# RISK RANKING:
# DEVELOPMENT OF A SINGLE METRIC FOR RISK RANKING BY THE NZFSA

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**SUMMARY**

From 2002 – 2005 the risk ranking project conducted by ESR for the NZFSA developed a process, and used expert opinion to produce severity and incidence estimates for a number of food/(microbiological) hazard combinations. The challenge is now to rank these, by devising a single metric that describes the burden of disease by combining information about severity and incidence. A further challenge will be to devise this metric in a way that is also applicable to chemical hazards. The health effect most commonly associated with foodborne microbiological hazards is acute gastrointestinal disease; chemical hazards cause a wider variety of adverse health effects, usually after exposure over a much longer time period.

Alternatives for estimating the burden of illness derive from economic evaluations of health care:

- Cost analysis: costs in monetary units;
- Cost-effectiveness analysis: costs in monetary units, consequences measured in natural units;
- Cost-utility analysis: costs in monetary units, consequences measured in healthy years (quality adjusted life years (QALYs), or disability adjusted life years (DALYs));
- Cost-benefit analysis: costs in monetary units, consequences in monetary units.

Inclusion of only costs (even from a broad societal perspective) ignores the burden of disease on individuals and quality of life.

Estimation of this burden on individuals in a cost-benefit analysis through derivation of monetary values requires assignment of economic value to health states, which may be unacceptable to some stakeholders. A particularly difficult issue is the assignment of a monetary value to mortality.

A cost effectiveness analysis approach might consider consequences in terms of incidence e.g. number of cases avoided. This does not take into account the variety of outcomes which may result from infection with foodborne microbiological hazards. For example, infection with STEC results in a high proportion of serious disease states, compared to norovirus infection.

The inclusion of both societal costs as well as intangible costs (due to pain and suffering due to illness, or years lost to premature death), captures the burden on both society as a whole and individuals. Estimation of intangible costs in the form of a HALY measure provides a consistent basis for comparison across disease states for gastrointestinal illness and its sequelae, as well as potentially future estimates of different endpoints associated with chemical hazards.

The DALY measure is the preferred option. This is partly because it is associated with loss of quality of life due to illness, and therefore the burden, rather than the gains that might be obtained from different types of treatment, where the QALY might be more appropriate. The DALY was also specifically designed to estimate burden of disease in an international context, and this should permit comparison with overseas estimates. The International Collaboration on Enteric Disease Burden of Illness Studies has recently established a DALY Working Group to explore the methodology and the potential for an estimation of the global burden of foodborne disease.

# 1 INTRODUCTION

This report contributes to a project with the following goal:

- the development of a single metric of risk ranking that can be applied to both chemical and microbiological hazards, and is applicable to the varied risk ranking needs of the NZFSA.

From 2002 – 2005 the risk ranking project conducted by ESR for the NZFSA developed a process, and used expert opinion to produce severity and incidence estimates for a number of food/(microbiological) hazard combinations. The challenge is now to rank these, by devising a single metric that describes the burden of disease by combining information about severity and incidence. A further challenge will be to devise this metric in a way that is also applicable to chemical hazards. The health effect most commonly associated with foodborne microbiological hazards is acute gastrointestinal disease; chemical hazards cause a wider variety of adverse health effects, usually after exposure over a much longer time period.

The purpose of this risk ranking exercise is to assist the NZFSA Science Group in setting priorities, particularly in relation to the Domestic and Imported Food Reviews.

This report is intended to discuss the available options, and choose a single metric for disease burden estimation in the public health context. Having chosen a single metric, the intention for the remainder of the project period (to 30 June 2007) is then to develop burden estimates for food/hazard combinations, selected in consultation with the NZFSA.

# 2 ECONOMIC EVALUATION OF HEALTH CARE

## 2.1 Approaches to the Economic Evaluation of Healthcare

Single metric estimates of the burden of illness caused by foodborne pathogens are required for risk ranking. Alternatives for estimating the burden of illness derive from economic evaluations of health care. These evaluations all examine the costs of illness in monetary terms, but vary in the way that the consequences of health care are measured.

Most of the following summary of these estimates is derived from two books: "Methods for the Economic Evaluation of Health Care Programmes" (Drummond *et al.*, 2005), and "Valuing Health for Regulatory Cost-Effectiveness Analysis" (Institute of Medicine, 2006).

Economic evaluation of health care makes use of several approaches:

- Cost analysis: costs in monetary units;
- Cost-effectiveness analysis: costs in monetary units, consequences measured in natural units;
- Cost-utility analysis: costs in monetary units, consequences measured in healthy years (quality adjusted life years (QALYs), or disability adjusted life years (DALYs));
- Cost-benefit analysis: costs in monetary units, consequences in monetary units.

### 2.1.1 Cost analysis

Cost analysis does not consider the consequences of health care, only the resources consumed. These may include costs to:

- The health sector;
- Other sectors;
- Patient/family;
- Productivity losses.

The first three of these costs are sometimes called direct costs; the last is sometimes designated indirect cost. The specific costs to be included are dependent on the viewpoint for the analysis; often a societal viewpoint is taken, which is the broadest view. For an economic cost of illness of infectious intestinal disease, an analysis would include costs for GP consultation and transport, over-the-counter or prescribed medicines, laboratory diagnostic tests, hospital costs, and production losses due to time off work (Scott *et al.*, 2000).

Two alternate estimations of costs are possible:

- Prevalence approach: stream of healthcare costs accruing to all patients alive during a specific time period;
- Incidence approach: discounted expected sum of current and future costs of all cases within a specified time period.

The estimation of productivity changes is often complex; with the simplest being the human capital approach to valuing the changes arising from the patient or family member taking time off work in order to receive health care (or recover). This uses estimates of gross

earnings of those in employment (and some studies attribute an equivalent value for those not in paid employment). An alternative is the friction cost method, in which the amount of production lost to disease depends on the time-span organisations need to restore the initial production level (e.g. by training or recruiting another employee).

### 2.1.2 Cost-effectiveness and cost-utility analysis

Cost utility analysis was originally considered a subset of cost-effectiveness analysis, and some analysts (particularly in the US) still use the same term for both.

Cost effectiveness analysis has been described as of most use in situations where a decision maker is considering a limited range of options within a given field. A common single outcome or consequence measure is chosen to evaluate a range of options. This outcome is often specified as a measurable clinical parameter (e.g. life years gained, disability days saved, points of blood pressure reduction). One example might be the evaluation of a variety of strategies for the detection of cancer, measured as cost per case detected.

Cost-utility analysis evaluates the consequences of programmes adjusted by health state preference scores or utility weights i.e. states of health associated with the outcomes are valued relative to one another. In general terms this means that one can assess the quality of (for example) life years gained, not just the crude number of life years. This approach is described as particularly useful for programmes that produce substantial reductions in morbidity rather than mortality, and also for situations where comparisons must be made across a broad set of interventions. An example is for evaluating neonatal intensive care for very low birth weight infants, where survival is an important outcome, but also the quality of that survival is critical (Drummond *et al.*, 2005).

Cost-utility analysis incorporates simultaneously the changes in the quantity of life (mortality) and changes in the quality of life (morbidity). The latter is sometimes known as Health Related Quality of Life (HRQL). The quality adjustment is based on a set of values or weights called utilities. In this context, utility is considered the relative desirability of the health state. The overall measure derived is usually reported as a Health Adjusted Life Years (HALY) measure: most frequently as quality adjusted life-years (QALY) gained, or disability adjusted life years (DALY) lost. The latter were developed by the World Health Organisation for their Global Burden of Disease and Injury study (Murray and Lopez, 1997).

There are three steps in calculating a HALY (Gold *et al.*, 2002):

- Describing health as a state or disease condition;
- Developing values or weights for the health state or condition (on a 0 – 1 scale);
- Combining values for different health states or conditions with estimates of life expectancy, thus creating a measure of the quality of life and the period over which that quality of life is experienced.

The values or weights are further discussed below. Cost-utility and cost-effectiveness analyses do require the risk manager to make decisions regarding the ratio of acceptable interventions i.e. the cost per QALY gained, or DALY avoided.

#### *2.1.2.1 Utility measures*

In order to incorporate both the quantity of life (mortality) and quality of life (morbidity) into a common unit of measurement, it is necessary to use a set of values or weights, sometimes

called utilities. These reflect the relative desirability of the health state, with perfect health and death representing the opposite extremes. There is a variety of methods for eliciting these preferences from individuals or health experts, including scaling methods (rating scales category scale, visual analogue scale, ratio scale), and choice methods (time trade-off, paired comparison, equivalence, person trade-off, and standard gamble). These are time-consuming and complex processes, and often raise ethical issues.

An alternative is to bypass this task by using one of the pre-scored multi-attribute health status classification systems. The four most widely used of these are:

- Quality of well-being (QWB);
- Health Utilities Index (HUI);
- EQ-5D from the EuroQol Group;
- Short Form 6D (SF-6D).

These systems classify patients or health states according to a set of attributes (e.g. the EQ-5D system uses: mobility, self-care, main activity, social relationships, pain, and mood). Levels of these attributes are defined and assigned a numerical value.

QALY estimates have used preference values based on a number of techniques, including choice methods and classification systems, derived from either population samples, patients, or health professionals. The HRQL weights are based on individual experience of health, and not connected to a particular disease. Rather the generic health states weightings are based on values of individuals for either their own health state, or those that are described to them (Gold *et al.*, 2002).

In an attempt to create comparable data across countries, DALY weightings are assigned to specific diseases, rather than health states. For DALY estimates, values for diseases and other nonfatal outcomes are obtained from health professional expert groups using a standardised person trade-off procedure, in an attempt to reconcile cultural and cross-national differences (Gold *et al.*, 2002). The person trade-off method asks experts to establish "equality in life" extension between healthy people and people with indicator conditions.

A disadvantage of the DALY approach is that, being based on particular diseases, no account is taken of comorbid conditions, which is more common amongst aging populations in industrialised nations. In theory, the QALY approach can take account of comorbidity, although there are considerable methodological difficulties (Gold *et al.*, 2002).

According to the WHO definition, (http://www.who.int/healthinfo/boddaly/en/index.html), DALYs are calculated as the sum of the years lost to premature mortality (YLL) and the years lost due to disability (YLD).

YLL = N x L

N = number of deaths
L = standard life expectancy at age of death in years

YLD = I x DW x L

I = number of incident cases

DW = disability weight
L = average duration of the case until remission or death in years

### 2.1.3 Cost-benefit analysis

Cost benefit analysis requires the attachment of monetary values to (beneficial) health outcomes. While this is difficult (particularly for mortality), it has the advantage that a direct comparison of costs and benefits can be made. In simple terms, if the monetary benefits exceed the cost, there is a net social benefit. This type of analysis also has the advantage of being applicable to situations where resource allocation decisions are being made across both health and non-health programmes.

Monetary measures of health outcomes include:

- Human capital: values healthy time in terms of the person's renewed or increased production in the market place (a counterpart to the productivity losses estimated in cost analysis).
- Revealed preferences: based on risk-money tradeoffs as expressed by consumers, particularly applicable to occupational risks.
- Contingency valuation studies/willingness to pay: in which questions are asked of respondents about their risk preferences, given stated costs and health outcomes.

An example is the USDA analysis of foodborne disease, which included the costs of health outcomes for mortality (value of a statistical life, derived partly from expected lifetime income), and morbidity from long term sequelae of infection resulting in partial income losses.

## 2.2 Discussion

The review above offers a number of options for devising a metric that incorporates both incidence and severity for illness caused by foodborne pathogens. Inclusion of only costs (even from a broad societal perspective) ignores the burden of disease on individuals and quality of life.

Estimation of this burden on individuals in a cost-benefit analysis through derivation of monetary values requires assignment of economic value to health states, which may be unacceptable to some stakeholders. A particularly difficult issue is the assignment of a monetary value to mortality, both from acceptability, as well as economic theory viewpoints (approaches to the valuation of a statistical life are not settled).

A cost effectiveness analysis approach might consider consequences in terms of incidence e.g. number of cases avoided. This does not take into account the variety of outcomes which may result from infection with foodborne microbiological hazards. For example, infection with STEC results in a high proportion of serious disease states, compared to norovirus infection.

The inclusion of both societal costs as well as intangible costs (due to pain and suffering due to illness, or years lost to premature death), captures the burden on both society as a whole and individuals. Estimation of intangible costs in the form of a HALY measure provides a consistent basis for comparison across disease states for gastrointestinal illness and its

sequelae, as well as potentially future estimates of different endpoints associated with chemical hazards. Cost-utility analysis has been described as most useful in situations where morbidity is the major burden rather than mortality; as is the case for acute gastrointestinal disease.

The DALY measure is the preferred option. This is partly because it is associated with loss of quality of life due to illness, and therefore the burden, rather than the gains that might be obtained from different types of treatment, where the QALY might be more appropriate. The DALY was also specifically designed to estimate burden of disease in an international context, and this should permit comparison with overseas estimates. The International Collaboration on Enteric Disease Burden of Illness Studies has recently established a DALY Working Group to explore the methodology and the potential for an estimation of the global burden of foodborne disease.

At present DALY disability weights are available for gastrointestinal illness, and its longer term outcomes in a generic sense, but are not differentiated for specific agents (although agent specific duration of illness estimates are used). These weights are derived from studies of the burden of infectious intestinal disease in the Netherlands (Kemmeren *et al.*, 2006). Further work to better define these values, and develop agent specific values is in progress and should be available during the first half of 2007 (Arie Havelaar, RIVM, personal communication, December 2006).

There will be issues concerning the transferability of these values to gastrointestinal illness caused by other pathogens, as well as the issue of transferability between countries. Nevertheless the DALY represents the best options for developing a single metric for ranking food safety issues at this time.

The application of DALY estimates to the health effects of chemical hazards will be more difficult. While there are likely to be disability weights available for both the cancer and non-cancer outcomes of concern from exposure to chemical hazards, attribution of the incidence of these outcomes to chemical exposures will be challenging.

# 3 EXISTING SINGLE METRIC ANALYSES

This section collates relevant information from work already conducted within New Zealand on burden of disease estimates. The following section reviews disease burden estimates from overseas, but only those relevant to food safety.

## 3.1 New Zealand

### 3.1.1 Economic cost of foodborne infectious disease

This analysis used estimates of the incidence of ten infectious intestinal diseases (Lake *et al.*, 2000) to develop disease specific economic costs of those diseases (Scott *et al.*, 2000). Crude attribution estimates were used to identify the foodborne component of these incidences and costs. Essentially this represented a cost analysis, including direct medical and non-medical costs, as well as estimates of indirect costs from lost productivity (of both employed and non-employed people), and an assigned value of a statistical life for the small number of deaths caused by infectious intestinal illnesses. This study made no attempt to estimate indirect costs or burden associated with long term sequelae of gastrointestinal illness, which can represent a significant contribution to the total cost.

An earlier analysis along similar lines, for campylobacteriosis in Canterbury in 1995, has also been published (Withington and Chambers, 1997).

### 3.1.2 The Burden of Disease and Injury in New Zealand

This report, published by the Ministry of Health in 2001, utilised the (discounted) DALY concept to estimate the burden of:

- Infectious diseases (including respiratory tract infections);
- Infant conditions;
- Injuries;
- Cancers;
- Endocrine, metabolic, haematologic and immunological conditions (including diabetes);
- Cardiovascular diseases;
- Chronic respiratory diseases (including asthma);
- Other chronic disorders;
- Musculoskeletal disorders;
- Neurosensory disorders;
- Mental illness.

The burden of infectious diseases included ICD 9 CM A codes (001 – 139) relevant to foodborne illness. However, the DALY estimates in the infectious diseases category are dominated by other illnesses, principally respiratory tract infections and meningitis which have a higher incidence (see Table A2).

Disability adjusted life year (DALY) estimates were determined for the years lost to premature mortality, and years lost to disability. The second of these parameters was based on incidence, duration, and a disability weight. In the absence of New Zealand specific

values for disability weights, overseas values (often from the Netherlands) were used. The issue of whether disability weights derived in one culture can be applied to another was raised, but not resolved.

All infectious diseases caused 3% of all DALYs lost, and (along with muscoloskeletal diseases) contributed the least to the overall burden.

## 3.2 Overseas Analyses Relevant to Food Safety

### 3.2.1 The Netherlands

The costs of human *Campylobacter* infections and sequelae in terms of both the cost of illness and the DALY burden in the Netherlands have been reported (Mangen *et al.*, 2005). The same approach was taken in a study towards priority setting for foodborne pathogens (Kemmeren *et al.*, 2006). This extended the campylobacteriosis study to also include *Toxoplasma gondii*, *Salmonella* spp., *Listeria monocytogenes*, *E. coli* O157, noroviruses, and rotaviruses. Attribution was not addressed in these studies; all transmission routes were considered together. The DALY burden of illness was greatest for toxoplasmosis.

### 3.2.2 USA

#### *3.2.2.1 Cost of bacterial foodborne disease (Buzby et al., 1996)*

This USDA Economic Research Service study evaluated the cost of illness (direct and indirect) for several bacterial diseases (salmonellosis, campylobacteriosis, infection with *E. coli* O157, listeriosis, intoxication with *Staphylococcus aureus* and *Clostridium perfringens*). Attribution for overall percentage of these illnesses due to foodborne transmission was assigned on the basis of expert opinion and outbreak studies.

The estimates in the original report are periodically updated and an interactive foodborne illness cost calculator has been created (http://www.ers.usda.gov/data/Foodborneillness/).

#### *3.2.2.2 Food Safety Research Consortium*

The Food Safety Research Consortium is a collaboration of several universities and private research institutions (http://www.rff.org/fsrc/). One of their activities is the development of a computer model to prioritise opportunities to reduce foodborne illness risk: the Foodborne Illness Risk Ranking Model (FIRRM). Phase 1 of model development has been released, but Phase 2 is still in development.

This model includes two methods of health valuation: economic and QALY. The economic measures are based on either cost-of-illness (medical costs and productivity losses) or willingness to pay measures.

The QALY estimates are based on health indices using the QWB index. In Phase 2 the EuroQol health index (EQ5D) will be introduced.

Phase 1 of model development included *Campylobacter*, *E. coli* O157, *Listeria monocytogenes*, and *Salmonella* spp. Phase 2 will include *Cryptosporidium*, *Cyclospora*, *Shigella*, *Vibrio*, *Yersinia*, norovirus and *Toxoplasma gondii*.

Attribution is addressed primarily through two options: outbreak data and expert judgement. At present the outbreak analysis performed by the Centre for Science in the Public Interest is used, although this will be replaced by the CDC analysis, once available. An expert elicitation has also been performed to provide attribution values.

#### *3.2.2.3 Institute of Food Technology*

A group of researchers, including Decisionalysis Canada, has been commissioned by the IFT, as part of a cooperative agreement with the US FDA, to develop a combined approach to ranking chemical and microbiological hazards. To address the issue of developing a common measure of burden of disease for hazards with such a diversity of health outcomes, a pseudo-DALY approach was devised. This uses semi-quantitative measures to discretise severity and duration dimensions:

- Severity: mild, moderate, serious, fatal;
- Duration: short term, medium term, long term.

These labels are assigned default values and are then multiplied to generate a health burden value. The burdens associated with each outcome are then weighted according to the relative frequency as a result of exposure. The frequency of outcomes are based on a probabilistic approach to exposure, and a dose-response relationship. The model allows the analyst to choose from a variety of options, particularly at the dose-response stage.

The details of this model are not available as the model has not yet been publicly released.

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