum, Bacillus cereus, Staphylococcus aureus.*	No systematic review available; use available data points and imputation if possible
4	Non-invasive *Salmonella, Shigella*, cholera, EPEC, ETEC, *Campylobacter*, norovirus and other diarrhoeal diseases	Use CHERG estimates for diarrhoea and portion out by etiology for patients under and over 5 years
5	Hepatitis A virus, M. *bovis*	Use WHO estimates of incidence and mortality for hepatitis A and human tuberculosis

4.3 Meeting between the EDTF and the Source Attribution Task Force (SATF)

4.3.1 Expert panel make-up

The EDTF prefers the expert panels on source attribution to be global rather than regional. These global panels will focus on enhanced regional representation. Also it was pointed out that subpanels would be needed for developed and developing countries.

The following panels were agreed upon:

- a global panel on brucellosis;
- a global panel on hepatitis A;
- a global panel on all other diarrhoeal diseases – developed countries (no typhoid fever); and
- a global panel on all other diarrhoeal diseases – developing countries.

4.3.2 List of pathogens and type of questions for attribution

The list of pathogens for attribution was finalized. The ETDF recommended eliminating the second-level expert attribution because of the change to global panels. It is not likely that it will be possible at this level to tease out specific foods, with an awareness of production systems in specific regions. If second-level attribution cannot be eliminated, then simpler versions of the questions that will be submitted to the expert panels need to be developed; for example, a more general question related to point of contamination for food would be preferable. A potential question is: If you had to eliminate this pathogen in food, what percentage of your effort would you invest in interventions at reservoir, processing, food service and home levels?

It was decided that the second-level attribution would be done for *Campylobacter, Salmonella*, STEC and brucellosis. The specific food types and the point in the chain of contamination are likely to be important.

5. Chemicals and Toxins Task Force

5.1 Cadmium

Exposure to cadmium will be estimated using urinary cadmium levels as biomarker, with a focus on the general population rather than groups from highly contaminated regions. Where such biomarker data are not available, the intake information from the WHO Global Environment Monitoring System (GEMS) database might be used. Cadmium exposure has been associated with several disease outcomes; adverse renal and bone effects were selected for the burden of disease estimates.

- *Renal effects*. Although efforts have been made quantitatively to associate cadmium exposure to biomarkers for tubular dysfunction and albuminuria, there is no disability weight available for these adverse effects. Current scientific understanding of these biomarkers is inadequate to link them quantitatively with ESRD. To estimate the incidence of cadmium-related ESRD, it is feasible to use the dose–response relationship between cadmium exposure and the resulting decrease in the estimated glomerular filtration rate (eGFR) (9). Using the country-specific distribution of eGFR, the incidence rate of stage 4/5 ESRD due to cadmium exposure can be estimated using the distributional shift of GFR.
- *Bone effects (osteoporosis/fractures)*. The relationship between cadmium exposure and osteoporosis has been established. However, there is no disability weight for osteoporosis. Since osteoporosis is a risk factor for fractures, which have disability weights, attempts will be made to estimate the cadmium-attributable incidence of fractures. The dose–response relationship between urinary cadmium levels and bone mass density can be used to obtain country-specific bone mass loss and, where available, the WHO FRAX fracture prediction parameters can be used to link bone mass density with the risk of fracture. WHO FRAX is a tool developed by WHO to evaluate fracture risk (10). Thus, urinary cadmium levels can be used to estimate the risk of fracture. Where such data are not available, an alternative method using the dose–response relationship between cadmium exposure and the risk ratio of fractures will be considered.

5.2 Methylmercury

Mercury intoxication results in many disease outcomes, but the most sensitive is considered to be impaired neurological development of children exposed prenatally, with loss of intelligence quotient (IQ) as endpoint. To estimate the number of methylmercury-induced cases of intellectual disability in the population, an exposure-based approach will be used, with mercury levels in hair or blood as biomarker and a focus on the general population rather than highly exposed subpopulations.

The systematic review identified over 1300 articles from a range of countries and regions with data on mercury levels in hair or blood collated in table format. One study was

selected for each country, using the following criteria: a nationally representative study, general population data, preferably with distribution of values (not a mining community or clinical cases, but a control group in a "hotspot" study could be included), recent survey, preferably measurements on hair, but some studies with blood measures were included (a conversion factor was applied to estimate hair mercury levels).

There is the option to include data from subpopulations in hotspots close to mining or fishing communities; however, exposure in a mining community affects predominantly males and may not be relevant to fetal exposure. In addition, exposure is likely to be to ingested or inhaled elemental mercury, not methylmercury.

Two options for filling data gaps on biomarkers were discussed: (a) using a regression model to link total fish consumption to levels of mercury in hair, using national survey data; or (b) using revised GEMS/Food cluster diets to assign known levels of mercury in hair to other countries in the same cluster for which no data are available.

5.2.1 Prediction of level of intellectual disability from IQ loss

Loss of IQ is not a disease as such; thus, an estimate is needed of the shift in the distribution of people with different degrees of intellectual disability (mild (IQ 50–70); moderate (35–50); severe (20–35); or profound (<20)). There are disability weights for the various degrees of intellectual disability.

To link IQ loss due to methylmercury exposure to the stage of intellectual disability requires data on the percentage of population in each IQ range, and a slope factor linking mercury levels in the hair of pregnant women to IQ loss in their offspring, taking into account the beneficial effects of eating fish as well as the risks, and the uncertainty around hair data. The mercury-associated shift in mild intellectual disability rates can then be predicted using birth rate data, estimating the number of children in each stratum of maternal mercury hair values, and converting these to increments of IQ loss using the slope factor of Axelrad et al. (11). Because decrements in intellectual disability may be compounded by diet, medical care, etc., the CTTF will use WHO adjustment factors for the WHO regions to make regional estimates (12).

5.3 Lead

For lead, an exposure-based approach is used, similar to that for methylmercury. Lead levels in blood will be used as biomarker for young children, and systolic blood pressure for adults. Again, the focus is on the general population rather than highly exposed subpopulations. Lead exposure may result in many disease outcomes, but the most sensitive is considered to be impaired neurological development in children, with IQ loss as endpoint. In adults, the endpoint is cardiovascular disease.

The main sources of lead exposure are soil and dust, paint chips, tapwater and diet. Other potential exposures are from dietary supplements, clay, lime, and cooking pots. For dietary exposure, total diet studies are considered to be the best information source.

There are three such studies that include information on children, in China, Europe and the USA (13, 14). New data on consumption and exposure in Europe are also available from the European Food Safety Authority (EFSA) (14).

To predict intellectual disability from IQ loss in young children, the shift in degrees of intellectual disability will be estimated (see the discussion on methylmercury, section 5.2). Because the estimates are largely independent of non-dietary exposures to lead, a bilinear dose–response model is best for converting lead levels in blood to IQ loss.

To predict cardiovascular disease from biomarker data for adults, lead levels in blood will be converted to systolic blood pressure using known slope factors. Using data on blood pressure, the relative risk slopes for three types of cardiovascular disease – ischaemic heart disease, cerebrovascular disease (stroke) and hypertensive disease – can be calculated for four age groups (15–44, 45–59, 60–69 and 70–79 years). Death rates from cardiovascular disease are needed to convert current relative risk to incidence of cardiovascular disease due to lead exposure, and to identify relevant disability weights for the three cardiovascular disease types.

5.4 Peanut allergens

There are three types of data on peanut allergy: self-reported, IgE prick test results and food challenge data. It was agreed to use self-reported data to estimate prevalence, since these are available for more countries.

Incidence rates will be derived for countries with data, on the assumption that incidence rates are equivalent to prevalence rates (once peanut allergy occurs in a young child it is expected to be lifelong). The CTTF discussed how data could be extrapolated to countries and regions with no data. One option is to refer to the International Study of Asthma and Allergies in Childhood (ISAAC) (which covers over 100 countries) (15). There is not sufficient time or resources to do additional analytical work on serum samples to determine the proportion with peanut allergy. However, it would be possible to use the ISAAC figures for the proportion that were deemed to be sensitized (which would include other allergies, asthma, rhinitis and eczema) and apply a standard proportion to derive an estimate of the percentage with peanut allergy.

There are disability weights that could be used for peanut allergy and anaphylactic shock.

5.5 Dioxins

A body burden approach will be taken for dioxins. Dioxin levels in breast milk will be used as a marker of body burden. The approach will focus on women of childbearing age. Dioxin exposure may have many adverse outcomes, but the most sensitive are changes in thyroid function and reproductive toxicity (prenatal effect on development of male reproductive organs and postnatal disturbances of sperm count). Exposure to high levels of

dioxin may result in an increased risk of cancer, but this will not be covered in the burden of disease estimates, since dioxin exposure through the food supply is believed to be below the level associated with an increased risk of cancer.

Results of surveys of dioxin levels in breast milk are available from WHO for many countries for 2000–2010, but these data represent pooled samples. Data from European countries suggest that dioxin levels in breast milk may have decreased with time. It was decided to estimate the body burden for various countries on the basis of the geometric mean for breast milk ± 1.5 standard deviations (SD) and the geometric mean for blood ± 2.0 SD (actual body burden). The estimations of standard deviation are based on individual breast milk and blood data from various countries.

An estimate of the human dioxin body burden that results in a 5% loss of sperm count following prenatal exposure was derived from dose–response modelling of animal data with extrapolation to humans (reference body burden). The reference body burden was then compared with the actual body burden to estimate the percentage of pregnant women with a body burden that would result in a 5% sperm count reduction in their offspring. However, a 5% reduction in sperm count is of clinical importance only if it reduces the sperm count below the cut-off point for impaired fertility (taken as 20 million per ml). The percentage of pregnant women with a body burden that would result in impaired fertility in their offspring was then calculated (P_{if}). This probability serves as the starting-point for the DALY calculation, assuming that impaired fertility leads to primary infertility.

Similarly, an estimate of the human dioxin body burden resulting in a 5% loss of total T4 (TT4) hormone in the blood of women of reproductive age was derived from dose–response modelling of animal data with extrapolation to humans. This reference body burden was compared with the actual body burden that results in a 5% reduction in TT4 level. However, a 5% reduction in TT4 level is of clinical importance only if it reduces the TT4 level below the cut-off point for impaired thyroid functioning (taken as the $P_{0.05}$ of the human TT4 blood level). The percentage of the population of women of reproductive age with a body burden that would result in impaired thyroid functioning was calculated (P_{thy}). This probability serves as the starting-point for the DALY calculation, assuming that impaired thyroid functioning leads to hypothyroidism.

The calculated percentages, P_{if} and P_{thy}, will be combined with demographic data to estimate country-specific prevalence and incidence rates for impaired fertility and hypothyroidism.

5.6 Arsenic

Biomarkers of arsenic typically include urinary arsenic (adjusted for urinary creatinine), and toenail arsenic. Urinary arsenic level is a biomarker of recent arsenic exposure, while toenail arsenic levels reflect exposure to arsenic over a longer duration (usually months). Since single doses of arsenic are rapidly and extensively cleared from the blood via the

kidneys, blood arsenic concentrations have been considered to reflect only recent exposure. However, arsenic concentration in blood can be used as a biomarker to measure the steady-state concentrations produced by chronic and continuing exposure.

An exposure-based approach will be taken to assess the number of cases of arsenic poisoning. Selected disease outcomes are bladder, lung and skin cancers. These three cancer endpoints are the health effects that are best documented in the scientific literature. Although there is growing evidence of an association between arsenic exposure and an increased risk of liver cancer, this is not included in the current assessment. Cardiovascular disease has also been linked to arsenic exposure (16), but including cardiovascular disease as outcome would require additional work.

The main pathways of exposure to arsenic are via water and food, with systemic accumulation of arsenic from soil and from water used in food preparation. There are many effects on body functions. Some studies have reported an interaction between smoking and arsenic exposure, leading to bladder and lung cancers. Folate deficiency is also a cofactor in the incidence of cancers. As the level of deficiency increases, adverse health effects increase, but there is not enough information to quantify the relationship with arsenic. Increased selenium in the diet tends to decrease the incidence of skin lesions, but this effect has also not been quantified.

Dietary exposure to inorganic arsenic will be estimated using the 13 GEMS/Food cluster diets, together with lower and upper bound concentration levels reported by EFSA; conversion factors for different foods will be taken from the literature.

Cancer prevalence rates will be estimated by combining exposure to arsenic in food with a cancer slope factor. Cancer slope factors may be used to estimate the risk of cancer associated with exposure to a carcinogenic. For each cancer, age-specific incidence rates will be calculated for males and females. It was noted that arsenic exposure increases the risk of reaction to other potential carcinogens, and that the incidence of related cancers increases with age.

5.7 Cyanogenic glycosides

An exposure-based approach is taken for cyanogenic glycosides. The selected disease outcome is paraparesis occurring in konzo-affected populations. Evidence is available for only five countries in sub-Saharan Africa. Some acute cyanide poisoning has been reported for other regions, but the information is not sufficient for assessment. The CTTF discussed whether impaired neurocognitive function should be included as a disease outcome. However, the one study that provided some evidence for this link in one country (17) had an inadequate sampling frame. It was therefore agreed not to include incidence of impaired neurocognitive function in the burden of disease estimates.

Linamarin is a cyanogenic glycoside found mainly in cassava, with high levels in bitter cassava and very low levels in sweet cassava. Three factors are likely to result in a high

rate of konzo: dependence on bitter cassava in the diet, a lack of legumes and meat in the diet, and living conditions that increase the probability of incorrect preparation of cassava, especially bitter cassava. The available data for five African countries will be extrapolated to other African countries that have similar consumption levels of cassava, legumes and meat, to estimate the incidence of konzo-related paraparesis. It was noted that the consumption levels used in the extrapolation exercise are national per capita levels. It is therefore possible that specific groups in other African and non-African countries may have similar dietary patterns that are not reflected in the national figures.

See Table 2 for an overview of biomarkers and selected disease outcomes for each agent.

Table 2. Overview of biomarkers and selected disease outcomes for each agent

Agent	Biomarker	Disease outcomes
Cadmium	Urinary cadmium levels	Renal dysfunction and bone effects (osteoporosis, fractures)
Methylmercury	Hair/blood mercury levels	IQ loss
Lead	In children: blood lead levels In adults: systolic blood pressure	In children: IQ loss In adults: cardiovascular disease
Peanut allergens	-	Peanut allergy and anaphylactic shock
Dioxin	Breast milk dioxin levels	Thyroid dysfunction and reduced sperm count
Arsenic	Urinary and toenail arsenic levels	Bladder, lung and skin cancers. Possibly cardiovascular disease
Cyanogenic glycosides	-	Konzo

6. Parasitic Diseases Task Force

The list of parasites examined by the Parasitic Diseases Task Force (PDTF) was reviewed and the need for additional commissioned work was discussed. For the parasites for which the work has been completed, the PDTF discussed what data had to be extracted for the CTF database templates. A review of the available data revealed a conflict between the FERG data and the GBD 2010 data for some of the parasites.

6.1 Foodborne trematodes

The results of the GBD 2010 study (2) will be used for foodborne trematodes (*Fasciola, Clonorchis, Opisthorchis*). The work for GBD 2010 was undertaken in collaboration with FERG. The paper by Fürst et al. reports 665 000 DALYs, whereas GBD 2010 reports 1.8 million DALYs, despite being based on the same dataset (18). The reasons for this discrepancy are not clear. The results of the paper need to be discussed and the data carefully analysed; the PDTF will contact the authors of the paper to obtain the raw data.

6.2 Echinococcosis

A report on echinococcosis estimates provided by IHME was reviewed by the PDTF. Many of the figures, such as the incidence totals for Eastern and Western Europe, are questionable. For alveolar echinococcosis, raw data are available from work commissioned by FERG. These data include public health data (published and unpublished), data from hospital records and published data from, for example, Russian government records and Chinese surveillance. There are also surveillance data of 20 000–30 000 Tibetans in highly endemic areas and natural history models.

The PDTF recommends that these commissioned data be used rather than the GBD 2010 data for alveolar echinococcosis. The data will be provided to the CTF.

A review of cystic echinococcosis by Budke et al. has been published (19). The data from this review are reasonably complete, although it is not clear what the data gaps are, i.e., which countries have no cases and which countries have no data. PDTF will contact Dr Budke to request the data on cystic echinococcosis in order to complete the CTF template.

6.3 Cysticercosis

The commissioned work on cysticercosis has resulted in the publication of two papers (20, 21). The first deals with the sequelae of cysticercosis, while the second addresses neurocysticercosis-induced epilepsy. The latter showed that 29% of epilepsy is induced by neurocysticercosis. There are no WHO figures for epilepsy, so this percentage will be

applied to the GBD 2010 epilepsy figures and adjusted for high-income countries and for people who do not eat pork.

The PDTF met with Dr Tarun Dua from the WHO Epilepsy Team to discuss WHO figures on epilepsy. Country-specific data on epilepsy are not available. WHO currently accepts the GBD 2010 epilepsy data. A systematic review is being carried out by WHO, but the data are not yet publicly available.

With the epilepsy data, the proportion of neurocysticercosis-induced epilepsy and information on other syndromes associated with neurocysticercosis from the commissioned work, the PDTF can fulfil the data requirements for cysticercosis.

6.4 *Trichinella*

A systematic review on *Trichinella* has been performed (22). CTF has extracted the data on incidence and will fill in the CTF database.

6.5 Anisakiasis

The results of the GBD 2010 study (2) will be used for anisakiasis.

6.6 Toxoplasmosis

The review on congenital toxoplasmosis is finished and will be published in the *Bulletin of the World Health Organization* (23). The review looked at several sets of data on seroconversion. Globally, there are an estimated 1.5 cases of toxoplasmosis per 1000 births. Incidence has been estimated for every country. The PDTF has already submitted data on congenital toxoplasmosis to the CTF.

Source attribution still needs to be carried out for all forms, as well as a systematic review of non-congenital forms.

6.7 Ascariasis

FERG had not contracted researchers for ascariasis as it had been agreed that FERG would wait for the GBD 2010 estimates. Ascariasis infection is common but associated mortality is low; GBD 2010 estimated 2700 deaths per year due to ascariasis. Thus the burden of ascariasis consists largely of YLDs. The disability weight used in GBD 2010 to estimate the burden of ascariasis was 0.012, which pertains to mild abdominal discomfort. The PDTF suggests adding a more severe disability weight to a proportion of cases.

The PDTF discussed a systematic review to assess the proportion of ascariasis that is

acquired through food. Because the PDTF has concerns about the prevalence YLDs of GBD 2010, it is proposed to discuss with the CTF the use of GBD 2005 figures.

6.8 Intestinal protozoa

The intestinal protozoa *Cryptosporidium, Giardia and Entamoeba* were covered in a review. The few available studies on sequelae of these intestinal protozoa found that sequelae of *Cryptosporidium and Giardia* are not very severe. Good prevalence data are available, stratified by age, sex and region. The PDTF needs to convert these data to incidence of disease (not of infection). Input is needed from CHERG, since incidence of disease is higher in younger age groups and the estimates need to fit in the overall estimates for diarrhoea episodes, morbidity and mortality (imputed using Bayesian methods).

To estimate incidence, inpatient proportions have to be derived by pathogen and applied to the overall diarrhoea estimates provided by CHERG (through the EDTF).

7. Source Attribution Task Force

FERG is charged with developing models of the causes of foodborne illness as well as incidence estimates. The challenge of limited data is even more severe in causal modelling than in modelling of disease incidence, and expert judgement must be used to inform the modelling. Often in such situations, modellers make these judgements informally, as part of model development.

Expert elicitation is a formal, systematic and transparent method for synthesizing expert judgement about uncertain parameter values where data are limited but there is a basis for developing an informed professional judgement about the values. FERG commissioned an expert elicitation study to provide parameter estimates and uncertainty bounds where the available data are not adequate to allow direct estimation of the parameters needed to model the causes of foodborne illness. The present meeting assessed the progress of the study.

A presentation was given, providing an overview of the use of expert elicitation in risk modelling and the elicitation designed for FERG. The guidance of FERG was sought regarding the design of the study. The presentation served as the basis for follow-up meetings at FERG5, during which the elicitation design was finalized.

It is important to note that, for pathway attribution, the point of attribution is the point of exposure; for food attribution, the point of attribution is the point of entry into the household/food setting. The EDTF also proposed to quantify the contribution from major parts of the food production chain by food source (primary production, food processing and preparation by consumer). Not all hazards are introduced or originate from “non-food” pathways. For some hazards, the food is the reservoir (e.g. cassava cyanide and peanut allergens); or the hazard may be formed during processing (e.g. acrylamide or bacterial toxins); and some hazards will be eliminated from the food chain during processing.

The questions of the expert elicitation will be calibrated and pretested to catch language or other issues related to the understanding of the questions. Each thematic task force will identify three people for the pretesting.

7.1 Expert panel make-up

Together with the hazard task forces, the SATF has made decisions about the composition and size of the expert panels (Table 3), and has finalized the list of agents and type of questions for attribution.

Figure 2. The transmission routes included in the expert elicitation

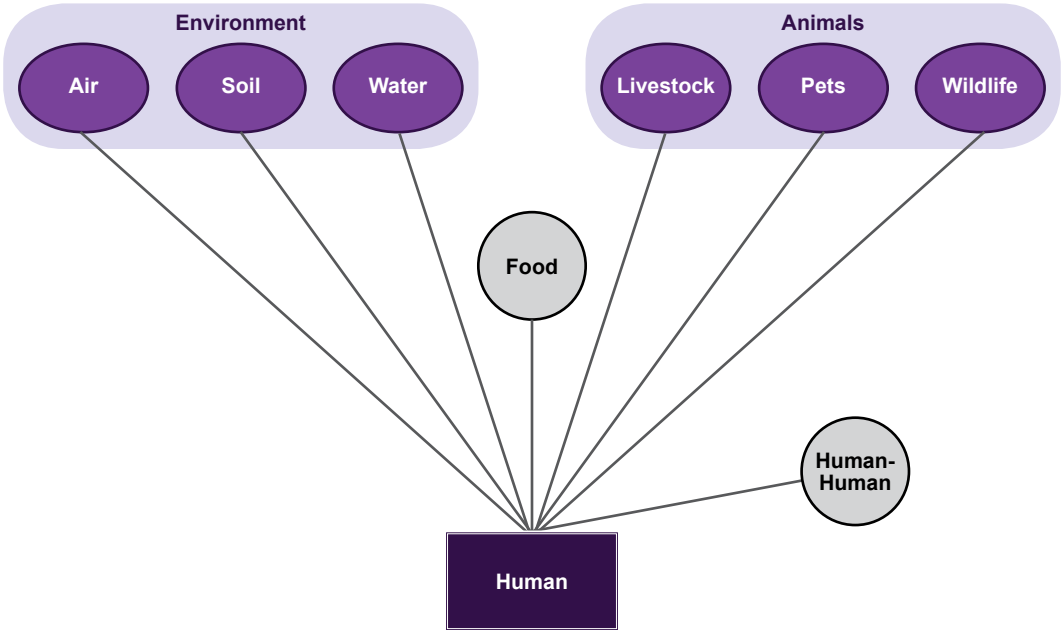


Table 3. Overview of panels, pathway attribution and food attribution per hazard

CTTF	
Panels	Global panel for metals, 10 experts
Pathway attribution	Inorganic arsenic, lead, cadmium
Food attribution	No EE needed; exposure data available
PDTF	
Panels	Global panel for protozoa, 10 experts Global panel for *Echinococcus*, 10 experts Global panel for *Toxoplasma*, 10 experts Global panel for *Ascaris lumbricoides*, 10 experts
Pathway attribution	*Cryptosporidium* spp., *Entamoeba histolytica, Giardia intestinalis, Echinococcus granulosus, Echinococcus multilocularis, Toxoplasma gondii, Ascaris lumbricoides*
Food attribution	*Cryptosporidium* spp., *Entamoeba histolytica, Giardia intestinalis, Echinococcus granulosus, Echinococcus multilocularis, Toxoplasma gondii, Ascaris lumbricoides*

EDTF	
Panels	Global panel for brucellosis, 10 experts Global panel for hepatitis A, 10 experts Other diarrhoeal diseases: One panel for developed countries, 15 experts One panel for developing countries, 15 experts
Pathway attribution	All
Food attribution	All, except heavy metals, *Shigella*, *Vibrio*, norovirus, ETEC, EPEC, *Salmonella*, hepatitis A

7.2 Identification and selection of experts

Experts will be identified and selected using a snowballing process. The first points of contact will be identified through FERG members and other networks, such as the Global Foodborne Infections Network (GFN) and GEMS/Food. These first points of contact will be asked to help identify additional experts who match the selection criteria. The qualifications of each of the identified experts will be reviewed to ensure that they meet the criteria and that geographical representation considerations are met. This process of referral will continue until the desired sample size is reached or an exhaustive list has been compiled. The final selection will be made on the basis of a standardized one-page summary of each expert's experience, including geographical experience, along with a curriculum vitae.

The skills and experience required for members of the panels for enteric and parasitic diseases are as follows.

- Public health specialist, veterinarian, food safety specialist or environmental health specialist, with expertise in food- and waterborne diseases caused by the specific pathogens to be considered.
- Knowledge of existing data on human incidence of enteric or parasitic diseases that can be transmitted by food, of food- and waterborne outbreaks, or of data on prevalence of the relevant pathogens in animals, food, or the environment.
- Knowledge of the important transmission pathways and sources of human infections, obtained for example through practical experience in assessing the epidemiological data mentioned above.
- Commitment to participate in an expert elicitation, providing estimates for the proportion of foodborne diseases attributable to specified hazards, amounting to a one-to-one interview of approximately 2–3 hours, followed by the completion of a questionnaire over a period of 1–2 months.

The skills and experience required for members of the panels for diseases caused by chemicals are as follows.

- Practical experience in reviewing, analysing, and evaluating population-based

exposure data for inorganic arsenic, lead, cadmium, or dioxin, and the environmental exposure routes of these chemicals.

- High standing as an internationally recognized scientist, as evidenced by a publication record, including for example government reports and surveillance reports.
- Commitment to participate in an expert elicitation, providing estimates for the proportion of exposure from different routes for the specified chemicals, amounting to a one-to-one interview of approximately 2–3 hours, followed by the completion of a questionnaire over a period of 1–2 months.

The timeline for the Scientific Judgement Elicitation on Food Attribution of Foodborne Illness Study is shown in Table 4.

Table 4. Timeline for the Scientific Judgement Elicitation on Food Attribution of Foodborne Illness Study

By	Complete
March 2013	Study plan, draft elicitation instrument, draft administration scripts, enteric calibration questions
1 May	Adaptation of instruments to parasites Pre-tests Recruitment of regional study administrators Criteria and frame for recruiting panel members
15 May	Written materials finalized
1 September	Training of regional administrators Identification and recruitment of panel members
1 October	Finalize chemicals elicitation instrument Administration of 1-on-1 sessions with panel members
15 November	Chemicals elicitation Individual elicitations returned to study team
1 December	Data analysis with distributions provided to modellers
28 February 2014	Draft report
30 March 2014	Final report

7.3 Concluding work of the SATF

The concluding work of the SATF will be to compare the results of the Scientific Judgement Elicitation on Food Attribution of Foodborne Illness Study with those of other source attribution studies. For this purpose, the SATF will identify and critically review published source attribution studies conducted for enteric and parasitic diseases and relevant papers, reports and data for chemicals and toxins, and compare these with the expert elicitation study from the same subregion. On the basis of the results, the SATF will discuss the feasibility of integrating the results for certain hazards in certain regions.

8. Computational Task Force

The FERG Computational Task Force was established in March 2012, following a decision made during the FERG Core Group meeting in Durres, Albania, in November 2011. The CTF was created to translate the FERG data on burden of foodborne disease into DALYs.

The CTF is composed of active members and supervisors. Active members are responsible for conducting the different CTF activities, while supervisors provide advice and interact with the other task forces.

8.1 Objectives of the CTF

The CTF has objectives at global level and activities at country level.
The objectives at global level are:

- to assemble and review the data emerging from:
  - systematic reviews by FERG and other WHO advisory bodies,
  - global burden studies (in particular GBD 2005, WHO cause-specific mortality estimates for 2008, and GBD 2010),
  - other relevant literature;
- to create the computational tools to:
  - incorporate uncertainty, derive attribution estimates and aggregate different regional datasets (from WHO, GEMS, etc.),
  - develop and use modelling approaches to address missing data;
- to perform the global and regional calculations and generate the output DALYs for FERG, in interaction with other FERG task forces and, where relevant and feasible, in liaison with the WHO burden of disease group and GBD.

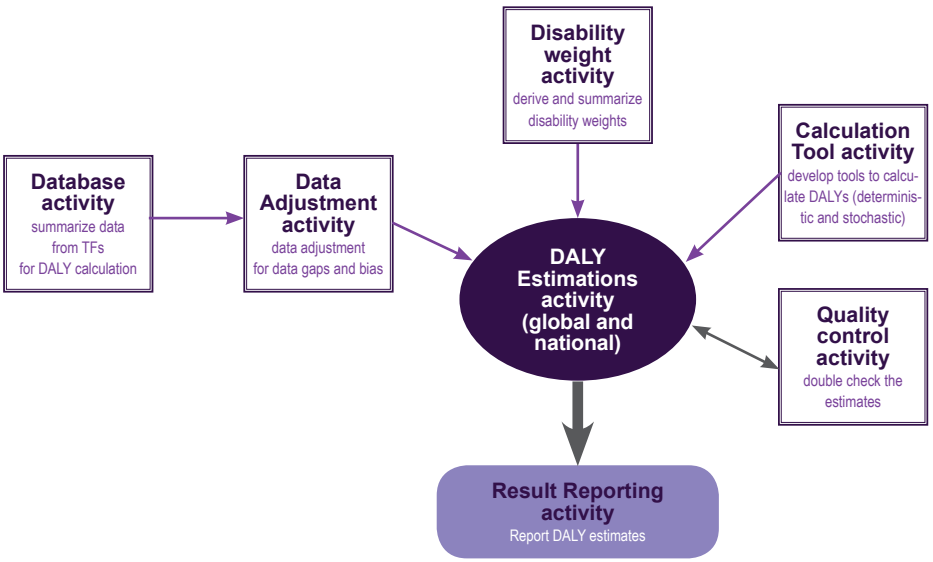
At country level, the CTF aims to:

- deliver the appropriate computational tools to countries undertaking the FERG country studies (with the tools adjusted as necessary to suit the national purpose and to be user-friendly).

To fulfil these objectives, the CTF has six activities, as summarized in Figure 3. The database activity involves the development of a physical database that can be filled with data on mortality, morbidity incidence and disease duration. Furthermore, it aims to highlight data gaps and bias that need to be considered within the data adjustment activity. The data adjustment activity develops tools to impute missing incidence and mortality data. The disability weights activity lists available GBD 2010 disability weights for the sequelae of the FERG diseases and agents. If no disability weights are available for certain sequelae, a strategy is developed to derive one. The objectives of the calculation tool activity are to develop tools: (a) to calculate DALYs, using both deterministic and stochastic approaches, and (b) to incorporate the results of the source attribution in the calculations. The quality control activity double-checks the database, models and DALY estimates and proceeds with sensitivity analyses. The result reporting activity will

present the incidence, mortality and DALY estimates in tables and maps, by GEMS and WHO subregions. Three agents were selected by the EDTF, PDTF and CTTF for the first DALY calculation process: *Salmonella, Toxoplasma and aflatoxins*.

Figure 3. CTF structure and activities



The first meeting of the CTF was held on 2–4 October 2012 at the Institute of Tropical Medicine, in Antwerp, Belgium. The meeting reviewed the progress of the CTF activities, tackled the technical difficulties encountered and fine-tuned the CTF workplan for 2012–2013. During the FERG5 meeting, the CTF discussed each of the activities and had meetings with the individual hazard task forces.

8.2 Disease models

For most of the agents, the CTF has constructed disease models, describing the disease outcomes. Disease outcomes for a specific pathogen may be unrelated or may follow an evolutive process over the lifetime. The disease models serve as a basis for identifying all the sequelae associated with a specific agent and for building the database.

8.3 Database

The CTF has developed a database template, which can be used to summarize the foodborne disease data (incidence, mortality and disease duration) collected by the task forces in the framework of the commissioned systematic reviews. On the basis of this template, one database will be developed for each agent. The hazard task forces will be in charge of entering the collected data into the databases, which will then be transferred to the CTF for data gap tracking, data adjustment and DALY calculation. A manual has been drafted describing the necessary steps for filling in the database. Missing incidence

data are indicated by leaving the relevant cell empty. If a country is disease-free, a 0 should be entered in the specific cell. If there is no information on age and sex distribution, the relevant cells should be left empty. Distributions around incidence and mortality data are also required when available. Both 5 and 95 percentiles, and 2.5 and 97.5 percentiles distribution, will be included in the database. Other types of distribution are also available. The template includes the previous version of GEMS/Food cluster diets, because the current ones were not available when the template was developed. The new GEMS/Food cluster diets will be added in a separate column. The database and manual will be fine-tuned and a revised version made available by the end of April 2013.

During the meeting it became clear that there is a need for someone to coordinate the data collection for each of the agents and for people to liaise with the hazard task forces. The tasks of the liaison person are to get the complete disease models, to structure the database according to the disease model and to send the structured databases to the hazard task forces for completion.

8.4 Data adjustment

The data adjustment activity develops tools to impute missing incidence and mortality data.

There are two possible approaches to adjusting data: an expert-driven approach and a data-driven approach.

(1) *The expert-driven approach*. Some experts who were commissioned to conduct the agent-specific systematic reviews and disease burden assessment have already used an agent-specific approach to impute incidence and mortality data for countries where they are lacking.

(2) *The data-driven approach*. In this case, the same methodology is used for all agents. Several approaches are possible, all based on the principle of clustering countries using some common variables or co-variates. A conservative imputation model will be applied (at least in the testing phase of the model selection process), using the GEMS/Food cluster diets to cluster the countries (GEMS-driven model). The CTF will also propose another approach based on the selection of socioeconomic, health, non-health and food-related predictor variables that capture similarities between countries with respect to foodborne disease risk; countries with similar risk can be clustered. The variables will be selected from a list of 1200 in FAO/WHO/WDI (World Development Indicators) databases. Five models are currently under consideration:

1. hierarchical Bayesian regression model,
2. frequentist regression model,
3. agent-specific linear regression model,
4. principal components to predict incidence,
5. Bayesian regression within clusters.

One of these will be chosen on the basis of its mean prediction error and its performance compared with the expert-driven and GEMS-driven models.

Regression-based predictions of foodborne disease mortality rates and agent-specific incidence rates (for aflatoxin and congenital toxoplasmosis) have already been generated using the different approaches. A report on these results will be drafted and a paper on the data adjustment approach will be written and submitted prior to submitting the FERG results methodology. More datasets are needed to accomplish the comparison in a more strategic and statistically reliable way. For this purpose, it is essential that the hazard task forces make new datasets available in the near future. The sooner the data are made available, the sooner the comparison will be possible, allowing a final decision to be made for the imputation strategy. The latter will be presented to WHO for final validation.

8.5 DALY calculation tool

The DALY calculation tool is an existing DALY package in the R environment (a software environment for statistical computing), which consists of a graphic user interface (GUI) for stochastic DALY calculation. Over the past months the DALY calculator tool has been further developed to allow an unlimited number of outcomes, user-defined age groups and implementation of conditional probability-based models. Furthermore, a link between the database (in Excel) and the DALY calculation tool has been established and functions for sensitivity analysis have been added, as well as a function that translates DALY calculator output into graphs, tables and maps. The resulting burden of disease calculations, in terms of DALYs, YLLs and YLDs, will be reported per 100 000 person-years, per case, per GEMS/Food region and per WHO subregion.

Final fine-tuning of the DALY calculation will be done in the coming months, including finding a solution for disease durations that are longer than life expectancy and including disability weights and functions for source attribution. For the latter, a list of agents and the type of distribution is needed.

By the end of April 2013, the DALY calculation will be tested by estimating DALYs for aflatoxin and toxoplasmosis.

8.6 Disability weights

The sequelae included in the overall planning document were mapped to GBD 2010 disability weights. The GBD 2010 disability weights focus on functional impairments and are described without a disease label (no etiological information).

Once the disease models have been finalized, the mapping of disability weights for sequelae will be revised. It will be important to ensure that the health state description of the disability weight reflects the epidemiological data to which it is matched. The revised list of matched disability weights will be validated by the hazard task forces. Discussion

is needed about what should be done for cases that have multiple health outcomes at the same time.

8.7 Quality control

A data gap strategy has been developed. A checklist will be developed for the hazard task forces and liaison persons to ensure that all the required input is entered in the database. The checklist will be finalized by the end of April 2013.

8.8 Next steps

The CTF needs to synchronize the time planning with the hazard task forces in order to implement the DALY calculation. This means that CTF and the hazard task forces need to plan the transfer of the final validated disease models and the data to the CTF. Contact persons within the hazard task forces need to be appointed, to work in close collaboration with the CTF liaison persons. The latter will facilitate the finalization of the disease models and data collection.

9. Country Studies Task Force and Knowledge Translation and Policy Group

9.1 Country Studies Task Force

The Country Studies Task Force (CSTF) is charged with developing protocols for burden of disease studies at country level and overseeing the execution of such studies, which include policy situation analyses. The objective of the CSTF is to provide guidance to countries on conducting national burden of FBD studies that:

- deliver burden of disease estimates in the area of foodborne diseases;
- contribute to capacity development in the areas of burden of disease and knowledge translation within the country;
- provide results that are translated into food safety policy for the country involved; and,
- contribute to estimates of the global burden of foodborne disease being prepared by FERG.

WHO has produced a pamphlet describing the purpose and value of country studies (24).

9.2 Knowledge Translation and Policy Group

In an effort to avoid the usual gap between the availability of evidence and translation of that evidence into policies and practices, WHO created a special Knowledge Translation and Policy Group (KTPG) as part of the FERG. The KTPG aims to: strengthen the capacity of countries to conduct foodborne burden of disease and cost of illness studies; develop tools to strengthen the capacity of researchers to translate food safety research into policy; strengthen the capacity of policy-makers to use burden of disease data; bridge the gap between collection of scientific evidence and food safety policy-making; and foster institutionalized interaction between food safety researchers and policy-makers throughout the research process (25).

9.3 Topics discussed at FERG5

Three principal topics related to the CSTF and the KTPG were discussed at FERG5:

1. the CSTF and KTPG workplans and schedules to the end of the FERG;
2. the situation analysis manual as one of the tools to support country studies;
3. a communications strategy for the global and regional results from FERG.

9.3.1 Revision of the situation analysis manual

A needs analysis for situation analysis and knowledge translation training was commissioned in 2012. For this analysis, a Web-based survey was conducted along with key informant interviews. During the meeting, members reviewed the report, as well as situation analyses prepared for Uganda and Japan. This discussion resulted in a draft proposal to further refine the existing situation analysis manual.

Key elements of this revision are:

- the inclusion of specific food safety examples wherever possible;
- the addition of section on knowledge translation, following the situation analysis and burden of foodborne disease estimates, with references to existing knowledge translation tools, including the templates already prepared by the KTPG;
- the addition of guidance on risk communication, based on the ideas developed in the overall FERG risk communication strategy.

The draft proposal for refining the manual is currently being circulated within the KTPG. Once finalized, it will include specific tasks for the KTPG. Once the proposal is complete (end of May 2013), the manual will be revised and distributed at least one month prior a joint country study workshop, which is scheduled for October 2013, so that the four pilot countries can further develop their own documents before the meeting.

9.3.2 DALY calculator

Communications with the pilot countries indicated that the DALY calculator being developed by the CTF for the global and regional results was likely to be unsuitable for capacity-building in countries. It is therefore proposed to develop a more transparent spreadsheet-based calculator to support country studies. This calculator would incorporate the inputs agreed by FERG as the basis for burden calculations (life expectancy tables, outcome trees, disability weights, duration, etc.) so that results would be aligned with those of FERG, but would be able to be amended by individual countries to accommodate country-specific inputs, such as attribution, and for training purposes. This calculator would be used for training and calculations during the joint country study workshop.

9.3.3 Joint country study workshop

A joint country study workshop was seen as desirable to allow two-way communication between FERG and the pilot countries, to provide training and further development of the studies, and to solicit responses from the pilot countries about the support tools developed by FERG.

The specific objectives of the joint country study workshop are:

- to provide training in DALY calculations and the calculator;
- to complete, as far as possible, the four pilot studies;
- to obtain feedback on the country study tools and how they might be improved;
- to allow the pilot countries to exchange experiences and make recommendations for future country studies; and
- to develop case study material to add to country study resources.

The intended participants for the joint country study workshop are the four pilot countries plus facilitators.

Terms of reference need to be developed for this workshop. The CSTF Chair will prepare a first draft.

9.3.4 Finalization of country study tools

WHO regards the suite of tools developed to support country studies as an important output from FERG. It is intended that this resource will be used for future national studies, which can be promoted through other programmes once FERG has completed its work. The existing tools will be refined following the joint country workshop, in particular to provide additional guidance manuals on their use, and to make them more user-friendly (an instructional design expert will be needed for this latter step). The objective is to finalize a suite of tools that can be used by countries with minimal direct guidance.

9.3.5 Communications strategy

The results from the global and regional estimates of the burden of foodborne disease need to be communicated in a way that promotes their use for policy development and action on food safety. With the guidance of a risk communication expert from WHO, the CSTF and KTPG discussed ideas about the objectives for the FERG communications. Further development of the strategy will be led by WHO, but the underlying ideas will be incorporated into the country studies situation analysis manual.

9.3.6 Publications

A number of scientific publications will be produced as outputs of the FERG initiative, including an editorial describing knowledge translation of the global and regional estimates, and a paper describing the experience and process for the pilot country studies. The editorial will be prepared by the KTPG, while the paper will be led by the CSTF Chair. An outline of each will be ready by approximately September 2013.

Table 5. Workplan and timeline of the CSTF and KTPG

Period	Activity
April to October 2013	Preparations for joint country study workshop and development of communications strategy for global and regional FERG results
October 2013	Joint country study workshop
October 2013 –December 2013	Finalization of country study tools
Early 2014	Contribution to FERG publications (editorial, paper)
April to July 2014	Pilot studies to examine global and regional results in their own context

10. Conclusions

There is 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 task force has outlined its priority activities for the coming year and WHO will use these to solicit the funding required to complete the FERG project.

10.1 Progress achieved at FERG5

The hazard task forces, 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.

The SATF finalized the expert elicitation protocol for chemicals and toxins (inorganic arsenic, lead, cadmium and dioxins), for parasitic diseases (*Entamoeba histolytica, Cryptosporidium spp., Giardia intestinalis, Echinococcus granulosus, Toxoplasma gondii, Echinococcus multilocularis and Ascaris lumbricoides*) 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 task forces. This expert elicitation will be the first time that the methodology has been applied at a global level for food safety and will involve disease experts from all six WHO regions. The logistics of such an enormous task were also mapped out and agreed during the meeting.

The CTF was able to agree the disease models for the majority of the pathogens, as well as meeting individually with each task force to advance the DALY calculations. The database was revised, methods for imputation of missing data were advanced, and disability weights were mapped to all outcomes.

The CSTF and KTPG agreed the aims and 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

10.2 Priority activities for 2013–2104

10.2.1 Overall FERG

- There is an extensive amount of work to be done to bring together all the data produced by the hazard task forces, review the selected models and prepare for the final calculations. This will involve all the members of FERG, resource advis-

ers and commissioned scientists.

- The final global atlas will be written and published.
- Some 8–10 scientific articles will be published in peer-reviewed journals.
- A communication plan will be developed and implemented, aimed at promoting the global estimates, encouraging countries to use the estimates to inform food safety policy and recognizing the support from technical partners and donors involved in FERG.

10.2.2 EDTF

The EDTF will:

- identify regional variations in the percentage of tuberculosis due to *M. bovis*;
- finalize probabilities for outcome tree for brucellosis;
- complete the systematic review of *Listeria*;
- complete the systematic review of intoxications;
- liaise with CTF to address co-morbidity issue for enteric pathogens and HIV/malaria;
- complete norovirus estimates;
- update the systematic review for eight enteric pathogens;
- estimate the global burden of Guillain-Barré syndrome, and estimate the percentage of Guillain-Barré cases due to *Campylobacter* infection.

10.2.3 PDTF

The PDTF will:

- Complete the systematic review of acquired toxoplasmosis, frequency and sequelae;
- review the data for Intestinal protozoa.

10.2.4 CTTF

The CTTF will:

- complete the systematic review of cardiovascular disease and arsenic;
- complete the systematic review of incidence of konzo due to cyanogenic glycoside exposure for sub-Saharan African countries.

10.2.5 SATF

The SATF will:

- identify and train facilitators for expert evaluation;
- enrol disease experts to the expert panels;
- undertake the expert evaluation and analyse the results;
- provide the results to the CTF for calculation of the proportion of disease attributable to food and identification of the main pathways for each hazard.

10.2.6 CTF

The CTF will:

- fine-tune the database template and DALY calculation tool (add function for source attribution);
- test the data adjustment tool using available databases;

- plan the transfer of the disease models and the data to the CTF;
- validate the final disease models with the hazard task forces;
- finalize the listing of disability weights using the validated disease models;
- initiate data collection for each agent.

10.2.7 CSTF and KTPG

The CSTF and KTPG will:

- conduct a country studies workshop with the pilot countries;
- finalize the country studies toolkit;
- complete the situational analysis and knowledge translation tools.

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ISBN 978 92 4 150796 7