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Risk prioritization
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Abstract. Risk profile is the first step of stochastic quantitative process risk models, by identifying the potential pathogen-matrix combinations of safety concern, then enabling the risk ranking of these combinations. This in turn may assist food industries about existing or emerging food safety issues and the authorities (risk managers) in making informed decisions on further commissioning a systematic quantitative risk assessment to address public health concerns. Risk ranking can be based on a variety of criteria, associated with exposure to and the severity of a hazard. Among the most recent and popular ones is the Disability or Quality Adjusted Lost Years (DALYs), which assesses the relative impact of different diseases based on incidence rate, cost of illness, hospitalizations and deaths. There is also a great number of tools for risk ranking publicly available either in the form of XL-based software (e.g., Risk Ranger) or as web-based platform (e.g., iRisk). As a follow up, there has been an increasing trend of developing strategies for prioritizing risks based on critical questions addressing all the aforementioned issues. A detailed list of such approaches is appended here and advantages or the concerns for a universally accepted methodology are discussed.

Keywords. Risk ranking – Hazard prioritizing – Severity exposure – Assessment – Epidemiology – Profiling tools – Ranger – SIEFE DALYs – QALYs – Disability Lost.

Priorisation des risques. Outils et méthodologies récentes

Résumé. *Le profil de risque est la première étape des modèles de risques de processus stochastiques quantitatifs, qui identifie les combinaisons pathogène-matrice potentielles en matière de sécurité sanitaire des aliments, et permet ainsi de classer les risques liés à ces combinaisons. Ceci, ensuite, peut être d'utilité aux industries alimentaires en ce qui concerne les enjeux existants ou émergents de sécurité des aliments, et aux autorités (gestionnaires de risques) pour la prise de décision informée quant à poursuivre par une évaluation quantitative systématique des risques pour aborder les préoccupations de santé publique. Le classement des risques peut être basé sur différents critères, liés à l'exposition à un danger et à sa gravité. Parmi les plus récents et les plus connus figure celui des années de vie corrigées de l'incapacité (DALY) ou des années de vie ajustées par leur qualité, qui évalue l'impact relatif de différentes maladies en se basant sur le taux d'incidence, le coût de la maladie, les hospitalisations et les décès. Il existe aussi un grand nombre d'outils pour classer les risques, qui sont disponibles publiquement soit sous forme de logiciel basé sur XL (p.ex., Risk Ranger) ou de plate-forme basée sur le web (p.ex., iRisk). Depuis lors, il y a eu une tendance croissante au développement de stratégies pour la priorisation des risques, fondées sur des questions critiques qui abordent tous les enjeux cités auparavant. Une liste détaillée de ces approches est annexée ici, et une discussion est présentée portant sur les avantages ou les préoccupations pour une méthodologie acceptée universellement.*

Mots-clés. *Classement des risques – priorisation des dangers – Gravité de l'exposition – Évaluation – Épidémiologie – Outils de profilage – Ranger – SIEFE DALYs – Années de vie ajustées par leur qualité (QALYs) – Années perdues du fait d'une incapacité.*

I – Introduction

Risk assessment (RA) is used to systematically assess the level of risk associated with particular hazards. It helps building an inventory of "typical" risk contributing factors and elaborate possible risk mitigation strategies. As a mission statement, RA constitutes an official science-based decision support methodology for Risk Managers, such as Competent Governmental Authorities, in their effort to protect public health from threats posed by exposure to contaminated foods with existing or emerging hazards. It is typically performed by focussing on one hazard in a (range of) food (categories). At a risk management level, which is commonly governmental or sometimes industrial, RA may assist in the following:

(i) Addressing aspects that have the highest impact on risk in a case, enabling the design and application of measures for risk mitigation.

(ii) Identification of foods that pose greater risk when cases are compared and suggest focussing resources, e.g., for monitoring, surveillance, studies, risk mitigation, etc.

(iii) Identification of vulnerable groups and improper (flawed) hygiene during food handling in domestic environments.

(iv) Establishment of food safety policies, in terms of risk-based food standards, which are necessary benchmarks for industry's food production safety assurance.

Risk managers are confronted with numerous public health challenges. In response to each of these challenges, they need to make a series of decisions associated with immediate (first) action to address the health problem, allocation of time and resources for informed decision-making and identification of best course of action, also balancing the societal and financial burden of the targeted public health issue with the help of stakeholders. The immediate action is based on the urgency and the priority of the problem and the outcome of risk profiling. This will further suggest or not the need for commissioning a full RA, setting risk mitigation strategies and determining risk management options.

II – Risk profiling

Risk profiling is a compilation of overviews for each of the pathogens that may be found in the various food products (Mataragas *et al.*, 2008). This allows identification of relevant pathogens-food chain (or food matrix) combinations of concern and lead to the development of risk ranking and risk matrix. The types of information required for conducting risk profile basically stem from the principles of RA and particularly are associated with the following: (i) hazard identification and/or their toxins that may be found in foods (problem statement); (ii) assessment of exposure in terms of how the food becomes contaminated, and whether/how the hazard changes along the food chain, frequency of consumption and uptake of illness causing dose; (iii) severity of the hazard, i.e., the illness-causing dose, host sensitivity, attack rates, etc.; and finally (iv) risk rating/ranking based on serving size and the integration of the above. Potential resources include literature reports, epidemiological data, expert opinion, industrial feedback, current legislation aspects or risk mitigation strategies, etc. (Pointon *et al.*, 2006). From the Food Industry standpoint, risk profiles can be used as preliminary food safety information, whereas at governmental level risk profiling constitutes the first step in risk ranking and a basis to identify priority issues for examination via the development of quantitative stochastic risk process models.

As far as the risk process models are concerned, as a rule of thumb, the risk of foodborne disease can be simply converged to the product of ***exposure*** (*P*) to a certain hazard at the time of consumption multiplied by the ***severity*** (*S*) of the hazard (i.e., $P \times S$). The exposure is a function of hazard dynamics along the food supply chain, i.e., increase or reduction of chemical contaminant corresponding to growth or death for microbial hazards, as well as of the amount and frequency of consumption. The severity component of risk is commonly quantified by its ability to cause acute or chronic damage (‘sequelae’) and can be mathematically represented by dose-response models, which also define the minimum infectious dose or the No Adverse Effect Level (NOAEL). Based on that, the Accepted Daily Intake and the more recent risk metrics, such as Appropriate Level of Protection and Food Safety Objectives may be set as the publicly available standards for food safety nationwide or worldwide.

III – Risk ranking

In a science- and risk-based food safety system, risk managers prioritize food safety hazards and preventive interventions using the best available data on the distribution of risk and how risk can be reduced most effectively and efficiently. As stated before, for foodborne pathogens, this requires an answer to the question: which pathogens in which foods cause the greatest impact on public health?

Risk ranking can be based on a variety of tools and methodologies, depending on the level of available information, and the expected accuracy and purpose of the estimate. It is important however that each methodology is encompassing both the impact of exposure and severity of different hazards in different foods. The tools that have been globally proposed include *Stepwise and Interactive Evaluation of Food safety by an Expert system (SIEFE)* (van Gerwen et al. 2000), *Risk Ranger* (Ross and Sumner 2002), *iRisk* (Chen et al. 2013) and the newly introduced metrics of disease burden, such as *Disability (or Quality) Adjusted Life Years* (*DALYs* or *QALYs*) (Batz *et al.,* 2011; Gkogka *et al.,* 2011). A detailed review of the risk ranking tools, also including comparisons and discussing on the utility and pros and cons of each tool can be found in the 2012 report series of Institute of Life Science Europe (ILSI Europe: "Tools for Microbiological Risk Assessment"; Bassett *et al.*, 2012) and the recent opinion of European Food Safety Authority on the development of a risk ranking framework on biological hazards (EFSA Journal 2012;10(6), page 2724).

In the following paragraphs, the aforementioned tools will be briefly described as an introduction to the most sophisticated and epidemiological based ***risk prioritization*** methodologies which have been recently released at Nation levels, for prioritizing both existing and emerging risks.

SIEFE is comprised of two levels, both applying the risk assessment principles (van Gerwen *et al.,* 2000). The first level is a semi-quantitative approach that could also be characterized as risk profiling coupled with risk ranking and aims to identify the risk-determining phenomena. Based on the outcomes and guidelines of this level, a thorough and systematic risk assessment is carried out in the second level, with particular numerical outputs, potentially accounting for variability and uncertainty, too (van Gerwen *et al*., 2000; Perni *et al.,* 2009).

Risk ranger is a simple publicly available *XL* spread-sheet which is based on eleven questions answered in nominal, ordinal, or continuous numerical scale, including user-defined values (Ross and Sumner 2002). As such, inputs include qualitative statements and quantitative data about risk-factors associated with specific food-hazard combination and target a specific population of concern along the food supply chain from farm to table. Through a series of mathematical and logical steps based on spread sheet functions, the software returns a risk ranking value on a logarithmic scale from 0 to 100, as well as an estimated number of cases *per* annum for the population of concern or the probability of illness per day and per consumer, attributed to the target food-hazard combination. Notably, the software is not a database, and thus, does not rely on epidemiological or literature evidence, not does it require *a priori* knowledge of the food-hazard combination. Its outputs derived only from simple (mostly multiplicative) calculations which depend on the inputs of the user, without engaging any sophisticated mathematical (e.g., predictive models) or statistical (e.g., Monte Carlo simulations) to describe variability and uncertainty. Nonetheless, it remains a simple and easy-to-interpret tool for rapid risk ranking based of food-pathogen combinations based on empirical food process and post-process stages and consumer consumption data.

DALYs integrate incidence data with indices of severity and duration. This in turn enables the relative ranking on the same DALY scale of diseases attributed to different causative agents the dose of which is estimated on different scales, such as chemical *vs* microbial, as well as of diseases with acute (e.g., an invasive foodborne infection or direct intoxication) or chronic impact (e.g., cardiovascular disease, cancer, etc.) (Havelaar *et al.,* 2012). DALY is the sum of two components (equation 1), one reflecting the years of life lost (*YLL*) due to mortality of a specific disease, and one representing the numbers of years lived with disability, also due to a certain disease (*YLD*).

$$DALY = YLL + YLD \qquad (1)$$

YLL is calculated by adding all fatal cases (*d*) due to all health outcomes (*l*) of that specific disease, each case multiplied by the expected individual life span (*e*), at the age of death, with a life expectancy according to models life tables proposed by WHO (equation 2):

$$YLL = \sum_i d_i \times e_i \qquad (2)$$

YLD is calculated by accumulation over all cases (*n*) and all health outcomes (*l*) of the product of the duration of the illness (*t*) and the disability weight (*w*) of a sporadic disease:

$$YLD = \sum_i n_i \times t_i \times w_i \qquad (3)$$

The following Table 1 shows a representative ranking of some well-known foodborne infections and intoxications caused by microbial hazards. The major criteria taken into account are the numbers of cases, the number of hospitalizations, the number of deaths and the average estimated financial burden of each disease, due to medical costs and productivity losses. It is evident that ranking of these diseases would not be realistic if it was solely based on a single criterion, because it would have ignored other aspects of the disease burden which are critical for the individuals or the society. For instance, the number of illnesses is not enough to place Norovirus on top of the ranking because the QALYs of *Salmonella*, which causes on average 5 times less cases than Norovirus, are increased due to the higher number of hospitalizations and deaths associated with this infection. Likewise, even though *L. monocytogenes* is the pathogen with the lowest number of cases in Table 1, it is not ranked at the end, due to the high fatality rate, which approximates the 20% of confirmed cases. EHEC is placed above *Clostridium perfrigens*, inspite of causing 10-times less cases, apparently because it has higher hospitalization rate and mortality than *Cl. perfrigens*.

iRisk is a publicly available web-based platform that performs ranking of multiple food-hazard combinations, according to their disease burden (DALYs) and targeting (consumer) populations of varying disease sensitivity (Chen *et al.,* 2013). Ranking is based on user-inputs through data entry templates and friendly interface for scenario building, in relation to particular food-hazard combinations and consumer groups of specific sensitivity to the relevant disease. The output of the system is determined by built-in mathematical functions and Monte Carlo simulations, based on the provided inputs and Analytica Decision Engine. The generic built-in risk scenario of iRisk is composed of a total of seven elements, of which three are the major grouping elements, namely (i) the food, (ii) the hazard and (iii) the population. These three are further divided into another four sub-modules as follows: (iv) the process model that determines the spatiotemporal behaviour of the hazard within the food matrix and along the entire food supply chain from primary production to consumption; (v) the consumer model containing the necessary information on consumption patterns; (vi) the hazard characterization component representing the severity of the hazard through a dose response model; and (vii) the DALY template, which is defined as the product of duration and severity of the disease according to the figures of cost, morbidity and mortality associated with the disease.

Table 1. Ranking of foodborne diseases according to QALYs (adopted by Batz *et al.,* 2011).

Pathogen	Ranking based on QALYs	QALYs	Cost of Illness ($ mil.)	Cases	Hospitalizations	Deaths
Salmonella spp.	1	16.782	3.309	1.027.561	19.336	378
Toxoplasma gondii	2	10.964	2.973	86.686	4.428	327
Campylobacter spp.	3	13.256	1.747	845.024	8.463	76
Listeria monocytogenes	4	9.651	2.655	1.591	1.455	255
Norovirus	5	5.023	2.002	5.461.731	14.663	149
Escherichia coli O157:H7	6	1.565	272	63.153	2.138	20
Clostridium perfrigens	7	875	309	965.958	438	26

IV – From risk ranking tools to strategies for risk prioritization

Recently, there have been some efforts in developing nation-wide risk prioritization strategies for ranking existing public health risks. Table 2 summarizes the risk ranking strategy adopted by three of these approaches, in New Zealand (McKenzie *et al.,* 2007), Belgium (Cardoen *et al.,* 2009) and Canada/USA (Ng and Sargeant, 2013). Due to the long-term heterogeneity in the existing methodologies for risk prioritization, such strategies aim to establish a universally accepted benchmarked strategy that quantitatively prioritizes diseases. The majority of risk prioritizing methodologies rely on the setup of measurable criteria for assessing the impact of various disease and food combinations, the definition of levels for each criterion and assignment of weights for the specified levels and/or criteria, thereby reflecting the relative importance of each criterion on the overall risk prioritization and finally aggregation of all inputs by additive or multiplicative formulas in order to numerically estimate the overall risk level.

The major concerns of the current (classical) methodologies are associated with the extent to which the selection of criteria and their levels are arbitrary, whether they sufficiently address the impact of interaction between criteria and quantitatively elicit the impact of factors contributing to the public health risk and the comparability of the numerical output. To remedy the scientific and mathematical bottlenecks, more sophisticated supporting-algorithms for these approaches have been introduced including Conjoint Analysis (Ng and Sargeant, 2013), Hierarchical Bayes and Classification and Regression Trees (CART) (Cardoen *et al.,* 2009). From public health perspective, it is of utmost importance that the outputs of risk prioritization of different methodologies are measurable and comparable, so that international validation is likely in the future. To do that, the available strategies should provide a reference risk-ranking output of universal acceptability, such as DALYs, or at least provide normalized outputs that can be expressed along a common scale. The Netherlands developed an advanced strategy of risk ranking using multiple criteria analysis (MCA) method for prioritizing risks by emerging zoonoses, based on their transmission between animals, from animals to human and between humans, also taking into account economic damage and the disease burden as a function of morbidity and mortality (Havelaar *et al.,* 2010). A pre-defined epidemiological database of selected disease is embedded in the platform and can be freely accessed at http://ezips.rivm.nl/. The mathematical methodology of this approach shares some features with the conjoint method of the Canadian/UA system. The criteria are relatively weighted based on expert consultation as indicated in Table 2 and transformed in order to facilitate further calculations of relative risk. The weights are extracted from the collective analysis of scores assigned to multiple random disease transmission scenarios by Risk managers, disease specialists and students from medical or veterinary schools. The diseases are ranked in a normalized scale from 0 to 1, whereas the user may introduce newly emerging diseases, through parameterization of disease attributes in relation to the seven prioritization criteria. The total number of criteria to be used, as well as the scale, the levels and the weights of each criterion are amenable for modifications by the user. Then the user-defined disease is graphically ranked relatively to the built-in zoonoses from the system database on the same normalized scale.

Table 2. Overview of nation-wide risk prioritization strategies

Study	Criteria	Scores *per* criterion	No of diseases Food/Hazard combination	Algorithm	Type of output
McKenzie *et al.* (2007) New Zealand	Probability of entry (POE) Likelihood of spread (LOS) Consequence of spread (COS) LOS/COS assessed for: Free-living wildlife, humans, captive wildlife, livestock and companion animals	• POE: 0.2, 0.4, 0.6, 0.8, 1 • LOS: 1, 2, 3, 4 • COS: 1, 2, 3, 4	48 exotic and 34 endemic wildlife pathogens	Product of POE x LOS x LOS	Numerical for different sub-populations as indicated in column ‘criteria’
Cardoen *et al.* (2009) Belgium	**Public Health** 1. Severity to humans 2. Occurrence in the Belgian population **Animal Health** 3. Occurrence in live animals in Belgium 4. Severity for animals Commercial/economic impact for the sector **Food** 5. Occurrence in food or in carcasses	Score 0 to 4 or ND/?: **Occurrence criteria** • Rare • Moderate • Significant • High • ND/? **Severity criteria** • Benign • Weak • Moderate • Severe • Lethal	35 experts x 51 food and water zoonotic agents	XL spreadsheet Weights decided by managers based on Las Vegas methodology Groups of importance identified by CART Uncertainty calculated with bootstrapping with *R*	Ranking according to the sum of weighted scores Scale 0-20

Table 2 (cont.). Overview of nation-wide risk prioritization strategies

Study	Criteria	Scores *per* criterion	No of diseases Food/Hazard combination	Algorithm	Type of output
Havelaar *et al.* (2010) The Netherlands	1. Probability of entry 2. Transmission between animals 3. Economic damage in animal reservoir 4. Transmission from animals to human 5. Transmission between humans 6. Morbidity 7. Mortality	1. %/year 2.Prevalence /100.000 animals 3. Million Euros per year 4. Prevalence /100.000 humans 5. Prevalence /100.000 humans 6. <0.03, 0.03-0.1, 0.1-.3, >0.3 7. % (0 to 100)	Built-in database of zoonoses: selection from 1415 human pathogens of which, 868 are zoonoses Expert consultation: • Risk managers from Dutch Ministries of Agriculture and Public Health Authorities • Infectious disease specialists • Students in medical/veterinary faculties	Multiple Criteria Analysis Uncertainty by Monte Carlo Simulation CART for clustering	Normalized result in a scale from 0 to 1
Ng and Sargeant (2013) US and Canada	**21 characteristics** ***a) Assessed separately for human and animals*** Case-fatality Duration Severity 5-years trend 5-years incidence Efficacy of control measures High risk groups Scientific knowledge ***b) For humans*** Economic burden Transmission from animals to humans Transmission between humans ***c) For animals*** Economic and social burden on trade Transmission between animals Transmission from human to animals	Categorical and numerical levels Magnitude differed with criteria	62 existing and emerging diseases Evaluated by 707 Canadian and 764 US experts	Conjoint Analysis (CA) Hierarchical Bayes Monte Carlo Markov Chain Metropolis/Hasting algorithm	Disease score from –infinity to +infinity based on (CA): Important scores *per* criterion (weights) Part-worth utility values

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