Overview of UK bovine spongiform encephalopathy (BSE) risk assessment

Grist E.P.M.*, Gallagher E., Wooldridge M. Centre for Epidemiology and Risk Analysis (risk analysis workgroup), Veterinary Laboratories Agency, Addlestone, Surrey, KT15 3ND, United Kingdom.

Summary

As one of the group of diseases known variously as transmissible spongiform encephalopathies (TSEs) or prion diseases, BSE has been causally associated with new variant CJD (vCJD) in humans (Collinge et al 1997, Bruce et al 1997). Confronted with many uncertainties on exposure pathways and transmission of the agent, the need for quantitative assessment of risk of human disease has achieved paramount importance. In this presentation we review all such BSE risk assessments undertaken in the UK to address this issue and consider how their results may be influenced by underlying model assumptions.

Introduction

BSE is a fatal disease characterised by spongiform tissue that develops in the brain. The BSE pathogen is generally perceived as a malformed prion protein (PrP^{sc}) that accumulates in a host by a process of 'catalytic conversion' of normal cellular PrP^{c} protein (Prusiner, 1991). Ultimately this results in the onset of illness and untimely death. However, early clinical symptons of BSE are vague or variable, making diagnosis difficult. Additionally, the long incubation period and variation of individual susceptibility both within and across different species has constrained attempts to understand BSE epidemiology. These aspects have combined to ensure that quantitative assessment of BSE risk is an endeavor necessarily fraught with uncertainty.

Objectives

In this presentation we provide an overview of all risk assessments undertaken in the UK to estimate BSE exposure risks to humans. In the light of statistical methodologies recently adopted in the field of risk analysis, we compare and contrast quantitative approaches and consider how risk results may be influenced by underlying model assumptions. In particular, we focus on three separate stages making up any BSE risk assessment: (1) source term estimation, (2) exposure pathway identification and (3) risk estimation. Each is considered separately.

Materials, methods and results

Source term estimation is the most fundamental part of any BSE risk assessment. This calculation estimates the amount of BSE *infectivity* (or infective load) contained in the pathogenic source under consideration. BSE infectivity is typically expressed in Infectious Dose 50 (ID_{50}) units, where 1 ID_{50} unit is the estimated mass of infected tissue that each individual in a population would need to orally ingest for 50% to become infected. This leads to a convenient working definition of the infective load as 'the potential of a specific mass of tissue to cause infection'.

Secondly, possible exposure pathways are identified and represented by an event tree model. Using data from different sources, the proportions of total infectivity to flow down each branch of the event tree are estimated, either as an average value or as a 'best' expert estimate. The event tree model therefore provides a framework for estimating the individual and societal risk to be associated with each exposure pathway.

Finally, risk is evaluated either through a deterministic or probabilistic assessment. In the former, 'point estimates' are derived. These are based on the most pessimistic estimates for (input) parameters in the risk model. However, such an assessment provides the risk manager with no information on the degree of uncertainty to be associated with each (output) risk estimate. Justification for the approach is to be found in the precautionary principle that, faced with a multitude of uncertainties, the most cautious outcome is provided by an evaluation of the worst case scenario. Although expected to be pessimistic (in other words, things should be better in reality), the calculation may sometimes underestimate because the method is reliant only upon the accuracy of the input values assigned to model parameters .

In recognition of this shortcoming, most risk assessments go on to proceed with *a probabilistic risk assessment* which generates 'interval estimates', typically through first-order Monte Carlo simulation. The computation attempts to take uncertainty into account by allowing (input) model parameters to take any value within a *range* of feasible values. Instead of a single calculation performed with a single set of *fixed* parameter estimates, risks are derived from repeated calculations in which the (input) parameters are drawn randomly from probability distributions. This generates an (output) distribution and percentile confidence interval (rather than a single point) for each risk estimate. However, different statistical approaches will in general yield different ranges for the associated range of (output) uncertainty.

Discussion

Major areas of uncertainty encountered in these risk assessments may be summarised as follows:

1. The prevalence of BSE infection individuals in a specified population
2. The magnitude of the cattle-to-human or sheep-to-human 'species barrier' factor
3. Whether there is a minimum (threshold) dose of prion required to initiate infection
4. Whether prions ingested by an individual accumulate over the course of time.
5. The nature of prion transportation and destruction through environmental pathways

The importance of each in the context of BSE risk assessment will be emphasized.

References

Bruce, M.E., Will, R.G., Ironside, J.W., McConnell, I., Drummond, D., Suttie, A., McCardle, L., Chree, A., Hope, J., Birkett, C., Cousens, S., Fraser, H., & Bostock, C.J. (1997). *Transmissions to mice indicate that new variant CJD is caused by the BSE agent.* Nature **389** 498-501.

Collinge, J., Hill, A.F., Desbruslais, M., Joiner, S., Sidle, K.C.L. and Gowland, I. (1997). *The same prion strain causes vCJD and BSE.* Nature **389** 448-450.

Prusiner S.B., (1991) *Molecular biology of prion diseases*. Science **252**, 1515 -1522.