An Estimation of the Magnitude and Duration of Bovine Sponginform Encephalopathy in Spain.

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Abstract

The objective of this study was to estimate the magnitude and duration of the Spanish BSE epizooty as well as the impact of a hypothetical mass slaughtering of animals in the epizootic curve. The model was based on the live curve of the exposed cohort and the incidence by age-distribution observed in the firsts years of the Spanish BSE epizooty. The model predicts a peak of cases between 2003 and 2004 and the extinction of the disease in 2012. Mass slaughtering of animals considered at risk would not significantly reduce the number of cases but would accelerate eradication 2 years. Absolute numbers derived from this model should be treated with caution, but general trends could be of major interest when deciding control and eradication measures. Until now the evolution of the disease in Spain it's following the prediction of this model. An up date overview of the Spanish BSE epizooty is also included.

Introduction

Several countries around the world, including Spain, have discovered their first cases of BSE in the last years, when Great Britain, the country that first detected the epizooty (1986), was on the downslope of the epizootic curve. This highlights the unfortunate reality that the BSE epizootic is more widespread than previously thought (Donnelly CA and others 2002). In Spain, the first confirmed case was declared in Galicia in 2000, and up to March 2006, a total of 625 infected animals were detected.

In 1988, the role of contaminated meat and bone meal (MBM) was demonstrated (Wilesmith JW and others) and in 1994, the European Commission banned the use of this MBM (Decision 94/381/CE) in ruminants. In June of 1998 these types of meals were forbidden in Spain. There is no evidence to date of horizontal transmission (Hoinville and others 1995) though some studies have pointed to a possible enhanced risk for calves born from infected dames (Donelly CA and others 1997).

At the beginning of the epizooty in Spain, a programme of passive surveillance began which consisted in the analysis of animals that died on farms and that had showed clinical neurological signs consistent with BSE before dying. The disease was confirmed by histopathology and immunohistochemistry and when a positive was detected all animals included in its "live cohort" were slaughtered as a preventive measure. A live cohort is defined as all animals living on the same farm born anywhere from 12 months before the birth of the BSE infected animal to 12 months after its birthdate. Currently, the scheme of the prevention and eradication program consists in the application of a quick test, which constitutes an important advance because it allows routine diagnosis (Grassi J 2003) of all animals sacrificed in the slaughterhouse as well as ones that die on farms. When positives arise the identification and slaughtering of live cohorts follow the same criteria. In 2001, a massive sacrifice of 83.000 animals considered at risk was carried out as part of control and prevention measures (FEOGA, 2002).

Due to the impossibility of identifying animals in early stages of BSE incubation, or made in vivo detection of the disease, the estimation of the magnitude and duration of epidemic curve would be of major interest not only for the implementation of eradication measures but also to estimate the potential danger to public health.

Models based on the observed frequency of clinical cases and the age distribution of animals that died from BSE, have been used to estimate the prevalence and incidence of BSE in the UK (Anderson and others 1996, Kao and others 2002), and similar models have been designed for the Swiss BSE epizootic (Doherr and others 1999).

The objective of this study was an estimation of the magnitude and duration of the Spanish BSE epizootic as well as the impact of a hypothetical mass slaughtering of animals in the epizootic curve. The model was based in the survival curve of the animals considered exposed to MBM and the incidence by age-distribution observed in the Spanish BSE epizooty. An overview of the Spanish BSE epizooty is included.

Materials and methods

Data sources
Information about cattle population was obtained from the Livestock Census, ranged by age and sex, and temporal series of cattle meat production published by the Ministry of Agriculture. The bovine census in Spain is divided into three groups: animals younger than 12 months, those from 12 to 24 months and those older than 24 months. Thus, age-distribution for animals younger than 24 months were obtained from national statistics while older animals; age-distribution was calculated following Swiss cattle distribution (Doherr, M.G and others 1999). Information referring to BSE cases was obtained from the monographic web of the BSE situation in Spain (www.eeb.es) and data on specific slaughtering caused by BSE from FEOGA publications (FEOGA, 2002).

BSE epizooty in Spain
In order to understand the Spanish situation of BSE epizooty the following aspects were analysed: Temporal evolution of the epizootic from 2000 to 2006; Spatial distribution, prevalence in each Autonomous Community (AC), calculated according to the number of tests done in 2002; affected animals, which were categorized by breed and mean age (calculated when the diagnosis was confirmed).
Additionally, information about number of animals tested and confirmed cases was obtained for the period 2001 to November 2002 categorized by clinical suspicion, emergency slaughter, animals with ante mortem symptoms, fallen stock, animals for human consumption, and animals belonging to the "live cohort" of a confirmed case. Attack rates by groups were calculated and compared. The absolute number of tested animals destined for human consumption was compared with the number of animals older than 30 months declared to have been slaughtered by the Spanish Ministry of Agriculture statistics (SGEA 2002).

Definitions and modelling
A cohort study was performed for the prospective estimation of potential clinical BSE cases. Back calculations were employed for the first years of the epidemic (2000-2001).
The exposed cohort was considered to be all cattle censed on December 31, 1998, assuming an effective feed ban started January 1, 1999. This cohort could be further broken down into age-cohorts (all animals born in the same year). Exposure to contaminated meat and bone meal (MBM) was considered homogeneous in the cohort.
The study of the evolution of the exposed cohort, the live curve (LC), was designed to follow the evolution of each age-cohort and to take into account the following criteria: a) the exposed cohort was considered closed and any hypothetical maternal transmission was studied separately; b) losses of animals were mainly due to regular slaughtering for human consumption (recorded by age and sex). Additionally, two different eradication schemes were used, resulting in different live curves (LCs). LC1: the evolution of the exposed cohort counting the animals that died from BSE on farms and the 44 animals slaughtered per BSE-positive animal detected (estimation of the animals killed when included in the "live cohort" of a BSE case occurring between 2001 and 2002). LC2: the evolution of the exposed cohort counting the animals lost in LC1 and adding those that would be included in a hypothetical, more extensive slaughtering of animals considered at risk. This number (83.000 animals per year) was the number of animals slaughtered in 2001 as control measure (FEOGA, 2002).
The estimation of expected cases was based on both live curves, calculated from the observed incidence, grouped by age, and resulted in two different figures; F1, based on LC1 and F2, based on LC2. Taking into account the variable and increasing number of tests performed from 2000 to 2002, observed incidence by cattle-age in 2002 was used for retrospection and prediction (animals which could have been detected in 2000 and 2001 if the same number of tests had been applied, and from 2003 to the end of the live curves, assuming a stable incidence by age).
Confidence Intervals for number of cases were calculated assuming a normal distribution when the expected number of cases was $n > 30$ and a Poisson distribution when $n < 30$.

Results

Spatial distribution
From 2001 to 2002 a of 32 provinces were affected from the total 50 Spanish provinces. An inventory of the distribution of the tests performed per AC showed that 90% of tests were done in the two ACs where the maximum number of cases were detected: Galicia = 35 and Castilla León = 36 (Figure 1). The number of cases per AC, in 2002, was closely related to the number of tests carried out the same year ($r = 0.991$, $r^2 = 0.88$, $p = 0.001$). The highest prevalence was found in north central and western Spain (Figure 2). During the following year a similar distribution was observed.

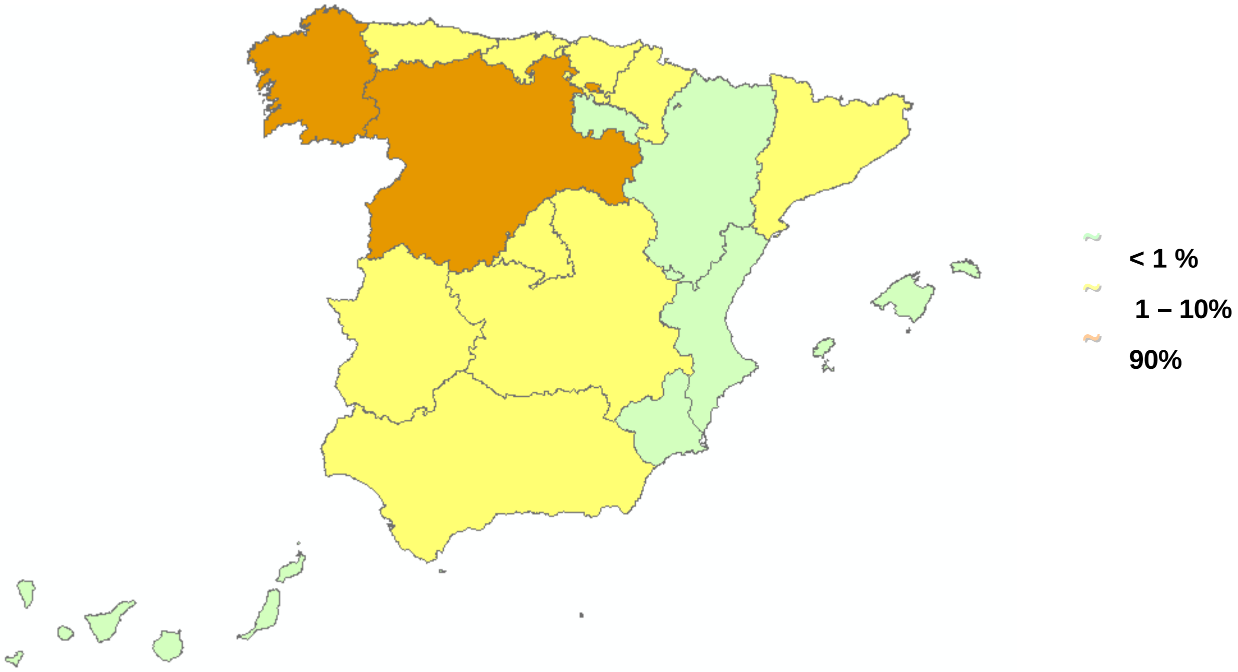


Figure 1. Proportion of test realized by Autonomic Community (2002).

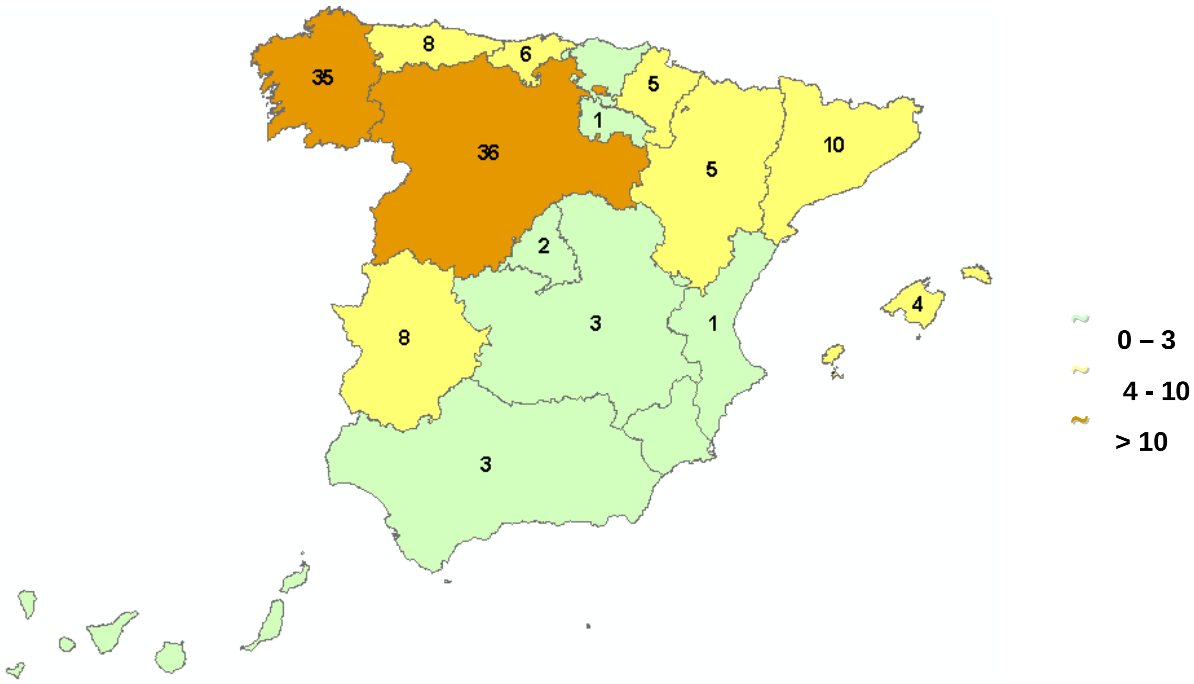


Figure 2. Number of BSE cases by AC (2002).

Spanish cases
The normal pattern of Spanish cases during the first two year was dairy cattle with a mean age of 6.5±0.13 years old, ranged between 3.6-14.8, and a mode of 5 years old. Case distribution by age showed that 50% of cases were between 5 and 7 years old, (Graphic 1). The breed most affected was Friesian (62.7%), which was consistent with its predominant position in the censed cattle population. No significant differences among breeds were found for mean age ($p = 0.141$) (Table 1) during the three years of the epizootic (5.37± 0.7; 6.34±2.1; 6.5±1.5, $p=0.475$), indicating that the pattern of cases is stable. The following years the same pattern was observed.

Graphic 1. Age-distribution of BSE cases detected in Spain from 2000 to 2002.

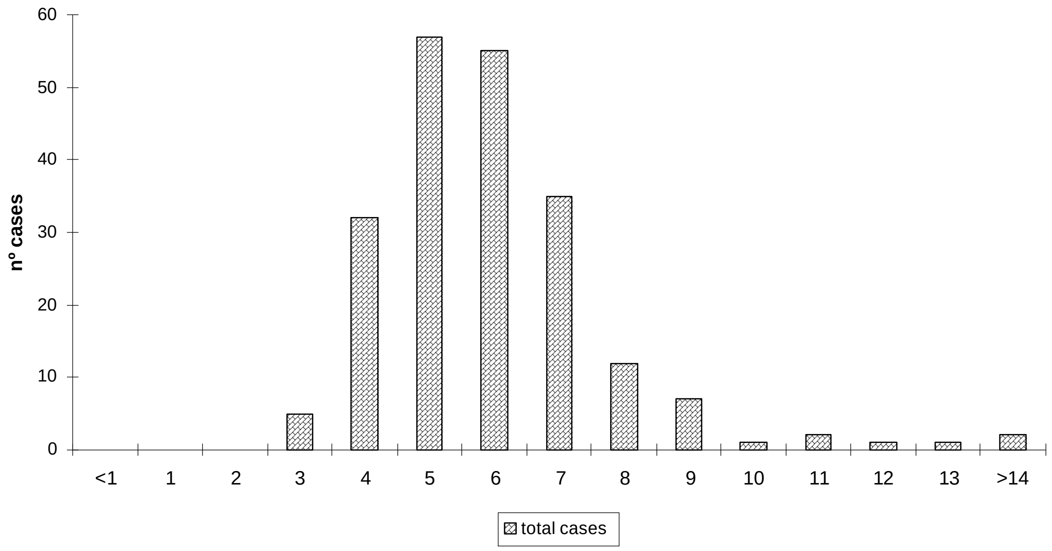


Table 1. BSE cases detected by raze the respective mean and range age.

Raze	Cases		Age	Range	
	N	%			
asturiana	4	2,0	9,0	4,4	14,8
avileña	1	0,5	8,8	8,8	8,8
cruce	41	20,1	6,9	4,9	13,3
charolesa	2	1,0	6,4	6,3	6,5
felckvich	1	0,5	5,3	5,3	5,3
frisona	**128**	**62,7**	**6,3**	**3,6**	**14,7**
jersey	1	0,5	7,1	7,1	7,1
limousine	6	2,9	6,2	5,1	8,1
mestiza	1	0,5	6,1	6,1	6,1
parda	7	3,4	5,7	4,3	7,0
pirenaica	6	2,9	7,0	6,0	8,4
retinta	3	1,5	6,0	5,1	6,9
cruce carnico	3	1,5	7,1	5,9	8,0
Total	**205**	**100**	**6,5**	**3,6**	**14,8**

The analysis of the tested and confirmed cases, grouped as described in materials and methods, showed that more than 80% of tested animals were destined for human consumption and the attack rate in that group was less than 0.008, the lowest of all groups (Table 2). The second most highly tested group was animals that died on farms, this group had a higher attack rate, 0.08. In contrast, the highest attack rate was detected for suspicious animals (26.9), the group that formed the smallest group, proportionally, of animals tested. 100% of cattle 24 months or older, destined for human consumption, were tested. This pattern was similar from 2003 to 2005.

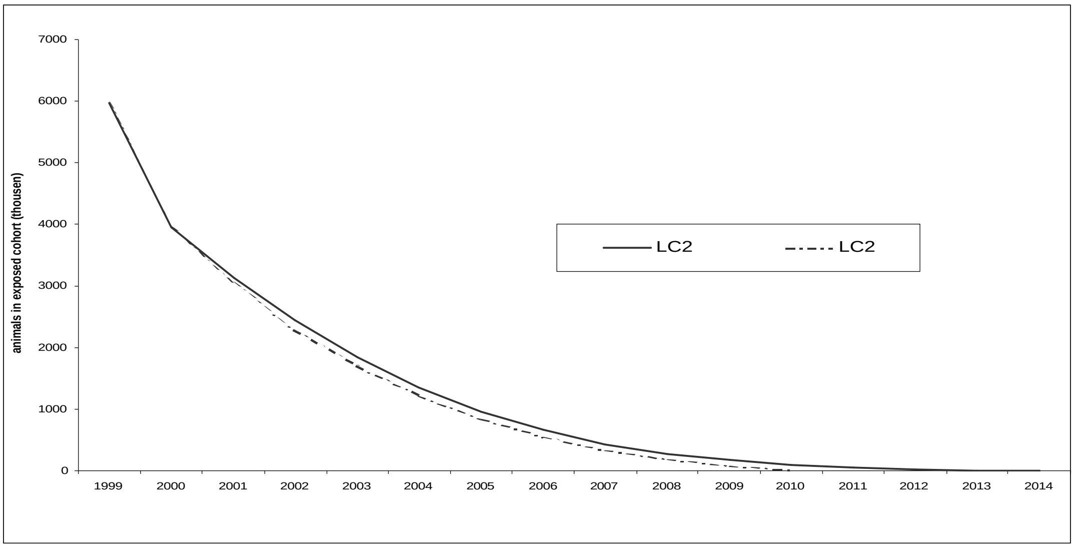
Table 2. Number of cases tested and confirmed for BSE in Spain in 2001 and up to Nov. 2002 and attack rate (AR) by category. POS: positive.

	2001			2002		
	Tested	POS	AR	Tested	POS	AR
Clinical suspicion	96	9	**9,375**	52	14	**26,923**
Emergency slaughter	3.827	6	**0,157**	1.293	2	**0,155**
Sint. ante mortem	632	1	**0,158**	1.067	7	**0,656**
Fallen Stock	50.925	31	**0,061**	68.370	56	**0,082**
Human consumption	327.055	35	**0,011**	376.507	31	**0,008**
Animals in "live cohort"	4.053	1	**0,025**	4.764	5	**0,105**

Expected cases of BSE

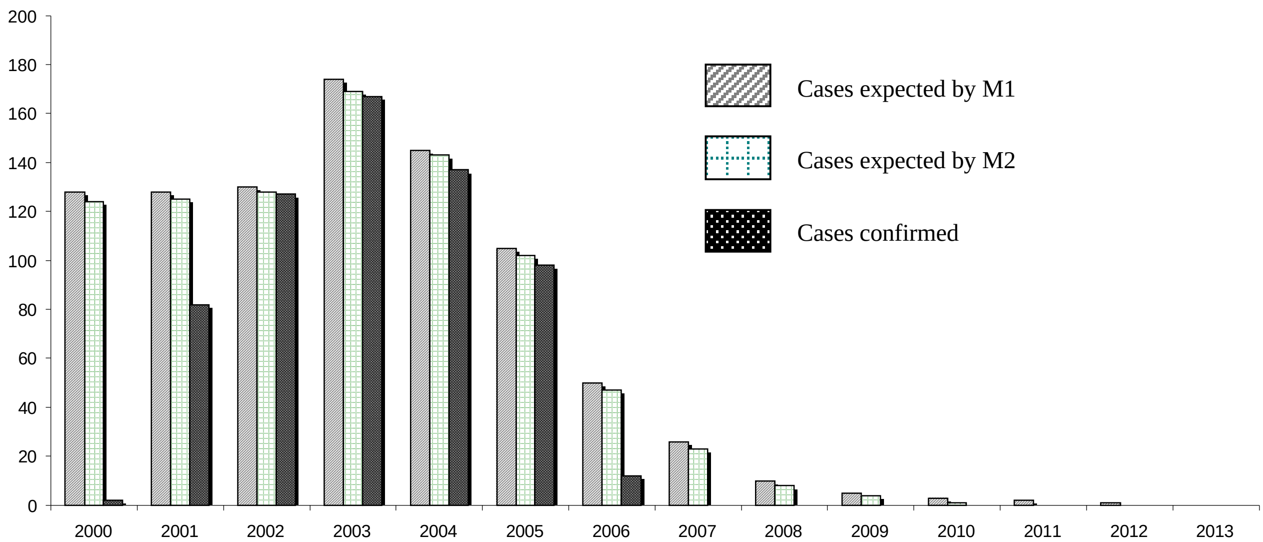
With regard to the evolution of the exposed cohort, a notable decrease was observed in the number of animals during the first years (2000-2001) in both LCs, reflecting the age at which large numbers of animals are slaughtered for human consumption (under 3 years). The decline in the number of animals would be expected to be slow and progressive until the extinction of the cohort, which one would expect to occur in different years depending on the LC. LC1 predicts less than 50.000 surviving animals after 2010 and the disappearance of the cohort in 2012. LC2 anticipates the end of the cohort between 2009 and 2010 (Graphic 2).

Graphic 2. Live curves based on regular slaughtering for human consumption and eradication measures: LC1: animals killed when included on a case "live cohort"; LC2: animals killed as LC1 and a massive slaughtering of risk animals.

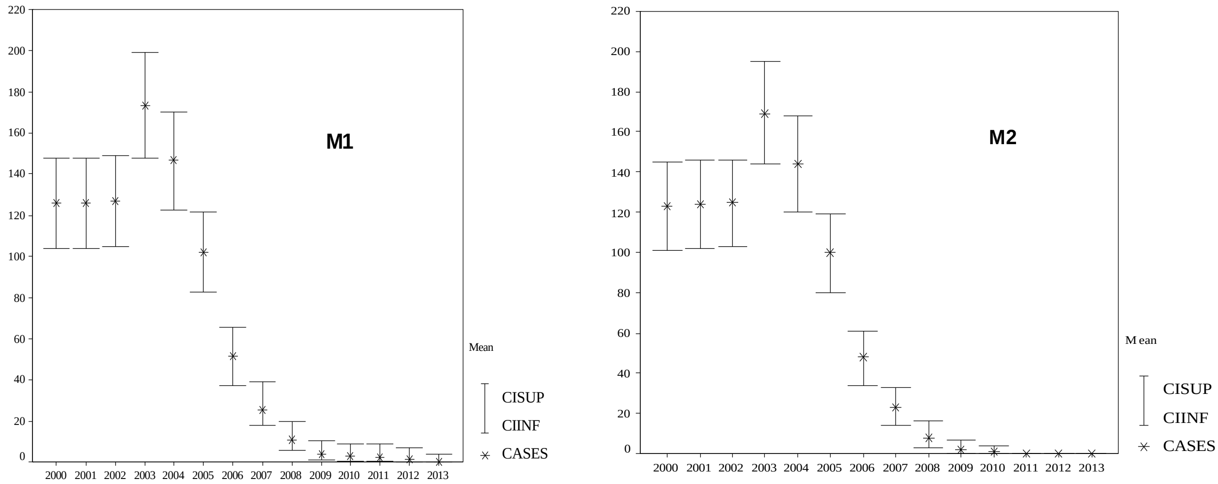


In 2000 and 2001, at least 126 cases (CI= 148-104, • =0.05) would have been detected if the testing scheme had been similar to 2002's and only animals in the live-cohort (LC1) had been slaughtered. The peak of the epizootic curve would be expected to occur between 2003 and 2004, followed by a progressive decrease in the number of cases, linked to the decline of animals in the exposed cohort. The maximum number of cases would be expected in 2003 with 174 (IC: 200-148, • =0.05) by S1, while S2 anticipates 169 cases (IC: 194-144, • =0.05) for the same year and a progressive decline in cases until 2009 when both possibilities (S1 and S2) predict less than 5 cases (IC: 10-1, • =0.05) and only sporadic cases until 2010 and 2012, respectively (Graphic 3 and 4).

Graphic 3. Number of expected cases on 2000 and 2001 assuming same scheme of testing than in 2002, and prospective estimation based on the 2 different live curves.



Graphic 4. Confidence intervals for number of expected cases by each model.



Discussion

Limits of Information Sources Consulted

The Spanish census of cattle provides little information about animal characteristics. No information about age distribution for animals older than 24 months was found in any of the different sources consulted. For this reason, and taking into account the similarity in age–distribution of BSE cases detected in Switzerland and Spain (Doherr and others 1999), the exposed cohort age-distribution for animals older than 24 months was designed following the Swiss dairy and breeding cattle structure.

As for information from the BSE surveillance programme, results of the quick tests performed in 2002 were amassed by AC while BSE case reports were made available by province. This limited information compelled the authors to estimate prevalence by AC and assign the same prevalence to all provinces included in an AC even though some of them had never reported a BSE case.

Temporal and spatial distribution

During the first three years of the BSE epizooty in Spain, the number of cases detected has increased significantly. There might be two main reasons to explain this development. First, the change in the testing scheme, which increased a 41% in 2002 than 2001, detecting 53% more cases, and, second, ageing of the exposed cohort. When considering the increase in testing, one should take into account the correlation found between the number of tests and cases detected. Possible underestimation of the real incidence from 2000 to 2002 would be expected, as other authors have previously described for their own countries (Doherr MG and others 1999, Donnelly CA and others 2002).

In spite of this under detection of BSE cases, the spatial distribution was wide and heterogeneous throughout Spain, with a noticeable dependence on the number of tests performed in each region. The prevalence distribution showed a more intensive epizooty in the northern half of the peninsula and in the west (Figure 3), which corresponds with is closely related with the bovine census distribution during 2001 (Figure 4).

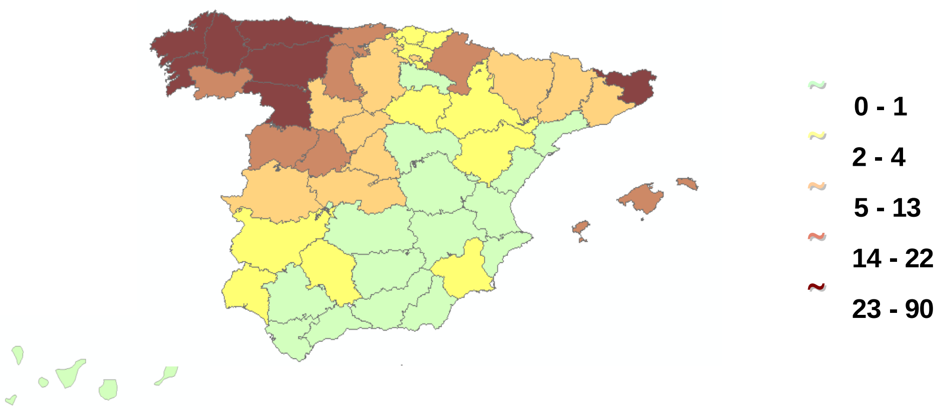


Figure 3. Spatial distribution of BSE cases in Spain (Total number of BSE cases from 2000 to 1 April 2006 by Province).

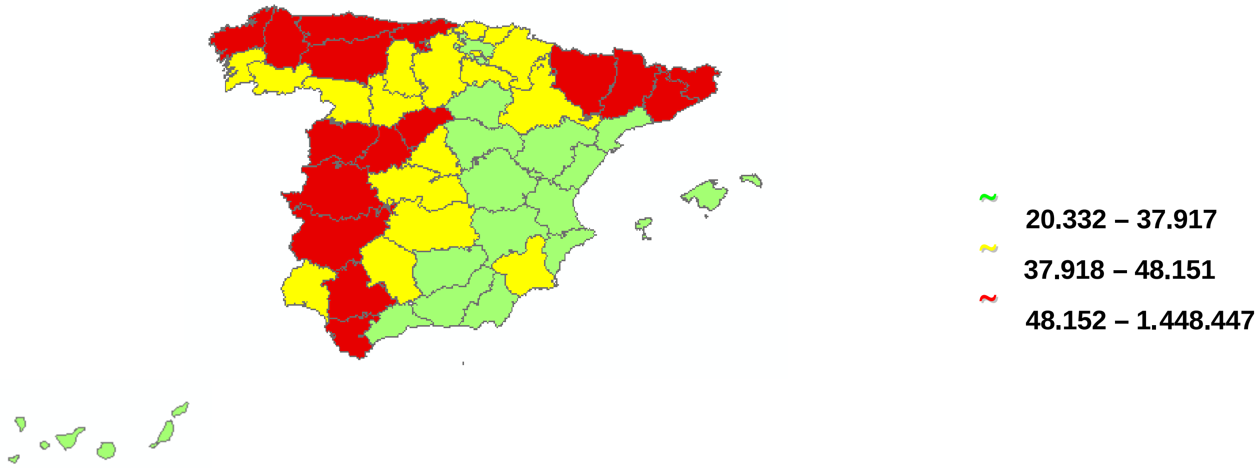


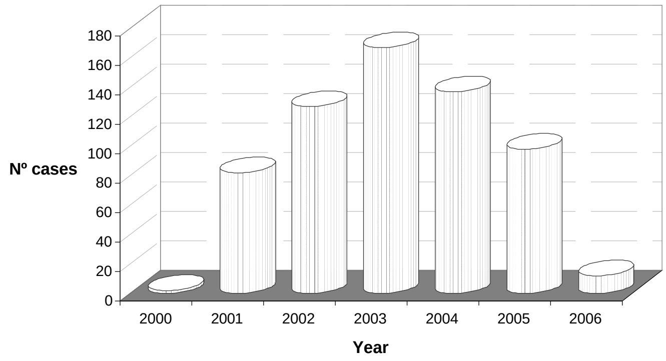
Figure 4. Bovine census distribution during 2001 (Total number of heads by Province).

BSE affected animals in Spain from 2000 to 2002 displayed a pattern of age distribution similar to cases identified in other countries (Switzerland or England), with 6 year olds being the most common (Doherr and others 1999, Ghani and others 2002). This finding seemed to agree with the usual assumption of an incubation period of 5 years, presuming that the greatest exposure and infection occurred during the first year of calves lives (Ghani and others 2002). Thus, cases confirmed between 2000 and 2002 might have been exposed to contaminated feed between 1995 and 1997. In the present study, due to the large number of different types of cattle farms found in Spain and the diversity of livestock gathering procedures, the authors considered that exposure to MBM could have occurred at different times on different farms. Thus, the worst situation was allowed for: homogeneous exposure throughout the cattle population, irrespective of age and location. To understand the basis of the model in Spain, it also should be mentioned that, up to the present time, no cases have appeared after the feed ban, contrary to what occurred in several European countries (Ducrot and others 2000, Doherr and others 2002). Thus, if we assume there was an effective ban on the MBM, it is possible to argue that there was one primary focus of contamination and that a single cohort of all animals censed in 1999 was potentially exposed to the contaminated feed.

Magnitude and duration of the BSE epizooty in Spain

With respect to the number of expected cases, the magnitude of the epizooty in 2000 and 2001, would have been at least similar to 2002 and, thus, the notable increase of the number of cases detected during those years, would be mainly attributable to the change in testing schemes. Moreover, the potential underreporting of BSE cases, described by other authors (Donnelly CA and others 2002) and estimated to be at least 50-75% (Doherr and others 1999), would double the number of expected cases per year. With these considerations in mind, it is possible to suppose that the beginning of the epizooty might have occurred a few years before 2000.

The model suggested that the peak of BSE detection would be expected to occur between 2003–2004, five or six years after the official feed ban went into effect (late 1998). The prediction of the models was correct (Figure 5) (www.eeb.es). This prediction agrees with observations in United Kingdom and Switzerland, where the peak of the epizooty was reached in the 4-5 years after their respective feed bans, (UK ban in 1988, peak in 1992-1993; Swiss ban in 1990, peak in 1994-1995). The increase in the number of cases might correspond both to the cohort growing older and expanded efforts in testing and culling. According to the first observation, animals that at the beginning of 1999 were younger than 24 months old, would be reaching the risk age (5-7) between 2003 and 2004. With regard to the second observation and keeping in mind the correlation found between number of tests performed and cases detected, the epizooty might only appear to be growing because eradication policies raise the number of cases detected. This hypothesis is consistent with the modification of the epizootic curve in Switzerland when quick tests were incorporated into the eradications measures (1998), detecting a great many more cases at a time when the Swiss epizooty seemed to be ending. In Spain, quick tests were incorporated in 2001 and thus, as mentioned above, this might explain an increase in the number of cases (www.eeb.es).



Year	Cases		Age (years)
	N	%	
2000	2	0,32	5,290410959
2001	82	13,12	6,288018034
2002	127	20,32	6,382147592
2003	167	26,72	6,780477401
2004	137	21,92	6,777900886
2005	98	15,68	6,678613363
2006*	12	1,92	7,479452055
Total	**625**	**100**	**6,52**

* Data as of 1 April 2006

Figure 5. Number of BSE cases in Spain (2000-2006)

Regarding the differences found between both schemes of eradication, little repercussion of the massive slaughtering was found in terms of cases avoided, but was more relevant for the epizooty duration. Assuming only the slaughtering of live cohort animals, the most widespread eradication policy, the end of the epizooty would be expected to occur 13 years after the first case was declared, which is consistent with previous observations (Anderson and others 1996, Doherr and others 1999). Massive slaughtering would accelerate eradication two years.
However, the model is strongly influenced by the initial assumption that no further exposure occurred after 1999. If contaminated feed was circulating after that year, all the predictions for the epizooty would have to be modified by the number of years that went by before the halt of contaminated feed consumption was achieved.

The model provides the estimation of the past and future patterns of the epizooty in Spain and the impact of a possible and controversial additional slaughtering of animals considered at risk. Absolute numbers of cases derived for the model should be treated with caution and the influence of the testing schemes on the curve shapes should always be taken into account. Nevertheless, the epizootic trends and the live curves observed at the end of the epizooty between 2010 and 2013 are very likely to be reliable.

Conclusions

- The maximum peak of BSE cases would be expected to occur between 2003 and 2004, 5-6 years after the official feed ban was put into effect.
- The exposed cohort will disappear in 2013, assuming animals in the live cohort will be slaughtered only when confirmed cases occur. Thus, the end of the epizooty would be expected for the same year, 13 years after the first case was detected.
- A hypothetical mass slaughtering of animals might have little effect, in terms of cases avoided, but would accelerate eradication two years.
- 100% of animals destined for human consumption are regularly tested.

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