2.7 SCIENTIFIC UNCERTAINTY AND COMPLEXITY IN PUBLIC HEALTH

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Introduction

This chapter provides an overview of some of the key ways in which uncertainty and complexity about risks are addressed in the public health field using examples from two disciplines, clinical medicine and environmental health.

Uncertainty, arising out of limits to knowledge, is to some degree part of every health decision, whether about the safety of individuals or of populations. Will a medical intervention work for a particular individual? What are the possible side effects? For public health decisions in medicine these same questions are scaled up to the population level (e.g. has a drug proven to be clinically effective in human populations – does it do more good than harm?). For public health decisions involving the application of chemicals or agents that pose hazards to health or the environment, questions may arise about the benefits as well as the risks of their use (e.g. the role of pesticides in providing more plentiful and cheaper food).

Thus, decisions about public health often entail risk tradeoffs, striking a balance between good and harm when neither the likelihood nor the severity of the outcomes may be known for certain (Graham and Wiener, 1995; Wiener, 2002). The guiding principles in medicine of 'do no harm' or of precaution cannot unilaterally dictate the choices decision makers face. They must strike a balance between false negatives (not taking action on risks that appear low, but in fact turn out to be high) and false positives (taking action because a risk appears high, but turns out to be low) (Wiener, 2002). Both may have costs, sometimes to different individuals or sectors of society. Thus, many public health decisions must be considered and debated in a larger societal context. Communication amongst scientists, decision makers, and stakeholders plays a critical role.

This chapter traces some of the parallels between the fields of medicine and environmental health in the analytical tools, the institutions and decision processes used to frame the issues of uncertainty and complexity, to analyse them, and to communicate them. Both disciplines, for example, have a strong natural science foundation relying heavily on empirical evidence and on the scientific knowledge of disease causation and the effectiveness of treatments or other disease control measures. Both confront uncertainty, complexity, and risk on two fundamental levels: (1) at a scientific level where uncertainty may result from lack of knowledge of or understanding of complex biological, chemical and physical processes and (2) uncertainty about the interaction or influence on complex social systems where other objectives, risks, perceptions must be considered and weighed.

The chapter has four major sections. In the first, uncertainty and complexity are defined in the context of medicine and environmental health. The second explores the field of clinical medicine and public health and the ways found to address uncertainty in

the key evidence underpinning medical knowledge and decisions. The third section covers the field of environmental health and introduces how the tools of risk assessment are used in conjunction with tools of uncertainty analysis to characterise sources and extent of uncertainty in estimates of risk from chemical, physical, or biological hazards. The final section places both disciplines into a broader societal context which recognises that scientific evidence and uncertainty are often only one input to a public health debate.

Defining uncertainty and complexity in public health

To understand the strategies that scientists and decision makers have developed to deal with uncertainty, complexity and risk it is first important to define and understand each term as it is used in public health applications.

In common parlance, uncertainty is often loosely used to describe all kinds of variation. Theoreticians, on the other hand, describe uncertainty more precisely as falling into two categories: *aleatory*[1] uncertainty and *epistemic*[2] uncertainty. To avoid the confusion arising from use of 'uncertainty' in both terms, we have used the simpler terminology whereby *variability* is used for aleatory uncertainty and *uncertainty* is used only to describe epistemic uncertainty (Paté-Cornell, 1996). Both are defined below.

Variability is defined as heterogeneity of values over time, space, or different members of a population and is generally a property of a system itself (IPCS, 2008). It can arise from stochastic or random processes or from processes that are controllable in various ways. For example, the distribution of heights or of the activity of a key detoxifying enzyme in a human population is at some fundamental level determined by the laws of genetics. The particular combination of genes received by any individual is a largely a matter of chance. However, characteristics like height can be further modulated by other factors, like diet, that are theoretically controllable.

Uncertainty is defined as incomplete 'imperfect knowledge concerning the present or future state of an organism, system, or (sub)population under consideration' (IPCS, 2004a). It arises from data that are limited (e.g. sparse, of questionable quality or relevance) and from processes that are not fully understood or predictable. Missing data may also reflect biases in the way decisions are made about what studies to fund or to publish.

Why do these distinctions matter? They matter because they lie at the heart of the different strategies we take toward dealing with the variation observed in human populations, exposures, and responses. Variability, as defined here, cannot be reduced. Uncertainty can theoretically be reduced by conducting research, collecting data, etc. – in essence adding to the knowledge base.

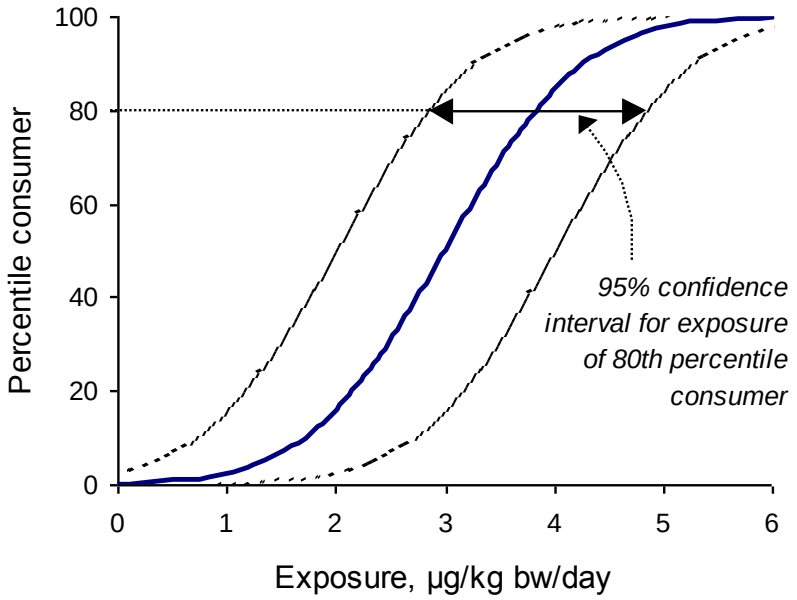
If variability is well characterised, decision makers can more easily make decisions in which the implications are clear. We set building standards for doors, for example, such that must be of a height to accommodate some high percentage of the population. We know that there are some particularly tall people who will have to stoop to enter, but the tradeoffs can be explicit.

[1] Aleatory: of or pertaining to natural or accidental causes, cannot be explained with mechanistic theory. Generally interpreted to be the same as stochastic variability (WHO, 2008)

[2] Epistemic: of or pertaining to human knowledge. (WHO, 2008)

On the other hand, if for some reason we were very uncertain about heights in a population, setting standards could be more difficult. Now there is risk involved in the decision. Making doors way too large has implications for construction costs as does making them too small (e.g. costs of retrofits); small doors may cause injuries to an unacceptable number of unsuspecting people.[3]

Figure 1: Example of cumulative distribution for variability of exposure between consumers (thick curve), with 95% confidence intervals (thin curves) showing uncertainty for each percentile consumer.



Note: Other confidence intervals (e.g. 90% or 99%) could be shown, depending on the level of confidence wanted by risk managers. bw = body weight. (Source: IPCS, 2008)

To use an example drawn from public health, consider exposure to a particular chemical in food. Regulatory authorities often think of controlling exposure, not just to the average citizen but to a high percentage of a population. Variability exists in the exposures that might be experienced by individuals due to differences in concentrations of the chemical in various foods, in dietary intake patterns, and other factors. At any given point in time, this variability might be characterised by a cumulative distribution as illustrated by the bold line in Figure 1. If the variability is perfectly known, a decision maker interested in knowing what exposures are experienced by 80% of the population needs only find the corresponding point on the X-axis. In reality, distributions of exposure like this are rarely known perfectly. Analysts might rely on small samples of the population, on data collected at some earlier point in time or location, or on models

[3] We see this kind of scenario playing out with rapid increase in obesity in the USA. This unexpected change in what was thought to be relatively stable population variation in weight has led to the need for hospitals to design bigger doors, beds, stretchers and wheel chairs to accommodate these large patients.

whose predictive capability may not be fully known. The consequence of these sources of uncertainty is that the 80th percentile is not precisely known; as indicated by the 95% confidence interval in Figure 1 which ranges from exposures of around 2.5 to 5 mg/kg /day. If the consequences of these different levels were to differ dramatically in terms of public health risk or regulatory action, the decision maker might well be in a quandary. He or she must consider the whether and how to act, given the uncertainty, including whether the better course of action is to collect more information in hopes of reducing uncertainty. The field of decision analysis, and in particular value of information analysis, has long existed to help with delineation and quantification of these tradeoffs (Raiffa and Schlaiffer, 1961; Raiffa, 1968; Morgan and Henrion, 1990).

Complexity enters into public health assessment and management when more and more variables are introduced and/or systems are characterised by more than one cause and effect relationship. It can exist on at least two levels: (1) at the biological, chemical and physical level that affects the ability to understand and characterise natural systems and (2) at a societal level where there exists a multiplicity of stakeholders, actors, actions and consequences for a given decision context. In the latter case, *complexity* can range from the level of an individual making a decision about a treatment choice in consultation with his or her physician to that of a national government making regulatory decisions about complex environmental problems with far ranging implications for health, the environment, and the economy.

Finally, there is a third kind of issue that is particularly challenging to decisions of all kinds – one that arises because of differences in interpretation of results or in fundamental underlying perceptions, values, or motivations. Some have termed this general issue *ambiguity* (Stirling, 2003; Renn, 2008) with *interpretive ambiguity* referring specifically to differences in interpretation of the same information and *normative ambiguity* referring to when individual stakeholders or actors value the consequences, whether risks or benefits, differently. Highly uncertain or complex decision contexts are more prone to interpretive ambiguity (e.g. does the scientific evidence support a conclusion that climate change is occurring?) But, normative ambiguity may persist even if all the facts are in and known for certain. For example, on an individual level, one patient may choose a nearer term death over an effective medical intervention that could prolong his or her life, but with significant side effects. Environmental projects often involve difficult choices amongst alternatives that may have fundamentally different goals. On a hazardous waste site, for example, decision makers have had to decide the extent to which a sensitive ecosystem (e.g. wetlands) should be dug up to remove chemical contamination that threatens a water supply and thus, public health. They must decide how much risk to public health from a particular hazard is 'acceptable' and how much should be spent to reduce it.

Although ambiguity has not been the explicit focus of this edited volume, it is important that it be recognised and distinguished from uncertainty and complexity. Dealing with normative ambiguity requires different kinds of strategies and negotiations in the policy making process. Better science alone will not suffice.

Addressing uncertainty and complexity in medicine

This section of the paper discusses the scientific and institutional tools used to deal with uncertainty and complexity in medicine, from individuals to populations. Decisions in clinical medicine are focused on treating existing disease, making early diagnoses of disease (e.g. screening for breast or cervical cancer) so as to provide treatment before much damage to the human body is installed, and identifying and addressing risk factors that are associated with development of a disease (e.g. cholesterol levels in blood or high blood pressure) so as to prevent ill health from occurring. Clinical medicine deals with decisions about the treatment or prevention of disease in individuals while public health focuses on promoting health and preventing disease in populations.

In the medical context, both operate from the basic premise that interventions should first and foremost 'do no harm'. This is one of the basic principles of medicine, and is based on Hypocrate's teachings. The reality is more complicated: 'doing no harm' may actually require 'doing the least harm' when interventions for preventing or treating disease involve risks as well as benefits (e.g. risks of weight gain and diabetes from treating schizophrenia with antipsychotic drugs[4], the risk of impotence in treating prostate cancer).

When working with an individual patient, physicians must help patients weigh the risks and benefits of undertaking an intervention or alternative interventions for treating a particular condition. They must take into account not just what the scientific evidence suggests for the 'average' patient, but also the implications of any risk factors for the particular patient (e.g. health status, age, drug or alcohol use, other medications, genetic susceptibilities, etc.). Even in the best of circumstances, statistics tells us that predicting outcomes for individuals is always more uncertain than for the average given these kinds of interindividual variability. In addition, these factors are not always known or revealed to the physician making the calculus more uncertain.

Decision making for populations is more complex and can involve tradeoffs in which the benefits and risks of interventions do not always accrue to the same individuals. In some circumstances, the benefits of interventions for populations are higher than benefits to any one individual. One example is vaccines for preventable diseases where the full benefit of protection comes from maintaining low levels of transmission among populations but relies on the decisions of individuals who receive the shot but who also bear the risk, albeit very small, of side effects from the vaccination itself. But if many individuals take the shot, all are protected; if few take the vaccine, person-to-person transmission levels increase and the disease spreads.

Any of these decisions, whether about the health of an individual or of the public, rely on a similar framework built from the scientific evidence base itself, the processes used to weigh and characterise it (including any uncertainties), and the ways in which it is communicated to and discussed with the other key stakeholders in the process. These elements are discussed further below.

[4] 'Alaska courthouse illustrates two views of antipsychotic drugs'
http://www.iht.com/articles/2008/03/24/business/drug.php

Medicine and public health: Evidence-based decision-making

Throughout much of history, physicians have relied on case histories drawn from their own practices, from the experience of their colleagues, and from the medical literature to inform their decisions about adopting a treatment or a screening measure for patients presenting with a disease or risk factor. The discussion of case histories still plays an integral role of training new physicians and keeping practising physicians up to date; daily 'rounds' to patient bedsides conducted by teams of doctors, and periodic 'grand rounds' convened to discuss particular cases or new scientific evidence reflect this tradition. With the Internet, the concept of 'grand rounds' has gone global with websites like Public Health Grand Rounds (http://www.publichealthgrandrounds.unc.edu/) sponsored by the US Centers for Disease Control and the North Carolina School of Public Health as a forum for discussing case studies from around the world.

The evidence base has evolved; decisions in medicine and public health are increasingly drawn from a range of evidence including experiments in basic sciences and epidemiological studies in human populations. Our discussion focuses is on epidemiological studies as they represent a logical extension of the effort to reduce the uncertainty associated with making decisions based on case studies. Case studies are inherently small samples and, as such, can be inadequate representations of patterns and associations in larger populations. Epidemiology has evolved using the tools of statistics to systematise the design of studies from the methods used for selecting sample populations for study to those used for making inferences about the significance any relationships revealed in the studies.

Medicine has increasing come to rely on the use of randomised clinical trials (RCTs) to evaluate decisions about specific medical interventions. Randomised clinical trials are clinical epidemiology studies that compare outcomes between groups of patients undergoing an intervention (e.g. a particular drug or treatment) with comparable groups who received no treatment or perhaps, the current standard one. Effectiveness and avoiding harm to recipients are the overriding interest and concern, as interventions should be warranted only if they produce better results than doing nothing, or than other known interventions. Those proposing the intervention have the onus of demonstrating effectiveness, as well identifying unwanted side effects of deploying the intervention, so as to help medical practitioners decide what interventions to use and when.

Individual epidemiological studies remain subject to errors in design and interpretation that continue to be a source of great debate. In addition, biases in the process of publication of research results can contribute to uncertainty in the overall state of knowledge. Medical journals have been shown in the past to give precedence to studies that show a positive effect, rather than to those that do not show an effect – a problem known as publication bias. If studies showing the efficacy of a treatment are published and the studies of its inefficacy are suppressed, one can easily see how doctors' decisions might be inadequately informed.

Institutional efforts to improve the evidence base for medical decision-making: The Cochrane Collaboration

Since the 1970s, a health profession-led movement to assess and promote the production and dissemination of good quality evidence on medical interventions has grown. It has been influenced in part by a textbook by Archie Cochrane on 'evidence-based medicine' that stressed the importance of randomised controlled trials (RCTs) in assessing the effectiveness of treatments (Cochrane, 1972). One outcome of this movement is the development of organisations like the Cochrane Collaboration[5] which was established in 1993 and is described briefly below. It represents an effort to provide a more complete and systematic review and presentation of scientific evidence.

The Cochrane Collaboration is an international non-profit organisation that produces and disseminates systematic reviews of healthcare interventions and promotes the search for evidence in the form of clinical trials and other studies of interventions. The systematic reviews are produced by volunteer healthcare professionals working in specific topics, with editorial teams overseeing the preparation and maintenance of the reviews, with the application of the rigorous quality standards. In 2004, for example, 11 500 people over 90 countries were working in the collaboration, half of them authors of the reviews. Others search manually for non-indexed publications, develop review methods, translate original trial papers, represent consumer views and support the editing process.

Cochrane review groups are sub-networks providing an editorial base to specific areas of health, focusing on the reviews of trials for treatment of breast cancer or schizophrenia for example. Cochrane centres support people in a geographic or linguistic area, providing training, translation, of other support for contributing to the systematic reviews. The resulting database of systematic reviews is published quarterly as part of The Cochrane Library and now has over 2000 reviews. The electronic publication allows for inclusion of more details of the materials and methods, data presentation and analysis that printed documents, as well as flexibility for regular updates as new information comes in. The resulting reviews are continually improving in content and quality.

Systematic reviews of RCT results provides guidance about what is known about effectiveness of interventions, i.e. whether the intervention achieves the intended outcomes, whether it carries potential risks, what the risk factors are, and who will benefit from its use.

National institutions for public health

Whether or not particular interventions are permitted for use in a society often must rely on more than just the presentation of scientific evidence. Such a decision may need to rely on a political process involving a more complex web of stakeholders who want to have a say. For example, stakeholders include pharmaceutical companies engaged in the development of new drugs and treatments, scientists involved in the research to test the safety and effectiveness of medical interventions, health care practitioners, the health care

[5] http://www.cochrane.org/

industry, the insurance industry, academia and other institutions supporting medical research, health systems purchasers, and finally user groups such as associations of patients and societies promoting research and action on given diseases.

Many countries have seen the development of one or more national agencies to provide guidance and quality control over medical research, the evaluation of the effectiveness of medical treatment, the safety quality and safety of proposed treatments, and the process for considering and balancing differing views or competing interests of the various stakeholders. In the USA, for example, the National Institutes of Health primarily supports research, having as its mission 'science in pursuit of fundamental knowledge about the nature and behaviour of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability.' The Food and Drug Administration, by contrast, is specifically charged with overseeing the approval of drugs and medical devices before they can be sold in the USA.

In the UK, the National Institute for Health and Clinical Excellence (NICE) provides such guidance. NICE[6] for example produces guidance in three areas of health: public health - guidance on the promotion of good health and the prevention of ill health; health technologies – guidance on the use of new and existing medicines, treatments and procedures; clinical practice – guidance on the appropriate treatment and care of people with specific diseases and conditions.

Ultimately, decision making in health, whether at the individual, institutional, or national level involves consideration to a number of other factors other than effectiveness, and where RCTs are not the feasible or appropriate judgement method. On an individual level, the views, experiences, priorities of the person with the illness need to be considered as part of the decisions on choice of treatment. Organisational context may also influence the feasibility of adopting a course of action or another, such as resources required for the intervention to be successfully implemented, or whether it will be acceptable for healthcare workers. Different study methods inform these questions, including focus group discussions, or participant observations. Bringing together the experience in these methods has not been as extensive as in the RCTs synthesis. However, rather than relying solely on one type of 'superior' evidence (i.e. the RCT), it is better to identify the appropriate method is used in addressing specific question (Pettigrew and Roberts, 2007).

Dealing with other aspects of uncertainty in clinical medicine is considered to require better ways to identify relevant evidence, to make connections between patient data and wider knowledge, the training of doctors on decision making and in communicating with patients about uncertainty (Djulbegovic, 2004; Plsek and Greenhalgh, 2001). Methods to systematise experience in addressing those issues are developing but much of those sources of uncertainty are addressed through clinical experience and judgement.

Addressing uncertainty and complexity in environmental health

Decision makers faced with the protection of public health from the potential adverse effects of chemicals or physical agents in our air, water, soil and food must often deal

[6] http://www.nice.org.uk/

with a further increase in the types and sources of uncertainty. Unlike in studies of the safety and efficacy of medicines, where humans receive doses they are likely to encounter in actual use, evaluation of the potential harm to public health from hazardous agents in the environment requires an expanded set of tools. Human encounters with hazardous agents in the environment often occur at levels much lower than ones at which frank health effects occur, and health effects may thus occur at frequencies that are difficult to detect without very large and sophisticated epidemiological studies. Health effects of some exposures may take decades to become manifest.

Uncertainties abound. What are the likely human health effects of a particular agent whose effects have only been studied in animals? What are the sources of the agent and how might humans be exposed to it? Do those exposures pose a threat to human health? Does the source involve an industrial sector that also provides important services to the economy or society at large? The evaluation and decision process also necessarily involves an increase in the complexity of the actors and stakeholders since management of certain risks to public health increasingly involve tradeoffs with other risks to public health, the environment as well as to the economy.

A common response to uncertainty is some degree of precaution (Wiener, 2002). 'Look before you leap'. Many international institutions and governments around the world have chosen to incorporate this general concept of precaution either implicitly or explicitly, sometimes as general guidance and at others with more specific directives, but most with the objective of limiting or preventing chemicals or processes that carry uncertain risks.[7]

In reality, the answer cannot be simply to ban products or activities simply because they may have risks (Wiener, 2002). Society undertakes any number of activities that have benefits as well as risks (e.g. taking medicines, driving, producing energy, etc.). Nor can the answer be to wait until we are absolutely certain before taking action. Principle 15 of the Rio Declaration of the United Nations Conference on Environment and Development, which codified the precautionary approach at the global level, states: 'In order to protect the environment, the precautionary approach shall be applied widely by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation' (UN, 1992).

More nuanced questions must be asked: 'how much risk and with what degree of uncertainty? What benefits and with what certainty? In a famous US case, in which the US Occupational Health Administration was challenged over their attempts to set a 'safe' standard for benzene exposure in the workplace, the US Supreme Court ruled that that 'safe' did not have to mean 'no risk' but instead 'no significant risk' and gave the US Occupational Safety and Health Administration the authority to determine what constitutes a 'significant' risk (Wiener, 2002).

These more difficult questions can only be answered with a better understanding of the science and technology behind each risk and the uncertainties that remain. These issues need to be communicated clearly and can then be subject to public debate in order to reach decisions about how much risk to accept, e.g. how much risk is 'significant'.

[7] A detailed discussion of precaution, precautionary approaches, principles, and practices is beyond the scope of this chapter. However, given the influence of these topics on policy and regulation, readers are recommended to consult the wealth of literature on this topic (Martuzzi, 2007; Wiener, 2002, 2005.)

Thus, it is not surprising that in practice, decision makers often look to a careful process of laying out the evidence, known as risk assessment. The outcome then takes its place in the broader decision-making and risk management process.

Risk assessment

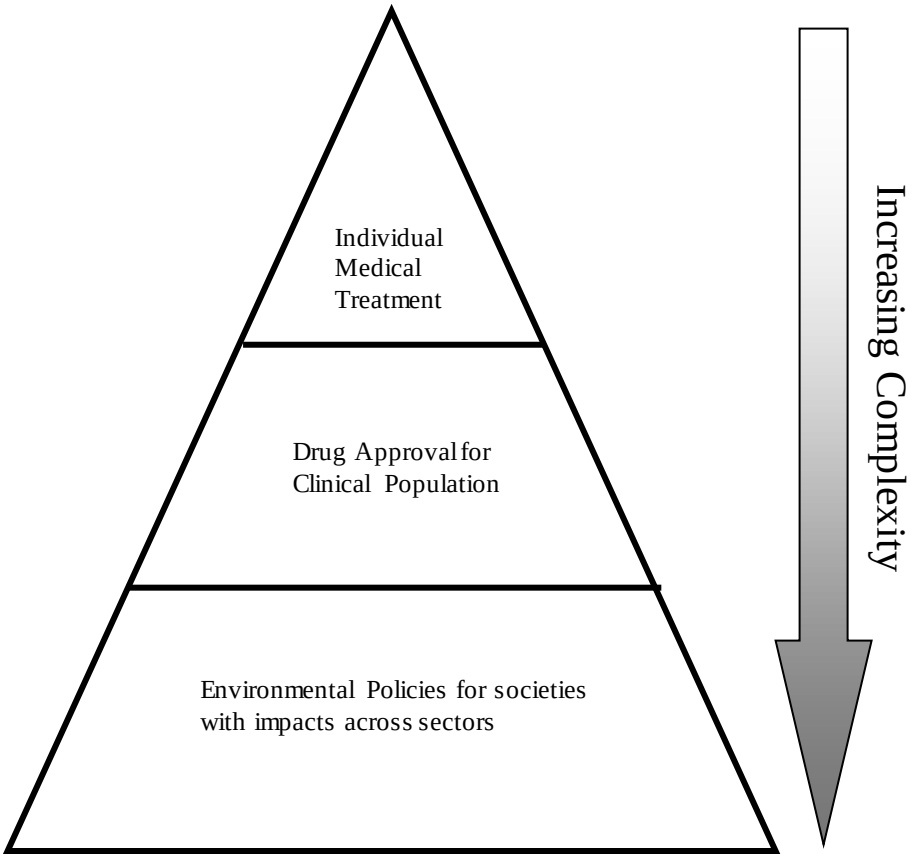
The basic paradigm for the risk assessment process was essentially codified by the US National Academy of Sciences (NRC, 1983) but it has been modified and enlarged upon by many national (NRC, 1989; NRC, 1996; RCEP, 1998) and international organisations including the International Programme on Chemical Safety (IPCS), a collaboration of a cooperative programme of the World Health Organisation (WHO), the International Labour Organisation (ILO) and the United Nations Environment Programme (UNEP) (IPCS, 2004a). The paradigm incorporates four basic components, shown in relationship to one another in the left side of Figure 2 and defined below:

- ***Hazard Identification:*** The identification of the type and nature of adverse effects that an agent has an inherent capacity to cause in an organism, system, or (sub)population.
- ***Hazard Characterisation[8]/Dose-Response Assessment:*** Characterisation of the qualitative, and if possible quantitative, relationship between the dose of a chemical or agent (or its derivatives) and the expected adverse response in an organism, system, or (sub)population. May also be expressed in terms of exposure, for example, a concentration-response relationship.
- ***Exposure Assessment:*** Characterisation of the potential sources, routes, magnitude, and duration of exposure of an agent (or its derivatives) to an organism, system, or (sub)population.
- ***Risk Characterisation:*** The qualitative and, wherever possible, quantitative description, including attendant uncertainties of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system, or (sub)population, under defined exposure conditions.

In short, this paradigm recognises that in order to be able to estimate the risk, or probability of harm, to public health from a particular agent, there must first be some non-zero probability that an agent is inherently hazardous; second, there must be some understanding of how large a dose is necessary to create the hazardous effect; and finally, there must be some estimate of the probability and magnitude of exposure to human populations. Without some probability of exposure, even a particularly hazardous substance may not need to be controlled. This paradigm further recognises that uncertainty may exist about any one or all of these components – in the probability of a causal relationship, in the nature of the dose-response relationship, and in the actual exposures experienced by individuals or populations over time. It calls for these uncertainties to be clearly identified in the final characterisation of risk.

[8] IPCS (2004a) favours 'Hazard Characterization' over 'Dose–response Assessment' for the second step although their definition includes dose–response.

Figure 2: The NRC Risk Assessment/Risk Management Paradigm in Human Health



Source: NRC, 1983

Though not listed in the original paradigm, *risk communication* has come to be recognised as a critical fifth component interlinking all of the other components and playing a critical role both prior to and after the results of any risk assessment. We will come back to risk communication later in the chapter.

Scientists and decision makers have struggled with how to characterise uncertainty and what to do with it in some cases long before the NRC codified the process of risk assessment. However, more than many public health fields, environmental health risk assessment has engaged in serious efforts to develop more quantitative characterisations of uncertainty. In the examples that follow, we seek to illustrate the different ways in which uncertainty has been characterised in hazard identification, in dose-response assessment, in exposure assessment and in risk characterisation. We can only touch on some of the many steps that may comprise a complicated risk assessment, but hope to convey the ways in which scientific evidence and expert knowledge are utilised in the risk assessment and ultimately, in risk management.

Hazard Identification for Carcinogens: The International Agency for Research on Cancer (IARC)

A key component of any risk assessment involves a response to the question: 'What is the likelihood of a true causal relationship between a particular action, for example a release of or exposure to a hazardous agent, and an adverse effect in human populations? How solid is the evidence? Society lacks resources to address all hazards so characterisation of how well these causal links are understood can be a critical first step in setting priorities. While these questions are relevant to both cancer and non-cancer effects we focus on cancer to illustrate this phase of the risk assessment process.

Few health effects inspire as much dread as cancer. The International Agency for Research on Cancer (IARC) was established in 1965 and almost immediately experienced a great demand for advice on the carcinogenic risks of chemicals, 'including requests for lists of known and suspected human carcinogens' (IARC, 2006). IARC ultimately responded with the development of a systematic programme for making these judgements on the available evidence with the help of international expert opinion. What has evolved is a sophisticated process for review of the state of scientific knowledge resulting in a qualitative assessment, or classification, of the degree of certainty about the carcinogenicity of thousands of hazards.

The IARC's results are published in the form of 'Monographs'. 'The monographs represent the first step in carcinogen risk assessment, which involves examination of all relevant information in order to assess the strength of the available evidence that an agent could alter the age-specific incidence of cancer in humans. They are developed based on the efforts of IARC 'Working Groups' consisting of scientists who 'generally have published significant research related to the carcinogenicity of the agents being reviewed and who demonstrate an' absence of real or apparent conflicts of interests.' (IARC, 1996). The outcome of the Working Group deliberations is essentially a qualitative assessment of the strength of the evidence for the carcinogenicity of a chemical, physical, or biological agent in (1) humans, and (2) in experimental animals (summarised in Table 1).

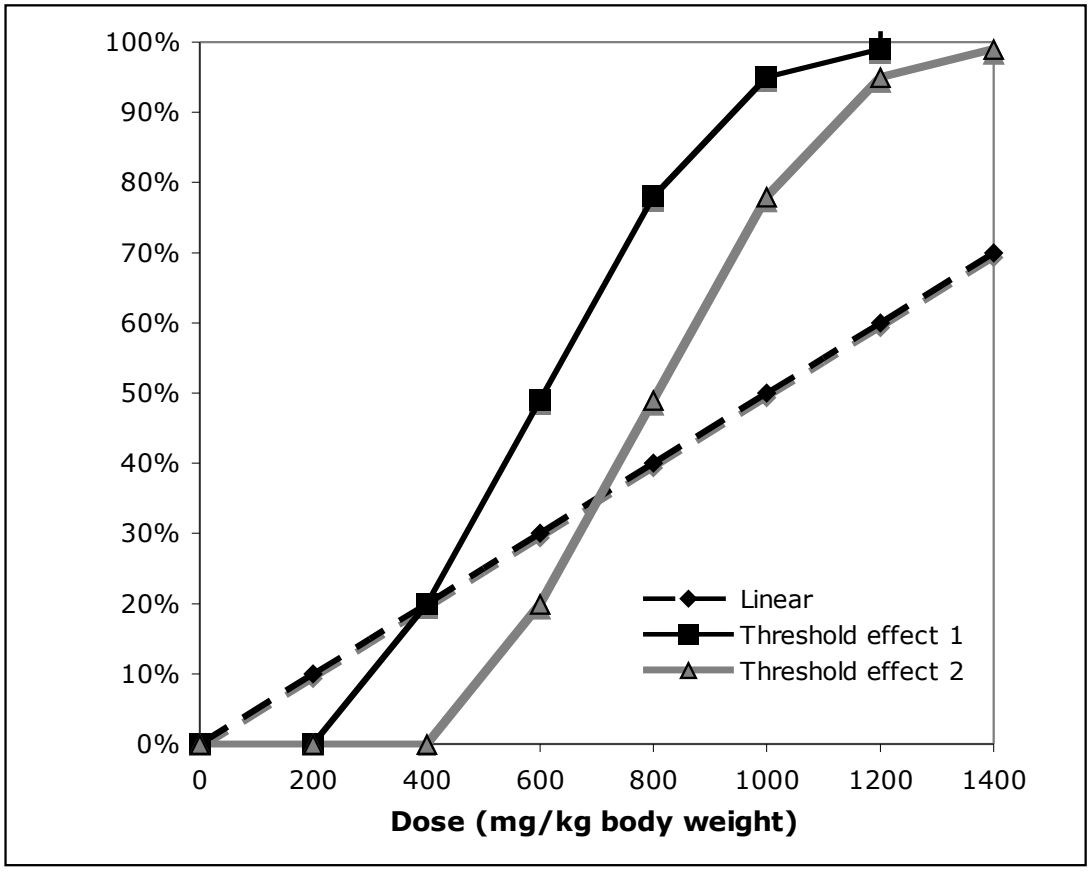
Though qualitative, the impact of the IARC monograph cancer classification programme has been powerful. The IARC evaluation process, though not without its critics, is more thorough and extensive than can be taken by many individual agencies and indeed countries. Many national and international authorities rely on the IARC monographs to set their own priorities for chemicals to consider in their regulatory programs, as a source of data for risk assessments, to identify sources of uncertainty relevant to assessing risks and to setting research priorities in their own countries.

Table 1: IARC Cancer Classification System

Evidence for Carcinogenicity in Humans	Evidence for Carcinogenicity in Experimental Animals
***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence. ***Limited evidence of carcinogenicity*:** A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence. ***Inadequate evidence of carcinogenicity*:** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available. ***Evidence suggesting lack of carcinogenicity*:** There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure.	***Sufficient evidence of carcinogenicity*:** The Working Group considers that a causal relationship has been established between the agent and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms. ***Limited evidence of carcinogenicity*:** The data suggest a carcinogenic effect but are limited for making a definitive evaluation. ***Inadequate evidence of carcinogenicity*:** The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available. ***Evidence suggesting lack of carcinogenicity*:** Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent is not carcinogenic.

The answer to this question depends on the dose-response relationship. The dose response relationship is a manifestation of a more intricate set of chemical and biological events that determine the specific mechanism or mode of action. However, to simplify the discussion our example deals only with dose-response as illustrated in Figure 3 which depicts hypothetical relationships between dose on the X-axis, expressed as milligrams (mg) per kilogram (kg) of body weight, and the response on the Y-axis, expressed as the percent of individuals showing a particular effect. The simplest form of a dose response curve is a linear one, in which an increase in dose results in a predictable increase in response related to the slope of the line. In such cases, for example, for 'genotoxic' carcinogens that are thought to interact directly with genetic material, the presumption is that there is no dose that is completely 'safe'. In many cases, however, the reality is more complicated; the rate of response changes with dose and there may exist a dose below which no adverse response is seen, referred to as a threshold. Many non-carcinogens, and some carcinogens, are believed to have a mode of action that will give rise to a threshold.

Figure 3: Hypothetical dose-response relationships



If sufficient data exists to demonstrate a clear threshold in humans, one could simply set a standard below the threshold. But this has rarely been the case. Uncertainty arises from the paucity of data in human populations; if human studies are available at all, questions may arise about how well the data represent potential responses particularly sensitive populations (for example infants, the elderly, or the infirm). Or, as is more often the case, scientists must rely primarily on data from animal studies; questions then arise about the reliability of extrapolation between species or from the high doses in animal experiments to the lower doses in the environment, among other issues.

Default 'safety' factors

Scientists and decision makers have historically dealt with these uncertainties with a degree of precaution, by applying one or more default safety factors to the lowest level of an experimental dose for which an adverse effect has been observed (LOAEL), or if available, to the no observed adverse effect level (NOAEL). The experimentally determined effect level is then divided by a safety factor to arrive at a dose that is presumed to be acceptable for the whole human population.

As long ago as the 1950s, Lehman and Fitzhugh of the US Food and Drug Administration introduced the 100-fold safety factor to provide an added margin of safety to protect the public from lifetime exposures to pesticide residues and food additives (Lehman and Fitzhugh, 1954). The factor of 100 was not just an arbitrary number; Lehman and Fitzhugh had observed that interspecies variation in responses fell within a factor of 2–3 and that the responses of sensitive individuals fell within a factor of 10 of average individuals. The US and other international agencies have adopted use of these default safety factors, typically factors of 10, one for interspecies differences and the other for human interindividual variability. Additional uncertainty factors are sometimes used to allow for database deficiencies, for the severity and irreversibility of effects, and in some cases for the possible effects in children.

Many decision makers have favoured these default safety factors because they are thought to be 'conservative' and precautionary by 'erring on the safe side.' Although they have some basis in scientific evidence, they have come under increasing scrutiny by the regulated community. How conservative, if fact, are they when applied to a particular chemical in a particular circumstance? Without some understanding of the possible answer to this question, a dialogue about their implications, for example about the implicit tradeoffs between degree of protection and cost, cannot easily take place.

As a result, several national and international organisations have begun to introduce more flexible systems that allow consideration of chemical-specific data in the development of what are now more neutrally referred to as 'adjustment' factors. The development of chemical specific adjustment factors discussed below reflects this movement toward more explicit consideration of the nature and quality of evidence for individual chemicals.

Chemical specific adjustment factors

The concept of chemical-specific adjustment factors (CSAFs) was introduced to provide a method for the incorporation of quantitative data on interspecies differences or human

variability in either toxicokinetics[9] or toxicodynamics[10] into the risk assessment procedure, by modifying the relevant default uncertainty factors of 10. These factors are discussed in detail elsewhere (IPCS, 2005a) but their development merits a brief discussion to show how a risk manager can use information on interindividual variability to think specifically about what percentile of the human population to protect in developing the adjustment factors.

Consider a simple case where adequate human data are believed to exist to develop a CSAF for human variability in toxicokinetics based on the measurements of a parameter that describes the rate at which a given chemical is detoxified in the body. The human data would be analysed and characterised in terms of a probability distribution (for example, a lognormal distribution) of values. If sufficiently representative, this sample might reflect the distribution of possible values for this parameter in the general human population. Replacement of the default subfactor by a CSAF would require that decision maker select a particular percentile of the distribution based on how protective he or she wanted the safety factor to be. The CSAF would be calculated as the ratio of the parameter estimate at the percentile of interest to the parameter estimate at the mean.

Choice of the percentile would be a policy decision and could be influenced by aspects such as the severity of the effect, the robustness of the data, the nature of the distribution and risk management considerations. However, the analyst might provide a range of percentiles for the risk manager to consider; the further out on the tail of the distribution, the higher the CSAF, and the greater the percentage of the population theoretically protected.

Dealing with uncertainty in exposure assessment

In the continuum of characterisation of uncertainty, the field of exposure assessment has gone the furthest toward adopting quantitative probability methods. In part, this development has come about because of the relative ease with which exposure can (at least appear to) be measured or modelled. As the previous section on CSAF indicated, probabilistic characterisations of particular toxicological parameters are gaining currency; however, predicting the magnitude and probability of causal and dose-response relationships in humans, although they exist (Cooke *et al.*, 2007; Evans *et al.* 2004a, b; Roman *et al.*, 2008) are much less common.

The need to characterise uncertainty in exposure also is motivated by the information decision makers should have to answer specific kinds of questions, for example:

- What are the most important routes of exposures to a population?
- What is the distribution of exposures among different members of an exposed population?
- What are the key sources of uncertainty in the exposure assessment? How should research efforts be targeted to improve the precision of the exposure estimates?

[9] Toxicokinetics describes the process of the uptake of potentially toxic substances by the body, the biotransformation they undergo, the distribution of the substances and their metabolites in the tissues and the elimination of the substances and their metabolites from the body.

[10] Toxicodynamics refers to the process of interaction of chemical substances with target sites and the subsequent reactions leading to adverse effects (essentially mode of action).

- How effective are proposed control or management strategies to reduce exposure?
- How significant are differences between alternative strategies?

These questions cannot be answered correctly without some understanding of uncertainty, of the strength and quality of evidence underlying the estimates. Optimal decisions cannot be made about the need to control an exposure or how and when to allocate research funds. A rank ordering of exposures based on mean estimates, for example, may not be truly valid if the data underlying estimates of the highest exposure is much more uncertain than one or more of the lower exposures. Faced with the fuller information, a decision maker might well choose to refine the estimate or to delay a decision on controlling the top exposure.

Early exposure assessments tried to deal implicitly with uncertainty by essentially incorporating a degree of conservatism in their choice of single point estimates to represent exposure. They relied on vague concepts like 'upper-bound exposure' and 'maximally exposed individual' which had no specific quantitative basis and thus led to lack of comparability both within and between assessments. The assumptions on which these point estimates were based were not always made transparent.

More recently, there has been increasing emphasis on the characterisation of the exposure of different individuals in the population. For example, the United States Environmental Protection Agency's (USEPA) guidelines for exposure assessment, issued in 1992, called for both high-end and central tendency estimates for the population (USEPA, 1992). The high end was considered as that which could occur for the 90th percentile or higher of exposed individuals, and the central tendency might represent an exposure somewhere near the median or mean of the distribution of exposed individuals.

Since the 1990s, there has been increasing emphasis also on characterisation of the distinction between variability and uncertainty in exposure assessments (Morgan and Henrion, 1990; NRC, 1994; Paté-Cornell, 1996). During this time, there was also growing interest and use of probabilistic simulation methods, such as those based on Monte Carlo or closely related methods, as the basis for estimating differences in exposures among individuals or, in some cases, in estimating the uncertainty associated with any particular exposure estimate (USEPA, 1997; Cullen and Frey, 1999).

These converging developments have brought the field of probabilistic exposure assessment from the background to a central part of exposure assessment today in many applications. The transparency afforded by probabilistic characterisation and separation of uncertainty and variability in exposure assessment offers potential benefits in the context of increasing common understanding as a basis for greater convergence in methodology.

A tiered approach to characterising uncertainty

Analysts recognise that data are not often sufficient to support the kind of quantitative analysis that is desirable and that instead, a tiered or phased approach many be necessary. A tiered approach refers to a process in which the exposure or risk assessment progresses systematically from relatively simple to more complex. The accompanying text box gives a summary of the tiered approach advocated by the IPCS (2008) in its guidance on characterising and communicating uncertainty in exposure assessment.

Tiered approaches have been advocated by other regulatory programs in Europe and the US: by the European Union's (EU) chemicals regulation, REACH, or the Registration, Evaluation, Authorisation and Restriction of Chemicals (EU, 2005); by the European Food Safety Authority (EFSA, 2006) for exposure assessment; by the USEPA's Risk Assessment Guidance for Superfund (USEPA, 2001) and Air Toxics Risk Assessment Technical Resource Manual (USEPA, 2004); California's Office of Environmental Health Hazard Assessment 'Hot Spots' air toxics programme (OEHHA, 2000). Tiered approaches to uncertainty are also used by other international organisations for non-exposure assessments, such as for contributions to global warming by the Intergovernmental Panel on Climate Change (IPCC, 2000).

Risk characterisation and uncertainty

The final step of the risk assessment paradigm is risk characterisation. It is a step in which the results of the steps described previously – hazard identification, dose-response, and exposure assessment are integrated into an overall assessment of the nature, likelihood, and magnitude of risks to human health. Because assessment and characterisation of uncertainty, its sources and implications should be a component of each step of the process, the final risk characterisation should also include a comprehensive and transparent discussion of uncertainty.

As suggested by Figure 2, the risk characterisation phase is one that is an important point of intersection with the risk management process, in which managers need to integrate the findings of the risk assessment into the broader decision framework. However this intersection is not just something that happens at the end; the information and analytical needs of risk managers should be communicated in early in the framing of the analysis. What are the relevant policy guidelines or regulatory standards that the outcome needs to be compared to? What information needs to be provided to help distinguish between different regulatory alternatives including decisions to take no action? How do the key sources of uncertainty need to be identified and characterised such that decision makers can evaluate the value of delaying a decision in favour of collecting additional data or conducting research? What information is necessary for communication of the results to the public and to other stakeholders? Anticipation and communication of the responses to such questions helps guide the framing and development of the risk assessment.

The form that risk characterisation takes will also be dependent on the data and extent of analysis conducted in earlier steps. Consequently, its form will not be discussed in detail here; we note simply that it may range from qualitative to fully quantitative and probabilistic consistent with the kinds of tiered approaches discussed earlier.

Text Box 1: The IPCS tiered approach to uncertainty analysis in exposure assessment

- **Tier 0 Screening Uncertainty Analysis.** Tier 0 uncertainty analysis is performed for routine screening assessments, where it is not feasible to conduct a separate uncertainty characterization for each case. Instead, default uncertainty factors that have been established for the type of problem under consideration may be applied. These screening-level assessments are designed to demonstrate if the projected exposures or risks are unlikely to exceed reference values.

- **Tier 1 Qualitative Uncertainty Analysis.** Where the screening assessment indicates a concern, a more case-specific uncertainty characterization is required to take account of any special circumstances of the case in hand (e.g. anything that might justify a smaller uncertainty factor than the default one) and to take account of any additional (higher-tier) data. Tier 1 analysis is intended to examine how likely it is that, and by how much, the exposure or risk levels of concern may be exceeded. Tier 1 is the simplest form of this enhanced uncertainty analysis, mostly based on a qualitative approach involving systematic identification and characterization of different sources of assessment uncertainties.

- **Tier 2 Deterministic Uncertainty Analysis.** In a higher-tier analysis, semiquantitative or quantitative sensitivity analysis, interval or perhaps factorial and probability-bound analyses are considered. The semiquantitative approach involves using available data to describe the potential range of values for the assessment parameters and performing sensitivity analysis to identify the parameters with the most impact on the exposure or risk predictions. Usually, Tier 2 uncertainty analysis consists of a deterministic point estimate sensitivity analysis. Sensitivity analysis in this context is often performed to identify the relative contribution of the uncertainty in a given parameter value (e.g. inhalation rate, emission rate) or a model component to the total uncertainty in the exposure or risk estimate.

- **Tier 3 Probabilistic Uncertainty Analysis.** Tier 3 analyses rely upon probabilistic methods to characterize the individual and combined effects of input and parameter uncertainties on the predicted results. Moreover, in some Tier 3 analyses, separate contributions of variability and uncertainty to overall assessment uncertainties may be differentiated. The starting point for any Tier 3 analysis is the quantification of probability distributions for each of the key exposure or risk model input values (e.g. mean and standard deviation of fitted statistical distributions, such as normal or lognormal distributions). These are often derived from existing measured or modelled values and in some cases based on expert judgements. Tier 3 uncertainty analysis examines the combined influence of the input uncertainties on the predictions by propagating either analytically (e.g. Taylor series approximation) or numerically (e.g. Monte Carlo simulation) parameter and input value uncertainties, as appropriate.

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Public health in a complex decision making context

The motivation to protect health, to 'do no harm' or to 'err on the side of safety' relies heavily on the role of scientific evidence as justification for decisions. The strong investment in research in support of 'evidence-based' medicine or of environmental health risk assessment both characterise the hope that 'if we could only get the science right' by reducing or at least characterising uncertainty that the 'right' answer would be easier to find. This is only partly true.

The reality is more complex. As discussed in the introduction this paper, and illustrated in Figure 4, public health risk is often only one component of a decision. There are alternatives to consider, the consequences of those alternatives, how those might be evaluated and judged not just by the prime decision makers, but by other stakeholders as well. There are often tradeoffs between several risks and benefits to be made.

Figure 4: Complexity in risk assessment and public policy-making

Other types of knowledge that may or may not be empirically based enter into discussions. Differing perceptions of risk can play a powerful role, both in individual and societal decisions (Slovic, 2000). In medical decisions, the fears, experiences, and priorities of the person with the illness need to be considered as part of the decision as they can affect the ultimate efficacy of the choice of treatment. Perceptions of the risk of particular technologies – genetically modified foods, nuclear power – can be extremely influential in public debates as proponents of these technologies can attest (Tait, 2008). They need to be openly acknowledged and discussed in the risk assessment and management process even if they may not be resolved.

At the same time, the literature on risk perception and judgements under uncertainty that lay people and experts alike can fall prey to common errors (Kahneman, Slovic, and Tversky, 1982; Gilovich, Griffen, and Kahneman, 2002). Decision makers need to be cognisant of these.

> *' [S]ound regulatory policy entails both responsiveness to public attitudes about risks and enlightened leadership by government officials.' ... '[If] the public is informed that some risk (say, nuclear power, or transgenic foods, or wolves, or urban youth, or fear of the dark) is not really a significant threat to public well-being, but if the public persists in feeling dread of the unfamiliar (abject fear of the unknown) and therefore presses for regulatory protection, perhaps government should think twice before translating dread into public policy.'* (Wiener, 2002)

Differences in the valuation of alternative outcomes or alternatives also need to be addressed. In the context of an individual medical decision about cancer treatment, for example, one patient may value the quality of remaining life lived more highly than prolonging life itself whereas another may feel the opposite. Uncertainty about the efficacy of the treatment may only be part of the decision. In other public health or decisions, outcomes may be both experienced and valued differently by disparate groups of people. Patient groups advocating for approval of experimental therapies they have found beneficial are sometimes pitted against patient groups who have experienced adverse side effects of the therapy. Outcomes may not even be measured using the same metrics (e.g. number of deaths avoided, monetary damages, ecological impacts) making weighing and choosing among priorities difficult.

Several methods do exist which try to provide a common basis for comparison amongst outcomes and alternatives. Cost-benefit analysis, which relies on monetisation of all costs and benefits, is one example. The WHO's Global Burden of Disease program[11] is another important public illustration of the use of an economic metric, the Disability Adjusted Life Year or DALY, to help governments identify key health priorities across diverse health outcomes (Lopez *et al.*, 2006). In brief, the DALY is 'a health gap measure that extends the concept of potential years of life lost due to premature death to include equivalent years of healthy life lost by virtue of individuals being in states of poor health or disability.'[12] One DALY can be thought of as one lost year of healthy life and the burden of disease as a measure of the gap between current health status and an ideal situation where everyone lives into old age free from disease and disability.' [13] It has been used to estimate the relative burden of disease attributable to communicable versus non-communicable disease and due to a wide range of risk factors from childhood nutrition to substance abuse and the environment.

While these methods can be useful additions to the debate, they may never resolve the fundamental *normative ambiguity* that exists for those who hold very different views of the risks and benefits. Policy makers, have the unenviable task of stepping in at the governmental level or at an individual project level to strike a balance. For example, in its

[11] See for details: http://www.who.int/healthinfo/bodproject/en/index.html.
[12] http://www.who.int/healthinfo/boddaly/en/
[13] Ibid.

creation of the Clean Air Act, the enabling legislation governing regulation of air quality in the USA, the US Congress decreed that only public health and environmental benefits – not cost – could be a consideration in setting National Ambient Air Quality Standards. However, later Presidential Executive Orders signed by Reagan (EO 12291) in 1981 and subsequently amended by Presidents Clinton (EO 12498) and Bush (EO 13422) required that any 'major' proposed regulations (i.e. that cost more than $100 million annually among other criteria) would have to undergo detailed analysis to see if the benefits exceeded the costs. Both these outcomes reflect the tug and pull of a long and complex stakeholder debates; the environmentalists arguably had the upper hand in the design of the Clean Air Act while business groups' concerns were reflected more in the later executive orders.

Much has been written on the merits and liabilities of different approaches to involving stakeholders in the risk and decision making processes (see Loftstedt and Van Asselt, 2008, and Renn and Walker, 2008, for an overview of some of the literature on these debates). This chapter can only touch on some of these broader issues that add to the complexity of dealing with public health issues in medicine and environmental health. The goal of introducing them is to make the point that framing and resolving a wider policy question affecting public health is not just a technical task, but a social and political process.

The NRC paradigm for risk assessment therefore must inevitably include risk communication (NRC, 1989). Effective communication along the way can often be just as important as the identification and characterisation of risks and their uncertainties. Figure 4, which puts stakeholders at the centre of a complex decision, shows interlinking – points of communication – between each of the elements of a decision. Thus, effective risk requires not just clear conversations between analysts and decision makers and careful communication to others of the final outcomes and decisions; it may mean careful involvement of key stakeholders early in the framing of a problem so that significant concerns are identified early on.

When breakdowns occur, the results can be disastrous. The early handling of Bovine Spongiform Encephalopathy (BSE) or Mad Cow Disease in Britain (see Text Box for details) is a instructive example of where poor communications about risks exacerbated a problem where risks were actually poorly characterised and where public perceptions and concerns were not addressed. It illustrates the conclusions of the literature on risk communication that shows that good communication processes are essential to gaining credibility and trust (NRC, 1989; Renn and Levine, 1991; Löfstedt, 2005).

Conclusions

This chapter has provided an overview of some of the approaches two fields of public health, clinical medicine and environmental health, use address uncertainty and complexity in decision-making. It serves as an introduction to the literature in these fields and to concepts and practices.

Similar patterns emerge from both clinical medicine and environmental health fields, namely:

- Strong emphasis on systematic evaluation of scientific evidence to characterise uncertainty and complexity (for example statistical methods, epidemiology, risk analysis),
- Development of independent institutions to assemble and review the scientific data (for example, The Cochrane Collaboration and IARC),
- Utilisation of tools from economics (for example, cost-benefit analysis, DALYs, and the like) to monetise and compare different kinds of risks and benefits.
- National and international institutions to provide guidance and/or regulations on the interpretation of existing data and development of new data to support decisions (for example, NICE, FDA, NIH, IPCS among others).

These approaches reflect attempts to establish more systematic and transparent processes for identifying relevant data, for assessing risks and benefits, for evaluating the uncertainties and ultimately the adequacy of the database for supporting the decisions at hand. They have played an important role in allowing institutions and countries to work more efficiently toward shared and consistent approaches to assessing risk. Increasing the transparency of these processes facilitates clearer communication about what is known and not known amongst scientists, stakeholders and decision-makers. It thus can be an important factor in gaining public credibility and trust in the institutions and decisions they make.

While this focus on the underlying science is often necessary and appropriate, it is not always enough. Even when the complexities and uncertainties surrounding the science of a particular decision are laid bare for all to see, fundamental disagreements arising from both interpretive[14] and normative *ambiguities* can remain. Tradeoffs almost always exist between different types of risks and benefits, which may be perceived, experienced, and valued differently by individuals or groups within society. These kinds of disagreements, in particular normative ones, place scientific efforts to deal with uncertainty and complexity squarely within a broader social and political context – one that requires yet another set of skills and tools beyond those discussed in this chapter.

[14] The influence of myriad factors, including academic training and normative views, among others, on scientific judgement is a much larger subject that cannot be taken on here. However, it is acknowledged in the ways institutions try to balance technical and political viewpoints on their scientific panels.

Text Box 1: BSE: Lessons on communication of risk and uncertainty

Since the first cases of mad cow's disease in 1986, BSE was a recurrent and important item of public concern, especially regarding the possibility of cross-species transfer, and the risk posed to humans by beef consumption. When transmission to humans was demonstrated, there was loss of public trust in institutions and experts in charge of food safety, a massive drop in beef consumption, major economic and political damage. The main problems with the risk communication strategy identified were:

- For many years however the official communications tended to downplay the risks characterizing public concerns as irrational "overreaction".
- Scientific estimates that BSE was unlikely to be transmitted to humans were translated as "no risk to humans" and the scientific uncertainty existing in those estimates were not included in the messages. British beef was portrayed as safe.
- Scientific issues were portrayed as the main reason behind the policy decisions, and hid other trade-off such as relating to beef industry and exports.
- The public was perceived as needing reassurance and simple messages, although there was no empirical evidence that this was the case.
- Having started with a risk communication strategy of consumer reassurance that asserted that British beef was safe, policy makers were inhibited from learning about the risks or responding to new evidence.
- The agency delivering those messages (Ministry of Agriculture, Fisheries and Food) was perceived as having a conflict of interest, as it was both responsible for food safety an for the promotion of beef.
- The BSE scientific advisory committee did not include any human health experts.
- Public opinion was seen as an object of policy and as a problem that needs to be managed, rather than as an input to policy, and risk communication strategies were therefore unidirectional, done after policy decision were made, with little effort to engage in reciprocal communication, so as to take perceptions of risk as input to risk assessment and management.

The government has since separated the functions of food safety and agriculture promotion. The Food Standards Agency established in 2000 has broken new ground and experimented with a number of innovative forms of reciprocal communication and deliberation.

Key Lessons:

- Avoid concealment, sedation and understatement when communicating about risks, as the public can understand trade-offs and uncertainty.
- Risk communication strategies that assert full certainty or risks to be zero when uncertainties remain, are unsustainable.
- Responsibility over risk assessment of product safety and commerce/industry needs to be independent and seen to be so.
- Risk perceptions and different perspectives need to feed into all stages of risk assessment and management, by engaging in communication with different stakeholders. Communication only after the decisions were made needs to be avoided.

Text Box 2: The IPCS tiered approach to uncertainty analysis in Exposure Assessment

- **Tier 0 Screening Uncertainty Analysis.** Tier 0 uncertainty analysis is performed for routine screening assessments, where it is not feasible to conduct a separate uncertainty characterization for each case. Instead, default uncertainty factors that have been established for the type of problem under consideration may be applied. These screening-level assessments are designed to demonstrate if the projected exposures or risks are unlikely to exceed reference values.
- **Tier 1 Qualitative Uncertainty Analysis.** Where the screening assessment indicates a concern, a more case-specific uncertainty characterization is required to take account of any special circumstances of the case in hand (e.g. anything that might justify a smaller uncertainty factor than the default one) and to take account of any additional (higher-tier) data. Tier 1 analysis is intended to examine how likely it is that, and by how much, the exposure or risk levels of concern may be exceeded. Tier 1 is the simplest form of this enhanced uncertainty analysis, mostly based on a qualitative approach involving systematic identification and characterization of different sources of assessment uncertainties.
- **Tier 2 Deterministic Uncertainty Analysis.** In a higher-tier analysis, semiquantitative or quantitative sensitivity analysis, interval or perhaps factorial and probability-bound analyses are considered. The semiquantitative approach involves using available data to describe the potential range of values for the assessment parameters and performing sensitivity analysis to identify the parameters with the most impact on the exposure or risk predictions. Usually, Tier 2 uncertainty analysis consists of a deterministic point estimate sensitivity analysis. Sensitivity analysis in this context is often performed to identify the relative contribution of the uncertainty in a given parameter value (e.g. inhalation rate, emission rate) or a model component to the total uncertainty in the exposure or risk estimate.
- **Tier 3 Probabilistic Uncertainty Analysis.** Tier 3 analyses rely upon probabilistic methods to characterize the individual and combined effects of input and parameter uncertainties on the predicted results. Moreover, in some Tier 3 analyses, separate contributions of variability and uncertainty to overall assessment uncertainties may be differentiated. The starting point for any Tier 3 analysis is the quantification of probability distributions for each of the key exposure or risk model input values (e.g. mean and standard deviation of fitted statistical distributions, such as normal or lognormal distributions). These are often derived from existing measured or modelled values and in some cases based on expert judgements. Tier 3 uncertainty analysis examines the combined influence of the input uncertainties on the predictions by propagating either analytically (e.g. Taylor series approximation) or numerically (e.g. Monte Carlo simulation) parameter and input value uncertainties, as appropriate.

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