6

Hazard characterization

6.1 THE PROCESS OF HAZARD CHARACTERIZATION

Codex defines hazard characterization as "the qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents, which may be present in food" (CAC, 1999). Hence, the hazard characterization provides a description of the adverse effects that may result from ingestion of a hazard, whether that is a microorganism or its toxin. Where possible the hazard characterization should include an indication, for the population of interest, of the probability to cause an adverse health effect as a function of dose. This would ideally take the form a dose–response relationship, if available, or using the *Median Dose* or *Infectious Dose 50 (ID_{50})*, the dose at which 50 percent of consumers become infected, or ill (see Section 6.3 for details). The hazard characterization may also include identification of different adverse effects for different subpopulations, such as neonates or immunocompromised people. Hazard characterization can be conducted as stand-alone process or as component of risk assessment.

A hazard characterization for a particular hazard may serve as a common module or building block for risk assessments conducted for a variety of purposes and in an assortment of commodities. A hazard characterization developed in one country may serve the needs of risk managers in another country when combined with an exposure assessment specific to that country, unless there are country-specific population effects. A hazard characterization developed for one specific food product may be adapted to another food product by taking into consideration

the food matrix effects, where possible. In general, hazard characterizations are adaptable between risk assessments for the same hazard. This is because the human responses to a specific hazard are not considered to be based on geography or culture. Instead, they are about the interaction between the hazard and the host only, recognizing that some hosts will be more susceptible than others.

Similar to other parts of risk assessment, hazard characterization can be iterative. For well-established hazards, such as *Campylobacter* or *L. monocytogenes*, the hazard characterizations tend to be well developed and may not require much revision unless considerable new information is available. However, for emerging hazards the hazard characterization may be less certain due to lack of data and information, and thus may require more frequent updating to reflect the increasing knowledge about the hazard. Characterization of hazards in food and water follow a structured, step-wise approach, as outlined in Figure 7 and described below.

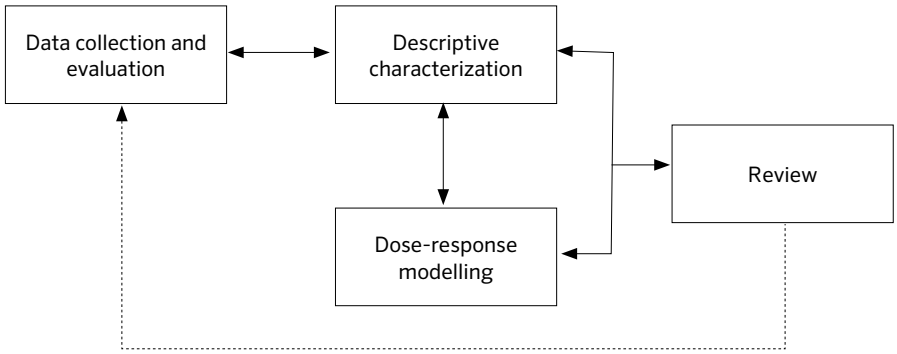


FIGURE 7. Process flow diagram for hazard characterization of pathogens

6.2 DESCRIPTIVE CHARACTERIZATION

Descriptive hazard characterization serves to structure and present the available information on the spectrum of human illness associated with a particular hazard, and how this is affected by the characteristics of the host, the hazard and the matrix, as indicated in Chapter 4. This is based on a qualitative or semi-quantitative analysis of the available evidence and will take the different illness mechanisms into account.

6.2.1 Information related to the disease process

When a hazard characterization is being undertaken, one of the initial activities will be to evaluate the weight of evidence for adverse health effects in humans to determine, or confirm, the ability of the hazard to cause disease. The weight of evidence is assessed based on causality inferences appropriately drawn from all available data. This entails examination of the quantity, quality and nature of the results available from clinical, experimental and epidemiological studies; analyses of hazard characteristics; and information on the biological mechanisms involved. When extrapolating from animal or *in vitro* studies, the biological mechanisms involved need to be considered to ensure they are relevant to humans.

When undertaking hazard characterization for waterborne and foodborne microbial hazards, the biological aspects of the disease process should be considered. Each of these steps is composed of many biological events. Careful attention should be given to the following general points.

- The process as a whole, as well as each of the component steps, will vary by the nature of the hazard.
- Hazards may be grouped in regard to one or more component steps, but this should be done cautiously and transparently.
- The probability of an event at each step may, or may not, depend on other steps.
- The sequence and timing of events are important.

For (toxico-)infectious hazards, it is recommended that the factors related to infection, and those related to illness as a consequence of infection (discussed in Section 13.1), are considered separately. While doing so, the following points should be considered when evaluating the available evidence.

- The definition of infection may differ between studies, i.e. is not universally accepted.
- Infection can be measured dichotomously (yes or no), but some aspects can be measured quantitatively.
- Detecting/measuring infection depends on the sensitivity of diagnostic assay.
- Target cells or tissue may be specific (one cell type) or nonspecific (many cell types), and local (noninvasive) or invasive or systemic, or a combination.
- The sequence of events and the time required for each may be important and may vary according to the hazard.

The information related to the disease should provide detailed insights into the disease process, either qualitatively and/or quantitatively. In most cases, this would be based on the available clinical and epidemiological studies. Narrative statements are helpful to summarize the nature of and confidence in the evidence, based on limitations and strengths of the data. Each source of information has its advantages and limitations, but collectively they permit characterization of potential adverse health effects. The analysis should include evaluations of the statistical characteristics of the studies, and appropriate control of possible bias, while identifying uncertainties, their sources, and their effects.

Characterization of the adverse human health effects should consider the whole spectrum of possible effects in response to the hazard, including asymptomatic infections and clinical manifestations, whether acute, subacute or chronic (e.g. long-term sequelae (Carbone, Luftig and Buckley, 2005)), or intermittent (see Table 2). Where clinical manifestations are concerned, the description would include consideration of the diverse clinical forms, together with their severity, which may be variable among strains and among hosts infected with the same strain. Severity may be defined as the degree or extent of clinical disease produced by a hazard, and may be expressed in a variety of ways, most of which include consideration of possible outcomes. For mild gastrointestinal symptoms, severity may be expressed as duration of the illness, or as the proportion of the population affected (morbidity). Where the symptoms require medical care or result in long-term illness, or both, severity may be expressed in terms of the costs to society, such as the proportion of workdays lost or cost of treatment. Some hazards and the related clinical forms may be associated with a certain degree of mortality and therefore severity may be expressed as mortality rate (e.g. *Vibrio vulnificus* infections and *L. monocytogenes* infections). Some hazards cause chronic illness, that is, the disease leaves long-term sequelae (Carbone, Luftig and Buckley, 2005), e.g. foodborne trematode infections. For these it may be desirable to consider and include the effects on quality of life as a result of the disease. Quality of life may be expressed in a variety of ways, depending on the nature of the illness. For instance, human life expectancy may decrease, chronic debilitation may occur, or quality of life may be affected by episodic bouts of disease. Increasingly, concepts such as Quality-Adjusted Life Year (QALY) or Disability-Adjusted Life Year (DALY), discussed further in Section 7.4.2, are being used to integrate and quantify the effects of different disease endpoints on the health of individuals or populations (Batz, Hoffmann and Morris, 2014; e.g. Havelaar *et al.*, 2000; WHO, 2000, 2015).

TABLE 2. Elements that might be included in characterization of adverse human health effects (Adapted from ILSI, 2000)

Clinical forms
Duration of illness
Severity (morbidity, mortality, sequelae)
Pathophysiology
Epidemiological pattern
Secondary transmission
Quality of life

In addition to a description of the human adverse health effects, information on the disease should include consideration of the epidemiological pattern and indicate whether the disease may be sporadic, endemic or epidemic. The frequency or incidence of the disease or its clinical forms, or both, should be addressed, together with their evolution with time and possible seasonal variations. The description should include consideration of the repartitioning of clinical forms according to specific groups at risk. Finally, the potential for, extent of or amount of transmission, including asymptomatic carriers, and secondary transmission, should also be characterized. Information collected on these aspects is important to guide the risk characterization.

In all cases, and with particular regard to further modelling, it is important that the characterization includes a definition of possible endpoints to be considered. Thought needs to be given to the appropriate criteria when defining *infection* of the host by the hazard, and the criteria of what constitutes a clinical *case*. In addition, a definition of the severity scale should be provided, specifying the indicator chosen (e.g. disease endpoint or consequences) and how it can be measured. The description should also include information on uncertainties and their sources.

To the extent possible, the characterization should incorporate information on the pathophysiology of the disease, i.e. on the biological mechanisms involved. Depending on the information available, this would include consideration of elements such as:

- the entrance route(s) of a hazard into a host;
- the effect of growth conditions on expression of virulence by and survival mechanisms of the hazard;
- the effect of the conditions of ingestion, including matrix effects;
- the effect of gastrointestinal status;

- the mechanisms involved in the penetration of the hazard into tissues and cells;
- the status of the hazard relative to nonspecific (innate) and cell-mediated immunity;
- the status of the hazard relative to humoral defences;
- the effect of intercurrent illnesses and treatments, such as immunosuppressive or antimicrobial therapy;
- the potential for natural elimination; and
- the behaviour of the hazard in a host and its cells.

The natural history of the disease needs to be completed by specific consideration of factors related to the hazard, the host and the food matrix, insofar as they may affect development of health effects, their frequency and severity.

6.2.2 Information related to the hazard

Basically, this information is analysed with a view to determining the characteristics of the hazard that affect its ability to cause disease in the host via transmission in food. The analysis needs to consider the biological nature of the hazard as well as the relevant mechanisms that cause illness (infectious, toxico-infectious, toxigenic, invasive or not, immune-mediated illness, etc.). In principle, the descriptive hazard characterization is applicable to all types of hazards and all associated illnesses. In practice, by nature of the data collected, the focus will be on acute effects, associated with single exposures rather than long-term effects associated with chronic exposure. Note that the possible interaction between repeated exposures, e.g. the development of acquired immunity, is an integral part of the descriptive characterization.

The ability of a hazard to cause disease is affected by many factors (Table 3). Some of these factors relate to the intrinsic properties of the hazard, such as phenotypic and genetic characteristics that affect virulence and pathogenicity, and host specificity. The characteristics of the hazard that determine its ability to survive and multiply in food and water, based on its resistance to processing conditions, are critical components of both exposure assessment and hazard characterization. Ecology, strain variation, infection mechanisms and potential for secondary transmission may also be considered, depending on the biology of the microorganism and on the context of the hazard characterization, such as the scenario that has been delineated during the problem formulation stage of a full risk assessment.

TABLE 3. Elements to consider in characterization of the hazard (Adapted from ILSI, 2000)

Intrinsic properties of the hazard (phenotypic and genetic characteristics)
Virulence and pathogenicity mechanisms
Pathological characteristics and disease caused
Host specificity
Infection mechanisms and portals of entry
Potential for secondary spread
Strain variability
Antimicrobial resistance and its effect on severity of disease

If not already included, then specific consideration should be given to the intrinsic properties of the hazard that affect infectivity, virulence and pathogenicity; their variability; and the factors that may alter the infectivity, virulence or pathogenicity. As a minimum, elements to addressed, as best as possible, are summarized in Table 3.

6.2.3 Information related to the host

Host-related factors are the characteristics of the potentially exposed population that may affect susceptibility to the particular hazard. These should take into account host intrinsic and acquired traits that modify the likelihood of infection or, most importantly, the probability of illness and its severity. There are many pre-existing (innate) host barriers, though they are not all equally effective against hazards. Each barrier component may have a range of effects depending on the hazard, and many factors may affect susceptibility and severity. These are identified in Table 4.

TABLE 4. Factors related to the host that may affect susceptibility and severity (Adapted from ILSI, 2000)

Age
General health status, stress
Immune status
Underlying conditions, concurrent or recent infections
Genetic background
Use of medications
Pertinent surgical procedures
Pregnancy
Breakdown of physiological barriers
Nutritional status, bodyweight
Demographic, social, and behavioural traits

Not all of the factors listed in Table 4 are relevant, or important, for all hazards. In all cases, however, an important issue in hazard characterization is to provide information on whom is at risk and on the stratification of the exposed population for relevant factors that affect susceptibility and severity.

6.2.4 Information related to the food matrix

The factors related to the food matrix are principally those that may affect the survival of the hazard through the hostile environment of the stomach. Such effects may be induced by protection of the hazard against physiological challenges, such as gastric acid or bile salts. These are related to the composition and structure of the food matrix, e.g. highly buffered foods and entrapment of bacteria in lipid droplets. Alternatively, the conditions in the food matrix may phenotypically affect the ability of the hazard to survive the host barriers. Examples include increased acid tolerance of bacteria following pre-exposure to moderately acidic conditions, or induction of stress–response by starvation in the environment. Stress conditions encountered during the processing or distribution of food and water may alter a hazard's inherent virulence and its ability to resist the body's defence mechanisms. These potential matrix effects can be important elements in hazard characterization. The conditions of ingestion may also affect survival by altering the contact time between hazard and barriers, e.g. initial rapid transit of liquids in an empty stomach. These factors are summarized in Table 5.

TABLE 5. Elements to consider in characterization of the effect of the food matrix on the hazard-host relationship

Protection of the hazard against physiological barriers, e.g. fatty foods, ingestion of pathogen in, or after, ingesting a large volume of fluid
Induction of stress response
Effects on transport of hazard through the gastrointestinal tract

6.2.5 Relationship between the dose and the response

The final, and essential, element in the descriptive hazard characterization is the relationship, if any, between the ingested dose, infection and the manifestation and magnitude of health effects in exposed individuals. Specific modelling aspects are covered in Sections 6.3 and Chapter 11.

Description of the dose–response relationship involves consideration of the elements or factors related to the hazard, the host and the matrix, insofar as they may modulate the response to exposure. Where appropriate information is

available, it also involves a discussion about the biological mechanisms involved, in particular whether synergistic action of hazards, may be a plausible mechanism for any harmful effect, or whether a single hazard may cause adverse effects under certain circumstances. Elements to consider are listed in Table 6.

TABLE 6. Elements to consider in describing the dose–response relationship (Adapted from ILSI, 2000)

Organism type and strain
Route of exposure
Level of exposure (the dose)
Adverse effect considered (the response)
Characteristics of the exposed population
Duration – multiplicity of exposure

Where clinical or epidemiological data are available, discussion of the dose–response relationship will generally be based on such data. However, the quality and quantity of data available will affect the characterization. The strengths and limitations of the different types of data are addressed in Chapter 10. A specific difficulty is obtaining data to characterize infection, the translation of infection into illness, and illness into different outcomes. In many cases, the analysis may only be able to describe a relationship between a dose and clinical illness. Other difficulties arise from several sources of variability, including variation in virulence and pathogenicity of the microorganisms; variation in attack rates; variation in host susceptibility; and type of matrix, which modulates the ability of hazards to affect the host. Therefore, it is essential that the dose–response analysis clearly identify what information has been utilized and how the information was obtained. In addition, the variability should be clearly acknowledged and the uncertainties and their sources, such as insufficient experimental data, should be thoroughly described.

In cases where a dose–response model cannot be ascertained or is not needed, such as for a qualitative MRA, an indication of the likely dose required to cause a certain probability of infection/illness should still be given. In particular, the dose that results in infection/illness in 50 percent of exposed consumers – often referred to the ID_{50} or median dose – may be a simple, yet practical, indicator. However, such a dose should not be interpreted as a threshold or minimal infective dose (see box below). For example, some hazards are highly infective and only a very small dose is required, such as for norovirus, for which it has been estimated that the ID_{50}

may be as low as 18 viruses (Teunis *et al.*, 2008). For other hazards a larger dose is required to cause 50 percent illness, as is the likely case with *L. monocytogenes* in the general population (FAO and WHO, 2004; Buchanan *et al.*, 2017).

It should be recognized that for many organisms a very low dose may cause illness, even though the probability of this happening may be very low. However, often the exposure distributions, i.e. distribution of doses, is highly right-skewed and so most exposures occur at (very) low doses. As a result, these low doses, together with a small probability of illness may still represent a large number of illnesses in a population; such exposures are consistent with the concept of *sporadic* illness.

6.3 QUANTIFYING THE DOSE–RESPONSE RELATIONSHIP

Illness can be the result of intoxication, toxico-infection or infection. In the first case the illness is the result of ingestion of toxins which are preformed in the food. The health risks of certain toxins, e.g. cyanobacterial toxins in water or aflatoxins in foods, usually relate to repeated exposures and hence tend to be chronic; these require another approach, which resembles hazard characterization of chemicals. Other toxins have more acute effects like botulinum toxin, *S. aureus* enterotoxin or *Bacillus cereus* cereulide. In toxico-infection organisms produce toxins in the intestines that either produce adverse effects there, or are transported and create effects in other places in the human body. For infections the organisms invade human cells, either in the intestine or elsewhere in the human body.

To determine the probability of adverse effects, a dose–response relation is needed to translate the doses resulting from exposure assessment. For this, a mathematical model is needed, as well as the value(s) of its parameter(s), including variability and uncertainty where possible. Attention should be paid to the following aspects.

- The dose ingested is characterized by the multiplication of the concentration and the amount of food (or water) ingested (that are both variable).
- The definition of the response(s), e.g. infection, disease, sequelae.
- The specific model used, e.g. exponential, Beta–Poisson.
- The set of parameters, including their variability and uncertainty, potentially relevant for a specific population group and/or food commodity and/or organism subgroup.

BOX 1

The *Minimal Infective Dose* model posits that there is a dose below which there is no infection and hence no risk, and above which infection always occurs. However, such models are now considered invalid. Microbial dose–response models today are based on the single-hit assumption, i.e. each individual cell has a discrete, nonzero probability of establishing infection. Models based on this assumption can be found in numerous peer-reviewed papers and are also recommended in the WHO/FAO Guidelines for Hazard Characterization of Pathogens in Water and Food (FAO and WHO, 2003). Therefore, the Minimal Infective Dose concept, the phrases "minimal infective dose," "infectious dose," or statements like "the dose–response is between 10^4 and 10^5 cells" should not be used. It is appropriate to use an infectious dose for a certain (quantitative) response like ID_{50} or ID_{10}, representing the dose at which 50 or 10 percent, respectively, of those exposed get infected. This concept holds true for toxico-infectious and infectious organisms. Sometimes the ID_{50} is used or interpreted as a threshold of infection; however, such an interpretation is incorrect and should be avoided. A minimal toxic dose might exist for illness cause by food containing preformed toxins (e.g. staphylococcal enterotoxins), where there is a level below which there is no observable response.

Plots of empirical datasets relating the response of a group of exposed individuals to the dose (often expressed on a logarithmic scale) frequently show a sigmoid shape (Figure 8, left) and a large number of mathematical functions can be used to model such dose–response relationship (Haas, Rose and Gerba, 2014; Teunis, 1997). It is important to also investigate this curve on the log-log scales, since the "low exposure" (X-axis) and "low probability" (Y-axis) part of the relationship (Figure 8, right) is often particularly relevant (Williams, Ebel and Vose, 2011a) as explained at the end of Section 6.2.5. It should be noted that the uncertainty bounds appear different in width when viewed on the log-log scale compared with the linear scale, though this is simply the result of the mathematical transformation. When extrapolating outside the region of observed data, different models may predict widely differing results (Coleman and Marks, 1998; Holcomb *et al.*, 1999). It is therefore necessary to select between the many possible dose–response functions and justify the decision. In setting out to generate a dose–response model, the biological aspects of the hazard–host–matrix interaction should be considered carefully (Teunis, 1997).

For some dose–response models, some of the well-established models and parameter values may be appropriate (see Table 7). In those cases, relevant assumptions need to be evaluated. It could also be decided to extend the dose–response relation with additional data or derive a fully new dose–response model. Guidance is provided in Chapter 13 for deriving new or updating existing dose–response models.

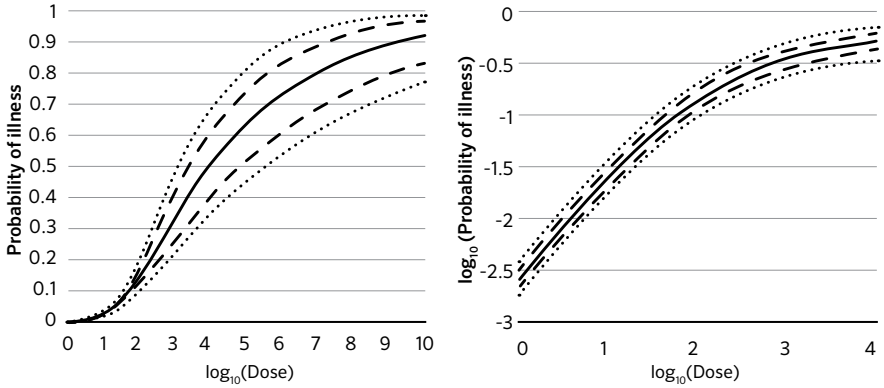


FIGURE 8. Example *Salmonella* dose–response model, including expected response (solid line), approximate 2.5th and 97.5th uncertainty percentile lines (dashed) and upper and lower uncertainty bounds (dotted) (FAO and WHO, 2002a p. 87) on linear-log scale (left) and on log-log scale (right)

TABLE 7. Dose–response models and parameter estimates commonly used in QMRA

Organism	Reference	Model	Parameters	Lower bound (Percentile)	Upper bound (Percentile)
Salmonella spp.	FAO/WHO (2002a)	Beta-Poisson	α=0.1324 β=51.43	0.0940 (2.5th) 43.75 (2.5th)	0.1817 (97.5th) 56.39 (97.5th)
Listeria monocytogenes [a]	FAO/WHO (2004)	Exponential (susceptible) Exponential (healthy)	$r=1.06\times10^{-12}$ $r=2.37\times10^{-14}$	2.47×10^{-13} (5th) 3.55×10^{-15} (5th)	9.32×10^{-12} (95th) 2.70×10^{-13} (95th)
Campylobacter spp.[b]	FAO/WHO (2009d)	Beta-Poisson	α=0.21 β=59.95		
Shigella dysenteriae/ *E. coli* O157	Cassin *et al*. (1998)	Beta-binomial	α=0.267 β=Lognormal (5.435, 2.47^2)		
Vibrio vulnificus	FAO/WHO (2005)		$\alpha=9.3\times10^{-6}$ β=110 000		

[a] For *L. monocytogenes*, newer animal model data (Roulo *et al.*, 2014; Smith *et al.*, 2003, 2008; Williams *et al.*, 2007, 2009) and outbreak data (Pouillot *et al.*, 2016) suggest much higher r-values and hence lower ID_{50} values than predicted by this model which was based on the method of Buchanan *et al.* (1997) of matching expected loads of *L. monocytogenes* across the food supply to the total annual cases in a community, and which relies on many untested assumptions.
[b] The dose–response relation is for infection. The conditional probability of disease following infection was 33 percent (29/89) and can be described by a beta(30,61) distribution.

7

Risk characterization

7.1 THE PROCESS OF RISK CHARACTERIZATION

Codex defines risk characterization as

> *… the process of determining the qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterization and exposure assessment (CAC, 1999).*

Hence, the risk characterization integrates the findings from those three components (see Figure 2) to estimate levels of risk, which can subsequently be used to make appropriate risk management decisions.

Risk characterization is the final step in the risk assessment process (Figure 2), which is initiated by risk managers who pose specific questions to be answered by the risk assessment. As noted previously, the questions posed by risk managers are usually revised and refined in an iterative process of discovery, discernment and negotiation with risk assessors. Once answered, the risk managers have the best available science-based information they need to support their decision-making process.

Risk characterization is the risk assessment step in which the risk managers' questions are directly addressed. While risk characterization is the process, the

result of the process is the risk estimate. The risk characterization can often include one or more estimates of risk, risk descriptions, and evaluations of risk management options. Those estimates may include economic and other evaluations in addition to estimates of risk attributable to the management options.

Although the Codex risk assessment framework is a common context for undertaking risk characterization, it is by no means the only context. In actual practice, an assessment of the risk may include some or all of these steps. The scientific analyses comprising any one of these steps may be sufficient on their own for decision-making. Risk assessments can follow a *bottomup* or *topdown* approach. A bottom-up approach links knowledge about the prevalence and concentration of a hazard in a food source with knowledge about the causal pathways, transmission routes and dose–response relations. Alternatively, top-down approaches use observational epidemiological information to assess risk, typically making use of statistical regression models (Williams, Ebel and Vose, 2011b). Also, models exist that use elements from both approaches, e.g. for source attribution. These approaches have different starting points, use different types of data and serve different purposes. For example, in Denmark (Hald *et al.*, 2004) and the United States of America (Guo *et al.*, 2011), the number of human cases of salmonellosis attributed to different animal sources was estimated without a precise exposure assessment and without using a dose–response model. A further example is provided by De Knegt *et al.* (2015). Bottomup and topdown MRA approaches have been published on aiding risk managers in the use of risk metrics, such as the *Appropriate Level of Protection* (ALOP) and *Food Safety Objective* (FSO) with case studies using *L. monocytogenes* in deli meats (Gkogka *et al.*, 2013a) and *Salmonella* spp. in raw chicken meat (Gkogka *et al.*, 2013b).

7.2 QUALITATIVE RISK CHARACTERIZATION IN RISK ASSESSMENT

7.2.1 Introduction

The risk characterization generated as part of a qualitative risk assessment will ideally be based in numerical data for exposure assessment and hazard characterization. Nevertheless, it will generally be of a descriptive or categorical nature that is not directly tied to a more precisely quantified measure of risk (e.g. CFIA, 2019 Section 3.4.1). Qualitative risk assessments are commonly used for screening risks to determine whether they merit further investigation and can be useful in the preliminary risk management activities described in (FAO and WHO, 2002b), but may also provide the needed information and analysis to answer

specific risk management questions. The major difference between qualitative and quantitative risk characterization approaches is in the way the information is synthesized and the communication of the conclusions.

7.2.2 Performing a qualitative risk characterization

Qualitative risk characterization requires an overall textual estimate of the risk that will be based on a combination of the various prior steps. This is a complex process as it should still obey basic principles of probability theory when combining probabilities but there are no clear rules to the outcome of the combination of (possibly subjective) textual descriptions of probability. As a hypothetical example, Table 8 illustrates a comparison between the process for computing risk estimates in quantitative versus qualitative risk assessments. When combining the equivalent qualitative statements, the only inference that can be made is that the final risk is either of equal magnitude or lower than the probability at Stage 1. This qualitative process can lead to errors in probability logic and may be impossible if there is uncertainty to address or multiple pathways to combine (Wooldridge, 2008). Alternatively, Wooldridge (2008) proposes the risk characterization process consist of a summary of the individual conclusions for each of the steps of the risk assessment (including descriptions of uncertainty).

TABLE 8. A comparison of the process for computing the final risk estimate in risk characterization in quantitative and qualitative risk assessments. (Table adapted from Table 4 in Wooldridge (2008))

Stage	Quantitative risk assessment		Qualitative risk assessment	
	Probability	Computation	Probability	Computation
1	0.1		Low	
2	0.001	P(Stage 2) = P(Stage 1) x 0.001 = 0.0001	Very Low	P(Stage 1) x "Very Low" → Very Low (or lower)
3	0.5	P(Stage 3) = P(Stage 2) x 0.5 = 0.00005	Medium	P(Stage 2) x "Medium" → further reduction from very low
4	0.9	P(Stage 4) = P(Stage 3) x 0.9 = 0.000045	High	P(Stage 3) x "High" → further (small) reduction
Risk estimate		**0.000045**		**Very low (or lower)**

Despite its name, a qualitative risk assessment still relies on as much numerical data as possible to provide suitable inputs. The search for information, and thus for numerical data, should be equally as thorough as for a quantitative risk assessment. Also, where there are crucial numerical data deficiencies, expert opinion must be utilized. The major difference between qualitative and quantitative risk assessment approaches lies in how the data and expert opinion are treated and combined.

Transparency in reaching conclusions

A qualitative risk characterization should show clearly how the risk estimate is reached. The precise way of doing this will vary depending in part on the complexity of the risk assessment and in part on the risk assessor(s) preferences. Methods used include:

- a *tabular* format, with data presented in the left-hand column, and the conclusions on risk in the right column; or
- a *sectional* format with a summary or conclusion at the end of each data section.

Examples of these formats that illustrate good practice (i.e. documentation of evidence and logic) are presented in Table 9 and Table 10. The examples are based on particular steps in an overall risk assessment for which the question is "What is the probability of human illness due to microbe 'M', in country 'C', due to the consumption of meat from livestock species 'S' infected with microbe M?"

TABLE 9. Example of a possible tabular format for presenting data linked to risk estimates and conclusions

Step being estimated: What is the probability of a randomly selected example of species S in country C being infected with microbe M?	
Data available	**Risk estimate and conclusions**
The prevalence of microbe M in species S in Country C was reported as 35 percent (Smith & Jones, 1999*). The prevalence of microbe M in region R, a district within country C, was reported as 86 percent (Brown, 2001*).	The studies suggest that the probability of a randomly selected example of species S in country C being infected with microbe M is medium to high. However, the two studies indicate that considerable variability by region is likely.
There are no particular geographical or demographic (with respect to S) differences in region R, compared with the rest of C (Atlas of World Geography, 1995*). The diagnostic test for microbe M, used in the livestock surveillance programme in country C is reported to have a sensitivity of 92 percent and a specificity of 99 percent (Potter & Porter, 1982*).	With only two studies available, there is also considerable uncertainty of the actual range of prevalence by region, as well as the probability of infection in a randomly selected example of S. In addition, the timing of these surveys may suggest an increasing prevalence of M in C. The reported parameters for the diagnostic test used do not alter these conclusions.
*Fictional references for illustrative purposes only	

TABLE 10. Example of a possible sectional format for presenting data linked to risk estimates and conclusions

SECTION X. What is the probability of human ill health, given infection with microbe M?
Data available
• No specific dose–response data have been found for microbe M. • Health authorities for country C provide the following data (Zhou and Kopko, 1999*). > Incidence over the period was reported as 22 cases per million of the population per year (22 per million is 0.000022 percent of the population per year). • Clinical incidence recording and reporting systems in Country C are considered to be of high quality (Bloggs, pers. comm.*). • Experts' opinions indicate that once clinical symptoms appear, cases are likely to consult a medical practitioner (Lopez *et al.*, 1992*). • Cases tend to be seen in the very young or the very old (Lopez *et al.*, 1992*). • A surveillance study undertaken by practice-based serological testing indicated that 35 percent of the population of C had been exposed to microbe M and had sero-converted (Hunt, Hunt and Seek, 2001*). This was a countrywide, statistically representational study. *Fictional references for illustrative purposes only
Conclusions
Data suggest a high level of exposure to microbe M in country C, but a very low incidence of clinical disease. Expert opinion indicates underreporting of clinical disease due to lack of medical practitioner involvement is unlikely to account for this. Overall, therefore, the probability of human ill health, given infection with microbe M, is likely to be low. The level of uncertainty in the data specific to country C appears to be low, making this conclusion reasonably certain. However, data also indicate that there are specific groups at higher risk of clinical illness, specifically the very old and very young. From the data currently available it is not possible to indicate how much higher this risk is likely to be.

Limitations of qualitative risk characterization

It may be difficult to conceive of a fully qualitative risk assessment that will provide useful advice to risk managers, except in a few special cases. In those special cases, the number of factors that could affect the risk may be very low or every factor that affects the risk may change the risk in the same direction. Since risk managers may make decisions on the basis of economics, qualitative descriptions may be difficult to translate directly to financial benefits and/or costs. In other cases, it may be virtually impossible to assess the combined effect of multiple stages because the relative contributions of factors, expressed in qualitative terms, cannot be logically combined to determine their overall effect on risk. In some cases, a qualitative best-effort may still be needed, and any assumptions and uncertainties need to be clearly explained. Thus, while a fully qualitative risk assessment can identify pathways or scenarios that lead to extremes of risk, the relative risk from all other scenarios cannot be logically differentiated. Logical qualitative reasoning can provide conclusions like "the risk of X is logically less (or greater) than that of Y"

where Y is another, more precisely quantified, risk that has previously been deemed acceptable (or unacceptable). One can also argue that both of these approaches are forms of best- and worst-case quantitative risk assessment. Cox, Babayev and Huber (2005) discuss these limitations in greater detail and provide examples.

Qualitative analyses often suffer from the inability to determine what pieces of evidence were influential, how they were combined, and ambiguity concerning the meaning of any assigned risk characterization labels. Without explicit criteria identifying what is meant by descriptions such as high, moderate, and low risk, there is little to distinguish the conclusions from arbitrary and possibly value-laden judgements about the level of risk. These shortcomings tend to make qualitative risk characterization unacceptable in many decision-support situations.

Another limitation of qualitative risk assessment may be to blur the lines between risk assessment and risk management. For example, a risk assessment that concludes the level of the risk under consideration to be "low", may be perceived to be making a management evaluation of the risk, and therefore confusing the roles of assessor and manager.

It is possible to present an unstructured analysis as a more structured analysis by including standard documentation headings such as exposure assessment, hazard characterization and risk characterization. Examples that illustrate qualitative approaches that do link evidence and conclusion are presented in Section 8.1.

If the risk assessment will be read by a broader audience, assessors should be mindful that interpretation of words or terms used as descriptors might vary between languages or regions. Even when there is a consensus between assessors and managers over the interpretation of the terms used, some limitations of qualitative risk assessment can be identified.

7.3 SEMI-QUANTITATIVE RISK CHARACTERIZATION

7.3.1 Introduction

Semi-quantitative approaches to risk characterization involve assigning numbers to qualitative estimates in the form of probability ranges, weights or scores. These are combined by addition, multiplication, or other mathematical operation with the objective of achieving a greater level of objectivity compared to a qualitative approach. It is the role of risk characterization to provide an unbiased estimate of the level of the risk being considered. Semi-quantitative approaches avoid this problem by using a specific, quantitative meaning rather than terms like "Low probability."

Table 11 and Table 12 provide some example definitions for probability, exposure and severity categories where probability ranges have been assigned to qualitative descriptions.

TABLE 11. Example category definitions for the probability of an event occurring and for the frequency of exposure per year

Category	Probability range (Probability of event per year)	Category	Exposures per year
Negligible	Indistinguishable from 0	Negligible	Indistinguishable from 0
Very Low	$< 10^{-4}$, (except 0)	Very Low	1-2
Low	10^{-4} to 10^{-3}	Low	3-10
Medium	10^{-3} to 10^{-2}	Medium	11-20
High	10^{-2} to 10^{-1}	High	21-50
Very High	$> 10^{-1}$ (except 1)	Very High	>50
Certain	1		

TABLE 12. Example definitions of health effect / severity category labels

Category	Severity description
None	No effect
Very low	Feel ill for few days without diarrhoea
Low	Diarrhoeal illness
Medium	Hospitalization
High	Chronic sequelae
Very high	Death

7.3.2 Performing a semi-quantitative risk characterization

Semi-quantitative methods require the development of decision rules guiding how the categorical risk levels are combined and which are logical, align with general principles of probability, and are transparent in terms of the operations performed. The options to conduct the risk characterization using semi-quantitative methods spans the continuum between qualitative and quantitative approaches, with no single approach endorsed as the single "best" approach in all circumstances. Approaches include, but are not limited to, the combination of labels or scores in algebraic form with a fixed equation (e.g. specifying multiplication or addition of scores); using specified probability ranges/bounds in place of quantitative point estimates of risk; or using a combinatorial risk matrix. The level of complexity

of the approach varies widely as the exact set of rules to combine the categorical risk levels are often designed specifically for the risk assessment being conducted. Examples of the types of approach that may be used include the following:

Using an algebraic approach: Components of the risk characterization (and overall risk assessment) are assigned numerical values to represent categorical levels and an equation is specified that defines how these values are combined. An example using an algebraic approach is RiskRanger by Ross & Sumner (2002). The probabilities involved in exposure and severity are converted to scores from 0 to 1, which are combined (usually by multiplication but including additions, e.g. for recontamination) and subject to logical tests in the software (e.g. to prevent unfeasible risk estimates). The result is a "comparative risk" and, in conjunction with the number of consumers, a predicted number of cases of illness is obtained. An example of its use is presented in Section 8.1.7.

Using probability bounds: The categorical labels are assigned probability ranges which are then combined. Often, in the course of carrying out a qualitative risk assessment, one can roughly estimate the probability of exposure, etc., from comparison with other, previously quantified risks or from good data pertaining to the problem. If time or the available data are insufficient to carry out a complete quantitative risk assessment, one can use these categorical labels to express the risk level in a more structured way than a simple description of the evidence one has acquired.

However, when terms like "low risk" or "very low risk" are used, it is very important to consider the number itself, but even more so to examine the context to see what the number means. For example, consider where the probability of botulinum toxin in one tin of food from a single supplier is 0.0001. This number itself (0.0001) seems very low. However, since this number refers to only a single tin in a potentially very large population of tins, e.g. 10 million, the resulting number of "toxic tins" equals $0.0001 \times 10\ 000\ 000 = 1\ 000$, which would be considered a very large number of toxic tins, given the nature of the illness. On the other hand, if the probability of one tin per year in the entire world containing botulinum toxin is 0.01, then this value is 100 times larger than the value above (0.0001), but the actual risk is much lower (i.e. one "toxic tin" in 100 years) – this risk is actually quite low, considering that the yearly worldwide tin use is in the trillions rather than millions. Therefore, the denominator of the probability needs to be clearly defined (per serving, per person per year, over the whole population, etc.) and the probabilities need to be considered in this context (risk per serving, for a person per year or for the whole population), to classify them as "high" or "low". In addition, the severity needs to be considered when moving from probability to risk.

As an example, consider that a qualitative risk assessment has determined that:

- the probability a serving could be contaminated is "Very High",
- the number of servings a random person consumes is "Medium" and
- the probability of illness given consumption of the contaminated product is "Low".

Using the example definitions from Table 11 and Table 12, one can conclude the composite probability to be between "Low" and "Medium" by multiplying the corresponding bounds from each of the probability ranges, as shown in Table 13.

TABLE 13. Example of combining category labels

Component	Category	Numerical range
Probability that serving is contaminated	Very High	10^{-1}–1
Number of servings in a year	Medium	10–20
Probability of illness from a contaminated serving	Low	10^{-4}–10^{-3}
Probability of illness in a year	Low to Medium	10^{-4}–2×10^{-2}

This approach enables people to make more consistent, logical conclusions: a "Low" exposure probability per serving and a "High" probability of illness given exposure cannot, for example, be categorized as a "Very High" probability of illness per serving.

It is possible to use categorical labels to perform some rudimentary type of probability manipulation. For example, by carefully defining the ranges assigned to each term, it is possible to combine a "Low" exposure with a "High" probability of subsequent health effect to determine the appropriate categorization for the total risk. It is only possible to maintain consistency and transparency in combining categorical labelling of elements of a risk assessment if numerical ranges have been defined for each label. Nonetheless, combining categorical labels should be approached with considerable caution (see Chapter 9).

Using a risk matrix: A risk matrix uses combination rules to combine categorical labels, and an example of such a matrix is show in Table 14

This approach has been adopted for many years in other areas of risk assessment but has also received criticism because of the difficulties of defining a robust, defensible treatment of risk characterization (and risk assessment in general). See Levine (2012) and Cox Jr. (2008) for a discussion of these issues and suggestions for improvement.

TABLE 14. A hypothetical example of a risk matrix to combine likelihood and severity as could be applicable to risk characterization using probability ratings as presented in Table 15

		Negligible	Minor	Severity moderate	Significant	Severe
Likelihood	**Very likely**	Low Medium	Medium	Medium High	High	High
	Likely	Low	Low Medium	Medium	Medium High	High
	Possible	Low	Low Medium	Medium	Medium High	Medium High
	Unlikely	Low	Low Medium	Low Medium	Medium	Medium High
	Very unlikely	Low	Low	Low Medium	Medium	Medium

TABLE 15. Semi-quantitative allocation of categorical labels to probability ranges

Probability	Risk Rating
>70%	Very likely
40% to 70%	Likely
10% to 40%	Possible
1% to 10%	Unlikely
<1%	Very Unlikely

Limitations of semi-quantitative risk characterization

Any semi-quantitative risk characterization has limitations which can result in inaccuracies in risk estimates. These are discussed in more detail in Section 9.2.3, and include:

- Number of categories: There is no rule regarding the number of categories that should be used, e.g. 5 or 25 categories of severity.
- Granularity of scale: Consider a risk whose probability of occurrence falls just above the boundary between two categories. If a risk management strategy reduces that probability by a small amount, then it could be dropped down one category. However, this change is indistinguishable from a change that reduces the probability by a factor of 10, and thus also reduces the category by one level.
- Difficulty combining probability scores: It is difficult to create a rule with scores that replicates the probability rules.

Data requirements

The basic principle of risk assessment is to collect as much data as possible, providing that the inclusion of more data may affect the decision being made. The data collected for a qualitative risk assessment are often sufficient for semi-quantitative risk assessment needs. The difference between the two is that semi-quantitative risk assessment has a greater focus on attempting to evaluate the components of the risk to within defined quantitative bounds. Thus, at times, one may do a statistical analysis on a data set to attempt to more precisely estimate a probability providing it will give the assessor more confidence about how to categorize the risk.

Semi-quantitative risk assessment is usually used as a means to compare several risks or risk management strategies. At times there may be sufficient data to be able to perform a full quantitative risk assessment for a select number of risks, i.e. food–pathogen combinations. A quantitative model can provide more information about specific strategies to apply to that particular risk issue, but the quantitative results can also be used to place these more precisely evaluated risks into context with others of concern in a semi-quantitative environment.

Transparency in reaching conclusions

Semi-quantitative risk assessment is a system for sorting out risks, focusing on the big issues, and managing the entire risk portfolio better. The scoring system is inherently imperfect, but so is any other risk evaluation system. If the scoring system being used can be shown to produce important errors in decision logic, then one can use potentially more precise quantitative risk assessment arguments or change the scoring system to something more suitable.

Semi-quantitative risk assessment may offer some advantages in achieving transparency. No sophisticated mathematical model is necessary, for example, which is appealing to the lay person. However, the use of mathematical models as an obstacle to transparency may be overemphasized. Most food safety risk assessments require understanding of complex microbiological information and a reasonable understanding of human medicine and of epidemiological principles, which tend to be postgraduate topics. In contrast, quantitative risk assessment uses mathematics that are generally covered at an undergraduate level. The main obstacle to transparency of quantitative models is that there are only a few people who have specialized in the field.

The key transparency issue with semi-quantitative risk assessment arises from the granularity of the scales used in scoring. The usually rather broad categories mean

that any distinction between risks, that can be considerably different in probability and/or severity magnitude, is lost. This means, for example, that one food industry could be unfairly penalized because its product lies just above a category bound, or that industry or regulator only have the incentive to push a risk just over, or below, a category boundary.

7.4 QUANTITATIVE RISK CHARACTERIZATION

7.4.1 Introduction

As described in Section 5.2.3, quantitative assessment can be either deterministic or stochastic. Examples of deterministic quantitative risk assessments can be found most readily in the food additive safety assessment (also known as chemical risk assessment) literature. However, most of the literature, guidance and the best-known examples of quantitative microbiological risk assessments are stochastic. This approach offers many advantages over deterministic risk assessment, and these advantages are described in Chapter 11. FAO and WHO have produced numerous examples of stochastic QMRAs, through the Microbiological Risk Assessment Series, as have many food safety authorities around the world; some examples are provided in Section 8.2

Quantitative risk characterization addresses risk management questions at a finer level of detail than a qualitative or semi-quantitative risk characterization and facilitates a more precise comparison between risks and between risk management options. This extra level of detail can be at the expense of a far greater time to completion, a reduction in scope and a greater difficulty in understanding the model. Probabilistic techniques are more complex and therefore introduce a greater likelihood of error or misunderstanding. Quantitative risk assessments may also rely on subjective quantitative assumptions (WHO and OECD, 2003), and the mathematical precision of these quantitative results can inadvertently give a false impression of the degree of accuracy in characterizing risk. This has been recognized for a long time in the risk analysis community, e.g. Whittemore (1983) noted, "Quantitative risk analyses produce numbers that, out of context, take on lives of their own, free of qualifiers, caveats and assumptions that created them."

7.4.2 Quantitative risk measures

Quantitative measures of risk combine the two quantitative components of risk: (a) a measure of the probability/amount of the hazard consumed (i.e. exposure) and (b) the subsequent severity of the health effect (Kaplan and Garrick, 1981).

Measure of exposure

The probability of exposure in microbiological food safety risk assessment must relate to a specified level of exposure, which is the result of the exposure assessment component (Chapter 5). The subsequent probability measures of risk are expressed generally as risk of an outcome (e.g. probability of illness per serving) or as population risk (e.g. probability of the population experiencing more than 10 illnesses per year).

There are advantages and disadvantages in selecting each probability measure. The first option underlines the probabilistic content of the risk measure, while the second can be misread to make one believe that the risk event will occur deterministically with the specified frequency. However, explicit identification of the distribution of the risk measure, or associated probability intervals, helps to counter that perception.

The probability measure needs to be chosen carefully and in collaboration with the risk managers. This allows any explanation of the risk assessment results to be made as clear as possible to the intended audience.

Measure of health effect

There are different ways of expressing risk (EFSA, 2012a). Codex Alimentarius defines risk as "A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard(s) in food" (CAC, 2019). There are different metrics that have been developed to characterize and compare risk including the number of an adverse outcome, the QALY, the DALY, as well as metrics for monetary valuation of public health (EFSA, 2012b). Each of these metrics has some advantages and disadvantages, and there is no universally preferred choice. Each individual metric provides a different perspective on the public health risk of foodborne pathogens and the choice should be based on the purpose and scope of the risk assessment. The selected measure(s) of health effect will reflect what the risk manager cares about.

There are many potential adverse health effects that a risk manager might be interested in, in addition to those about which the affected individual is directly concerned. This, in turn, means that there are many possible ways to measure and express the magnitude of the risk, sometimes called the *risk metric*, that might be selected as the required output from a risk assessment. The selection of a particular measure of risk is therefore not necessarily straightforward, and must be discussed between the risk manager, the risk assessor, and other interested stakeholders. In addition, for quantitative modelling, the unit(s) required must be defined whilst

considering the practical aspects of modelling so that the outputs can be produced and reported in those units.

A) Number of adverse outcomes: The number of adverse outcomes (e.g. illnesses, hospitalizations, deaths) is the simplest metric that can be used in risk assessment. This number (or the probability) of adverse outcomes can be estimated as "per serving" or "per annum" and standardized for population size (e.g. per 100 000 per year). In general, the per annum relative risks inherently have a greater degree of uncertainty than the corresponding per serving relative risk because of the additional uncertainty associated with the number of annual servings (EFSA, 2012b). Another factor that affects relative risk on a per annum basis is the size of the susceptible subpopulations, relative to the total population, which are substantially different, e.g. young, old, pregnant, immunocompromised (YOPI). Note that not all subpopulations may be equally susceptible to all hazards, e.g. susceptibility to infection may differ between subpopulations.

- **Risk of some outcome per serving** requires that a serving be defined (e.g. 100 g of cooked chicken, 150 ml of orange juice, or use of a serving size probability distribution). The risk of some outcome per serving measure provides an easy comparison of the risk from direct consumption of different food products. It can also be helpful in establishing cost–benefit type arguments where, for example, one is looking for the lowest risk for a given nutrition requirement.
- **Individual risk** can be specified for a random individual within the population of concern, or for a random consumer of the product. If a random consumer of the product is assumed this presupposes that there are no significant secondary infections or cross-contamination effects. Random individuals can be assumed to be part of various subpopulations if one wishes to explore the risk to different subpopulations. Examples of different individual risk estimates include:
    1. The probability per year that a random individual will suffer illness X from exposure to bacteria Y in food Z.
    2. The probability per year that a random individual will suffer any deterioration in health X from exposure to bacteria Y in food type Z.
    3. The probability that a person will suffer some adverse health effect in their lifetime from exposure to bacteria Y in foods.
    4. The expected number of foodborne-related adverse health events for a random individual from consuming food type Z in a year.
    5. The distribution of the number of foodborne-related adverse health events for a random individual from consuming food type Z in a year.
    6. The per capita expected incidence of health impact X from food type Z.

7. The expected incidence of health impact X per kg consumed of food type Z by the nation.

   This risk per person is usually a very low number (e.g. 0.000 013 expected illnesses per person per year), making it difficult to understand and compare. These values can be made more understandable by considering the risk over a large number of people (e.g. 1.3 expected illnesses per 100 000 people per year).

- **Population–level risk** considers the risk distributed over the population or subpopulation of interest. It may or may not distinguish between subgroups within that population, such as by region, ethnicity, age or health status. The following are some examples of population–level risk estimates:
  1. Total expected number of cases of foodborne illness within the population in a year.
  2. Expected number of hospital bed–days taken up per year as a result of a particular foodborne pathogen.
  3. Probability that there will be at least one outbreak (or one death, one illness, etc.) in the population in a year.
  4. Probability that there will be more than 10 000 illnesses in the population in a year.

  These estimates can be produced for separate subpopulations if required and aggregated to a single measure for the whole population.

B) Health adjusted life years (Burden of disease): Summary measures of public health can characterize and compare the health effect of diverse risks and health outcomes. These are particularly useful when a risk assessment is considering different pathogens. For example, deciding between risk management options that pertain to two different pathogens requires a method that accounts for the differences in severity between those pathogens. In contrast, if a risk assessment is concerned with a particular product–hazard pairing, and the severity of outcomes is independent of exposure pathway, then these summary metrics are less critical. For example, deciding between risk management options that pertain to controlling illnesses for a particular product–hazard pair is less dependent on the differences in severity between the options (because this is the same).

Different methods have been developed that provide a common metric for more fully valuing and comparing health risks. Health-Adjusted Life Years (HALYs) are nonmonetary health indices and are summary measures of population health

permitting morbidity and mortality to be simultaneously described within a single number (Gold, Stevenson and Fryback, 2002). HALYs are used in economic cost–effectiveness analyses, also sometimes referred in the literature as cost–utility analysis or weighted cost–effectiveness analysis (Mangen *et al.*, 2010). The two most prominent HALYs are QALYs and DALYs.

The DALY is based on the amount of life quality lost multiplied by the duration of that health state (Van der Fels-Klerx *et al.*, 2018). They are useful for overall estimates of burden of disease, comparisons of the relative effect of specific illnesses and conditions on communities, and in economic analyses. The DALY method presumes perfect health for the entire life span, and therefore measures the loss due to ill health. The QALY concept is analogous, but measures the increase in quality of life, and its duration, as a result of an actual or putative intervention.

The DALY approach allows one health state to be compared with another, and with mortality itself. Integrated health measures provide information to put diverse risks into context. DALYs lost is the summation of two quantities:

1. YLL: Years of life lost (the difference between the age at death and the life expectancy)
2. YLD: Years lived with a disability (multiplied by the extent of the disability)

Given values of these disability rates, and data on time course (distribution) of severity of outcomes, the DALYs in units of total years of impact in the population under consideration can be computed (Ssemanda *et al.*, 2018). This formulation recognizes that different illnesses will have different patterns of severity and longevity of disability (Haas, Rose and Gerba, 2014). The DALY methodology has been widely used in both national (Lake *et al.*, 2010; Monge *et al.*, 2019; Scallan *et al.*, 2015; Ssemanda *et al.*, 2018) and global (Mangen *et al.*, 2010) disease burden estimations or to compare the burden of disease estimates attributed to different cooking practices (Berjia, Poulsen and Nauta, 2014). The DALY approach has also been used by WHO to quantify the global burden of foodborne disease as it incorporates life years lost through specific types of disability, pain or other reduced quality of life, including premature mortality. The WHO Initiative to Estimate the Global Burden of Foodborne Diseases (WHO, 2015) provides estimates of global foodborne disease incidence, mortality, and disease burden in terms of DALYs for 31 foodborne hazards (including 11 diarrhoeal disease agents, 7 invasive infectious disease agents, 10 helminths and 3 chemicals).

A related approach to integrate the spectrum of health outcomes is the QALY approach. QALYs differ from DALYs primarily by the nature of the weights used.

Rather than using expert-derived "disability weights," the QALY concept uses "quality weights" which are based on survey or preference data to assess the relative perceived quality of life under certain health impairments. Such an approach allows for the differentiation among subpopulations, socioeconomic conditions, and differences in underlying society (Haas, Rose and Gerba, 2014).

The DALY method is considered by some to be preferable to the QALY method for making societal resource allocation decisions. The QALY method was intended to evaluate the benefit in quality of life improvement through a medical intervention, i.e. compared to the cost, while DALY mostly seeks to quantify the burden of disease due to a particular hazard in a particular context.

A strong point of the overarching HALY approach is that utility and disability weights are not income constrained. However, HALYs do not capture effects that are not health related and HALY effects cannot be compared to other nonhealth projects, as would be the case if all effects would be expressed in monetary values (Mangen *et al.*, 2010). HALYs are based on the assumption that a life–year is the appropriate metric for measuring health; as a result, the valuation of permanent disability and mortality is linearly valued by age of patients. DALYs and QALYs are semi-quantitative estimates based on disability scoring, and their accuracy depends greatly on the quality of input data and risk assessment models used for estimating the incidences of relevant health outcomes (Van der Fels-Klerx *et al.*, 2018).

C) Monetary risk metrics: The public health effect of foodborne disease can also be characterized using monetary metrics (Mangen *et al.*, 2010). However, health economics is a branch of economics with additional complexities (Arrow, 1963). Factors that distinguish health economics from other areas include extensive government interventions, uncertainty in several dimensions, asymmetric information (the physicians know more than the patients), barriers to entry, externalities (communicable diseases, fear of catching disease) and the presence of a third-party agent (professional health care provider).

Several different approaches have been developed for the monetary valuation of risk (Mangen *et al.*, 2010). The three general approaches are:

- the human capital approach, measuring a person´s production in the marketplace;
- cost of illness (COI) methods; and
- revealed or stated preferences which also include immeasurable factors such as suffering and pain.

With the human capital approach, the benefits of a health program or costs of disease is measured by the effect on a person's productive input. The human capital approach is generally restricted to the effects on labour productivity (e.g. foregone income) and makes no attempt to include intangible costs. It is therefore not considered a measure of individual or social welfare. Opportunity costs of time or a replacement cost approach are two methods usually used to value the time for nonmarket activities (e.g. home-keeping).

A second approach to measuring the public health impact of disease is the COI method. The COI approach does not measure intangible costs but traces the economic flow associated with an adverse health outcome through the quantification of measurable monetary costs. COI measures include (Mangen *et al.*, 2015):

1. the costs related to the resources used within the healthcare sector;
2. the resources used by patients and their families; and
3. productivity losses and other, not healthcare related, resources used that are indirectly related to illness (e.g. special education).

The COI method estimates the money spent on medical expenditures and the value of the productivity of the patient foregone as a result of foodborne illnesses, complications and deaths. It can be applied wherever there are quantitative data relating to the effect of disease and sufficient cost data for calculating resultant treatment costs and loss of income. Subject to data availability, it is possible to compare large numbers of food risks using COI (Van der Fels-Klerx *et al.*, 2018). COI can be applied for comparing diseases (Mangen *et al.*, 2015), for food–disease combinations (Thomsen *et al.*, 2019), for supply chain analysis of a single food–disease combination (Duncan, 2014; McLinden *et al.*, 2014; Monge *et al.*, 2019), and for comparing the cost–effectiveness of different interventions to reduce the foodborne risk (Lawson *et al.*, 2009).

A third approach uses stated preference studies that are based on the presentation of hypothetical scenarios on which to evaluate how much a person would pay for reductions in the risk of death or other adverse health states. Stated preventative studies can be designed for a specific health state, but are based on a hypothetical construction and, therefore, describe the intention of individuals to adopt particular decisions (Mangen *et al.*, 2010).

Matching dose–response endpoints to the risk measure

Exposure to microbiological agents can result in a continuum of responses ranging from asymptomatic carriage to death. Risk characterization needs to consider the

reported health outcome used in developing the dose–response relationship and may require estimating the desired risk assessment endpoint(s) from a more or less severe measurement endpoint. A fraction of exposed individuals will become infected. Infection may be measured as the multiplication of organisms within the host, followed by excretion, or a rise in serum antibodies. The *morbidity ratio* is the fraction of those infected who will exhibit symptomatic illness, as measured by clinical observation or reported by patients or consumer responses (Haas, Rose and Gerba, 2014). A fraction of those becoming ill will suffer severe symptoms (e.g. bloody diarrhoea), require medical care or hospitalization, or will die. In the case of death, this fraction is known as the *case–fatality rate* or *mortality ratio* (Haas, Rose and Gerba, 2014). It should also be noted that DALY and QALY are not typically dose–response endpoints; rather, the endpoints are infections, illness, death. A template (e.g. DALY/case) must be used to translate the risk estimate (e.g. cases) from a quantitative microbial risk assessment to DALYs, etc.

In addition, care must be taken to ensure that the implications of the case definition used in a clinical trial or epidemiological investigation are understood. For clinical trials, typical measurement endpoints include infection (e.g. as indicated by a faecal positive) or illness (e.g. as indicated by diarrhoea). Epidemiological surveys may provide information on morbidity and mortality ratios. These ratios might be dose-dependent, but epidemiological data may not indicate this relationship. In some cases, clinical trials have used a continuous dose–response measurement endpoint (e.g. volume of diarrhoea excreted) that might provide some insight about the dose-dependency of outcome severity (Coleman *et al.*, 2004).

Accounting for subpopulations

Subpopulations may vary with respect to susceptibility, exposure, or both. If the risk characterization seeks to distinguish risk by subpopulation (e.g. by age class), then the exposure assessment outputs should be kept separate for each subpopulation to reflect variation in exposure among them (e.g. the frequency, size and preparation of servings consumed by members of each age class). Even where separate dose–response relationship by subpopulation cannot be specified, it may be informative to characterize risk by subpopulation.

The subpopulations of interest to the risk managers (e.g. susceptible consumers) may not correspond directly to easily identified categories (e.g. age classes). There should be a reasoned basis for classifying consumers as members of different subpopulations, and that subpopulation definitions are consistent between the exposure and dose–response analyses.

7.4.3 Integration of hazard characterization and exposure assessment

Codex guidelines describe the need to assess exposure to a hazard and assess the level of risk that the exposure represents. Most quantitative risk assessments will implement the exposure and dose–response models separately, and risk characterization will connect these to estimate the risk. This need for connection should be included in the planning stage of the modelling whenever possible, to avoid having to adjust the output of exposure or the input of the dose–response to achieve consistency.

When there is a logical separation between variability and uncertainty in either the exposure assessment or hazard characterization, this distinction should be propagated through the integration to determine both the variability and uncertainty in the relevant risk measures. Failure to maintain separation between variability and uncertainty can profoundly affect the risk characterization (Nauta, 2000). Additionally, assumptions implicit to specific dose–response models or potential biases in the dose–response estimates can limit how exposure and dose–response can be combined.

In the following sections the dose concepts formulated previously are briefly reviewed and suggestions are offered to address issues of maintaining consistency of units, dose–response model rationales and reducing biases when integrating potentially inconsistent exposure and hazard characterizations.

Units of dose in exposure assessment

According to Codex (CAC, 1999) the output of the exposure assessment is defined as an estimate, with associated uncertainty, of the likelihood and level of a pathogen in a specified consumer portion of food. This exposure estimate is commonly represented by a distribution of the probability that a randomly selected portion of food is contaminated with the hazard, combined with a probability distribution representing the numbers (or concentration) of hazard in contaminated portions of food (i.e. contain one or more cells of the pathogen).

Whether the level of contamination is expressed as a number, i.e. colony forming units (CFU), or concentration (CFU/g or CFU/ml) is important when linking this exposure output to a dose–response model. Numbers of CFU potentially ingested are necessarily positive integers, so a discrete distribution may be the most natural choice for the estimated exposure. The use of a continuous distribution for modelling of individual exposures would be most appropriate when pathogen concentrations are relatively high but these can always be converted back to a

discrete distribution with some rounding function. Continuous distributions are often used for bacterial counts because they are more flexible and easier to manipulate than discrete distributions. If a concentration is used to express the level of exposure, the concentration has to be multiplied by the amount of food ingested to determine the individual exposure. If the concentration being modelled is in the form of a probabilistic mean, then one needs to use dose–response functions for which inputs are probabilistic (usually, Poisson) mean doses rather than those whose input is an actual dose (Haas, 2002; Pouillot, Chen and Hoelzer, 2015).

Units of dose in dose–response assessment

Dose–response models in microbiological risk assessment typically apply the concepts of "no threshold" mechanisms, independent action and the particulate nature of the inoculum (Chapter 11). This results in the application of single-hit models like the exponential model, the Beta-Poisson model approximation, the Weibull-Gamma model and the hypergeometric model (Haas, 1983; Teunis and Havelaar, 2000). These models assume each ingested cell acts independently, and all cells have the same probability of causing infection. The "no threshold" assumption implies the existence of some level of risk for any dose greater than zero.

A review of dose–response models is provided Chapter 13. The two principle types of data used for dose–response modelling are clinical feeding trials with human volunteers, and epidemiological outbreak data or data on disease incidence associated with foodborne exposure. These different types of human data have varying strengths and weaknesses, as discussed in Chapter 10.

Combining exposure and dose–response assessments

Consistency is important when combining exposure and dose–response assessments. The exposure assessment and hazard characterization should be applicable to the same hazard and the same population. For example, one might mistakenly apply a dose–response relationship, estimated using data from young healthy volunteers, to a less homogenous population that includes susceptible individuals. Such extrapolations should be avoided, if possible, by looking at alternative modelling approaches. However, if extrapolation is done, then it should be clearly explained, and the potential biases and uncertainties of such extrapolation should be incorporated in the assessment.

The output of the exposure assessment should be in units of ingested organisms (CFU, cells, virus particles, etc.) per individual and usually on a per-exposure event basis. In contrast, the input of the dose–response may not be on a per-individual level. For example, the exposure may be expressed as a mean or other summary

of a distribution of exposures over a group of individuals (e.g. Teunis *et al.*, 2010), though this should be avoided. Differences between individual– and group–level exposure summaries in a hazard characterization may create problems of consistency when combining them.

Exposure assessment and hazard characterization can be combined in a Monte Carlo simulation by calculating a probability of infection (or illness) associated with each sample from the exposure distribution. For a given sample containing a known number of cells from the exposure distribution, the probability of infection from the specified dose, would then be calculated based on the dose–response relationship. Exposure and risk predictions will generally be uncertain due to the uncertainty associated with alternative models of the exposure distribution and the risk of illness at any specified dose level. These uncertainties extend to predictions of risk when the exposure and dose–response are combined and should be properly represented in the output of the assessment.

Limitations of quantitative risk characterization

Just as with qualitative and semi-quantitative risk characterization, there are limitations of quantitative risk characterization. These primarily stem from its advantages and are related to the potential need for large quantities of data, as well as the use of complex models. Because of the data and modelling needs, some multidisciplinary teams tasked with performing quantitative risk characterization can be quite large, and thus costly and time-consuming. Deciding on how to incorporate uncertainty in the risk assessment and explaining uncertainty can be challenging. The complex nature of the models often makes the review of such models limited to select experts, as well as time consuming. This complexity can also provide a challenge to transparency as complex models may not be easily interpreted by nonexperts.

8

Examples

The examples below are provided to give a perspective on the breadth and depth of published risk assessments, to make the concept of risk assessment more tangible for Codex, FAO and WHO member countries, and to provide example guidance for their own development of risk assessment activities. These examples cover a range of situations, including country and regional level; from the early days of risk assessment to more recently; completed by government employees or in partnership with academic experts; a focus on a particular food product or covering large food categories; for one or more pathogens; for a specific part or the whole food chain. Most of the risk assessment focus on infectious pathogens, but one focuses on the toxin histamine produced by microbial action. Examples of qualitative and semi-quantitative risk assessments are provided in Section 8.1, while quantitative risk assessments can be found in Section 8.2.

8.1 EXAMPLES OF QUALITATIVE AND SEMI-QUANTITATIVE RISK ASSESSMENTS

8.1.1 Risk assessment for main determinants of antibiotic resistance in South East Asia

The emergence of antibiotic resistant bacteria and genes has been observed. A qualitative risk assessment was conducted to evaluate the relative effects of the main determinants of antibiotic resistance, and to estimate the risk of the emergence and spread of antibiotic resistance among humans in the WHO South East Asia region (Chereau *et al.*, 2017). Factors were examined at the policy

level (e.g. scope of policies and guidelines), system level (e.g. implementation of healthcare, wastewater, or agriculture and livestock management options), and at individual level (e.g. human behaviour).

The region considered includes the 11 countries Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, and Timor-Leste. Seven bacteria with high levels of antibiotic resistance were considered as part of the hazard identification. The study focused on those causing infections with high mortality, namely extended spectrum β-lactamase and carbapenemase producing *Enterobacteriaceae* and methicillin resistant *S. aureus* (MRSA).

The processes leading to the acquisition, selection, and spread of the resistant bacteria and genes in humans was described as part of the exposure assessment. This included the reservoirs, transmission routes, and biological determinants of the emergence and transmission of resistance. Exposure routes considered included the release from human and animal waste, aquaculture, and pharmaceutical industry, ingestion of contaminated food and water, direct contact with reservoirs (animals, soil, water), and human-to-human transmission (including health case workers).

A context assessment was also conducted to look at the environment in which the event is taking place, considering socioeconomic, ecological, other factors that may affect the exposure and/or risk.

The likelihood of occurrence of each event was rated using a qualitative approach using the following categories:

- Negligible: the event occurs under exceptional circumstances
- Low: the event occurs some of the time
- Moderate: the event occurs regularly
- High: the event occurs in most circumstances.

The events in the chain were chronologically integrated leading to transmission of antibiotic resistance in the human population using a matrix to calculate the risks from two consecutive, and dependent events. When multiple independent events contributed to the estimation of risk, the highest risk was used. The risk matrix used was from Wieland *et al.* (2011), which is designed to combine two risk estimates based on the assumption that the second event is fully conditional on the previous event (see Table 16).

The risk assessment concluded that South–East Asia is at high risk of the emergence and spread of antibiotic resistance in humans. The assessment provides an overall

picture of the factors affecting the emergence of antibiotic resistance emergence in humans in the region, and highlights the limited benefit of interventions that are sector specific as opposed to an overall holistic "One Health" approach.

TABLE 16. Risk matrix used to combine two consecutive, and dependent events (adapted from Wieland *et al.*, 2011)

Event 2 / Event 1	Negligible	Low	Moderate	High
Negligible	Negligible	Negligible	Negligible	Negligible
Low	Negligible	Low	Low	Low
Moderate	Low	Low	Moderate	Moderate
High	Low	Moderate	Moderate	High

8.1.2 Faecal pollution and water quality, WHO

The *Annapolis Protocol* (WHO, 1999) was developed in response to concerns regarding the adequacy and effectiveness of approaches to monitoring and managing faecal-polluted recreational waters. One of the most important changes recommended in the Annapolis Protocol was a move away from sole reliance on guideline values of faecal indicator bacteria to the use of a qualitative ranking of faecal loading in recreational-water environments. The protocol was tested in several countries, and an expert consultation was convened by WHO. A revised Chapter 4 in Volume 1 of the guidelines was produced from the expert consultation, which described a suitable approach to risk assessment and risk management (WHO, 2003). Tables were produced for water bodies affected by three different sources of human faecal contamination: sewage outfalls, riverine discharges and bather shedding. The tables were based on qualitative assessment of risk of exposure under "normal" conditions of sewage operation, water levels, etc., and classified the potential human risk. Table 17 reproduces the classification for sewage outfalls.

TABLE 17. Relative risk potential to human health through exposure to sewage through outfalls (reproduced from WHO, 2003)

Treatment	Directly on beach	Discharge type short outfall[a]	Effective outfall[b]
None[c]	Very High	High	NA[d]
Preliminary	Very High	High	Low
Primary (including septic tank)	Very High	High	Low
Secondary	High	High	Low

(cont.)

Treatment	Directly on beach	Discharge type short outfall[a]	Effective outfall[b]
Secondary plus disinfection[e]	Moderate	Moderate	Very Low
Tertiary	Moderate	Moderate	Very Low
Tertiary plus disinfection	Very Low	Very Low	Very Low
Lagoons	High	High	Low

a) The relative risk is modified by population size. Relative risk is increased for discharges from large populations and decreased for discharges from small populations.
b) This assumes that the design capacity has not been exceeded and that climatic and oceanic extreme conditions are considered in the design objective (i.e. no sewage on the beach zone).
c) Includes combined sewer overflows.
d) NA = not applicable.
e) Additional investigations recommended to account for the likely lack of prediction with faecal index organisms.

8.1.3 Drinking water guidelines, Australian National Health and Medical Research Council

As part of Australia's National Water Quality Management Strategy the Australian National Health and Medical Research Council produced the Australian Drinking Water Guidelines (NHMRC, 2011). The guidelines are not mandatory standards but are designed to provide an authoritative reference document and framework for good management of drinking water supplies to assure safety at point of use by consumers in all parts of Australia. The guidelines consider that the greatest risks to consumers of drinking water are pathogenic microorganisms, and as such cover similar issues for water that microbiological food safety risk assessment covers for food. However, it should be noted that microbiological growth and inactivation are likely to play a much larger role in microbiological food safety risk assessment because of the greater potential for microbial growth in foods, and the application of strong inactivation processes that do not occur in water in nature. The extensive guidelines document includes a qualitative method for assessing human health risks and recommends that risks should be assessed at two levels so that priorities for risk management and application of preventive measures can be established:

- **Maximum risk** in the absence of preventive measures; and
- **Residual risk** after consideration of existing preventive measures.

It is stated in the document that "the aim should be to distinguish between very high and low risks" (NHMRC, 2011). The level of risk of each hazard (pathogen or hazardous event) can be qualitatively assessed by combining the likelihood of the hazard occurring and the subsequent severity of the consequences, according to the example categories listed in Table 18, Table 19 and Table 20 (Tables 3.1, 3.2 and 3.3 in the original document), though these can be modified as needed. The guidelines document also includes qualitative hazard identification characterizations for a wide range of waterborne hazards that can be used to assist in the application of the tables.

TABLE 18. Qualitative measures of likelihood

Level	Descriptor	Example description
A	Almost certain	Is expected to occur in most circumstances
B	Likely	Will probably occur in most circumstances
C	Possible	Might occur or should occur at some time
D	Unlikely	Could occur at some time
E	Rare	May occur only in exceptional circumstances

TABLE 19. Qualitative measures of consequence or impact

Level	Descriptor	Example description
1	Insignificant	Insignificant impact; little disruption to normal operation; low increase in normal operation costs
2	Minor	Minor impact for small population; some manageable operation disruption; some increase in operating costs
3	Moderate	Minor impact for large population; significant modification to normal operation but manageable; operation costs increased; increased monitoring
4	Major	Major impact for small population; systems significantly compromised and abnormal operation, if at all; high level of monitoring required
5	Catastrophic	Major impact for large population; complete failure of systems

TABLE 20. Qualitative risk analysis matrix: level of risk

	Consequences				
Likelihood	**1 Insignificant**	**2 Minor**	**3 Moderate**	**4 Major**	**5 Catastrophic**
A (almost certain)	Moderate	High	Very high	Very high	Very high
B (likely)	Moderate	High	High	Very high	Very high
C (possible)	Low	Moderate	High	Very high	Very high
D (unlikely)	Low	Low	Moderate	High	Very high
E (rare)	Low	Low	Moderate	High	High

8.1.4 BSE/TSE risk assessment of goat milk and milk-derived products, EFSA

A research group in France found a suspected case of Bovine Spongiform Encephalopathy (BSE) infection in a slaughtered goat in 2002. As a result, the European Commission (EC) requested advice from the European Food Safety

Authority (EFSA) on the safety of milk and meat in relation to Transmissible Spongiform Encephalopathy (TSE) in goats and sheep. EFSA (2004a) published the following preliminary statement:

> *From the limited data available today it is concluded that in the light of current scientific knowledge and irrespective of their geographical origin, milk and milk derivatives (e.g. lactoferrin, lactose) from small ruminants are unlikely to present any risk of TSE contamination provided that milk is sourced from clinically healthy animals. Exclusion of animals with mastitis is considered to reduce the potential risk. Further assurance of healthy milk could include milk tests for total somatic cell counts indicative of inflammation.*

EFSA also commented in a press release (EFSA, 2021):

> *A comprehensive and quantitative assessment of the risks involved in the consumption of goat meat, milk and dairy products will only be possible if more scientific research data on the occurrence of TSE in small ruminants can be obtained. Such a quantitative risk assessment, if feasible, will take considerably more time.*

It is extremely difficult to assess the risk of BSE-contaminated product because there is no means to measure the number of prions present in a food product. In addition, no human dose–response relationship for prion levels currently exists. EFSA nonetheless needed to provide comment on the level of the above risk and relied on an expert panel to review the available data.

8.1.5 Geographical BSE cattle risk assessment, EFSA

In 2003, EFSA was requested by the EC to reassess geographical BSE risk (GBR) and concluded the following (EFSA, 2004b):

> *The Geographical BSE-Risk (GBR) is a qualitative indicator of the likelihood of the presence of one or more cattle being infected with BSE, pre-clinically as well as clinically, at a given point in time, in a country. Where its presence is confirmed, the GBR gives an indication of the level of infection.*
>
> *The GBR assessments are based on information submitted by countries concerned in response to a European Commission recommendation in 1998 setting out the information requirements for such an assessment.*

> *The information concerns in particular imports of bovines and meat and bone meal (MBM) from the United Kingdom and other BSE-risk countries, rendering standards for animal by-products, use of so called Specified Risk Materials (SRMs), feeding of MBM to ruminants, etcetera.*

Table 3.5 [Table 21] shows the current GBR levels of the seven countries assessed by EFSA so far, as well as their former classification where available.

TABLE 21. Geographical BSE Risk (GBR) in 2003 in seven countries as assessed by EFSA (2004b; Table 3.5). Earlier assessed levels are also shown

GBR level	Presence of one or more cattle clinically or preclinically infected with the BSE agent in a geographical region or country	GBR of the country or region Current status (status before)
I	Highly unlikely	Australia (I)
II	Unlikely but not excluded	Norway (I), Sweden (II)
III	Likely but not confirmed or confirmed at a lower level	Canada (II), Mexico (N/A), South Africa (N/A), USA (II)
IV	Confirmed at a higher level	none

Note: N/A = not applicable, i.e. not assessed before

8.1.6 Risk profile of *Mycobacterium bovis* in milk, New Zealand Food Safety Authority

The New Zealand Food Safety Authority[2] commissioned the New Zealand Institute of Environmental Science & Research Ltd to provide a risk profile of *Mycobacterium bovis* in milk (Lake *et al.*, 2009).

The risk profile is used in the New Zealand food safety system to rank food safety issues for risk management. It forms part of the preliminary risk management activities (Figure 1).

The pathogen was selected for assessment because

> *Although it is likely to have minimal public health significance, demonstration of the safety of New Zealand produced food with respect to this pathogen may have trade implications. The food most commonly associated with transmission to humans is cow's milk.*

[2] The former New Zealand Food Safety Authority is now part of the New Zealand Ministry of Primary Industries.

The system for assigning a category for a food–hazard combination uses two criteria: incidence (rate) and severity. A four-category scoring system was proposed for the rate (see Table 22), based on foodborne disease rates experienced in New Zealand (Lake *et al.*, 2005). Note that this generic scoring system was adapted to *M. bovis* in milk.

Similarly, a three-category scoring system was proposed for the severity (see Table 23), based on a comparison of the proportion of New Zealand foodborne cases that result in severe outcomes, namely long-term illness or death (Lake *et al.*, 2005). This generic scoring system was also adapted to *M. bovis* in milk.

TABLE 22. The four generic categories proposed in New Zealand for the incidence (rate) with examples (Appendix 1 in Lake *et al.*, 2005)

Rate Category	Rate range (per 100 000 per year)	Examples of food hazard combinations
1	>100	Significant contributor to foodborne campylobacteriosis
2	10–100	Major contributor to foodborne salmonellosis Significant contributor to foodborne noroviruses
3	1–10	Major contributor to foodborne yersiniosis, shigellosis
4	<1	Major contributor to foodborne listeriosis

TABLE 23. The three generic categories proposed in New Zealand for severity with examples (Appendix 1 in Lake *et al.*, 2005)

Severity Category	Fraction of cases that experience severe outcomes	Examples
1	5%	Listeriosis; Shiga toxin-producing *Escherichia coli* (STEC); hepatitis A; typhoid
2	0.5-5%	Salmonellosis; shigellosis
3	<0.5%	Campylobacteriosis; yersiniosis; noroviruses; toxins

Analysis for *M. bovis* in milk was hampered by a complete lack of prevalence information, so it was considered impossible to make even qualitative statements of exposure. The only available dose–response data were from animal experiments from 1934 and earlier, making it meaningless to consider a usual food safety risk assessment of exposure and hazard characterization. Therefore, the risk profile is based solely on epidemiological data in an attempt to inform decision–makers of

how important the issue is among other food safety issues that need to be managed. The analysis discussed the available evidence and gave the following scores:

- **Severity**: 1 (>5% serious outcomes)
- **Incidence**: 4 (<1 per 100 000 people per year)
- **Trade importance**: High

Note that the risk assessment title described this as a "qualitative" risk assessment. However, the numerical definitions of the broad category bands would place it within the range of semiquantitative risk assessments, as used in this document.

8.1.7 Seafood safety using RiskRanger, Australia

Sumner *et al.* (2004) discuss the continuum between qualitative and quantitative risk assessment for seafood, and introduce a semi-quantitative risk assessment method that had been coded into a freely-available software tool called RiskRanger (Ross and Sumner, 2002; Sumner and Ross, 2002; CB Premium, 2021). The tool requires answers to 11 questions, which describe the factors throughout the food chain that affect the food safety risk. The questions can be answered in either qualitative (with predetermined categories) or quantitative terms. Qualitative answers are converted to quantitative values according to lookup tables.

The model is intended to be population specific, so key inputs like total and/or regional population size are required. A score is calculated from the inputs, allowing the ranking of various food–hazard combinations. The scoring system is designed to have a scale of 0 to 100, where 100 represents the worst imaginable scenario, i.e. that every member of the population consumes a lethal dose every day. A score of 0 was arbitrarily set to equate to one mild diarrhoeal case per 100 billion people per hundred years, the logic being that the Earth's population is significantly less than 100 billion, so one would not expect to see an occurrence of the risk anywhere within a person's lifetime. The chosen range extends over 17.6 orders of magnitude, which equates to $100/17.6 \approx 6$ "risk ranking units" for each factor of 10 between risks.

The method has been designed to screen risks and to screen major categories of risk management options. The interface allows a risk manager to instantaneously consider what-if scenarios that can stimulate discussion of possible risk management strategies. The simplicity and generic nature of the model means that its results remain fairly crude. It also means that the questions that are posed are very general. The authors go into considerable detail to warn the reader of these limitations. There is, for example, no incorporation of uncertainty and variability in the model.

The tool was used to evaluate ten Australian seafood hazard–product combinations, considering different consuming subpopulations in Australia. The results are shown in Table 24 (from Sumner and Ross, 2002). The authors compared the ranked risks against observations in Australia. There had been no documented cases in Australia for risks with a score <32. All risks with scores between 32 and 48 (a range of three orders of magnitude) had caused several outbreaks of foodborne illness in Australia, with the exception of *Vibrio cholera*. Risks with scores >48 had all caused outbreaks of large numbers, some in specific regions.

TABLE 24. Result of using RiskRanger to evaluate hazard–product combinations for various subpopulations in Australia (from Sumner and Ross, 2002)

Hazard–product pairing	Selected population	Risk ranking
Ciguatera in reef fish	General Australian population	45
Ciguatera in reef fish	Recreational fishers, Queensland	60
Scombrotoxicosis	General Australian population	40
Algal biotoxin in shellfish – controlled waters	General Australian population	31
Algal biotoxin — during an algal bloom	Recreational gatherers	72
Mercury in predaceous fish	General Australian population	24
Viruses in oysters — contaminated waters	General Australian population	67
Viruses in oysters — uncontaminated waters	General Australian population	31
Vibrio parahaemolyticus in cooked prawns	General Australian population	37
Vibrio cholerae in cooked prawns	General Australian population	37
Vibrio vulnificus in oysters	General Australian population	41
Listeria monocytogenes in cold-smoked seafoods	General Australian population	39
Listeria monocytogenes in cold-smoked seafoods	Susceptible (aged, pregnant, etc.)	45
Listeria monocytogenes in cold-smoked seafoods	Extremely susceptible (AIDS, cancer)	47
Clostridium botulinum in canned fish	General Australian population	25
Clostridium botulinum in vacuum packed smoked fish	General Australian population	28
Parasites in sushi or sashimi	General Australian population	31
Enteric bacteria in imported cooked shrimp	General Australian population	31
Enteric bacteria in imported cooked shrimp	Susceptible (aged, pregnant, etc.)	48

As an important caution the authors cite that they have not been able to systematically and objectively evaluate the model's performance because there are few data sets describing exposure and foodborne disease incidence. That caution, however, is evidence that full quantitative models would also not have been possible.

The authors also found that the model was a powerful tool for teaching the principles of risk analysis.

8.1.8 Animal and animal product import risk assessment methodology, Biosecurity Australia

In 1998, a trade dispute between Canada and Australia over Australia's 24-year ban of uncooked salmon went to the WTO court (WTO, 1998). The former Australia Quarantine Inspection Service had produced a qualitative risk assessment analysing the disease threat in 1995, and another in 1996 – the former assessed the risk to be acceptably low while the latter reached the opposite conclusion. The difference in conclusion was due to a different qualitative risk assessment approach being used, rather than through the emergence of new information. The WTO Appellate Body found in favour of Canada because, *inter alia*, it considered that Australia had not implemented a proper risk assessment of salmon imports. This highlighted to the risk analysis community the potential problems of relying on a purely qualitative risk assessment methodology.

Australia's regulatory body assessing import risk was restructured, and it now falls under the responsibility of Biosecurity Australia. They have developed a semi-quantitative approach to assessing import risk (Biosecurity Australia, 2016). The risk evaluation is based on placing the estimated risk in a risk matrix (Table 25). The band of cells marked "very low risk" represents Australia's ALOP, or tolerance for loss.

The guidelines describe qualitative (e.g. low, medium, high), semi-quantitative (e.g. 0 → 0.0001; 0.0001 → 0.001; 0.001 → 0.01; 0.01 → 1) and quantitative (exact probability calculation) evaluation of likelihood of entry of an exotic disease into Australia. This has the potential advantage of using one environment to incorporate risk assessments along the qualitative to quantitative continuum. Qualitative evaluations of steps in a sequence that results in exotic disease entry are allowed through a matrix rule for combining such qualitative probabilities.

The consequence assessment component of the risk estimate for an exotic disease import risk is generally considered far more difficult than evaluating the probability of disease entry. This is because imports are regulated and fairly simple to model,

and their probabilities are well understood, whereas there are no data on the spread of disease in the naïve country, and disease spread is extremely complex to model.

Biosecurity Australia aimed to evaluate the probability and magnitude of a variety of effects should the disease enter the country. They devised a series of rules that allowed the incorporation of the geographical extent of the consequence (local, district, regional, national), and the level to which the consequence would be felt at that scale. Other rules combined the qualitative or semi-quantitative estimates of likelihood of these consequences (given the disease has entered Australia) to allow a placement of the unrestricted risk estimate (i.e. the risk from a product where no specific controls are in place to protect against the hazard in question) in Table 25.

If the unrestricted risk estimate fell into an acceptable region, the import would be allowed without any restrictions. If not, restrictions (testing, heat treatment, etc.) would be evaluated to determine the least trade-restrictive option that would allow the import product to meet Australia's ALOP.

Whichever approach (or combination of approaches) is chosen, the guidelines state that the approach should provide for the following:

- an assessment based on sound science;
- an assessment that is structured and transparent;
- an assessment that is internally consistent, and that can be repeated (with the same or a similar outcome) by another operator using the same framework and data;
- an outcome that will support the estimation of risk (a combination of likelihood and consequences);
- an outcome that will enable risk to be evaluated against the importing country's ALOP; and
- a framework within which the efficacy of risk management and the acceptability of a mitigated risk can be evaluated.

TABLE 25. Tabulation of risk as a combination of likelihood and consequence (Biosecurity Australia, 2016)

Likelihood of pest entry, establishment and spread	Consequence of pest entry, establishment and spread					
	Negligible	**Very Low**	**Low**	**Moderate**	**High**	**Extreme**
High	Negligible risk	Very low risk	Low risk	Moderate risk	High risk	Extreme risk
Moderate	Negligible risk	Very low risk	Low risk	Moderate risk	High risk	Extreme risk
Low	Negligible risk	Negligible risk	Very low risk	Low risk	Moderate risk	High risk
Very Low	Negligible risk	Negligible risk	Negligible risk	Very low risk	Low risk	Moderate risk
Extremely Low	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Very low risk	Low risk
Negligible	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Negligible risk	Very low risk

8.1.9 Multicriteria-based ranking for risk management of foodborne parasites, FAO/WHO

FAO and WHO were asked to review the current status of knowledge on parasites in food and their public health and trade impact (FAO and WHO, 2014). This was done to provide the Codex Committee on Food Hygiene with advice and guidance on the parasite–commodity combinations of concern, issues that need to be addressed by risk managers, and the options available to them. As part of this charge some work was undertaken to develop a quantitative ranking tool using expert opinion.

The experts defined global criteria for evaluating the 24 foodborne parasites and rated each parasite along these criteria. The criteria were: (1) number of global illnesses; (2) global distribution; (3) acute morbidity; (4) chronic morbidity; (5) percentage chronic; (6) mortality; (7) increasing illness potential; (8) trade relevance; and (9) socioeconomic effect. Each criterion was then weighted by the experts for importance and averaged. The three criteria for disease severity (3, 4 and 5) were combined into one criterion, giving a total of 7 criteria weights, reflecting the relative importance of each criterion to the overall score. The average of the elicited criteria weights used in the multi-criteria ranking are shown in Table 26. The overall score for each parasite is calculated as follows.

$$\text{Score} = C1*W1+C2*W2+\{C3*(1-C5)+C4*C5\}*W345+C6*W6+C7*W7+C8*W8+C9*W9$$

The resulting tool was able to give a global ranking of foodborne parasites by importance and their primary food vehicle.

TABLE 26. Average of elicited criteria weights used in the multi-criteria ranking (Table 3 from FAO and WHO, 2014)

Scoring Criterion		Criterion Weight
W1	Number of global foodborne illnesses	0.22
W2	Global distribution	0.14
W345	Morbidity severity	0.22
W6	Case-fatality ratio	0.15
W7	Increased illness potential	0.07
W8	Trade relevance	0.10
W9	Impacts on economically vulnerable communities	0.10

8.2 Examples of quantitative risk assessments

8.2.1 E. coli O157:H7 in tenderized vs non-tenderized beef, FSIS

Mechanical tenderization, performed using stainless steel blades or needles, moves pathogens from the surface of intact beef cuts to beneath the surface, thereby potentially shielding those pathogens from the lethal effects of heat during cooking.

The United States of America Department of Agriculture's Food Safety and Inspection Service (FSIS) aimed to estimate whether blade-tenderized steak posed a significantly greater risk than its nontenderized equivalent (FSIS, 2002). They created a quantitative simulation model that predicted the change in survival of bacteria due to the extra protection that was afforded by being embedded in the meat through the tenderizing process. They estimated the bacterial load on steaks after cooking and used this concentration as input into a dose–response model to estimate risk.

FSIS concluded that the probability of *E. coli* O157:H7 surviving typical cooking practices in either tenderized or non-tenderized steaks is minuscule and that differences in bacterial dose after cooking attributable to either type of steak were minimal. They predicted seven additional illnesses due to tenderization for every billion steak servings. This can be seen from Figure 9 below, where the dotted and solid lines for tenderized and non-tenderized steaks are virtually indistinguishable.

This was a comparative risk assessment, so the model contained only the elements that were necessary to make the comparison. Thus, the model began with the distribution of bacteria on steak prior to tenderizing, and then looked at the difference in human health risk posed by the same steak under different processing. Consequently, there was no need to consider any factors involved in the rearing and slaughtering of the animal.

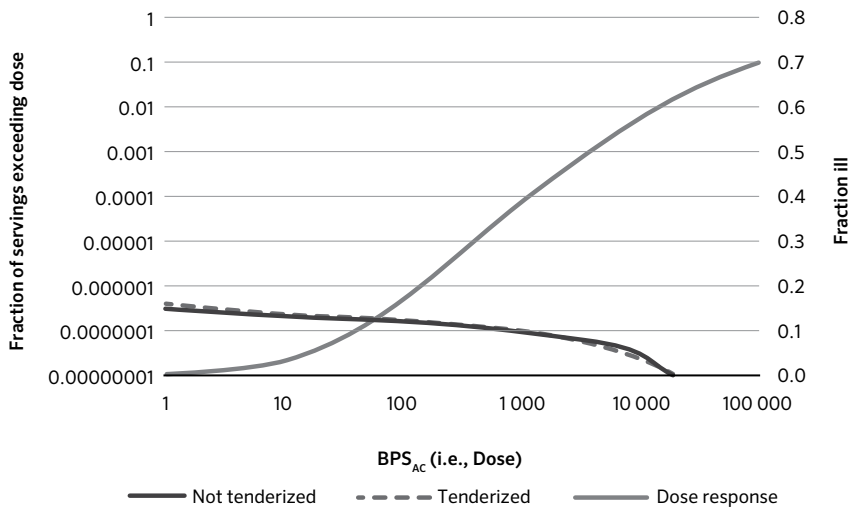


FIGURE 9. Model output (from FSIS, 2002) showing predicted bacteria per serving after cooking (Dose) and corresponding frequency of illness (Dose–response)

8.2.2 Listeria monocytogenes in ready-to-eat foods, FAO/WHO

FAO/WHO convened a drafting group to address three questions relating to *L. monocytogenes* that were posed by the Codex Committee on Food Hygiene (CAC, 2000). Those questions were to (i) Estimate the risk of serious illness from *L. monocytogenes* in food when the number of organisms ranges from absence in 25 g to 1 000 CFU/g (or CFU/ml) or does not exceed specified levels at the point of consumption; (ii) Estimate the risk of serious illness for consumers in different susceptible population groups (elderly, infants, pregnant women and immunocompromised patients) relative to the general population; and (iii) Estimate the risk of serious illness from *L. monocytogenes* in foods that support its growth and foods that do not support its growth at specific storage and shelf life conditions.

The risk assessment did not need to complete a full farm-to-fork model to answer these questions (FAO and WHO, 2004). The questions are also not specific to a particular country or product, which would require defining the scope of the model. The team decided to focus on the level of *L. monocytogenes* at retail; model the growth and inactivation from retail to consumption; and use a dose–response function to estimate the subsequent risk.

The team selected four ready-to-eat foods to be reasonably representative of the many different foods available. The quantitative analysis produced the results shown in Table 27.

TABLE 27. Estimated risk from *L. monocytogenes* as used in the risk assessment (FAO and WHO, 2004)

Food	Cases of listeriosis per 10^9 people per year	Cases of listeriosis per 10^9 servings
Milk	910	0.5
Ice cream	1.2	0.0014
Smoked fish	46	2.1
Fermented meats	0.066	0.00025

The risk assessment report provides a detailed explanation of the important limitations of the quantitative analysis. In particular, these included the need to rely on mostly European quantitative contamination data and on multiple sources for the prevalence estimates. Consumption data were mainly from North America, and the dose–response relationship was derived from epidemiological data from the United States of America. The summary response to the three Codex questions recognizes the caution that should be applied in interpreting the quantitative figures, by providing qualitative context.

> *The report notes that the risk assessment demonstrates that most cases of listeriosis result from the consumption of high numbers of Listeria. Those cases arise from foods where the L. monocytogenes level exceeds the criteria (either 0.04 or 100 CFU/g). The model predicts that consumption of low numbers of L. monocytogenes has a low probability of illness. Eliminating higher levels of L. monocytogenes at the time of consumption has a large impact on the predicted number of illnesses. (FAO and WHO, 2004)*

8.2.3 Shiga toxin-producing *E. coli* O157 in steak tartare patties, Netherlands

Nauta *et al.* (2001) simulated the exposure of the population in the Netherlands to Shiga toxinproducing *E. coli* O157 in steak tartare, using a farm-to-fork Monte Carlo model. This risk assessment provided an example of integration of exposure assessment and hazard characterization with a low-level dose and an individual–level dose–response relation. The baseline model predicted 0.29 percent contaminated tartare patties and a mean dose of 190 CFU per contaminated patty, as shown in Table 28.

TABLE 28. Baseline risk model results at the stage of raw steak tartare patties, for different routes of exposure and the means for the Netherlands (NL). (Pos. tartare = STEC O157 contaminated steak tartare patty), where the column headers refer to specific segments of the Dutch industry (article 10 slaughter with 'industrial' butcher, article 10 slaughter with 'traditional' butcher and article 4 slaughter)

	Art 10, ind.	Art 10, trad.	Art 4	NL
Prevalence	0.29%	0.30%	0.21%	0.29%
Mean cfu/pos. tartare	3.4	670	1700	190
Pos. tartare with one cfu STEC O157	72%	38%	36%	64%

The dose–response model developed for the hazard characterization was based on a well-documented outbreak in a primary school in Japan (Shinagawa, Hu and Yoshida, 1997). An exponential model, fitted separately to the data for children and adults, resulted in point estimates for the probability of infection by a single cell of r = 0.0093 for children and r = 0.0051 for adults.

The exposure distribution was combined with the dose–response model in a Monte Carlo simulation by applying the single-hit model in the form $1-(1-r)^n$, with *n* a random sample from the exposure distribution. The risk characterization predicted an attack rate of 0.0015 percent infections per person per year in the Netherlands; or 2 335 infections per 15.6 million people per year. This example incorporated variability but not uncertainty.

8.2.4 *Vibrio vulnificus* in raw oysters, FAO/WHO

An FAO/WHO assessment of the risk of illness due to *V. vulnificus* in raw oysters adapted a risk model previously developed in the United States of America for *V. parahaemolyticus* (FAO and WHO, 2005). A principle objective was to investigate potential effectiveness of mitigations after development of a baseline model. This risk assessment provides an example of integration of exposure assessment and hazard characterization, with different assumptions used in estimating the dose–response.

A dose–response relationship for *V. vulnificus* was obtained by fitting a Beta-Poisson model to estimated arithmetic mean risk for the population versus arithmetic mean dose (grouped by month and year). The magnitude of the difference between risk predictions obtained under two alternative interpretations of the dose–response is shown in Table 29. Assuming that the fitted population–level risk

versus dose relationship applied at the individual level resulted in predictions of risk that were consistently lower (by up to 75 percent) than the epidemiological estimates of mean risks. The predictions of risk obtained based on an aggregate-level interpretation of the dose–response were more consistent, on average, with the epidemiological estimates of mean risks used to obtain the dose–response fit, so this latter interpretation was used for risk characterization.

TABLE 29. Mean risk of illness due to *V. vulnificus* per serving or exposure

Season	Estimated data based on case reports and consumption statistics	Fitted as individual-level risk versus dose		Fitted as mean risk versus mean dose	
		Risk	Ratio to Estimated Data	Risk	Ratio to Estimated Data
Winter	1.40E-06	5.10E-07	0.36	1.10E-06	0.79
Spring	2.80E-05	1.70E-05	0.61	3.40E-05	1.21
Summer	4.90E-05	2.80E-05	0.57	3.90E-05	0.80
Autumn	1.90E-05	5.10E-06	0.27	2.30E-05	1.21

8.2.5 Histamine in fish sauce, Thailand

Fish sauce is a fundamental ingredient used in many South-East Asian dishes and is also used as a dipping condiment. Due to the nature of raw materials and the production methods for traditional fish sauce, high levels of histamine are found in many samples.

A risk assessment of histamine in Thai fish sauce was undertaken to respond to the request of the Codex Committee on Fish and Fishery Products (CCFFP) for sound scientific advice as a basis for the development of guidelines for the control of histamine in fish sauce (CCFFP, 2011).

Previous human trials and outbreak data were used to build a histamine dose–response model. Subsequently, the risk of developing histamine poisoning from fish sauce among Thai consumers was estimated. Consumption of fish sauce alone yielded a very small histamine intake for consumers. Different scenarios reflecting the effect of different histamine standards were also evaluated and are shown in the Table 30 below. As the analysis shows, the risk from fish sauce alone is essentially zero, and clearly less than the risk of histamine poisoning from fish alone. When the risk of histamine poisoning from fish and fish sauce was evaluated under two different standards, the risk increased slightly.

TABLE 30. Risk estimates using probabilistic approach (Table 5 in CCFFP, 2011)

Scenario	Mean risk per meal (SD)[a]
1. Fish sauce alone (a FS daily dose was consumed in one meal)	0.00 (0.00)
2. Fish alone[b] (a fish daily dose was consumed in a meal)	8.12×10^{-6} (0.4×10^{-5})
3. Fish + fish sauce (a FS daily dose was consumed in one meal) • 200ppm FS standard • 400ppm FS standard	8.39×10^{-6} (0.46×10^{-5}) 8.47×10^{-6} (0.52×10^{-5})

[a] Risk per meal refers to the predicted risk of an individual becoming ill of histamine poisoning when he or she consumes a daily dose of fish sauce (FS) or a daily dose of a scombroid fish or a scombroid fish with fish sauce. The risk was estimated as a probability of the histamine intake to exceed the No Observed Adverse Effect Level (NOAEL) limit of 50mg using Monte-Carlo simulations.
[b] Assumption: a fresh scombroid fish had a lognormal distribution with an average of histamine concentration of 5ppm and standard deviation of 10ppm.

8.2.6 Pathogens in fresh vegetables, Rwanda

This study analysed the farm-to-fork microbial risk for the fresh vegetable supply chain in Rwanda (Ssemanda, 2018). One of the major data gaps identified by the authors was that they could not attribute the estimates of food related illnesses to any food vehicle based on the available data. Despite these limitations, the authors were able to evaluate several scenarios related to the distribution chain.

1. Moving all vegetables from farms to food service establishments without going through markets.
2. Moving all vegetables from farms via supermarkets (with specialized refrigeration systems) to food service establishments.
3. Holding all vegetables under refrigeration (2 °C and 8 °C) from farm to fork and the introduction of a die-off model.
4. All vegetables are effectively washed and sanitized, accomplished by increasing the modelled logreduction by washing.
5. Assuming no contamination and crosscontamination occurs between vegetables and other surfaces throughout the chain.
6. Assuming that preventive measures and interventions implemented at farm level reduce prevalence and levels of pathogenic *E. coli* by 90 percent.
7. Assuming that the last three scenarios (4 to 6) are combined.

Simulation of the 7 scenarios resulted in varying fold-changes in the predicted microbial risk as shown in Table 31. Improvement in washing and sanitization at food service establishments resulted in less than a twofold change in the predicted microbial risk. About a two-fold reduction in risk was observed for the scenario

of channelling all vegetables through supermarkets instead of traditional markets (Route 3 in Table 31). Farm interventions reduced the predicted prevalence and levels of pathogenic *E. coli* in the baseline model by 90 percent, introducing a cold chain and skipping the market step resulted in a tenfold reduction in predicted microbial risk. The scenario of avoiding contamination and cross contamination along the supply chain led to a more than 4000-fold reduction in the predicted microbial risk. Lastly, combining the final three farm-to-fork measures resulted in an estimated reduction in risk of 1 million-fold.

TABLE 31. Number of illnesses per year and probability of illness per serving after 100 000 iterations of the baseline model and the what if scenarios (Table 6.4 in Ssemanda, 2018)

	No. of illnesses per year (in millions)		Probability of illness per serving		
What if scenarios [b]	**Mode**	**5th, 95th Percentile**	**Mode**	**5th, 95th Percentile**	**Fold change[#]**
Baseline/ Route 1[a]	12.1	6.96, 32.6	0.100	0.0572, 0.169	–
Improving washing and sanitization at FSEs	10.63	2.13, 27.8	0.1039	0.0151, 0.156	1.14
Route 3	6.26	0.828, 17.3	0.0535	0.0395, 0.0057	1.93
Farm Interventions	1.13	0.517, 3.101	0.01029	0.00395, 0.0165	10.71
Introduction of cold chain	0.288	0.218, 15.1	0.00042	0.0015, 0.1016	42.01
Route 2 (market step skipped)	0.139	0.195, 10.87	0.000455	0.0013, 0.0728	87.1
No contamination and cross contamination along the supply chain	0.00272	0.00339, 9.4	0.0000183	0.0002, 0.0564	4 449
Farm to fork measures and interventions	0.00001108	0.0000144,0.694	7.33×10^{-8}	0.000, 0.00494	1.1×10^{6}

[a] Baseline model or Route 1 represents a simulation of the supply chain through which about 90 percent of the vegetables are channelled from farms via traditional markets to food service establishments (FSEs)
– not applicable
Fold change were calculated by dividing the mode for the numbers of illness per year in the baseline model with the mode for the numbers of illness per year in the what if scenarios.
[b] What if scenarios arranged in descending order of the number of illnesses per year and probability of illness per serving.

8.2.7 *Campylobacter* and *Salmonella* in Chicken Meals, Senegal

The authors used a QMRA model to describe the risk of *Campylobacter* and *Salmonella* infection linked to chicken meals prepared in households in Dakar, Senegal (Pouillot *et al.*, 2012). The authors note that prevalence and concentration of pathogens in foods available in many countries are well-known data gaps for risk assessment. They also suggest that more information on home cooking practices, cooking processes, and the length and temperature of food storage before and after preparation are needed. They used data collected specifically for purposes of QMRA, including prevalence and level of bacteria on chickens from local markets, time–temperature profiles of chickens from purchase to consumption, observational data from meal preparation in kitchens, and data on pathogens prevalence on utensils, equipment and cooks' hands. Their model was developed in R software using the mc2d package for second-order Monte Carlo simulations. The simulation used 10 001 iterations in the variability dimension and 1 001 iterations in the uncertainty dimension. The model predicted that crosscontamination led to a high expected frequency of pathogen ingestion, and that significant *Salmonella* growth was predicted during food storage at ambient temperature before and after meal preparation. The model also predicted a significant decrease in risk could be achieved through reducing prevalence of chicken contamination at slaughter, and by using simple hygienic measures in the kitchen. The model indicated that most effective modification to home cooking practices include the use of a new board, knife, and dish when manipulating the cooked chicken, assuming that these objects are bacteria-free.

8.2.8 *Vibrio parahaemolyticus* in bloody clams, Thailand

A microbiological risk assessment of *V. parahaemolyticus* risk from *Anadara granosa* (Bloody clam) was conducted by researchers from Thailand and Japan. They developed two risk assessments (a farm-to-fork model and a fractional change model) based on new data collected primarily from Hat Yai City in southern Thailand, where seafood consumption is popular. The QMRAs were published as part of the FAO/WHO Microbiological Risk Assessment Series in a book entitled "Risk assessment of *V. parahaemolyticus* in seafood" (FAO and WHO, 2011a).

The purpose of the risk assessment was to estimate the risk of *V. parahaemolyticus* infection associated with consumption of one type of seafood in a defined setting and during a limited period. The work documents an example of a case study where scientists were able to conduct a series of clinical and microbiological studies to generate locally relevant data and elaborate a risk assessment model for a shellfish species other than oyster.

The authors report that the study estimated that only a few people per 10 000 people per year acquire *V. parahaemolyticus* infection as a result of consuming the boiled Bloody clam food. The risk estimate does not support the common perception that Bloody clam is a major cause of diarrhoeal illness, including *V. parahaemolyticus* illnesses.

At the same time, the investigators caution that this study may also underestimate the risk of Bloody clam-associated *V. parahaemolyticus* illness due to several critical data gaps. The authors recommended that a case–control study be conducted using patients in Hat Yai City with microbiologically confirmed *V. parahaemolyticus* infections, as this could provide data on various food and environmental exposure paths. These investigations might also provide more realistic evidence of behaviour that reduces or increases the risk of *V. parahaemolyticus* illness. The investigators also suggested that more bacterial data on Bloody clam throughout the food chain should be collected, focusing on detection of virulent strains. Finally, the authors encouraged the collection of more detailed data on behaviour regarding harvesting, storage, cooking and consumption patterns need to be collected.

A representation of the QMRA model for *V. parahaemolyticus* in Bloody clam from production to consumption is shown in Figure 10.

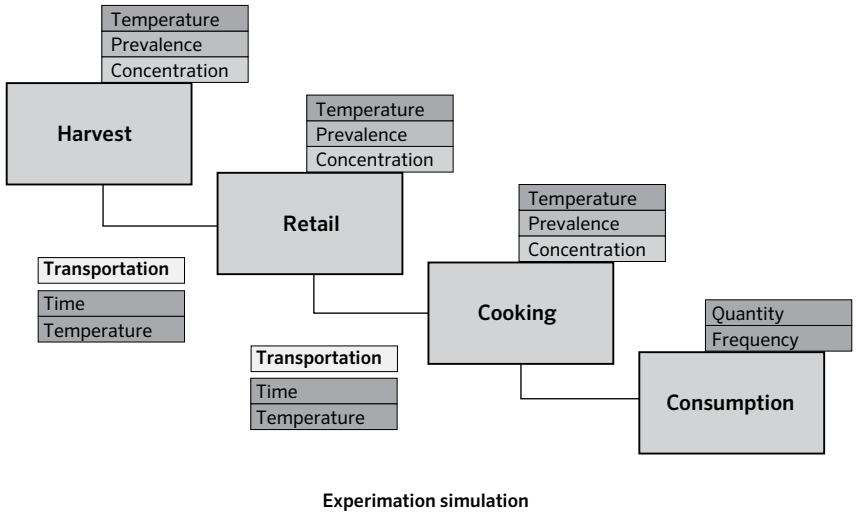


FIGURE 10. Schematic representation of the model framework for a production-to-consumption risk assessment of *V. parahaemolyticus* in Bloody clam (Figure II-6 in FAO and WHO, 2011a)

8.2.9 Salmonella in table eggs, EFSA

This risk assessment, originally developed by Thomas et al. (2006), was adapted by EFSA to answer a EC's, question about the risk of *Salmonella* in eggs (EFSA, 2014b). The EC asked EFSA to assess the public health risk posed by *Salmonella* from table eggs and to quantify the relevance of the period of time between laying and consumption and the storage conditions of eggs. The period of time between laying and consumption is related to the "Sellby date" and the "Bestbefore date". The Sellby date applicable to eggs is fixed at 21 days by the European Union (EU) Hygiene Regulation (EC) No 853/2004. This means that table eggs must be delivered to the consumers within of 21 days after laying. The Bestbefore date applicable to eggs is fixed in Regulation (EC) No 589/2008 at 28 days from laying.

EFSA applied a quantitative risk assessment model for *S.* Enteritidis in eggs to answer the question. The quantitative model excluded all stages before laying. A baseline scenario was defined according to the current Sellby and Bestbefore dates in the EU. Changes to time and temperature of storage at retail and in the household, were used to assess the effect of different storage practice scenarios (Table 32).

TABLE 32. Dates used in the model for the baseline and alternative scenarios (Table 11 in EFSA, 2014b)

Days post lay / Scenarios	Sell-by date (retail)				Best-before date (household/catering)					
	21	28	35	42	28	35	42	56	63	70
Baseline	●				●					
Alternative 1		●			●	●	●	●	●	●
Alternative 2			●			●	●	●	●	●
Alternative 3				●			●	●	●	●
Alternative 4		◇			●	●	●	●	●	●
Alternative 5			◇			●	●	●	●	●
Alternative 6				◇			●	●	●	●
Worst-case scenario				●						●

● Scenarios with egg storage at retail under current conditions
◇ Scenarios with egg storage under refrigeration conditions in all retail establishments

Storage temperature and time were modelled using distributions based on expert opinion. The remaining distributions were adapted from the model using expert opinion distribution or based on scientific literature. Table 33 below shows a summary of time and temperature of storage of eggs in the EU, from farm to retail as derived from industry expert opinion.

TABLE 33. Summary of time and temperature of storage of eggs in the EU, from the 'on farm' to the 'transport to retail' stages as derived from expert opinion (industry experts) (Table 6 in EFSA, 2014b)

	Time (hours)			Temperature (°C)		
Stage	**Min.**	**Most likely**	**Max.**	**Min.**	**Most likely**	**Max.**
On farm	0	45	168	4	15	30
Transport to grading	0	6	48	4	15	30
Grading	0	18	168	5	15	30
Transport to wholesale	0	5	48	0.1	14	30
Wholesale/ distribution centre	0	23	336	0.1	13	28
Transport to retail	0	7.5	36	0	14	30

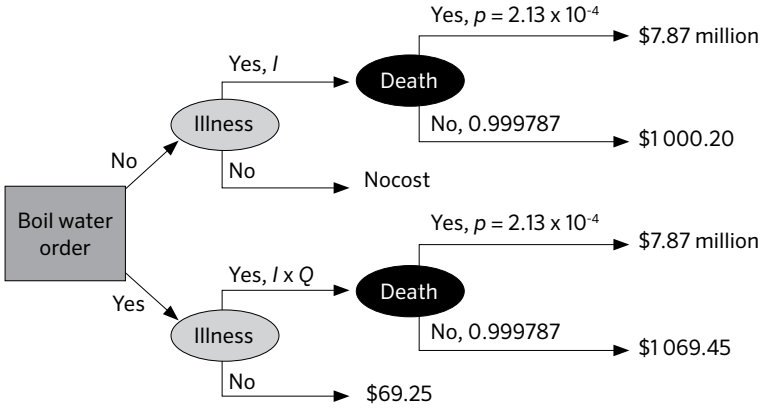
In the household setting, extending the storage time for table eggs resulted in an increase in the number of illnesses per million servings, except when eggs are well-cooked. Extending the Sellby date by one week (from 21 to 28 days), but leaving Bestbefore date unchanged, was estimated to result in a relative risk of illness of 1.4 and 1.5 for uncooked and lightly cooked egg meals, respectively, compared with the baseline. If the Bestbefore date was also extended by one week (from 28 to 35 days), the relative risk was 1.6 and 1.7. In the worstcase scenario considered in this assessment (Sellby date of 42 days, Bestbefore date of 70 days), the relative risks of illness were 2.9 and 3.5.

EFSA found that the implementation of refrigeration of all eggs during the retail stage (i.e. with temperatures assumed to range from 0 °C to 12 °C) limited this increase in risk in the household setting to some extent. Compared with the baseline scenario, the risk was reduced with an extension of up to three weeks in the Sellby date, and one or two weeks of the Bestbefore date for a sell-by date of 35 and 28 days, respectively, if refrigeration was applied in all retail establishments. If the Sellby date or the Bestbefore date were prolonged beyond three weeks,

then the risk estimates were greater compared with the baseline scenario, even if refrigeration at retail was applied, assuming that the proportion of consumers who do not store their eggs under refrigeration remained unchanged.

8.2.10 Cryptosporidium in water – a cost–benefit analysis, United States of America

The authors developed a simple decision tree (Figure 11) for Boil Water Order (BWO), including the effectiveness of the BWO and illness and death as possible outcomes (Ryan *et al.*, 2013a, 2013b). For each branch in the decision tree the authors assigned the relevant probabilities, including the probability of illness, probability of death, and probability of the boiling process being ineffective. The boiling process may not be effective due to the boiling time being too short or the boiled water being transferred to a nondisinfected container, or other factors. Estimates for these probabilities, for costs of implementation and for the various outcomes were based on published literature. The uncertainty in these estimates were evaluated using a Monte-Carlo sensitivity analysis.



I–the probability of illness, *Q*–the probability that the boil water order is ineffective, *p*–the probability of death from illness, 0.999787–the probability of no death from illness

FIGURE 11. Decision tree for Boil Water Orders for *Cryptosporidium* showing the probabilities and estimated costs for illness and death outcomes (Ryan *et al.*, 2013a). (Reproduced with permission from John Wiley and Sons)

The authors used the decision tree to calculate a threshold value for the oocyst concentration in treated water using an exponential dose–response model. This

was done by equating the BWO and No BWO branches and solving for the daily dose and associated concentration. The authors concluded that this threshold concentration was equal to 0.046 oocysts/L in treated water or 46 oocysts/L in raw water, which was considered to be more practical to assess using water sampling. These concentrations were estimated to result in 9 illnesses per 10 000 people exposed, given the assumed 3-$\log_{10}$ reduction during water treatment. However, the authors also noted that:

> *[…] many water supplies that exceed this concentration may already be applying additional treatment, given that a concentration of 46 oocysts/L would require treatment beyond the 3-log removal required by the Long Term Enhanced Surface Water Treatment Rule. (Ryan et al., 2013a)*