

Assessment of the risk factors related to bovine spongiform encephalopathy

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Summary

The Office International des Epizooties (OIE: World organisation for animal health) recommends that all OIE Member Countries determine the status of bovine spongiform encephalopathy (BSE) in their cattle populations by conducting a risk assessment and meeting certain BSE surveillance criteria. The OIE has identified and listed the factors and criteria for this in the *International Animal Health Code*. The factors to be assessed include the consumption of meat-and-bone meal (MBM) by cattle, the importation of cattle and MBM which are potentially infected or contaminated with the BSE agent, the livestock population structure, the rendering processes and the animal feeding practices. In this paper, the authors present an overview of these risk factors and criteria, detailing the relevant components of each. In the second part of this paper, the authors provide a risk assessment to demonstrate the application of the OIE BSE guidelines. This is a probabilistic risk assessment of the factors related to BSE for Canada which conforms to the OIE approach to import risk analysis. The steps include the hazard identification, release, exposure and consequence assessments and the risk estimation. A scenario tree for the release and exposure assessments was used to model the events emanating from the initiating failure event of importing cattle potentially infected with BSE. The consequence assessment describes the costs and losses associated with the introduction and establishment of BSE in other countries. The risk estimate, integrating the release, exposure and consequence assessments, indicates a negligible probability that BSE was introduced and established in Canada; nevertheless, the economic consequences would have been extreme.

Keywords

Bovine spongiform encephalopathy – Canada – Meat-and-bone meal – Prions – Risk analysis – Risk assessment – Risk factors – Transmissible spongiform encephalopathies.

Introduction

Bovine spongiform encephalopathy (BSE) is recognised as an animal and zoonotic disease with extreme economic and public health consequences. Past and current trade in cattle, other ruminant animals and rendered animal proteins, all of which may be potentially infected with the BSE agent, has resulted in the introduction of the disease in some countries and necessitated the assessment of BSE factors by all countries. Bovine spongiform encephalopathy risk factors and the surveillance criteria to determine the BSE status of the cattle population of a country are identified in the *International Animal Health Code* of the Office International des Epizooties

(OIE: World organisation for animal health) (65) and elaborated in this paper. In most countries, the time period for the collected data and documentation on these factors and criteria extends from the late 1970s to the present day. In the second part of this paper, the authors present a probabilistic risk assessment of the factors related to BSE occurrence in the cattle population in Canada. This assessment, which follows the OIE risk analysis guidelines, may serve as an approach to be considered by other countries. The risk assessment presents the model and the specific evidence for the model inputs. It does not represent a review of the scientific literature or primary research but rather an objective and transparent presentation of the risk assessment approach and the evidence which was modelled.

Criteria to determine the bovine spongiform encephalopathy status of the cattle population

The OIE lists five criteria for determining the BSE status in the cattle population of a country. The first criterion is a risk assessment on the occurrence of BSE and the others are surveillance criteria.

A risk assessment of the factors for bovine spongiform encephalopathy occurrence

The OIE has identified the following factors as being important when conducting a risk assessment on the occurrence of BSE:

- ‘potential for introduction and recycling of the BSE agent through consumption by cattle of meat-and-bone meal or greaves of ruminant origin’
- ‘importation of meat-and-bone meal or greaves potentially contaminated with a transmissible spongiform encephalopathy (TSE) or feedstuffs containing either’
- ‘importation of animals or embryos/ova potentially infected with a transmissible spongiform encephalopathy’
- ‘epidemiological situation concerning all animal TSEs in the country or zone’
- ‘extent of knowledge of the population structure of cattle, sheep and goats in the country or zone’
- ‘origin of animal waste, the parameters of the rendering processes and the methods of animal feed production’ (65).

These factors represent risk factors and risk sources. A risk factor is defined here as an attribute or exposure that is associated with an increased probability of disease and may be part of the causal chain of BSE. The risk factors take account of the epidemiological aspects of BSE, including the routes of infection, the modes of transmission, and host, agent and environmental determinants. A risk source represents an activity or medium for introducing the BSE agent, such as the importation of cattle. The BSE factors primarily relate to the quantity of cattle and meat-and-bone meal (MBM) which were imported from BSE-infected countries, the practice of feeding MBM or greaves of ruminant origin to cattle, and the rendering processes for animal slaughter waste. The risk assessment process of the European Community Scientific Steering Committee (SSC) entitled ‘Geographical BSE risk’ (GBR) (44) assesses most of the same factors. However, the GBR also assesses the surveillance measures listed as criteria 2 to 5 by the OIE.

The nature, epidemiology, epidemic history and long incubation period of BSE require the assimilation of data over a long period of time, from the late 1970s to the present day. Most of the evidence collected on risk factors is complicated by the need for corroboration, so that historical information can be audited then either confirmed or eliminated.

Potential for introduction and recycling of the BSE agent through consumption by cattle of meat-and-bone meal or greaves of ruminant origin

In order to describe and quantify this risk factor, historical and current data and evidence on the feeding of MBM or greaves of ruminant origin are necessary. Greaves are an incompletely processed, protein-rich solid residue of the rendering process in which raw material composed of any animal by-products, including offal, fat trimmings, and bones from slaughterhouses and dead animals, are cooked to produce fats (tallow). Meat-and-bone meal is produced from the grinding and further processing of greaves.

Depending upon the circumstances of a country, information about the following matters may be required over the specified time period:

- a) the feed industry:
 - feed production by type of feed
 - number of production facilities
 - number of retailers/distributors
 - distribution within the country
- b) feed legislation:
 - federal, state and provincial legislation, including legislation involving feed bans of mammalian proteins to ruminants
 - compliance with this legislation
 - the frequency of inspection
 - the legislative controls put in place
- c) feeding practices:
 - the feeding, in relation to mammalian proteins and other protein supplements, of dairy and beef calves, dairy and beef breeding heifers, bulls and cows, feedlot steers and heifers and veal calves
 - the availability and per unit costs of the protein supplements to feed manufacturers or livestock producers
 - the per unit cost of undegradable intake protein (rumen undegradable protein, which is the portion of ingested protein that escapes rumen degradation and is digested directly in the abomasum and small intestine)
 - the feeding of mammalian proteins to other species, such as swine, poultry, and pet animals, such as dogs and cats, in order to corroborate the total use of mammalian protein within the country.

Importation of meat-and-bone meal or greaves potentially contaminated with a transmissible spongiform encephalopathy (TSE) or feedstuffs containing either

The Harmonised Commodity Description and Coding System (Harmonised System or HS) can be used to search the import statistics databases of a country, to determine the imports of

these products over the relevant time period. The exporting countries for which statistics need to be accessed are those countries reporting BSE listed on the OIE website (64). The relevant 6-digit and 10-digit HS Codes may be searched for the following imports:

- flours, meals, pellets of meat or meat offal unfit for human consumption, greaves
- meat waste and scrap of dead animals for the manufacture of animal feeds
- blood meal of dead animals for the manufacture of animal feeds
- bone meal for the manufacture of animal feed
- animal feed preparations and feed supplements, including feed concentrates
- complete feeds of bovines, dairy cattle and calves.

Other databases that can be used to corroborate and reconcile these findings from the import statistics of a country include the export statistics of the European Union and individual countries.

Importation of animals or embryos/ova potentially infected with a transmissible spongiform encephalopathy

The import statistics of a country can be searched to determine the number of ruminant animals, embryos and ova originating in TSE-infected countries that were imported over the specified time period, as well as their destination, use, quarantine and disposition. The species likely imported include cattle, sheep, goats, water buffalo (*Bubalus bubalis*), North American bison (*Bison bison*) and deer. Bovine spongiform encephalopathy has occurred contemporaneously with the BSE epidemic in captive exotic ruminants in British zoos, such as the greater kudu (*Tragelaphus strepsiceros*), gemsbok (*Oryx gazella*), nyala (*Tragelaphus angasi*), Arabian oryx (*Oryx leucoryx*), Scimitar-horned oryx (*Oryx dammah*), eland (*Taurotragus oryx*), ankole cattle (*Bos taurus*) and bison. Accordingly, examining the importation statistics on these exotic ruminants from BSE-infected countries may be warranted.

Sheep and goats have been experimentally infected with BSE via oral transmission with 5 g of infected bovine brain (50). Kao *et al.* (54) and Ferguson *et al.* (48) have modelled the potential occurrence of BSE in sheep. To date though, the natural transmission of BSE to sheep and goat populations has not been observed (41, 56). The International Embryo Transfer Society (IETS) does not consider the BSE agent as a hazard for the international movement of bovine embryos, based on the experimental work by Wrathall *et al.* (87). The conclusion of the European Community SSC on the safety of bovine embryos is similar (43). Embryo transfer from goats with experimentally induced infection did not transmit BSE (49).

Epidemiological situation concerning all animal TSEs in the country or zone

This factor refers to the occurrence of BSE in domestic cattle (*Bos taurus*, *Bos indicus*), water buffalo, bison, and exotic ruminants, scrapie in sheep (*Ovis aries*) and goats (*Capra hircus*), TSE in farmed mink (*Mustela vison*), feline spongiform encephalopathy in the domestic cat (*Felis catus*) and exotic cats, such as the cheetah (*Acinonyx jubatus*), ocelot (*Felis pardalis*), tiger (*Panthera tigris*) and lions (*Panthera leo*), and chronic wasting disease of deer of the Cervidae family including white-tailed deer (*Odocoileus virginianus*), mule deer (*Odocoileus hemionus*), and elk (*Cervus canadensis*). Epidemiological and other details on these animal TSEs may include:

- the species affected, the number of cases and the number of herds/flocks affected
- the incidence of the disease and the age, breed and sex distribution of cases
- the geographical distribution and countries of origin, if these TSEs are imported cases
- information concerning the epidemiology of each TSE
- laboratory confirmation and diagnostics
- carcass disposal such as incineration and burial
- surveillance programme for these TSEs (other than for BSE. The BSE surveillance programme is detailed below).

Although the origin of the BSE agent in Great Britain remains obscure, one hypothesis is that a scrapie agent may have been the primary origin. The principal spread of BSE to other countries, however, appears to originate from the importation of cattle and MBM from the United Kingdom (UK) and other infected countries. Risk assessments on the occurrence of BSE in a cattle population therefore focus on these risk sources rather than on the occurrence of scrapie in sheep and chronic wasting disease in deer (9).

Extent of knowledge of the population structure of cattle, sheep and goats in the country or zone

The population structure comprises the demography of the cattle, sheep and goat populations in the country, according to geographic region and over the relevant time period, including:

- the number of animals, herds or flocks
- stratification of the animal population by age, breed, husbandry type and herd or flock size
- slaughter statistics by age group or production function
- marketing systems such as auction markets, marketing boards, assembly yards
- culling rates and mortality rates by age group and production function
- animal identification and animal traceability

- average production of milk, beef, lamb, mutton and goat meat per animal unit
- the economic value of the particular sector, including the value of exports
- types and sources of feeds and feeding practices
- import and export statistics for live animals
- the numbers of farms with single species and multiple species operations
- trends in population size, geographic distribution and production.

Origin of animal waste, the parameters of the rendering processes and the methods of animal feed production

Detailed information on the rendering industry in the country over the specified time period is necessary since this represents part of the principal pathway for BSE infectivity to enter the cattle feed chain (28). This information should include the following:

- a description of all rendering processes, quantitative and qualitative parameters and practices
- the legislation and policies governing the rendering industry
- the types of rendered materials (dead stock, inedible offal, carcass condemnations, non-ambulatory animals, and specified risk materials [SRM], such as brain and spinal cord), the annual amounts of rendered materials produced and the distribution of rendering facilities
- production quality control, inspection and compliance
- the annual total domestic production, use and exports
- the annual total volume of imports, according to type of rendered materials
- the methods for incorporating rendered materials into feeds, production quality control, inspection and compliance
- the contamination of feeds with rendered materials.

Continuing disease awareness programme

The training and educational efforts directed at specific occupational groups should be described. These groups may include the following:

- farmers
- drovers
- livestock and zoo animal handlers
- abattoir personnel
- animal breeders
- veterinary diagnosticians
- rendering plant and feed mill operators

- official veterinarians (federal, state and provincial)
- veterinary practitioners
- teachers and students of colleges of agriculture and veterinary medicine.

This training may focus on the following elements:

- a description of the clinical signs and epidemiology of the disease
- the herd/flock, national and international implications of the disease
- notification legislation
- compensation programmes.

Additional details on the scope, modes, duration, frequency, intended audiences and structure of the education programme are also needed to assess its comprehensiveness and value.

Compulsory notification

Bovine spongiform encephalopathy must be a compulsorily notifiable disease in the country. The legislation enacted must include:

- the date the legislation came into force
- the definition of a case of BSE
- the measures to be taken in the event of a confirmed case, including the disposal of the carcass, offspring and other animals within the herd or flock
- the compensation provided.

Bovine spongiform encephalopathy surveillance and monitoring system

Surveillance strategies and a monitoring system must be in accordance with Appendix 3.8.4. of the 2002 OIE *Code* (65). Surveillance and monitoring records must be maintained for at least seven years and include:

- a description of the BSE surveillance and monitoring programme, including the sampling scheme, sample size, age and target groups
- the numbers of animals examined annually, their ages, geographical distribution, origin (indigenous/imported), breed, type (beef/dairy), reasons for examination and final diagnosis.

Diagnostic testing in an approved laboratory

Samples must be collected using the methods and protocols detailed in the latest edition of the OIE *Manual of standards for diagnostic tests and vaccines* (63). Examination of the brain or other tissues collected must be performed in an approved laboratory in agreement with the definition in Section 1.1. of

the *Code* (65). The laboratory should maintain records on the following information:

- the capacities of the laboratory (infrastructure, personnel, training, approval procedure)
- the dates on which these capacities were available
- the methodologies used for the examination of tissues
- the dates on which these methods were applied.

Risk assessment of the factors related to bovine spongiform encephalopathy for Canada

Hazard identification

Bovine spongiform encephalopathy is a chronic, degenerative disease affecting the central nervous system of cattle and belonging to the family of diseases known as TSEs (64, 72). The causative agent of BSE has not been fully characterised, but at present the most accepted theory is that the agent is a modified form of a normal cell protein known as a prion (4, 10, 51).

The prion is an abnormally configured protein, 'BSE prion protein (PrP)' or PrP^{BSE} in short. This abnormal protein or prion, which is normally encoded by the host protein (PrP), accumulates in and eventually causes the death of the nerve cells. This modified version of PrP is both less soluble and more resistant to enzyme degradation than the normal protein. It is accepted that the BSE agent:

- a) is smaller than most viral particles and is highly resistant to heat, ultraviolet light, ionising radiation, and common disinfectants which normally inactivate viruses or bacteria
- b) causes no detectable immune or inflammatory response in the host
- c) has not been observed microscopically (26, 51, 80).

Bovine spongiform encephalopathy has a long incubation period. This means that it usually takes four to six years for cattle infected with BSE to show signs of the disease, such as disorientation, clumsiness and, occasionally, aggressive behaviour towards other animals and humans (55, 72).

Most experts agree that BSE is spread to cattle through the feeding of contaminated MBM, originating from cattle with previously unidentified BSE infection. Offal tissues of particular risk include the brain, spinal cord, dorsal root ganglia and trigeminal ganglia (30, 82). An oral infectious dose (ID) of 50% (ID₅₀) indicates the oral dosage at which 50% of challenged cattle would become infected, where infection means evidence of replication of the BSE agent. The ID₅₀ is expressed as the product of the titre ID₅₀/g of tissue ingested by cattle and the amount of tissue (g) (31). It is estimated that, in a clinical case of BSE, about 8,000 cattle oral ID₅₀ of infectivity are present in

the carcass. The percentage of the total infectivity and the number of cattle oral ID₅₀ in a 537 kg clinical case, represented by the various tissues, is as follows:

- brain 64.1% and 5,000 ID₅₀
- spinal cord 25.6% and 2,000 ID₅₀
- trigeminal ganglia 2.6% and 200 ID₅₀
- dorsal root ganglia 3.8% and 300 ID₅₀
- distal ileum 3.3% and 260 ID₅₀
- spleen 0.3% and 26 ID₅₀
- eyes 0.4% and 3 ID₅₀ (29, 30).

Semen and embryos/ova are not seen as effective transmission vectors (40, 49, 87). Bovine spongiform encephalopathy does not appear to be spread horizontally (69, 86), but some studies suggest that maternal transmission may occur at an extremely low level (25, 44, 52, 85). No detectable infectivity has been found in the blood or blood components of cattle infected with BSE (83, 84), although experimental transmission of BSE has been achieved by blood transfusion between sheep (42, 53). It is difficult to assess the likelihood of the occurrence of BSE in small ruminants without additional information (41). In public health, BSE is a major concern for its zoonotic potential (75).

Bovine spongiform encephalopathy was first diagnosed in Great Britain in 1986. Only the UK has experienced a significant epidemic, which peaked at the end of 1992. The disease has been diagnosed in native-born cattle in Austria, Belgium, the Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Japan, Liechtenstein, Luxembourg, the Netherlands, Poland, Portugal, Slovenia, Slovakia, Spain, Switzerland, and the UK. There have been more than 180,000 cases worldwide since the disease was first diagnosed. From 1986 to 2001, more than 98% of the cases of BSE in the world were reported from the UK (6).

Release assessment

The release assessment consists of describing and quantifying the potential ability of risk sources to release or otherwise introduce the BSE risk agent into an environment accessible to animal populations. A release assessment typically includes:

- a) a description of the types, timing and amounts of risk agent and the probability of its release
- b) a description of how these attributes might change as a result of various actions or events.

For this paper, the release assessment describes the potential of a risk source to introduce the BSE agent into Canada. The risk source constitutes the past imports of cattle from BSE-infected countries (64) or countries likely to be infected, according to the GBR (44). Maternal transmission was not factored into this risk assessment, despite the evidence suggesting a low probability of developing BSE in offspring born closer to the onset of the disease in the dam (11, 20, 22, 23, 25, 46, 52, 85). Maternal transmission is assumed to be limited to the last

6 months of the incubation period of the dam and the probability of that occurring may be 0.5% (25). In a study of the offspring of BSE-affected pedigree beef suckler cows, none of 219 calves which had been suckled for at least one month developed the disease (17). The importation of MBM and feeds containing MBM into Canada from BSE-infected countries did not occur (3) and thus, does not represent a risk source for this release assessment.

Figure 1 portrays the release and exposure assessment scenario tree emanating from the initiating failure event of the importation of cattle from countries between 1979 and 1997 which were potentially infected with BSE. The scenario tree comprised eight model inputs and branch points and nine end-states. The initiating frequency (ϕ_0) represented the number of cattle imported while the model input f_1 represented the probability that the imported animal was infected with BSE. The release assessment consisted of these two inputs. The risk scenario pathways S_3 and S_6 were the pathways of interest in this scenario tree.

Probability that the imported bovine animal is infected with bovine spongiform encephalopathy (f_1)

A total of 665 cattle were imported into Canada from BSE-infected countries during the period 1979 to 1997. Of these, 120 were ordered to be exported or destroyed, and the

remaining 545 cattle either died or were slaughtered. In the case of these 545 animals, the carcass or inedible carcass parts may have been rendered to produce MBM (3) (Table I).

With respect to the type of cattle, there were 31 dairy cattle and 105 beef in the 136 animals imported from the UK, which either died or were slaughtered. The breeds of all the imported cattle from the other European countries were not available. However, of 545 cattle for which breed information was found, 490 (or 90%) were beef.

The incidence of BSE in the UK was dramatically different between dairy and beef female cattle. The number of clinical BSE suckler cases in the UK, as of July 31, 2002, was 21,315 (12% of the total number of BSE cases of 179,361) (14), although 5.9% of the cases were designated as mixed cases and 1.3% were not recorded as either dairy or suckler cows. For the purposes of this risk assessment, 88% was considered as the percentage of dairy cases and 12% as the percentage of beef cases. In 1989 the cattle population in the UK comprised 2,865,900 dairy cows (65% of the total number of cows) and 1,525,400 beef cows (15). In order to quantify the lifetime cumulative incidence rates of clinical disease (I) for dairy and beef cattle individually, Cohen *et al.* (9) developed the expressions below. The lifetime cumulative incidence rate represented the summation of the annual incidences from 1987 to 1996 over the commercial lifespan of cattle for each birth cohort from 1974 to 1995 in Great Britain (73). The first expression was employed to estimate the proportion of BSE

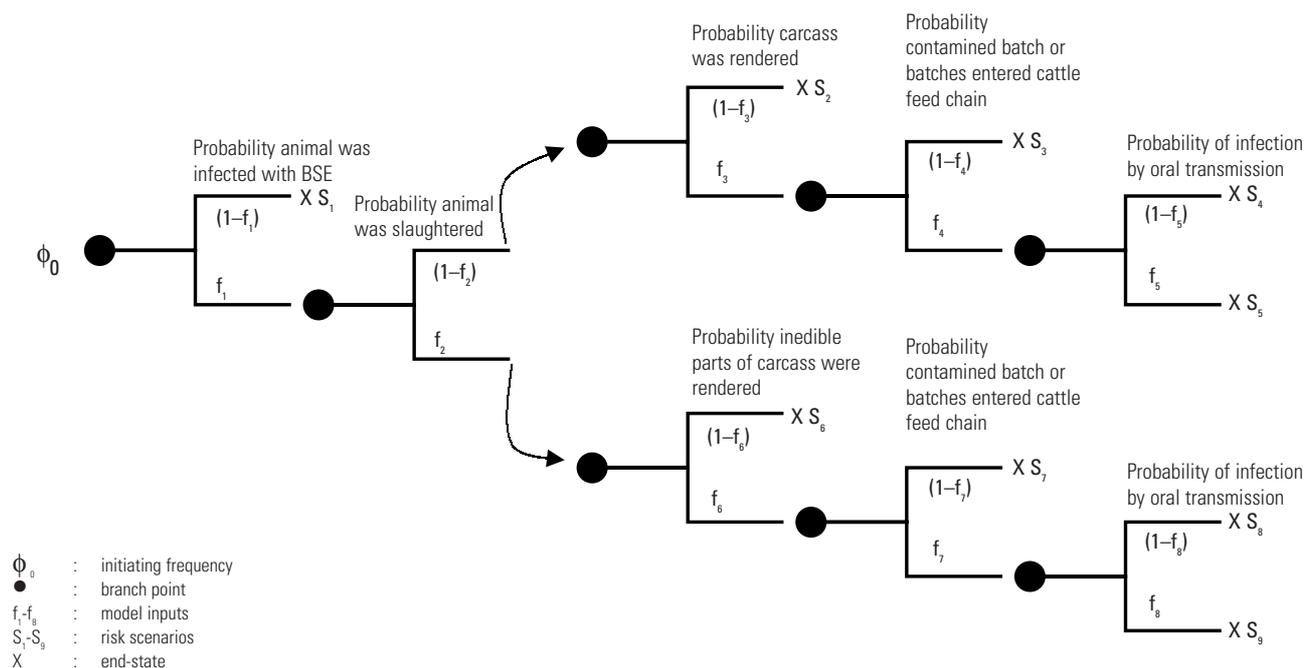


Fig. 1
Release and exposure assessment scenario tree emanating from the initiating failure event of importing cattle, potentially infected with bovine spongiform encephalopathy, from Austria, Denmark, France, Germany, the Republic of Ireland, Switzerland, the Netherlands, and the United Kingdom into Canada between 1979 and 1997

Table I
Cattle imported into Canada between 1979 and 1997, from countries reporting the occurrence of bovine spongiform encephalopathy, and their disposal

Country	Year imported	Imported	Ordered destroyed	Ordered exported	Total cattle Died (known)	Slaughtered (known)	Died or slaughtered
Austria	1981	6	0	0	0	0	6
Denmark	1993	9	1	1	0	0	7
France*	1980 (141) 1981 (75)						
	1985 (126)	342	0	0	0	0	342
Germany	1981	4	0	0	0	0	4
Republic of Ireland	1979 (2) 1982 (2) 1984 (4)						
	1989 (10)	18	4	0	3	9	2
Switzerland	1981 (17) 1985 (18)	35	0	0	0	0	35
The Netherlands	1981	1	0	0	0	0	1
United Kingdom	1979 (19) 1980 (19) 1981 (30) 1982 (27) 1983 (16) 1984 (13) 1985 (15) 1986 (12) 1987 (40) 1988 (12) 1989 (33) 1990 (14)	250	77	37	9	59	68
Total		665	82	38	12	68	465

* Includes 141 cattle imported from France, Germany, Italy, the Netherlands and Switzerland in 1980, for which individual figures were not available

cases in dairy cattle (BSE_D), where $BSE_D = 88\%$, BSE cases in beef cattle (BSE_B) = 12%, the proportion of the cattle population which were dairy animals (F_D) = 65% and the proportion of the cattle population which were beef animals (F_B) = 35%. As I_B = the lifetime cumulative incidence rate of clinical BSE for the beef cattle population, and F_B = the proportion of the cattle population that were beef animals, then $I_B F_B$ = the lifetime cumulative incidence rate of clinical BSE for the beef cattle population multiplied by the proportion of the cattle population that were beef animals. This term is resolved in the second expression.

Likewise, since I_D = the lifetime cumulative incidence rate of clinical BSE for the dairy cattle population, and F_D = the proportion of the cattle population which were dairy animals, then $I_D F_D$ = the lifetime cumulative incidence rate of clinical BSE for the dairy cattle population multiplied by the proportion of the cattle population that were dairy animals.

Expression 3 follows, since $I_B F_B + I_D F_D = I$, the lifetime cumulative incidence for the entire cattle population. Both the I_D and I_B terms can be solved as shown in expressions 4 and 5.

$$BSE_D = \frac{I_D F_D}{I_D F_D + I_B F_B}$$

$$I_D F_B = \frac{BSE_B}{BSE_D} I_D F_D$$

$$I_D F_D = \frac{BSE_B}{BSE_D} I_D F_D = I$$

$$I_D = \frac{I}{F_D \left(1 + \frac{BSE_B}{BSE_D} \right)}$$

$$I_B = \frac{I - I_D F_D}{F_B}$$

The lifetime cumulative incidence of clinical BSE disease in Great Britain was elaborated by Schreuder *et al.* (73), according to a twelve-month birth cohort from July to June inclusive, from July 1974 to June 1995 for dairy and beef cattle combined. Cohen *et al.* (9) computed the calendar year lifetime

cumulative year incidence of clinical disease by averaging the two contributing years. This information is presented below in Table II, for the years of birth 1974-1989, from which cattle had been imported into Canada. Although the lifetime cumulative incidence was based on the occurrence of BSE in Great Britain, the same rate was assumed for the UK.

The lifetime cumulative incidence of infection is a product of the lifetime cumulative incidence of clinical disease and 6.10. The latter factor is based on the ratio of the number of infected cattle in Great Britain as estimated by Donnelly and Ferguson and Ferguson *et al.* (24, 47) (954,000 infected animals in the years 1974 to 1995) and the number of confirmed clinical BSE cases (156,360 BSE cases in the years 1974 to 1995) (14). The model presented was the best-fitting age-dependent susceptibility function and incubation period distribution examined. Although Cohen *et al.* (9) employed the Schreuder *et al.* (73) lifetime cumulative incidence to represent the incidence for female cattle, and went on to estimate the lifetime cumulative incidence of clinical disease and infection for male cattle as 6% of that of female cattle, Table II does not differentiate incidence by sex. The dairy and beef lifetime cumulative incidence of infection according to year of birth from Table II were all interpreted as beta distributions. The beta distribution belongs to the family of probability density functions of continuous random variables taking on values in

the interval (0, 1). It is a useful distribution to model the uncertainty about the unknown probability p , prevalence of infection. The notation of the beta distribution employed here is beta (α_1, α_2), where α_1 and α_2 are shape parameters for the beta probability density function.

Denmark first reported the occurrence of indigenous clinical BSE in 2000, with an annual incidence of 1.14 cases per million cattle over two years of age (33, 64). The seven cattle imported from Denmark in 1993 were associated with a prevalence of infection in the 1992 birth cohort of beta (2, 1.0×10^6). The same beta distribution representing a baseline undetected prevalence of infection in a birth cohort was employed for importations from countries prior to their first report of BSE, except for birth cohorts where epidemiological modelling provided estimates of the number of infected cattle.

France reported clinical cases of BSE in indigenous cattle in 1991 at an annual incidence of 0.45 cases per million cattle over two years of age (34, 64). The age-specific incidence, modelled by birth cohort and assuming under-reporting of clinical cases, estimated that 7,300 domestic cattle in France (95% confidence interval [c.i.] of 4,700 and 9,800) were infected with the BSE agent from mid-1987 to mid-1996 (18). The 141 cattle imported from France, Germany, Italy, Switzerland and the Netherlands in 1980 were considered to

Table II
Lifetime cumulative incidence of bovine spongiform encephalopathy clinical disease and infection in birth cohorts in Great Britain from 1974 to 1989, and the number of beef and dairy cattle imported into Canada that died or were slaughtered and may have been rendered, according to year of birth

Year of birth	Lifetime cumulative incidence of clinical disease	Lifetime cumulative incidence of infection	Lifetime cumulative incidence of infection in dairy cattle (I_d)	Lifetime cumulative incidence of infection in beef cattle (I_b)	No. of dairy cattle imported from the United Kingdom into Canada according to year of birth	No. of beef cattle imported from the United Kingdom into Canada according to year of birth
1974	0	0	0	0	0	1
1975	0	0	0	0	0	1
1976	0.00003	0.00020	0.00027	0.00007	1	2
1977	0.00012	0.00073	0.00099	0.00025	1	2
1978	0.00020	0.00122	0.00165	0.00042	5	10
1979	0.00047	0.00287	0.00388	0.00098	11	22
1980	0.00081	0.00494	0.00669	0.00169	3	14
1981	0.00170	0.01037	0.01404	0.00356	5	8
1982	0.00500	0.03050	0.04129	0.01046	1	6
1983	0.01100	0.06710	0.09084	0.02301	3	6
1984	0.01600	0.09760	0.13214	0.03346	0	6
1985	0.02300	0.14030	0.18994	0.04810	0	10
1986	0.03800	0.23180	0.31382	0.07947	1	8
1987	0.05100	0.31110	0.42118	0.10666	0	5
1988	0.03900	0.23790	0.32208	0.08157	0	2
1989	0.01800	0.10980	0.14865	0.03765	0	2
Total					31	105

have originated from France for the purposes of this risk assessment, since the number of imported cattle from each country was unknown. These 141 cattle imported in 1980, the 75 cattle imported in 1981 and the 126 cattle imported in 1985 were associated with a prevalence of BSE infection in the 1979, 1980, and 1984 birth cohorts, respectively, of beta (2, 1.0×10^6).

The Republic of Ireland reported indigenous BSE clinical cases in 1989 with an annual incidence of 4.41 cases per million cattle over two years of age. One or more clinical cases of BSE originated from the 1981 birth cohort (36, 64). The age-specific incidence, modelled by birth cohort and assuming under-reporting of clinical cases, produced an estimated total of approximately 22,000 cattle infected with BSE in the Republic of Ireland during the period 1985 to 1996. About 4,400 cattle were infected in both the 1985 and 1986 birth cohorts, 2,100 in 1987 and 1,700 cattle in 1988 (19). The cattle imported from the Republic of Ireland into Canada from the 1978, 1981, 1983 and 1988 birth cohorts were associated with a prevalence of BSE infection of beta (2, 1.0×10^6), except for the 1988 birth cohort. The latter birth cohort was associated with a prevalence based on the modelling by Donnelly (19) and an estimate of the birth cohort population (about 1,630,708 cattle in 1985) (36) of beta (1,701, 1.6×10^6).

Switzerland first reported indigenous clinical cases of BSE in 1990 with an annual incidence of 1 case per million cattle over 24 months of age (38, 64). The expected number of infected cattle in 1984, based on modelling the BSE epidemic in Switzerland until the end of 1997 and assuming 50% under-reporting of clinical cases, was six cattle under two years of age. The denominator for a prevalence estimate for cattle imported from Switzerland in 1985 was 273,300 calves under one year of age (Swiss cattle population in 1996) (16). The prevalence of BSE infection in the 1984 birth cohort was represented by beta (7, 273,295) while that for the 1980 birth cohort was represented by beta (2, 1.0×10^6).

For Austria, Germany, the Netherlands and Italy, the first report of indigenous clinical cases of BSE occurred in 2001, 2000, 1997 and 2001 with an incidence of 0.96, 1.7, 1 and 14.1 cases per million cattle over two years of age, respectively (32, 35, 37, 39, 64). The prevalence of infection for the birth cohorts of imports from these countries were all represented by beta (2, 1.0×10^6).

Computer simulation (10,000 iterations of Latin hypercube sampling) with @RISK® risk analysis software and its binomial distribution function (RiskBinomial [n , p]) was used to estimate the number of BSE-infected cattle which may have been imported from BSE-infected countries during the years 1979 to 1997 (68). Latin hypercube sampling is sampling without replacement in which the cumulative distribution function curve of the model input is stratified into equal

intervals and a sample is taken from each stratification. The number of stratifications is equal to the number of iterations. The n value for the binomial distribution was represented by 545, which is the number of cattle which were imported and subsequently died or were slaughtered. The lifetime cumulative incidences of infection for beef cattle and dairy cattle by year of birth in Table II were converted to beta distributions for use as the p values in the binomial distribution for beef and dairy cattle of UK origin. Beta distributions represented the prevalence of BSE infection in the birth cohorts of cattle from the other countries, as indicated above.

The mean expected number of animals infected with BSE whose carcasses were rendered was 3 cattle while the 95th percentile was 24 cattle (Fig. 2).

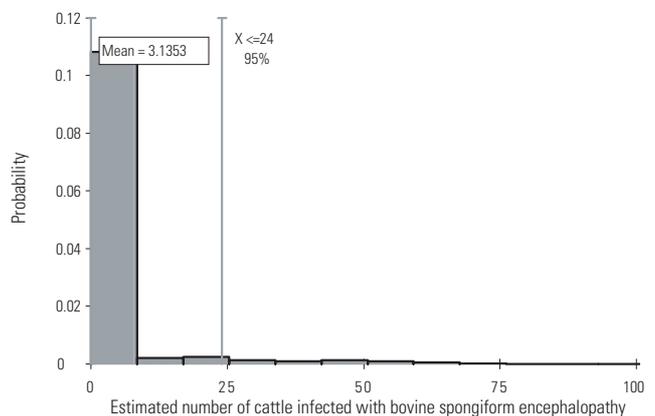


Fig. 2
Distribution of the estimated number of cattle infected with bovine spongiform encephalopathy imported into Canada from Austria, Denmark, France, Germany, the Republic of Ireland, Switzerland, the Netherlands, and the United Kingdom, that were slaughtered or died and may have been rendered (simulation output of the @RISK® risk analysis software, 10,000 iterations of Latin hypercube sampling) (68)

Exposure assessment

The exposure assessment consists of describing and quantifying the conditions for animal exposures to the BSE risk agent produced or released by a given risk source. The exposure assessment includes:

- a description of the intensity, timing, frequency, and duration of exposure
- the routes of exposure (e.g., ingestion)
- the number, species and characteristics of populations that might be exposed.

The exposure assessment in this case describes and quantifies the likelihood that BSE infectivity was introduced into the cattle feed chain in MBM before the 1997 MBM feed ban, and

the consequent likelihood of infection of at least one animal by oral transmission. It does not account for the potential contamination of blood meals as a result of the stunning procedure at slaughter (9).

The exposure assessment comprised model inputs f_2 – f_8 in Figure 1, all of which were probabilities.

Probability that the animal was slaughtered (f_2)

The ratio of the mortality rate and slaughter rate of beef and dairy breeding cattle was employed to estimate the proportion of 465 cattle which died or were culled for slaughter. Fifty-nine cattle from the UK and nine from the Republic of Ireland were slaughtered while nine and three, respectively, died. Annual mortality and slaughter rates in beef breeding cattle of 1.5% and 10.8% (58, 59, 60, 71) and 3.8% and 32% (95% of the Ontario Holstein dairy cow culling rate in 1995) in dairy cattle (57, 66, 71) were used to calculate the mortality/slaughter ratio for the two husbandry types. It was necessary to use the proportion of dairy and beef cattle imported, that is, approximately 12% of 665 imported cattle were dairy breeds (based on the available information on the breeds of cattle imported). The proportion of 465 cattle which were slaughtered was therefore $(0.88 \text{ beef slaughter} \times 0.90 \text{ beef breeds} + 0.89 \text{ dairy slaughter} \times 0.10 \text{ dairy breeds}) = 0.88$, giving a total of $409 + 68 = 477$ or 88% of the 545 imported cattle. A beta distribution with parameter values $(477 + 1, 545 - 477 + 1)$ was employed for this probability (f_2). The proportion of cattle which died was estimated as $(1 - f_2)$.

Probability that the carcass was rendered (f_3) and probability that inedible parts of the carcass were rendered (f_6)

The probability (f_3) that the carcass of an animal which died was rendered was represented as a beta pert distribution with parameter values (0.50, 0.75, 0.80). The beta pert distribution is a 3-parameter version of the beta distribution, that is, minimum, most likely and maximum parameters. Its interval is not restricted to (0, 1) but by the minimum and maximum values. The beta pert distribution is ideally suited for modelling expert judgement. It was assumed that between 50% and 80% of the animals that died were rendered, while the remainder were buried on the farm. The probability (f_6) was represented as a beta pert distribution with parameter values (0.99, 0.999, 1).

Probability of a contaminated batch entering the cattle feed chain (f_4 and f_5)

Of the 25 million tonnes of complete feed produced in Canada annually, 15% or 3,750,000 tonnes are fed to dairy cattle (3). All dairy feeds incorporated on average a 1% level of MBM before the 1997 MBM ruminant feed ban came into force. This percentage equates to approximately 37,500 tonnes of MBM

fed to dairy cattle annually. This amount represented about 10% of the 373,600 tonnes of MBM produced in Canada in 1995 (3), indicating that about 90% of the MBM manufactured in Canada was incorporated into feeds for poultry, swine and beef cattle. The levels of MBM incorporated in swine and poultry feeds (37% of the complete feeds produced annually were swine feeds and 16% were poultry feeds) at inclusion rates of 3% to 5% indicated an annual consumption of 397,500 to 662,500 tonnes of MBM. More MBM was consumed than was produced each year in Canada. The shortfall of about 50% of the rendered products used in livestock feeds was imported from the United States of America (USA). The USA has never had a case of BSE and has similar import controls and rendering processes to those in Canada (3). The level of MBM fed to beef cattle was considered quite low because of the availability of cheaper protein sources such as non-protein nitrogen, canola and soybean meal (3).

A beta pert distribution was employed to represent the proportion of MBM produced in Canada that was fed to swine and poultry and therefore eliminated from the cattle feed chain. For this input, 90% represented the maximum value, 85% the most likely value and 80% the minimum value.

Probability of at least one oral transmission of infection (f_5 and f_8)

Wahlström *et al.* (81) estimated this probability by setting an average number of secondary infections produced when one infected individual was introduced into a host population where all individuals are susceptible, that is, R_0 , which was estimated subjectively. Cohen *et al.* (9) examined the actual consumption by susceptible animals of the BSE-causing agent in MBM. In this risk assessment, the sub-model for this probability was estimated from the end consumption of each cattle oral ID_{50} remaining in the MBM at the time of feeding. Considering accumulative infectivity over a 3-day 'feeding period' (31), during which the infectious dose could accumulate in an individual, the term x was used to denote the total number of susceptible animal-feeding periods which share a single ID_{50} of infectious agent. Given that there is no natural upper limit on x , a Poisson probability model for $y = x - 1$ was used, where the parameter $\lambda = -\ln P(y = 0) = -\ln P(x = 1)$.

An assumption here is that the number of ID_{50} per kg of MBM follows an exponential distribution with $\lambda = 1/0.068 \approx 15$ (the expected number of ID_{50} remains $1/\lambda = 0.068$ per kg of MBM). The latter is based on the expected number of cattle oral ID_{50} remaining after the rendering of one infected carcass ($34 ID_{50}$) in what is considered to be a conservative quantity of 500 kg of MBM. The exponential model allocates substantive probability of a high concentration of BSE agent in the rendered MBM. Otherwise, the 'diluting effect' of the rendering process and feed formulation would greatly reduce the likelihood of any animal

receiving an infectious dose. If the 3-day MBM consumption is m kg, then the number (n) of ID_{50} contained in m kg follows an exponential distribution with $\lambda = 1/(0.068 \times m) = 15/m$, where the mean of the exponential distribution is $1/\lambda$. The probability of m kg containing at least one ID_{50} is the tail probability $P(n \geq 1) = e^{-3/m}$. If, in turn, the above is taken as the probability that one ID_{50} is ingested entirely by a single susceptible animal, i.e., the input for the Poisson distribution, then the λ parameter for the Poisson distribution is $-\ln[e^{-15/m}] = 15/m$.

The probability of various values of x , the number of individual animals (or animal-feeding periods) sharing the same ID_{50} , was as follows:

$$P(x = k) = P(y = k - 1) = e^{-\lambda} \frac{\lambda^{k-1}}{(k-1)!}$$

For each x value, an ID_{50} is more or less equally shared by the x susceptible individuals (more precisely, x susceptible animal-feeding periods), each receiving $1/x$ of the original ID_{50} dose. The dose-response curve for cattle oral BSE infectivity is necessary in order to calculate the ID percentage of this divided dose. Without an exact dose-response curve, a linear dose-response relationship was assumed, namely $1/x$ of the original ID_{50} dose representing a dose of $ID_{50/x}$. The probability that the particular ID_{50} would cause at least one infection, after factoring in susceptibility (P_s), is:

$$P(\text{oral transmission} \geq 1) =$$

$$1 - (1 - (P(x = 1) (P_s \times 0.50 + P(x = 2) \times [1 - (1 - P_s \times 0.50/2)^2] + P(x = 3) \times [1 - (1 - P_s \times 0.50/3)^3] + P(x = 4) \times [1 - (1 - P_s \times 0.50/4)^4] + P(x = 5) \times [1 - (1 - P_s \times 0.50/5)^5]))^n$$

where n = the number of cattle oral ID_{50} contributed by a BSE-infected carcass which has been rendered.

Given that a very conservative model of a linear dose-response relationship below ID_{50} was used, the first 5 or 6 terms in the above formula sufficed to give an estimate of the probability of oral transmission. Figure 3 illustrates the @RISK® software simulation output of the estimated probability of oral transmission of infection in which the expected probability is 0.03, while the 95th percentile is 0.29 (68). The following evidence and data were employed in the model inputs of this sub-model for the probability of at least one oral transmission:

- a) Number of ID_{50} presented by a BSE-infected rendered carcass (n)
 - BSE infectivity
 - rendering reduction in ID_{50}
- b) Average daily consumption of MBM by age (months)
- c) Proportion of dairy cattle population by age (months)

d) Age-dependent susceptibility of cattle to bovine spongiform encephalopathy infection (p_s).

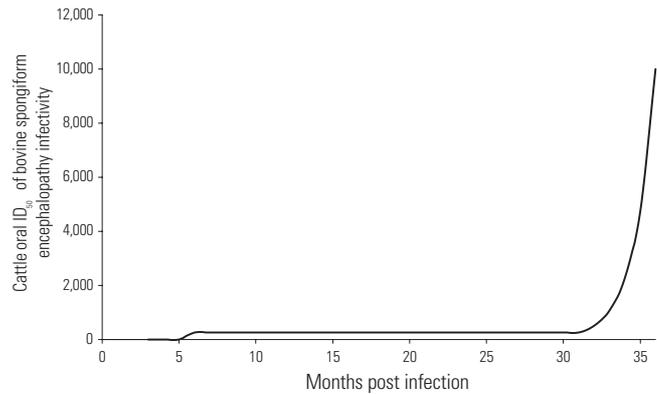


Fig. 3
Total infectivity found in calves experimentally infected with bovine spongiform encephalopathy, according to month post-infection, expressed as cattle oral infectious doses 50% (ID_{50})
 (adapted from Cohen *et al.* [9])

Number of infectious doses presented by a BSE-infected rendered carcass
BSE infectivity

The computer software @RISK® was used to determine the following:

- the month of infection
- the month of export
- the duration of BSE incubation
- the duration of clinical BSE
- the month of death and month of slaughter for imported cattle which died or were slaughtered, and their carcass or inedible carcass parts rendered (68).

The months refer to the age of the imported BSE-infected animal and (n) is the number of cattle oral ID_{50} presented by a BSE-infected rendered carcass

To estimate the amount of BSE infectivity introduced by an imported BSE-infected animal, a probability distribution for cattle of the incubation period in months was used. This distribution was based on the model and parameter values of Ferguson *et al.* (47), as presented by Cohen *et al.* (9). The probability density function for the incubation period (months) is $f(t)$, and,

$$f(t) = \left(\frac{\alpha_2 e^{-t/\alpha_1}}{\alpha_3} \right)^{\frac{\alpha_2^2}{\alpha_3}} \frac{\alpha_2 e^{-t/\alpha_1}}{e^{\frac{\alpha_2}{\alpha_3}}}$$

where $\alpha_1 = 1.146$, $\alpha_2 = 0.0241$ and $\alpha_3 = 5.71 \times 10^{-4}$, representing the 'best-fit' parameter values for the incubation distribution C of Ferguson *et al.* (47). The input t is expressed in years. The 5th percentile of this distribution is about 31 months, the median: 49 months, the mean: 52 months and the 95th percentile: 83 months.

For cattle which died and cattle which were slaughtered, probability distributions as to the age at death and slaughter were obtained by simulation, using 10,000 iterations of Latin hypercube sampling. The objective was to obtain a distribution of the truncated incubation periods, truncated according to age at death and age at slaughter, respectively. The mortality in beef breeding female cattle was set at a constant rate of 0.08% for 6 to 23 months of age; a constant rate of 1.5% for 2 to 10 years of age; and the function $1 - e^{-0.006 \times a}$, where $a =$ age in years, from 11 to 20 years. The annual slaughter rate in beef breeding cattle was set at 2.5% for year 2; 10% for years 3 to 10; and the function $1 - e^{-0.001 \times a}$ for years 11 to 20 (57, 66, 69). Similarly, the mortality rate in dairy female cattle was set at a constant rate of 0.2% for 6 to 23 months of age; 3.8% for 2 to 6 years of age; and the function $1 - e^{-0.004 \times a}$ for 7 to 20 years of age, while the annual slaughter rate was set at 5%, 20%, 30%, 30% and 10% for 2 to 6 years of age and $1 - e^{-0.0003 \times a}$ for 7 to 20 years of age, respectively (57, 66, 71).

Cattle from the UK and the Republic of Ireland were attributed an age at export of 6 to 24 months (discrete uniform distribution [6, 7, ..., 24]) while cattle from the other European countries were attributed an age at export of 6 to 10 months (discrete uniform distribution [6, 7, ..., 10]). A discrete uniform distribution of a set of values assigns equal probability for all the values. Cattle from Continental Europe exported to Canada during the 1970s and 1980s had been restricted to cattle of less than 11 months of age (3). The imported BSE-infected cattle were assumed to be infected between 2 and 12 months of age (discrete uniform distribution [2, 3, ..., 12]). Appropriate 'IF' functions of the spreadsheet computer software Microsoft® Excel were used to limit the value for which the month of infection preceded the month of export in the calculations.

The duration of clinical BSE was attributed a period of 2 to 6 months (9) (uniform distribution [2, 6]), a period of disease not curtailed by either disease control measures or the intervention of the owner. The uniform distribution consists of minimum and maximum parameters. Every value across the range of the uniform distribution has an equal likelihood of occurrence.

Truncated incubation periods were obtained by deleting those iterations of the simulation in which the following argument was true: (month of infection + incubation period in months + clinical duration in months < age at death or age at slaughter). For each distribution, truncated by mortality or slaughter rates, the months of incubation were transformed and scaled to a

36-month axis, employing the VLOOKUP function of the Excel spreadsheet software and data from an experimental pathogenesis study on BSE (9, 83, 84). In this study, the time course of infectivity was evaluated through the oral dosing of 30 four-month-old calves with 100 g of pooled brain stem from 75 cases of BSE. The study revealed increasing infectivity in the distal ileum at 6, 10, 14 and 18 months post infection (p.i.). Then infectivity was not detectable in the distal ileum until 36 months p.i. Infectivity was not detected in other parts of the gastro-intestinal tract nor in any other non-neural tissues at any stage, with the exception of trace infectivity in sternal bone marrow collected during the clinical stage at 38 months p.i. Infectivity was detected in the brain, spinal cord, dorsal root ganglia, and trigeminal ganglia at 32, 36, 38 and 40 months p.i. and in the distal ileum at 36, 38, and 40 months p.i. (45, 83, 84).

Estimates of the infectivity levels in tissues of an infected bovine (near the end of the incubation period or during the clinical phase) have been presented in cattle oral ID_{50} (29, 30). Figure 4 presents the total infectivity found in the experimentally infected animals according to month p.i. The total amount of infectivity in an animal with clinical BSE was assumed to be 10,000 cattle oral ID_{50} (9). The infectivity level in the distal ileum from six months of age up to 31 months of age was attributed an estimated quantity of ID_{50} found in an adult BSE clinical case.

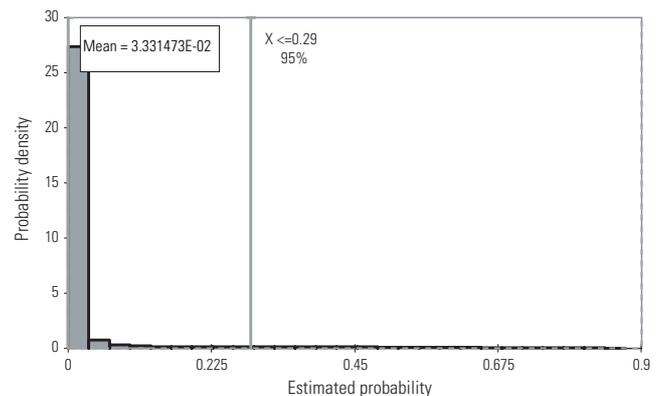


Fig. 4
Distribution of the probability of oral transmission of bovine spongiform encephalopathy (simulation output of the @RISK® risk analysis software (68) 100,000 iterations of Latin hypercube sampling)

Computer simulation using 100,000 iterations of the risk analysis program @RISK® software with Latin hypercube sampling gave an output distribution of the number of cattle oral ID_{50} present in carcasses of BSE-infected cattle which died or were slaughtered (68). Normal distributions of the \log_{10} total infectivity level obtained for slaughtered animals and

cattle that died were Normal (3.13, 0.73) and Normal (2.92, 0.70), respectively.

Reduction in infectious doses caused by rendering

The reduction of the infectivity of BSE and scrapie agents (measured as ID_{50}) caused by different rendering processes was investigated using small-scale equipment and quantities of MBM to simulate full-scale production (76, 77). For batch rendering, a 1:20 representation of full-scale production was achieved, whereas for other rendering processes the scale was 1:100. In one study, in which the BSE agent was incorporated into MBM at appropriate proportions of BSE-infected brain tissue, bovine or porcine intestine and bovine bone, a titre of $\log_{10} 1.7 ID_{50}/g$ resulted. Inactivation of the BSE agent was obtained in eleven rendering processes, as follows:

- with batch processing at atmospheric pressure
- with two of four continuous processes at atmospheric pressure and containing natural fat
- with two continuous processes at atmospheric pressure using high fat
- with three continuous wet rendering processes containing high fat
- in three batch rendering processes under pressure and with natural fat.

The inactivation in these eleven processes (with adjustment for the volume inoculated intra-cerebrally into mice) represented a reduction in titre of about $\log_{10} 1.4 ID_{50}$. Infectivity was detected following two of four continuous processes at atmospheric pressure and with natural fat content, and also after two continuous high fat vacuum processes. In one of the latter vacuum processes the infectivity titre was only reduced to $\log_{10} 1.6 ID_{50}/g$.

In another study (77), in which the scrapie agent was incorporated into MBM using brains of sheep clinically affected with scrapie and porcine bone and intestine, a titre of $\log_{10} 3.1 ID_{50}/g$ was achieved. The reduction in scrapie titre (with adjustment for the volume inoculated intra-cerebrally into mice) following processing were as follows:

- $\log_{10} 1.5 ID_{50}$ for batch processing at atmospheric pressure
- $\log_{10} 1.6 ID_{50}$ and $\log_{10} 2.3 ID_{50}$ for two continuous processes at atmospheric pressure and containing natural fat
- $\log_{10} 2.3 ID_{50}$ for a continuous process at atmospheric pressure using high fat
- $\log_{10} 1.6 ID_{50}$ for a continuous process with high fat content and under vacuum
- $\log_{10} 2.0 ID_{50}$ and $\log_{10} 2.8 ID_{50}$ for two continuous wet rendering processes containing high fat
- inactivation ($\log_{10} 2.8 ID_{50}$) for five batch rendering processes under pressure and with natural fat.

The rendering industry in Canada, comprising 32 plants, uses batch and continuous rendering under atmospheric pressure and vacuum rendering (3). The proportions of MBM rendered by the different processes is known under present conditions. However, this information is not known for the principal period of interest before 1997 when the ruminant MBM feed ban was implemented. The approach used was to employ the overall titre reduction of both the BSE and scrapie agents for the batch and continuous processes detailed above, except for the batch processes under hyperbaric steam. A Normal distribution based on the mean $\log_{10} 1.6 ID_{50}$ and standard deviation $\log_{10} 0.58 ID_{50}$ of the reduction in BSE agent titre was employed to represent the effects of rendering processes in Canada.

Computer simulation with @RISK® software to estimate the total infectivity titre following rendering was conducted on the difference between the total infectivity titre before rendering and the effects of different rendering processes (68). The resulting distributions were achieved with 10,000 iterations of Latin hypercube sampling, as Normal (1.53, 0.93) with a 95% c.i. of (0.0015 to 3.033) for slaughtered animals and Normal (1.32, 0.91) with a 95% c.i. of (–0.17 to 2.81) for animals that died.

The number of cattle oral ID_{50} remaining after rendering of either a slaughtered animal or an animal which died was estimated from the distribution with the highest level of infectivity, Normal (1.53, 0.93). The expected number of cattle oral ID_{50} per BSE-infected rendered carcass was 34 with a 95% c.i. of (1 to 1,079).

Average daily consumption of MBM by age (months)

The daily consumption of MBM by dairy cattle was estimated according to age (in months), based on the following feeding assumptions, which are proposed as representative of dairy feeding in Canada. For dairy heifers before their first calf, the feeding regime was composed of hay of 88% dry matter (DM), 20% crude protein (CP) (DM basis), haylage of 50% DM and 15% CP (DM basis), a supplement at the rate of 22% of the grain mix fed from one month of age to seven months of age, the supplement at the rate of 15% of the grain mix for calves eight to twelve months of age and the incorporation of MBM in the supplement at 4.5%. The age in months according to body weight in kg and the average daily gain were obtained from heifer growth charts for Holstein and Brown Swiss cattle (8). The nutrient requirements such as the daily g of CP, daily g of undegradable intake protein (UIP), and dry matter intake (DMI) were based on the 1989 Nutrient Requirements of Dairy Cattle (62) and the Ontario Ministry of Agriculture, Food and Rural Affairs (OMAFRA) dairy ration balancer (67) (B. Wheeler, personal communication). The OMAFRA dairy ration balancer increases the National Research Council (NRC) requirements for calcium and CP to account for the higher skeletal growth and weight in Canadian heifers when compared to US heifers. From 12 to 27 months, 27 months being the mean age at first calving (66), feeding haylage alone was assumed.

The feeding of protein feeds of animal origin such as meat meal, MBM and blood meal were considered too expensive and their availability was limited in the 1970s and 1980s. The principal protein supplements for dairy rations included soybean, linseed, canola and corn gluten meals, canola seed, cottonseed, corn gluten, brewers' grains, distillers' grains and non-protein nitrogen such as feed-grade urea. Commercial protein supplements such as 36% CP dairy supplement were formulated under a 'least cost' approach determined by the feed mills (27). The assumptions for feeding dairy cows were also based on the 1989 dairy cattle requirements (62) and the OMAFRA dairy ration balancer. A representative ration (B. Wheeler, personal communication) consisting of legume hay, grass hay, mixed hay, alfalfa haylage, corn silage, high moisture corn, soybean meal and commercial supplement containing 15% MBM was formulated. The quantity fed was based on a Holstein cow calving at 28 months of age, weighing 700 kg at the beginning of the cow's third lactation, producing a peak in milk yield of 45 kg per day at 45 days in milk from the third lactation onwards, and having a calving interval of 13.5 months. The latter parameter value represented the 50th percentile of the 65% to 70% of the dairy herds in the Province of Ontario enrolled in the Ontario Dairy Herd Improvement for 1996 (66).

Proportion of dairy cattle population by age (in months)

The number of dairy cattle by age (in months) was based on the number of dairy female calves under one year of age (490,800) at 1 July 2001, the number of dairy heifers (473,000) and the number of dairy cows (1,131,000) (74), and on the age distribution of more than 492,000 dairy cows in August 2002 which qualified for genetic evaluation under the Canadian Dairy Network (5). The numbers of calves and heifers from 0 to 27 months were estimated using a mortality rate of 10.8% for the first two months of age and 2.4% for heifers from weaning age (8.4 weeks) to first calving (57, 71) and the number of replacement heifers between 12 to 27 months of age.

Age-dependent susceptibility of cattle to bovine spongiform encephalopathy infection

Cattle appear to be susceptible to BSE infection (p) at all ages; however, young cattle appear to be more so. Young cattle were estimated to be ten times more susceptible than adults. Susceptibility declined exponentially with an annual constant rate of 0.85 after the age of four months to as low as 10% of its peak value. The susceptibility function was represented by the equation $\beta(a) = 0.1 + 1.8e^{-2a}$ where a is the age in years (9). Another model for age-dependent susceptibility indicated a peak in susceptibility between 6 and 18 months of age (2, 21, 24, 47, 86). The susceptibility function model indicated above was employed for this input since it provided for the highest

susceptibility at the time when dairy calves in Canada may have received increasing amounts of MBM from two to six months of age. The feeding regimes constituted declining levels to no MBM use from 7 to 13 months of age.

Consequence assessment

Consequence assessment consists of describing and quantifying the relationship between specified exposures to a risk agent and the economic consequences of those exposures. The consequences of disease outbreaks are associated with animal losses, production losses, costs of control and eradication, costs of monitoring and surveillance and trade embargoes and restrictions.

The impact of the introduction and establishment of BSE in Canada would be extreme, based on the animal and human health impacts, trade impact, impact on industry and the cost of eradication as exemplified in other countries. The consequence assessment consisted of a description of the costs and losses that were incurred in the UK and other countries. It is unlikely, however, that a BSE epidemic such as the one that occurred in the UK will ever be observed again.

Direct consequences

Animal health impact

The animal health impact is not a significant fraction of the economic consequences of BSE, except in the UK. In July 2002, the Department for Environment, Food and Rural Affairs (DEFRA) in Great Britain reported that a total of 179,361 cases were notified on 35,551 farms since 1986 (14). Most of the herds (63%) affected were dairy herds; 27% were beef suckler herds, and the balance were of mixed beef and dairy type. The within herd incidence peaked in 1992 at 2.7% (12).

In other BSE-infected countries, the incidence per million cattle aged over 24 months ranged from a high of 138 cases in Portugal to a low of one in Austria in 2001 (64). Cases of BSE reported by most of these countries consisted of clinical cases and cases detected by active surveillance of at-risk cattle populations and herd mates, birth cohorts and the progeny of BSE cases.

Public health impact

In 1996, the British Government announced a possible link between BSE and a new variant of Creutzfeldt-Jakob disease (vCJD) in humans, similar to BSE in cattle and scrapie in sheep (44). Variant Creutzfeldt-Jakob disease (vCJD) is a neurodegenerative disease similar to CJD, for which there is neither treatment nor cure. In September 2002, the number of definite and probable vCJD cases was 138 (127 cases in the UK, six in France, one in Hong Kong, China; one in Ireland, one in Italy, one in the USA, and one in Canada. It has been concluded,

however, that the patients in Hong Kong, China; the USA and Canada contracted vCJD while resident in the UK.) To date, vCJD has occurred almost exclusively in people under the age of 55, a number of whom were teenagers (61, 78). The cost to the Department of Health in the UK of staff time spent on BSE/CJD-related activities during 1988 to 1996 was approximately £820,000. The average cost per vCJD patient, estimated by the Economics and Operational Research Division, was about £20,000 in the UK. Depending on the type of care given, this could vary from £6,500 to £40,000 per patient (70). The losses associated with the premature deaths of productive wage earners and other societal losses would be more significant.

Indirect consequences

Economic considerations

Surveillance, control and eradication cost

In France, the annual direct costs of surveillance, control and eradication were estimated at approximately €835 million or €75 per bovine older than 24 months or €2 million per positive case detected. Testing healthy slaughtered animals to declare the meat fit for human consumption represented the major cost (€1.8 million per detected case), although this cost was mainly passed on to the consumers. The eradication measures involved the culling of the entire herd of origin of a BSE case and the culling of any cattle that originated from that herd. The total annual direct costs of eradication measures represented 13% of the total costs of control measures (7).

In the UK, expenditure on diagnosis and surveillance reached a total of approximately £7.7 million from 1988 to 1996. The removal of suspected cattle or carcasses from a property, valuing these animals, and the subsequent incineration of their carcasses cost £44 million over the period from 1988 to 1996. The cost of compensation in the UK from 1986 to 1996 was £136.4 million. Other costs, including such things as rent, utilities, wages and equipment costs, reached a total of £90.8 million. In addition, there was a dramatic rise in expenditure in the UK on compensation after the adoption, in April 1996, of the scheme to slaughter cattle over 30 months old. In April 2000, the UK Government estimated that the total net cost of the BSE crisis would be £3.7 billion by the end of the 2001/2002 financial year (70).

Potential trade losses

Trade impact

On 27 March 1996, the European Commission prohibited all UK exports of beef and cattle, and their by-products, to all other EU Member States and to the rest of the world. What had become a beef export market worth almost £600 million per year collapsed, leading to severe economic difficulties for those dependent on it. The European Community partners of the UK and many other countries, including Canada and the USA, have banned the importation of all live cattle from the UK.

Export markets were completely lost (70). In 1995, the UK exported 77,000 tonnes of beef and veal around the world. In the year 2000, the UK was forecast to export less than 2,000 tonnes (79).

The rendering industry faced the loss of markets for its major products – MBM and tallow – as a result of the ban on using MBM in any farmed animal feed and the EU export ban on British beef derivatives. The slaughtering sector was suffering as the build-up of unsaleable stocks of product resulted in significant physical and financial blockages. Temporary financial measures were put in place for the rendering and slaughtering sectors to ensure that these key elements of the meat chain continued to operate. Approximately £97 million in support was provided to individual rendering companies during 1996 to 1997 (13).

Impact on industry

The occurrence of BSE in Canada would affect many sectors of the cattle industry, including farmers, meat processing, rendering, transportation and distribution, and retail, among others. It could result in a substantial decline in the consumption of beef and beef products due to a perception of risk to human health and safety (1).

In the UK, the economic consequences of BSE to the industry have been considerable. Complex changes in the economics of beef and beef products have been experienced by many sectors of the community, including producers, retailers and consumers. Over the period from 1986 to 1995, the share of beef and veal within total meat consumption declined from approximately 31% in 1986 to 24% in 1995, being mostly replaced by poultry. Per capita beef consumption also declined by about 35%, or 6.7 kg per person per year (70).

Risk estimation

Risk estimation consists of integrating the results from the release, exposure, and consequence assessments to produce a measurement of the risk involved.

The mathematical model to estimate the probability of at least one infection for n imported animals was as follows:

$$P(I \geq 1) = 1 - ((1 - f_1) + f_1 \times ((1 - f_2) \times ((1 - f_3) + f_3 \times ((1 - f_4) + f_4 \times (1 - f_5)))) + f_2 \times ((1 - f_6) + f_6 \times ((1 - f_7) + f_7 \times (1 - f_8))))^n$$

The risk estimate is based on the expected number of BSE-infected animals which may have been imported, slaughtered or died, and whose carcass was subsequently rendered during 1979 to 1997, and the probability of the exposure of Canadian cattle to any BSE infectivity. An estimated mean probability of at least one BSE infection of 7.3×10^{-3} and a 95% confidence level of 2.0×10^{-2} were obtained (Fig. 5). This estimated

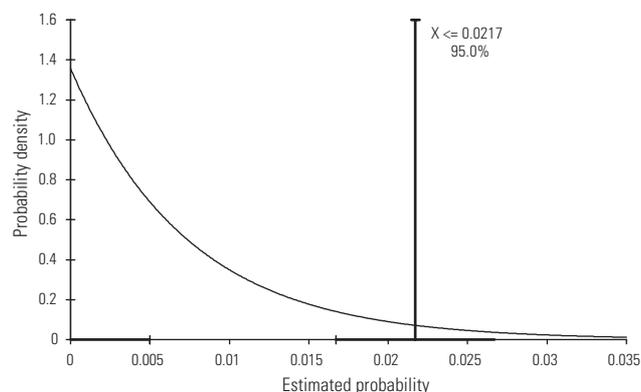


Fig. 5
Distribution of the probability of at least one infection with bovine spongiform encephalopathy (simulation output of the @RISK® risk analysis software (68) 100,000 iterations of Latin hypercube sampling)

probability indicated that, according to the scientific evidence and through computer simulation, 993 times out of a thousand, there would be no BSE infection in Canada as the result of the importation of cattle from the UK and Europe from 1979 to 1997. Furthermore, given this estimate it can be stated that the amplification and establishment of BSE in Canada, before the 1997 feed ban and after the 1997 feed ban, are negligible. The mitigating measures (import policies, disease control measures, detection systems on the farm and at slaughter plants) that were in place and have been added to since 1997 further decreased the likelihood of the introduction and establishment of BSE in Canada. These additional measures included the MBM feed ban and import bans on the following items from countries not recognised by Canada as being free of BSE:

- all ruminants and meats of ruminant origin
- all products containing rendered animal proteins
- ruminant SRMs
- veterinary biological products (containing bovine material).

Risk is a two-dimensional concept involving the likelihood and the consequences of an adverse event. Although the likelihood of the introduction and establishment of BSE into Canada is negligible, the consequences would be extreme.

The sensitivity analysis identified the most critical inputs for the model. With the rank order correlation sensitivity analysis, a correlation coefficient is calculated between the selected output variable and the samples for each of the input distributions. The higher the correlation between the input and the output, the more significant the input is in determining the value of the output. The tornado graph (Fig. 6) indicated that the ‘age in months’ input, showing the longest bar and a positive coefficient of 0.367, was the most important input for

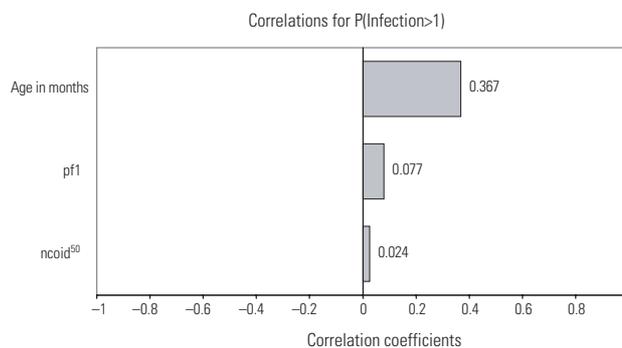


Fig. 6
Sensitivity analysis (tornado graph of the @RISK® risk analysis software) of the most significant inputs to the output distribution (the probability of at least one case of infection with bovine spongiform encephalopathy)

estimating the probability of at least one infection. The ‘age in months’ input was weighted by the proportion of the dairy cattle population by age. Associated with this input was the average daily consumption of MBM over three days in kg (m) and the age-dependent susceptibility to BSE infection (p_s). The sampling of ‘age in months’ from one iteration generated the corresponding value for m and p_s . Hence, the ‘age in months’ input was the most significant in determining the output probability of at least one infection with BSE, indicating that any effort to collect additional data should be directed to this input.

Two other inputs indicated a much lower level of correlation with the output. ‘pf1’, which represented the function assimilating the prevalence of infection by country and year of birth, was second in importance with a positive coefficient of 0.077. The number of cattle oral ID₅₀, represented by the input variable ‘ncoid₅₀’, revealed a correlation coefficient of only 0.024.

Conclusion

The Canadian risk assessment example indicates that the approach of the OIE Code, Section 1.3., entitled ‘Import risk analysis’, can be effectively applied to the assessment of risk factors associated with the occurrence of BSE in a country. A probabilistic risk assessment is the only approach for interpreting evidence and data and estimating the probabilities of a chain of events, actions and states of nature that could lead to the introduction and establishment of a disease such as BSE. The logical soundness of the risk assessment based on the principles of probability theory and statistical analysis is essential.

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cattle in Canada. Their exhaustive and thorough risk assessment document provided the cattle import data employed in this paper.



Évaluation des facteurs de risque associés à l'encéphalopathie spongiforme bovine

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Résumé

L'Office international des épizooties (OIE : Organisation mondiale de la santé animale) recommande à tous ses Pays Membres de déterminer le statut de leurs populations bovines au regard de l'encéphalopathie spongiforme bovine (ESB) en procédant à une évaluation des risques et en appliquant certains critères de surveillance relatifs à cette maladie. Le *Code zoosanitaire international* de l'OIE identifie et énumère les facteurs et les critères utiles à cette fin. Parmi les facteurs à évaluer figurent la consommation par les bovins de farines de viande et d'os, l'importation de bovins et de farines de viande et d'os susceptibles d'être infectés ou contaminés par l'agent de l'ESB, la structure des populations animales, les traitements d'équarrissage et le mode d'alimentation des animaux. Les auteurs donnent une description générale des critères et des facteurs de risque, en décrivant de façon détaillée les composantes importantes de chacun d'entre eux. Dans la deuxième partie de l'article, les auteurs procèdent à une évaluation des risques pour illustrer l'application des lignes directrices de l'OIE relatives à l'ESB. Il s'agit d'une évaluation probabilistique du risque des facteurs liés à l'ESB pour le Canada qui est conforme à l'approche de l'OIE en matière d'analyse du risque à l'importation. Les étapes comprennent l'identification du danger, l'appréciation de l'émission, de l'exposition et des conséquences, et enfin l'estimation du risque. Un arbre de scénario appliqué à l'appréciation de l'émission et de l'exposition a été utilisé pour modéliser les événements ayant découlé de l'erreur initiale qui a consisté à importer des bovins potentiellement infectés par l'agent de l'ESB. L'appréciation des conséquences comprend une description de coûts et des pertes associés à l'introduction et à la propagation de l'ESB dans d'autres pays. L'estimation du risque, qui intègre les résultats des appréciations précédentes (émission, exposition et conséquences), indique que la probabilité que l'ESB se soit introduite et propagée au Canada est négligeable, tout en reconnaissant que les conséquences économiques d'une telle introduction auraient été extrêmement lourdes.

Mots-clés

Analyse des risques – Appréciation du risque – Encéphalopathie spongiforme bovine – Facteur de risque – Farine de viande et d'os.



Determinación de los factores de riesgo ligados a la encefalopatía espongiforme bovina

R.S. Morley, S. Chen et N. Rheault

Resumen

La Oficina Internacional de Epizootias (OIE: Organización mundial de sanidad animal) recomienda a todos sus Países Miembros que esclarezcan la situación de la encefalopatía espongiforme bovina (EEB) en sus poblaciones de ganado vacuno, para lo cual deben llevar a cabo una determinación del riesgo y satisfacer una serie de criterios de vigilancia de la enfermedad. En el *Código zoosanitario internacional* de la OIE están definidos y repertoriados los parámetros necesarios para ello. Los factores de riesgo que deben evaluarse son: el consumo de harinas de carne y huesos por el ganado bovino; la importación de bovinos y harinas potencialmente infectados o contaminados por el agente de la EEB; la estructura de la cabaña ganadera; los procesos de transformación de cadáveres y despojos animales; y los sistemas de alimentación animal. Los autores presentan un resumen de los mencionados criterios y factores de riesgo, especificando en cada caso sus principales elementos. En la segunda parte del artículo describen un proceso de determinación del riesgo para ilustrar con un ejemplo la aplicación de las directrices de la OIE relativas a la EEB. Se trata de un estudio probabilístico de los factores de riesgo de EEB en Canadá, acorde con los planteamientos de la OIE en materia de análisis del riesgo ligado a las importaciones. Consta de varias etapas: identificación del peligro, evaluación de la difusión, de la exposición y de las consecuencias y estimación del riesgo. Utilizando un árbol de hipótesis de riesgo para determinar las probabilidades de difusión y exposición, se elaboró un modelo de todos los acontecimientos que podían seguirse del fallo desencadenante inicial, esto es, la importación de bovinos potencialmente infectados por la EEB. La evaluación de las consecuencias incluye una estimación de las pérdidas y costos derivados de la introducción y propagación de la EEB en otros países. La estimación del riesgo, que integra las evaluaciones de difusión, exposición y consecuencias, arroja una probabilidad ínfima de penetración y asentamiento de la EEB en Canadá, a la par que apunta a consecuencias económicas de extrema gravedad.

Palabras clave

Análisis del riesgo – Determinación del riesgo – Encefalopatía espongiforme bovina – Factores de riesgo – Harinas de carne y huesos.



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