

WHAT DOES IT MEAN WHEN THE RISK ASSESSMENT SAYS 4.73×10^{-5} ?

Andrew Langley

Sunshine Coast Public Health Unit
Queensland Health

A number is a number is a number ... and yet exactitude should not be confused with accuracy. This article describes some of the philosophical underpinnings of the methods of health risk assessment.

BACKGROUND

The development of risk assessment methodologies in the 1970s and 1980s proceeded along two paths. Qualitative risk assessment sought to categorise risk. In some situations, this was into broad categories such as 'safe' (or 'acceptable') and 'unsafe' (or 'unacceptable'); in other situations, a series of very well defined categories was used. An example of this is the grading of substances by WHO's International Agency for Research on Cancer into one of five levels of carcinogenicity.¹

Quantitative risk assessment provides a numerical estimate of risk. It is emphasised that it is an estimate or calculation rather than an actual value. McKone and Bogen describe three types of risk: 'actual', 'calculated', and 'perceived'.² Ideally, these would be equivalent, but often risks are unquantifiable and unknowable as we have insufficient information on which to base the calculations, or our tools are not subtle (or accurate) enough. There are numerous quantitative risk assessment methodologies. The most prominent are probably the Cancer Risk Assessment Guidelines of the United States Environmental Protection Agency (US EPA) developed in the early 1980s.³

Quantitative risk assessment has been most controversial when applied to carcinogens, because of debates about the level of conservatism (that is, the caution associated with particular assumptions and default values chosen for the risk assessment) in estimates of risk. US EPA methodologies have been the most influential in the area of cancer risk assessment, but these contain a range of conservative assumptions that have been adopted for the pragmatic purpose of implementing cancer risk assessment rather than being established scientific fact.⁴

For exposure assessment, a series of 'high end' (that is, conservative) estimates of particular exposure factors is used in some assessments. The compounding effect of simultaneously combining several 'high end' estimates may result in 'an exceptionally rare value output' (that is, extremely conservative estimates).⁴

The US EPA has commented that the 'high end' risk estimates generated by its methodology are not 'necessarily a realistic prediction of risk' and that the 'true

value' may be as low as zero.^{4,5} The conservative nature of the methodology has been defended as necessary, in order to deal with the uncertainties in risk assessment, especially those relating to carcinogenicity data derived from feeding studies with limited cohorts of animals.

Having a number for the estimate of risk is somewhat meaningless, unless there are benchmarks such as an 'acceptable' level of risk against which the estimate can be judged. Frequently, a value of 1×10^{-6} is used to determine acceptability. Further, it needs to be clarified whether this is a risk per annum or over a lifetime, using a default life expectancy of 70 years. When quantitative risk assessment was first being used, an acceptable value of risk over a lifetime of 1×10^{-8} was arbitrarily proposed.⁴ This was reduced to 1×10^{-6} , which was considered to be a *de minimis* risk, from the legal term *De minimis non curat lex* (the law does not concern itself with trifles). Paustenbach refers to a commissioner of the US Food and Drug Administration indicating that a risk of 1×10^{-6} did not mean that 1×10^{-6} exposed persons would develop cancer but rather that the risk was virtually nonexistent.⁶ A review of US decision-making shows that risks between 4×10^{-3} and 10^{-6} have been deemed acceptable.⁶

The media, lawyers, and engineers like the concept of quantitative risk assessment but the risks and the context of the risk do not have the 'one dimensional' character of a number. While the public often just wants to know whether something is 'safe' or 'unsafe', regulatory risk assessors usually have to deal with uncertainty. While the US EPA methodology explicitly requires uncertainty assessments (that is, qualifications) around the risk characterisation, these are often not done.

Despite these problems, while a quantitative risk assessment model may lack accuracy in its risk characterisations, it may have sufficient precision to enable risks to be ranked, and for cost benefits to be compared for a variety of interventions. If the conservatism can be identified and taken into account it can reasonably be stated that the actual risk is unlikely to exceed this estimate and, hence, if the estimate falls below the criterion for acceptable risk, the actual risk is unlikely to exceed the criterion.

The US EPA is tending towards using narrative descriptions of risk, and has proposed this approach in its review of the methodology for assessing carcinogens.⁷ A narrative description can provide more 'shading' to the nature and magnitude of the risk than a number that may not capture the 'subjectivity and multiple dimensions of risks'.⁸

RULES OF THUMB FOR ASSESSING QUANTITATIVE RISK ASSESSMENTS

It is important to determine whether the risk assessment has been documented clearly, coherently and completely and whether it has been exposed to peer review.⁹ A range of questions can then be asked:

- Why was the risk assessment done? What was the societal and risk management context in which the risk assessment was done? What is the meaning of the risk to those involved in the situation? What information did the risk manager want? Will the risk assessment affect the management of the situation?
- Was there a better way of managing the issue than using a risk assessment?
- How will the results of the risk assessment be interpreted? Is there a need to determine an 'acceptable' or 'tolerable' level of risk?
- Is a qualitative risk assessment sufficient or more appropriate than a quantitative risk assessment?
- Were there sufficient data relevant to the local situation to be able to undertake a quantitative risk assessment? Was there an excessive reliance on default data rather than on data that is from the relevant population or situation?
- Are all the equations and default assumptions and values available and transparent or is it a 'black box' where the details of the methodology are unclear? This is particularly important where the results are presented as definitive.
- Has the risk estimate been calculated to too many decimal points?
- Is the risk estimate a 'best estimate' of risk, or does it reflect the inclusion of multiple conservative assumptions (for example, relating to exposures and the dose–response slope for carcinogens), the compounding effect of which is to provide a very conservative estimate of risk?
- Is the risk estimate derived for typical members of the population or only highly-exposed people?
- Does the model give a good appreciation of uncertainty for each stage of the risk assessment?
- What are the effects of doing a sensitivity analysis using changes in assumptions or different data selections?
- How could this risk estimate be improved?

CONCLUSION

To assist Australian risk assessors, the National Environmental Health Council (enHealth) has recently

released a comprehensive risk assessment methodology, which includes a chapter on appraising risk assessment reports and risk characterisations.¹⁰ It also describes techniques such as the Monte Carlo method,¹⁰ which can— if done properly—help to improve the meaningfulness of quantitative risk assessments. The National Health and Medical Research Council (NHMRC) has established a Committee on Risk Assessment and Toxicity, which had its inaugural meeting in September 2002. Among its tasks is to advise the NHMRC on best practices in health risk assessment.

ACKNOWLEDGEMENTS

Bruce Markey assisted with the identification of historical references.

REFERENCES

1. International Agency for Research on Cancer. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. IARC monographs may be found at <http://monographs.iarc.fr>.
2. McKone TE, Bogen KT. Predicting the uncertainties in risk assessment. *Environmental Science and Technology* 1991; 25(10): 1674(8).
3. United States Environmental Protection Agency. *Federal Register* 1986; 51: 33–992.
4. Hrudey SE. Quantitative cancer risk assessment—Pitfalls and progress. Hester RE and Harrison RM (editors). *Issues in Environmental Science and Technology, No. 9*. Cambridge: Royal Society of Chemistry Risk Assessment and Risk Management, 1998.
5. Barnard RC. Major issues raised by the OMB report from the perspective of the regulatory agencies. *Regulatory Toxicology and Pharmacology* 1991; 14: 223–228.
6. Paustenbach DJ, Jernigan JD, Finley BL, Ripple SR, Keenan RE. The current practice of health risk assessment: Potential impacts on standards for toxic air contaminants. *Journal of the Air & Waste Management Association* 1990; 40(12): 1620–1630.
7. United States Environmental Protection Agency, Office of Research and Development. *Draft Revision to the Guidelines for Carcinogenic Risk Assessment*. Washington DC: United States Environmental Protection Agency, 1996.
8. Thomas SP and Hrudey SE. *Risk of Death in Canada: What we know and how we know it*. Edmonton: University of Alberta Press, 1997.
9. Vose D. *Risk Analysis: A Quantitative Guide*, 2nd edition. Chichester, West Sussex: John Wiley & Sons, 2000.
10. enHealth. *Environmental Health Risk Assessment: Guidelines for Assessing Human Health Risks from Environmental Hazards*. Canberra: Department of Health and Ageing, 2002. ☐