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Classical BSE in Great Britain: Review of its epidemic, risk factors, policy and impact

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ABSTRACT

The emergence and epidemic of classical Bovine Spongiform Encephalopathy (cBSE) represents one of the most important and unique episodes in disease control of a zoonotic disease due to its novelty and its impact. Since its detection in 1986 in the United Kingdom, it has also been detected in 25 countries. The novel nature of its infectious agent and the discovery of its zoonotic potential (causing the new variant of Creutzfeldt-Jakob disease in humans) caught the food industry, policy makers, scientific community and consumers off guard, with concerns over massive human exposure and health impact. Thirty-five years later, and following the feed bans of mammalian protein to livestock in 1996, the epidemic is now in its final stages, with expectations of occasional cases emerging until the year 2026. In the last six years, two cBSE cases from animals Born After the Reinforced feed Ban (BARB) have been identified in Scotland and England, delaying their application for BSE Negligible status. This paper provides a current and historical analysis of the cBSE epidemic situation in Great Britain and review the policies implemented, its impact and the possible factors explaining the occurrence of new cases.

The analysis and review reinforce the hypothesis that cBSE BARB cases occurrence may not be spontaneous, yet there remains much uncertainty of their aetiology. To date, 181,122 cBSE cases have been detected in Great Britain, of which 178 are BARB cases; and 178 human cases of the new variant of Creutzfeldt-Jakob have been diagnosed. The disease triggered major policy responses in the country, and worldwide, that have transformed the industry and our approach to animal health. Almost all its impact originated from societal reactions to the disease, from disposal of animals and products, to reduction of the national herd and its production efficiency, losses through trade restrictions and reduction in market prices and consumers' confidence, hardening of cleaning and control procedures in farms and hospitals, generation of heavy government investment plans through numerous support, surveillance and research schemes, and political and societal changes. BSE is an example of major system shock to a food industry, but which experience has resulted in better traceability systems of animals, increased capacity to develop robust diagnostic methods, numerous lessons learnt on policy coordination, implementation and communication, increased society awareness on food systems and overall improved the country's preparedness to future epidemics.

1. Introduction

Bovine spongiform encephalopathy (BSE) was first confirmed in Great Britain (GB) in 1986, with subsequent retrospective clinical evidence of occurrence detected in 1985 (Wilesmith et al., 1988). The disease became notifiable in the country in 1988, and was posteriorly linked in 1996 to a new variant of Creutzfeldt-Jakob (vCJD) disease in humans (Will et al., 1996). To date, 183,325 BSE cases (including atypical cases) in cattle and 178 human cases of vCJD haven been reported in the United Kingdom (UK), with an annual human mortality in 2020 of 1.98 cases/million (www.cjd.ed.ac.uk, 2020). Although the disease is now on a declining trend, the magnitude of the financial and public health impact makes it imperative that the aetiology and epidemiology of the disease is well understood.

BSE cases are differentiated, based on the molecular mass of PrP^{sc} (scrapie isoform of the prion protein) after protease degradation and Western blot analysis, into classical BSE (cBSE) and two atypical BSE types, namely H-BSE or L-BSE prions. These atypical BSE types were first

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reported in 2004 from cases in Italy and France (Biacabe et al., 2004; Casalone et al., 2004). So far, cBSE has been linked to variant Creutzfeldt-Jakob disease in humans (Scott et al., 1999), while human infection with atypical BSE has not been reported. Yet, some experiments with mice and non-human primates have shown evidence of the zoonotic potential of L-BSE prions (Beringue et al., 2007; Mestre-Frances et al., 2012).

The origin of BSE remains unknown, and different hypotheses have been formulated. It has been argued that BSE may have been a rare spontaneous disease in cattle which was amplified by the use of Meat and Bone Meal (MBM); or that it was acquired from Sheep Scrapie or a human TSE (Colchester & Colchester, 2005). The source of infection of classical BSE has been attributed to the consumption of mammalian MBM, which subsequently triggered a ban of such feed to cattle. Cases of BSE in cattle, which were born after the reinforcement of the feed ban on July 31, 1996, in GB, are referred to as BARB cases (Born After the Reinforced Ban). To date, there have been 184 confirmed BSE BARB cases in GB, including 6 which were confirmed as atypical BSE. These cases should not have had exposure to banned feedstuffs, and therefore there has been much interest and speculation about their aetiology. The last two cBSE cases were reported on October 2018 in Aberdeenshire, Scotland (APHA, 2018), and on September 2021 in Somerset (APHA, 2021). As a result, Scotland reverted from BSE negligible risk status to controlled risk status, as per the World Organization for Animal Health requirements (WOAH, 2022), while the latter case stopped England and Wales, who currently hold controlled risk status, from applying for negligible risk status.

The emergence of BSE, and the discovery of its zoonotic link, can be viewed as one of the largest shocks suffered by a food industry. The crisis affected all levels of the industry, and represented an enormous challenge for policy and risk communication. In this paper, we aim (1) to provide an analysis of the current status of the epidemic since its first discovery, with particular focus on classical BSE BARB cases and their distribution; and (2) to review the major policies implemented, the impact of the disease in society and the potential factors that can explain the occurrence of new cases.

2. Materials and methods

The study was conducted in three parts. The first part aimed to describe the epidemiological pattern of cBSE cases, and particularly of all the BARB cases identified in the UK. This included an analysis of spatial and spatio-temporal clustering of BARB cases. Secondly, a review of the literature was conducted to collect evidence of potential risk factors for their emergence. This review was complemented with an analysis of the free text data from investigation reports of the BARB cases detected after 2009, in order to further understand possible causes for their emergence. Finally, a review of existing policies and disease impact associated to BSE was conducted.

2.1. Assessment of the epidemiological trend of BSE cases in Great Britain

The Animal and Plant Health Agency (APHA) provided data on all BSE cases reported in GB up to the year 2021. For each case, data were obtained on date of detection, date of birth, holding number (based on CPH number[1]) and location, type of production (dairy or meat), pedigree status and the type of BSE (classical or atypical). All atypical cases were identified and removed from the database for analysis, as these may have a different causal pathway to cBSE.

Data were used to produce an epidemic curve of cBSE and cBSE BARB cases detected in GB. Changes in the animal-case profile between the recent cases (after 2009) and historical cases (before 2009) were investigated based on differences in the route of detection (passive or active surveillance) and age of cattle at detection. T-test statistical analysis was used to assess the difference in age between both groups. Spatial analysis was then conducted to understand their distribution, detect spatial clusters and identify potential spatio-temporal correlation of cases. Spatial and spatio-temporal clustering of BARB cases were assessed by means of the scan statistic. For the purely spatial analysis a Bernoulli model (Kulldorff, 1997) was used, with cases being holdings where at least one BARB case had been reported and non-cases included the remaining GB agricultural holdings keeping cattle according to the 2000 Agricultural Census. The spatio-temporal analysis was carried out using a retrospective space-time permutation model (Kulldorff et al., 2005) with time aggregation at level of the year. For both models 999 permutations were used and a p-value of less than 0.05 was considered as evidence of clustering. The analyses were implemented in SaTScan version 9.6 (Information Management Services Inc.).

2.2. Review of BSE policies, impact and BARB risk factors

A review of the existing scientific literature, via PubMed and through consultation of official reports from national and supranational institutions, was conducted. The review extracted data on: 1) evidence of risk factors associated with emergence of cBSE BARB cases, 2) impact of these cases on the national herd, 3) prospective economic and epidemiological modelling of cases, 4) the past and existing policies for the detection, surveillance and control of cases and protection measures to consumers, and 5) scientific opinions for future policies and control. For the review of BSE BARB cases risk factors, the search was conducted via PubMed using the terms 'BSE' AND 'Risk factor'. All articles were screened and studies were selected for review if these focussed on BARB cases or provided a comparative analysis of cases before and after the feed ban in the UK or other European countries. BARB cases were defined as those cBSE cases born after July 31, 1996, in the UK or those cBSE cases born after 2001 in the rest of Europe. In addition, studies that investigated risk factors of cBSE after the implementation of earlier partial feed bans were also included and named here as BAB cases. For the UK, BAB were cases born between 1988 and 1996, while for the rest of Europe BAB cases were those born between 1990 and 2001. The reason for including these was to explore whether some of the risk factors would be similar to those identified for BARB cases or could be used to generate hypotheses to explain their emergence.

In addition, the reports produced by APHA for the epidemiological investigation of cBSE BARB cases detected after 2009 were reviewed. These reports provided detailed information, in free text form, on: (1) case animal characteristics, such as breed and movement history, (2) herd size, (3) feed and water management and source, (4) other animal species on farm and (5) TSE history of the farm. The free text data was manually extracted and collated in a spreadsheet using Microsoft Excel (2013). This was then used to describe and compare the farm and animal characteristics and history of the cases, and to identify factors relating to the potential aetiology of the cases.

The review of BSE policies implemented was conducted based on the authors' knowledge of the most important and relevant policies and also through Google searches of key BSE and TSE legislations and policy documents relevant to the UK and the European Union (EU). Reports published by the UK government, European commission and European Food Safety Authority were also considered in this study. The review focussed on policies that had significant impact on BSE control and surveillance, establishment of public health protection measures and trade implications. The review of the economic impact of BSE was assessed using a combination of Google search, Google scholar and Pubmed, and through a series of specific investigations based on the knowledge of the epidemic and policies implemented. Some investigations were at a general level, such as the impact of BSE on trade or the cost of BSE surveillance, whilst others were targeted to assess economic losses due to specific policies, such as the selective cull policy or

[1] https://www.gov.uk/guidance/register-a-holding-so-that-you-can-keep-cattle.

the disposal of specified risk material (SRM), amongst others. In addition, when gaps in the economic impact of the disease were detected in UK studies, economic studies conducted in other countries were presented to illustrate the potential importance of such gaps. Existing BSE review and opinion papers were also used to further extract key lessons learnt and benefits of the BSE epidemic.

3. Results

3.1. cBSE epidemic in Great Britain

Fig. 1 shows the epidemic curve of cBSE in Great Britain since the detection of the first cBSE case in 1986. Fig. 2 shows the epidemic curve of BARB cases with data aggregated per year, together with estimated incidence. To date, a total of 181,122 cBSE cases have been found in GB, of which 178 are BARB cases (0.1%). The last non-BARB BSE case was detected in 2012. The first cBSE BARB case was detected in 2000, and the peak of these cases was observed in 2003 with 38 cases detected, two years after the implementation of active surveillance in the GB. The number of cases steadily declined since, with only one or two cBARB cases per year between 2011 and 2015, and then one case every three years between 2015 and 2021. A total of 13 cBSE BARB cases have been detected in the last decade (since 2010). The yearly incidence of cBSE BARB cases fell from a peak of 13.7 cases per 100,000 cattle in 2001 to one to two cases per 100,000 cattle for the period 2009 to 2015 (Fig. 2). The incidence for the period 2016 to 2021 was 0.29 cases per 100,000 cattle, with only two cases detected for this period. The yearly total number of cBSE cases detected has reduced from a total of 1,291 cases in 2000 (incidence of 12,847 cases per 100,000 cattle tested) to no more than a case per year since 2014.

Of all cBSE cases confirmed in GB, 98.9% were detected through passive surveillance (Table 1). This proportion has reduced to 60.1% for the period 2000–2009 and then to 3.2% for the period 2010–2021. Yet the majority (76%) of BARB cases were detected via active surveillance. The last BSE case found via passive surveillance was in 2008.

Analysis of age at detection of cBSE BARB cases showed there was an increasing trend between 2000 and 2010, and a subsequent irregular pattern with old animals (>10 years) and animals<6.5 years being detected. An average difference of 2.36 years of age (*t*-test $p = 0.01$) was detected between cBSE BARB cattle identified pre-2010 and post-2010 (Fig. 3). The average age of cBSE BARB cases in the last decade was 8.8 years compared to 6.23 years for cases in the 2000–2010 period. Yet, the cases in 2018 and 2021 were detected in animals with 5.4 and 6.6 years of age.

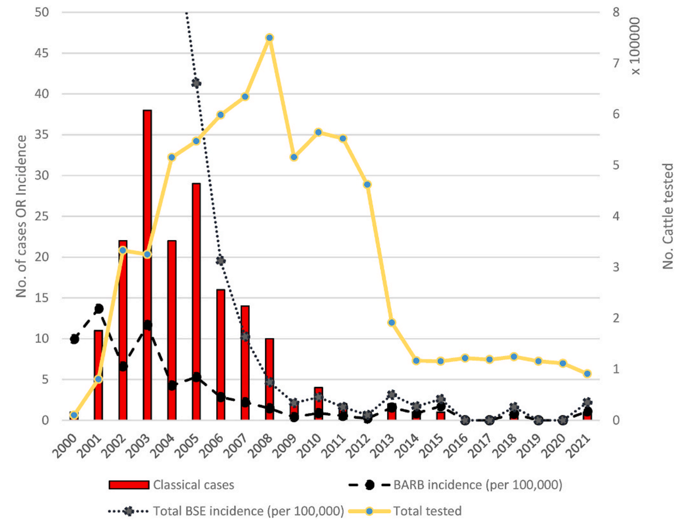

Fig. 2. Epidemic curve of classical BSE BARB cases (number of cases per year).

Once all duplicate CPH numbers were accounted for, the dataset consisted of a total of 166 holdings where cBSE BARB cases have been detected. However, two holdings were found to be under the same ownership (same herd mark) and located less than one km apart, although with different CPH numbers. Hence, it is estimated that a total of 165 holdings had experienced a cBSE BARB case in GB. Of these, 11 farms have had more than one case. One farm had three cases detected in 2005 (two were detected on the same day, by cohort surveillance), and the others had two cases each. For two farms, the second BARB case was detected as a result of clinical suspicion. For five farms, the subsequent BARB cases were detected by cohort surveillance. For 10 farms, the second cases were detected within a year of the first case. Only one of these repeat cases was detected in the post-2010 period.

The results of the assessment of spatial clustering identified a small area of 1.6 Km radius in Dorset where, out of four agricultural holdings, BARB cases were identified in three of them, in October 2002, May 2003 and January 2006 (one case per farm; relative risk = 379.09, P = 0.005). One spatio-temporal cluster was found, it included four cases from four

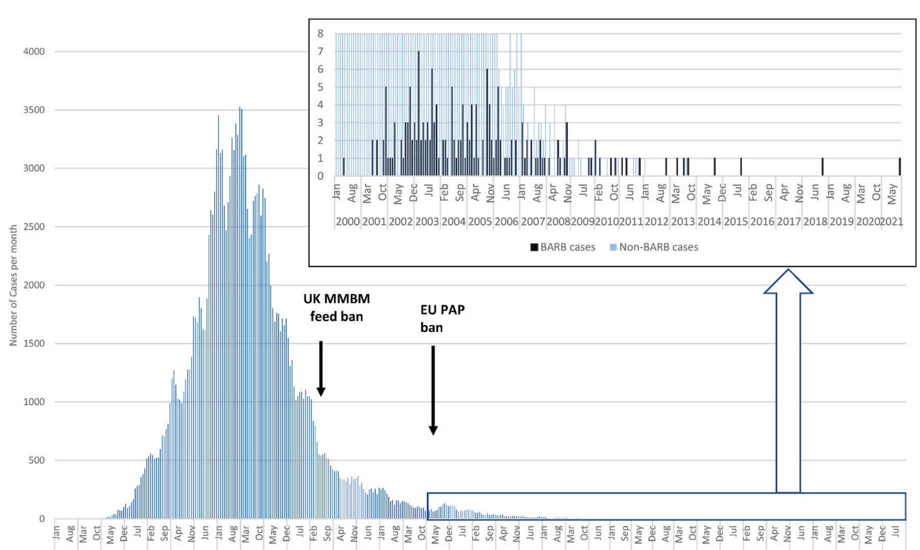

Fig. 1. Epidemic curve of classical BSE in Great Britain (number of cases per month). The dates of implementation of the UK ban on the use of mammalian meat and bone meal (MMBM) in livestock feed, and the European Union ban on the use of processed animal protein (PAP) in livestock feed are indicated.

Table 1
Detection of Classical BSE (cBSE) and Classical BSE BARB cases in Great Britain (Data extracted from Government statistics[a] – excludes 15 Atypical BSE cases).

	cBSE cases	cBARB cases	2000–2009				2010–2021			
			Non-cBSE BARB cases	cBSE BARB cases	Number of tests done	cBSE/ 100,000 tests	Non-cBSE BARB cases	cBSE BARB cases	Number of tests done	cBSE/ 100,000 tests
Passive Surveillance	179,183	42	2814	42	4081	69,982.8	1	0	46	2173.9
Active Surveillance	1939	136	1776	123	4,310,918	44.1	17	13	2,688,027	1.00
Total	181,122	178	4.590	165	4,314,999	110.2	18	13	2,688,073	1.15

[a] Cattle TSE surveillance statistics - https://www.gov.uk/government/publications/cattle-tse-surveillance-statistics.

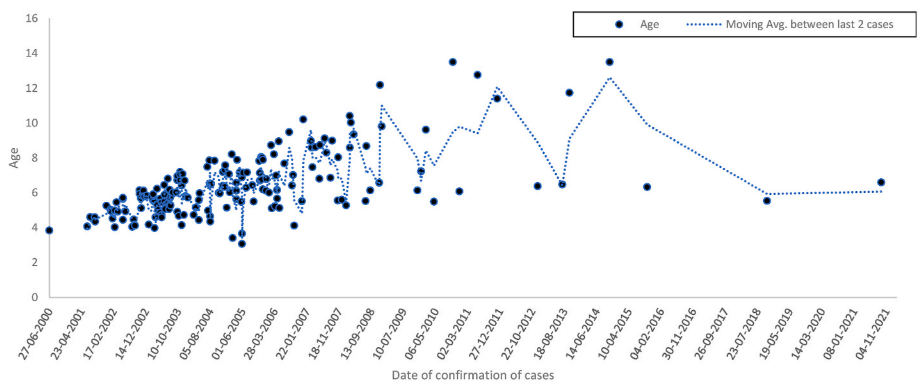

Fig. 3. Scatterplot of the age of classical BSE BARB cases and the date at detection of these cases.

different holdings (i.e. all cases were from 'single case holdings') located within a 17 Km radius area in Somerset, all observed during an eight month period (September 16, 2010 to April 19, 2011). Another farm located in the same area had a case in 2003. The ratio of observed to expected was 44.5 (P = 0.017; Fig. 4).

3.2. *Review of risk factors for emergence of cBSE BARB cases*

Several hypotheses have been formulated to explain the emergence of cBSE BARB cases, including spontaneous occurrence, contamination of feed with prions and environmental persistence of the agent in affected farms. The search provided a total of 571 published papers, of which 15 papers focused on risk factors associated with cBSE BARB or BAB cases and were selected for review (Fig. 5). The findings of the literature review on cBSE BARB and BAB risk factors are shown in Table 2. A descriptive study of the first 11 cBSE BARB cases in GB hypothesized that the likely source of infection was through feed contamination, based on the fact that all cases received commercial feed during the first year of life (Burke, 2009). Ortiz-Pelaez et al. (2012) undertook a case control study of BSE BARB cases reported up to July 31, 2009. In their study, control animals were clinical suspects that tested negative for BSE and were born in the same period as BARB cases. Risk factors identified were: (1) feeding with homemix concentrates (or homemix and proprietary concentrates) during the first six months of life; (2) age at detection, with cases tending to occur in older animals; and (3) previous history of BSE on the farm. A case-control study in Northern Ireland investigated the risk factors associated to 44 cBSE BARB cases from 40 herds. The study found evidence that cBSE BARB cases had increased odds of occurrence in dairy farms and with very weak evidence of association with areas with high herd density. Subsequent spatial analysis found evidence of spatial clustering of cases as opposed to random spatial distribution. Based on this, the authors rejected the hypothesis of spontaneous occurrence, and suggest that feed-borne routes are likely the route of infection. Yet, no clear direct evidence to support the latter argument was provided and the small number of cases in the study was an important limitation (Ryan et al., 2012).

In an earlier study conducted by Wilesmith et al. (2010), a notably uniform spatial distribution of BSE cases in the BARB phase compared to previous phases in the epidemic was observed. Based on this evidence, it was concluded by both Wilesmith et al. (2010) and Ortiz-Pelaez et al. (2012) that persistence of the BSE agent in the environment is an unlikely explanation for the occurrence of BSE BARB cases; and that the spatial distribution of BSE BARB risk is not consistent with the main source of exposure being from residual contaminated feed on farms or from a single feedborne source from within GB. Both studies indicated that the hypothesis for exogenous (non-GB) sources of contaminated feed as potential cause of cBSE BARB cases remains a plausible explanation.

Recent qualitative analysis of 60 cBSE BARB cases and unknown type of BSE BARB cases detected in 11 European countries, also failed to ascertain the source of infection for BARB cases (EFSA BIOHAZ Panel et al., 2017). This analysis included 24 BSE BARB cases from the UK (11 detected since 2009). The report concluded that feed-borne exposure was believed to be the most likely explanation. The long incubation period of the disease, spanning over several years, was the main challenge faced to determine exposure to contaminated feed. Arnold et al. (2017) indicated that the exponential decay of the disease, at a rate of 34% for EU countries, with a progressive reduction of exposure to risk factors, did not support a spontaneous origin of these cases. This was supported principally by the observed BSE data, with back-calculation modelling suggesting the best fitting model was that which declined ultimately to zero prevalence. No other studies directly investigated risk factors associated to cBSE BARB cases.

Several studies provided insight into factors associated with earlier feedban restrictions. Two studies identified the use of milk replacers or proprietary commercial feed as risk factors (Clauss et al., 2006; Jarrige et al., 2007). In Switzerland it was found that farms with a two Km and 10 Km proximity to feed manufactures had also higher odds of disease (Schwermer et al., 2007). Five studies showed evidence that potential

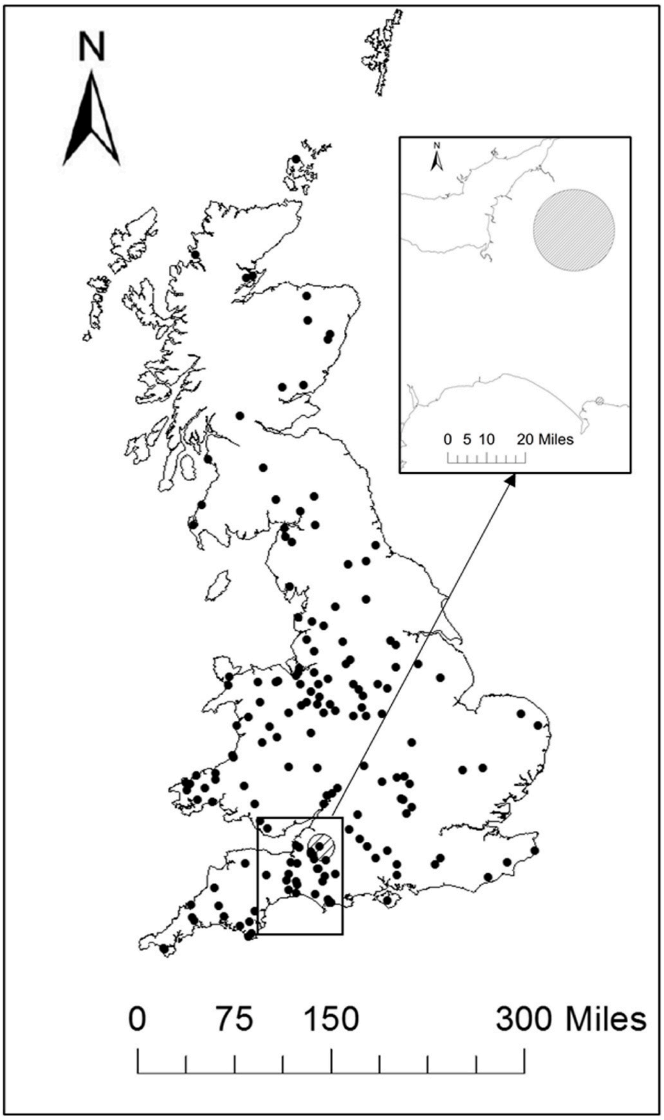

Fig. 4. Location of farms of origin of classical BSE BARB cases, jittered randomly within a circular disk of radius 5 km to preserve confidentiality, and the location of the spatio-temporal cluster.

cross-contamination from pig or poultry feed may have occurred (Abrial et al., 2005a; Allepuz et al., 2007; Jarrige et al., 2007; Ryan et al., 2012; Schwermer & Heim, 2007). Cattle herd density was found weakly associated in one study in Northern Ireland (Ryan et al., 2012). Three studies in France and Switzerland looking at spatial distribution of these cases found evidence of clustering (Doherr et al., 2002; Sala et al., 2012; Schwermer & Heim, 2007), while two studies in France and Spain did not (Abrial et al., 2005b; Allepuz et al., 2007). The authors suggest that regional effects influenced the occurrence of cases, including the late or lack of effective implementation of feedban measures. Studies in France however did not find evidence of differences in the spatial distribution of BAB cases born between 1990-1996 and 1996–2001 (Abrial et al., 2005b; Ducrot et al., 2005), while a study in Switzerland did not find a difference in the distribution of cases before and after the ban in 1990 (Schwermer et al., 2007).

3.3. Findings of investigation reports for classical BSE BARB cases detected after July 31, 2009

Nineteen farms provided epidemiological information for the investigation of 15 classical cBSE BARB cases detected since 2009. Six of the cases were born on a farm different from the farm of residence at the time when BSE was diagnosed. Four of these were purchased from local breeders within the same county; and two travelled as part of herd relocation to North Yorkshire and Scotland. The average herd size was 160 cattle, with the largest herd being 500 and the smallest 22.

Farms reported which feed suppliers were used during the time that the case animal was on the farm, and these were notably numerous and diverse. Thirty-five different feed suppliers were named by 17 farms, although one farm reported to use 13 different types of feed suppliers, while the rest had an average of 1.73 feed suppliers (2 farms did not supply this information). Only three of the feed suppliers were used by more than one of the case farms. One of these was a large national supplier that was used by four case farms; the other two were smaller companies, serving a limited local range, and were used by two case farms. Where the addresses of feed suppliers were given, they were usually within the local area of the farm. Two farms did not purchase feed, but purchased straw.

Four of the 19 cases were raised on a farm that used homemix feed for calves within their first six months of life. Feed storage was usually in bins, on the floor, or in bags. Eight farms mentioned their cleaning procedures, and descriptions differed greatly in the level of detail given, although mostly involved brushing/scraping, with no washing or disinfection mentioned.

Ten of the 19 farms declared that they owned sheep. Of these, six reported that no co-grazing between cattle and sheep took place. One farm reported that co-grazing may have occurred occasionally but that it was not typical, another stated that only lambs were co-grazed with cattle, and one reported that sheep grazed the same fields as cattle but not at the same time. One farm declared that co-grazing with sheep was typical practice. No likely contact with any other species or access to other species' feed was reported. Thirteen out of the 19 farms declared that dogs and/or cats were kept on the farm, although it was unclear whether the dogs would have had access to calf areas.

Nine farms reported previous BSE cases. Two of these also reported BSE cases that had calved within a month of birth of the BARB case, one of which noted that placentas were routinely removed after parturition (the other did not specify). Five of the farms reported that animals had access to a flowing watercourse (stream or river), all others were supplied only by mains water or a borehole on the farm.

As mentioned, only two cases were detected in the last seven years, which require special consideration. The cBSE case detected in 2018 was located in Aberdeenshire, Scotland. The affected cow showed clinical signs associated with a diagnosis of hypomagnesemia, but also compatible with BSE. Two days after treatment, she fell into a water course and the farmer decided to cull her. The cow died before the veterinarian arrived and was tested for BSE as part of the fallen stock active surveillance scheme. The case was a 5.4 year old pedigree cow (suckler) born in England and then moved to a holding in Scotland shortly after (in 2012), when the farm decided to relocate its herd. The herd was of a small-medium size (n = 22), which were raised together with a medium-size flock of ewes, although no co-grazing between species occurred. The place of birth was on land that historically contained a dairy and arable unit owned by the local council, and where three BSE cases were detected between 1992 and 1994. It was however reported that no feed storage/feeding equipment was present on the holding when the farmer started. The Scottish holding was used in the past to produce goats and store gardening products (compost). Cows were fed with home-grown haylage and grass. Straw was purchased from local farmers, concentrate feed was not used nor milk replacers were historically used for calves. The epidemiological investigation did not identify any plausible source of infection of this case (APHA, 2018).

The cBSE case detected in September 2021 was located in Somerset, England, on a farm of 300 dairy cows. The affected animal was a 6.6 year old homebred dairy cow who lived her whole life on the same farm. It developed milk fever (although not confirmed via biochemistry analysis), and was euthanized due to treatment failure. The carcass entered

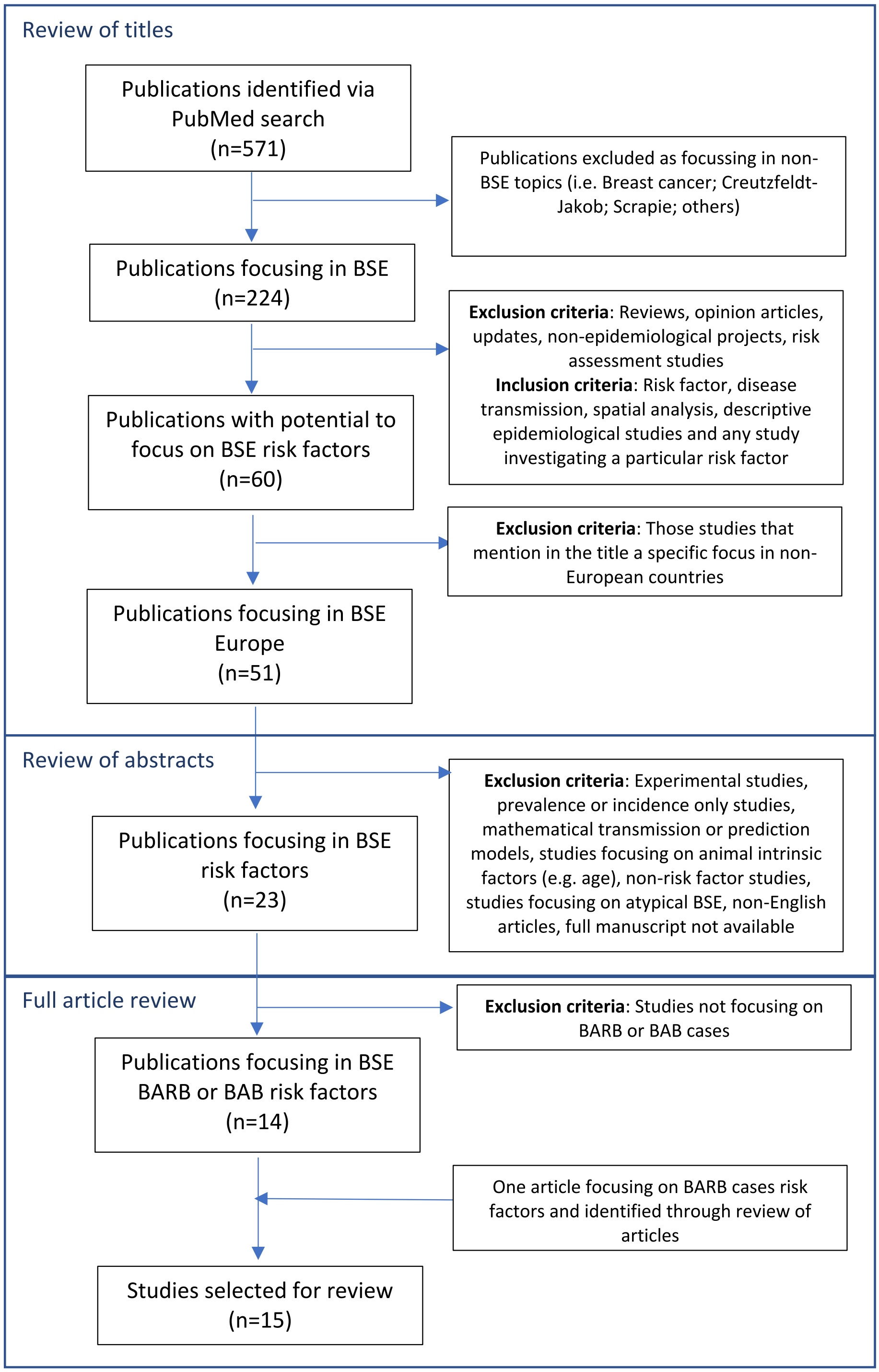

Fig. 5. Flow diagram of the literature review search results on classical BSE risk factors.

the fallen stock active surveillance scheme where it was diagnosed with cBSE. Historically, several BSE non-BARB cases were detected on the farm of origin, which were likely to have been fed with feed stored in silos on-farm. One of the silos that operated since the 1980s for dairy feed was still in use to store feed at the time of birth of the cBSE BARB case. The farm purchased commercial pellet feed from the same mill since the 1970s. It was reported that appropriate cleaning of that silo had never been carried out due to access problems, and as a consequence the epidemiological investigation suggested that the most likely source of infection was through residual material in the silo (APHA, 2021).

3.4. BSE policy response in Great Britain

Table 3 lists the key policies implemented in the UK for the control and surveillance of BSE. After evidence of disease transmission to cattle was obtained (Wilesmith et al., 1988), the policy of BSE control started with The BSE Order 1988 (SI 1988/1039), which came into effect on June 21, 1988. With this order the disease became notifiable and

Table 2
Risk factors and spatial analysis findings of studies investigating classical BSE cases occurring after initial and reinforced feedban in Europe.

Country and years of restrictions	Study	Type of study	BARB, BAB and control details	Risk factors and spatial clustering	Authors' Conclusion
Great Britain - 1988 ban ruminant -protein to cattle - 1994 ban mammalian protein to cattle - 1996 MBM ban to farm livestock - 2001 processed ban protein to livestock	Ortiz-Pelaez et al. (2012)	Case-control	**BARB:** 164 cases born after 1996 and detected until 2009; **Controls:** 499 BSE clinical suspects born after 1996	Homemix and proprietary concentrates during first six month of life (OR:2.56; 95%CI:1.29–5.07). Previous history of BSE on the farm (OR:0.59; 95%CI: 0.50–0.69) (protective). Increase age at detection. Areas with excess of BARB cases detected	Farms with previous cases more likely to notify BSE clinical suspicions. No evidence of environmental contamination. Some evidence of exogenous contamination and feed source of infection.
	Wilesmith et al. (2010)	Descriptive and spatial analysis	**BARB:** 164 cases born after 1996 and detected until 2008.	26 cases occurred as multiple cases. No evidence of BSE history in 53 (35.6 per cent) herds. The risk of infection of animals is reduced in the last phase of the epidemic, with uniforn geographical distribution.	Environmental contamination is unlikely to be a major risk factor for their occurrence.
	Burke (2009)	Descriptive Spatial analysis	**BARB:** 11 cases born after 2000	Commercial compound feed or commercially traded concentrate feed materials was used for all cases in their first year of life. Each farm however was supplied by different feed mill. No evidence of vertical transmission nor environmental contamination other than feed	Supports the hypothesis of foodborne infection of cases
	Stevenson et al. (2005)		**BAB** Cases born between 1988 and 1997	Lower mortality ratio for BSE in the Southwest and an increased ratio in the Southeast and Eastern regions of England. Areas with larger dairy cattle population. Areas with larger number of piggeries relative to cattle	Incomplete implementation of control measures in the Eastern counties. Low level cross-contamination of cattle feed with pig feednfluenced BSE incidence.
Northern Ireland - 1991 MBM to farm livestock; - 1996 removal of cadavers and SRM for animal feed - 2001 PAP ban to livestock	Ryan et al. (2012)	Case control	**BARB:** 9 herds with cases born after 2001, and 146 control herds; **BARB:** 31 herds with cases born post-1996, and 146 control herds ; **BAB:** 732 herds with cases born between 1991 and 1996; and 2365 control herds (no matching)	BARB risk factors: Dairy farm (OR: 14.53, 95%CI: 5.95–35.53). Spatial clustering of cases detected. BAB risk factors: Dairy farm (OR: 32.26, 95%CI: 16.11–49,79). Proportion of dairy farms in area. Number of piggeries in area. Number of poultry holdings in area.	Hypothesis of spontaneous occurrence was rejected. It was suggested that feed-borne routes are the most likely route of infection. No evidence found that contamination of BARB cases is different from non-BARB cases. BAB occurrence likely due to cross-contamination of cattle feed with MMBM from locally produced pig and poultry feed..
Germany - 1994 ban on feeding MBM to ruminants	Clauss et al. (2006)	Case-control	**BAB:** 110 dairy farms with cases born after 1994 and detected between 2000 and 2004; Controls: 4006 dairy farms	Proprietary concentrate feed used in animals of less than 12 months of age (OR:15.6, 9%CI:7.3–34.6). Proprietary milk replacer used in animals of less than 12 months of age (OR 12·9; 95%CI: 6·2–27·5). Combination of milk replacer and concentrate feed in animals of less than 12 months of age (OR:1·9; 95%CI: 1·6–2·2).	Possible contamination of MBM in cattle feed.
France - 1990 ban of MBM for cattle; - 1996 removal of cadavers and SRM for animal feed - 2001 reinforce ban	Jarrige et al. (2007)	Case-control	**BAB:** 184 cases; Controls: 184 cattle, matched geographically. Cases detected 2000–2002 and born after 1990	Consumption of proprietary concentrates before the age of two. Use of milk replacer (OR: 1.8, 95% CI: 1.0–3.1). Purchase of feedstuff for poultry (OR:1.8, 95%CI: 1.1.-3.0)	Contamination of MBM in cattle concentrate was the likely explanation for BSE occurrence. Possible cross-ontamination of cattle feed with poultry feed containing MBM may have occurred.
	La Bonnardiere et al. (2007)	Case-control	**BAB:** 145 farms with cases; Controls: 2900 farms; matched geographically; cases detected between 2001 and 2003; cases born between 1992 and 1998	Cows producing >10,000 kg of milk (OR:3.17; 95%CI:1.17–8:56). Age at 1st calving <27 month (OR: 2.15; 95%CI:1.21–3.82)	Rejected the hypothesis of association between farm intensification and BSE. Possible feed management associated to high yield may express increased risk.
	Ducrot et al. (2005)	Spatio-temporal analysis	**BAB**: 467 cases born after 1990 and 72 cases born after 1996; cases detected between 2001 and 2003	Highest risk area were different per birth cohort. Spatial patterns of risk were similar for the two type of BSE cases.	Hypothesis for spontaneous occurrence of BSE was rejected. Possible difference in effectiveness of control measures between areas. Transmission of infection likely to be the same for both type of cases.
	Abrial et al. (2005b)	Spatial analysis	**BAB:** 58 cases born after 1996; **BAB:** 445 cases born after 1990.	Significant spatial heterogeneity of both BSE cases. Areas of risk are the same for both cases.	Same source of contamination of both type of cases probable.
	Abrial et al. (2005a)	Spatial analysis	**BAB:** 467 cases born after 1990, detected between 2001 and 2003.	Increase density of pigs and poultry	Cross-contamination of MBM from pig or poultry feed has occurred

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Table 2 (*continued*)

Country and years of restrictions	Study	Type of study	BARB, BAB and control details	Risk factors and spatial clustering	Authors' Conclusion
Switzerland - 1990 - 1996	Schwermer and Heim (2007)	Case-control and spatial analysis	**BAB:** 34 cases born after 1996 (BAB96); **BAB:** 170 cases born after 1990 (BAB90); Controls: 44,689 farms; no matching	Spatial Cluster for both type of cases identified. Presence of small ruminants for BAB96 (OR:1.9, 9% CI:1.0–3.8). Presence of pigs for BAB90 (OR: 4.1, 95%CI: 2.9–5.7). Pig cattle ratio of more than one for BAB90 (protective) (OR: 0.1, 95% CI:0.08–0.21).	Clustered farms tend to also produce pigs. Cross-contamination of feed suggested as the likely cause. Contamination of feed with MBM remains the most likely source of infection.
	Schwermer et al. (2007)	Spatial analysis	**BAB:** 216 cases born after 1990 and detected until 2005	Feed producers positive for MBM as posible cluster centers for BSE cases . Proximity to feed producer by 2 km and 10 km increase risk	Cross-contamination was the likely route for BSE transmission after the feed ban.
	Doherr et al. (2002)	Spatial analysis	**BAB:** 354 cases born before 1990; Controls: 2000 holdings AND 239 BSE case born before 1990; no matching	Spatial clustering of cases detected. Stronger evidence of spatial clustering of cases born after the ban compared to those born before the ban	Possible regional effects of the feed ban on the exposure of cattle.
Spain 1998 (ban in 1996 but enforced in 1998)	Allepuz et al. (2007)	Spatial analysis	**BAB:** 49 BSE cases born after 1998; Controls: 175 cases born before 1998.	No spatial cluster detected on cases born after 1998. Correlation between pig population and BSE risk	Risk of infection was not homogenous. Control measures effectively reduced risk. Gradual implementation of measure may explain partly the association with pig population.

affected farms had movement restrictions imposed, where they were required to have their premises and equipment cleaned and disinfected at farmers' expense. The order also implemented a slaughter and compensation policy and a feed ban of ruminant-derived Meat and Bone Meal (MBM) to cattle farms, which did not include milk or any milk product or dicalcium bone phosphate. The BSE (No 2) Amendment Order 1990 (SI 1990/1930), subsequently extended the ban on the use of specified bovine offal to any animal feed. Exports to other EU Member States of such feed were also effectively banned. Third country exports were banned on July 10, 1991, by The Export of Goods (Control) (Amendment No 7) Order 1991 (SI 1991/1583) controlling the export to third countries of Specified Bovine Offals (SBOs) and feeding stuffs containing SBOs.) In that year, the Spongiform Encephalopathy Advisory Committee (SEAC) was established to provide independent advice to the government.

On March 20, 1996, SEAC announced that the CJD Surveillance Unit had identified a previously unrecognised and consistent disease pattern. The Committee concluded that although there was no direct evidence of a link, the most likely explanation was that these cases were linked to exposure to BSE before the introduction of the SBO ban in 1989. The government announced its intention to consult on further control measures. The legislation that followed required carcases from cattle aged over 30 months (OTM) to be deboned in specially licensed plants supervised by the Meat Hygiene Service and for the trimmings to be kept out of the food chain; and it banned the use of mammalian meat and bonemeal in feed for all farm animals.

On March 27, 1996, given the number of cases detected in the UK and SEAC's advice on the link to human health, the EU implemented a ban on the export from the UK of live bovine animals, their semen and embryos; meat of bovine animals slaughtered in the country; products obtained from bovine animals slaughtered in the UK which were liable to enter the animal feed or human food chain, and materials destined for use in medicinal products, cosmetics or pharmaceutical products; and mammalian derived meat and bone meal.

On March 29, 1996, on the advice of SEAC, the BSE (Amendment) Order 1996 (SI 1996/962) prohibited the sale or supply of any mammalian meat and bone meal (MMBM), or any feeding stuff known to include MMBM, for the purpose of feeding to farm animals, including horses and farmed fish. A voluntary recall scheme of MMBM and feed containing MMBM from farms, feed dealers and feed manufacturers was implemented in the UK, which successfully managed to recall 11,000 tonnes (Ortiz-Pelaez et al., 2012).

In 2001, the ban was further re-enforced following the new EU regulations (Council Decision 2000/766/EFSA-BIOHAZ-Panel EFSA Panel on Biological Hazards, 2014/9/EC), which prohibited the use of processed animal-protein to feed farmed animals, with the exception of dairy products. The rules were relaxed in 2008 to permit the use of fishmeal, but only to young unweaned calves. This total feed ban still continues in the UK. However, recently EU regulations (EU Regulation 2021/1372) have partially lifted the ban and currently authorize the use of pig and insect PAP in poultry feed, and the use of poultry and insect PAP in pig feed, as well as the use of ruminant collagen and gelatine in non-ruminant feed. This decision was justified on the basis of the lack of TSE infections in non-ruminants and on the outcomes of risk assessments (EFSA-BIOHAZ-Panel et al., 2018). With the UK now being outside of the EU, this new regulation has no effect, and Defra has commissioned their own risk assessment to decide on whether to implement a similar policy.

In 1999 and 2000, two limited surveys were undertaken in GB to assess prevalence levels in the healthy cattle population over 30 months old. Large scale active surveillance across the EU commenced in 2001 with the testing of 1) healthy cattle over 30 months old that were slaughtered for human consumption and 2) 'risk' cattle, i.e. those cattle over 30 months old that died or were culled (fallen stock) or were slaughtered for human consumption as casualties (e.g. with a broken leg) or failed an ante mortem inspection. The start of active surveillance in the UK was delayed from January to June that year due to the Foot and Mouth Disease restrictions occurring at that time. The age of 'risk' cattle to be tested was reduced to over 24 months by the Commission Regulation (EC) No 1248/2001 in June 2001. The age limit increased to 48 months on January 1, 2009, with a further increase in the age limit to 72 months for healthy slaughtered cattle on July 1, 2011. From February 1, 2013, healthy animals born within the EU (except for Romania, Croatia and Bulgaria) entering the food chain were no longer required to be tested.

Policies aiming to avoid consumer exposure to prion were also implemented, and responsible for the large economic impact on the industry. In 1989, the Bovine Offal (Prohibition) Regulations 1989 (SI 1989/2061) banned the use of high risk SBO for human consumption in England and Wales. Similar legislation was implemented in Scotland and Northern Ireland in 1990. These offals were the brains, spinal cord, thymus, tonsils, spleen, intestines derived from bovine animals aged more than 6 months at slaughter. In 1990, the BSE (No 2) Amendment Order 1990 (SI 1990/1930) extended the ban on the use of SBO to any animal feed. The rules on SBO were updated by the SBO Order 1995 (SI

Table 3
Major policies implemented in Great Britain for the control and monitoring of BSE.

Implemented	Policy	Measures
Jul 14, 1988	BSE order 1988 (SI 1988/1039)	BSE as a notifiable disease. Movement restrictions of cattle in affected farms. Cleaning and disinfection of affected farm at farmers expenses. Ban of ruminant-derive MBM feed to ruminants, except milk.
Aug 8, 1988	BSE (Amendment) Order 1988 (SI 1988/1345) and BSE Compensation Order 1988 (SI 1988/1346)	Provided for a slaughter policy and payment of compensation.
Dec 22, 1988	Zoonosis Order 1988 (SI 1988/2264)	Designated BSE as a zoonosis, enabling powers under the Animal Health Act 1981 to be used to reduce the risk to human health from BSE.
Jul 28, 1989	89/469/EEC	European commission impose export ban on live cattle born before in UK July 1988 and offspring of affected animals.
Nov 13, 1989	Bovine Offal (Prohibition) Regulations 1989 (SI 1989/2061)	Banned the use of certain specified bovine offals (SBO) for human consumption.
Mar 27, 1990	90/59/EEC	Export ban to live cattle aged over six months.
Apr 9, 1990	90/200/EEC	Ban of high risk offals for human consumption. These are brains, spinal cord, thymus, tonsils, spleen, intestines derived from bovine animals > six month old.
Sep 25, 1990	BSE (No 2) Amendment order 1990 (SI 1990/1930)	Extension of the ban on the use of specified bovine offals to any animal feed. Exports to other Member States of such feed also effectively banned.
Oct 15, 1990	Bovine Animals (Identification, Marking and Breeding Records) Order 1990 (SI 1990/1867)	Introduction of new record keeping arrangements requiring cattle farmers to maintain breeding records which, with movement records, were to be retained for ten years.
Mar 12, 1992	Bovine Offal Prohibition (Amendment) Regulations 1992 (SI 1992/306)	Prohibited the use of the head after the skull is opened (effectively minimising risks of contamination of head meat by the process of brain removal) and the removal of the brain, except in an area free at all times from any food intended for human consumption.
Jan 1, 1993	Animals and Animal Products (Export and Import) Regulations 1992 (SI 1992/3295)	Implemented Commission Decision 90/200/EEC in domestic law by prohibiting the export of bovine animals not complying with Community legislation listed in Schedule 3 (including BSE Decisions)
May 14, 1992	92/290/EEC	Prohibited intra community trade in bovine embryos derived from BSE suspect or confirmed dams or dams born after July 18, 1988
Jun 27, 1994	94/381/EC	Prohibited the feeding of mammalian protein to ruminants throughout EU
Jul 27, 1994	94/474/EC	Introduced new measures on beef exports. Bone-in beef for export was to come only from cattle certified not to have been on holdings where BSE had been confirmed in the previous 6 years.
Nov 2, 1994	Bovine Offal (Prohibition) (Amendment) Regulations 1994 (SI 1994/2628)	Extended the controls in the principal regulations to include thymus and intestines of all bovine animals, except those under two months which have died.
Nov 2, 1994	Spongiform Encephalopathy (Miscellaneous Amendments) Order 1994 (SI 1994/2627)	Extended the ban on the use of SBOs in animal feed, banned the use of mammalian protein in ruminant feeding stuffs and made notifiable laboratory suspicion of spongiform encephalopathies in species other than cattle, sheep and goats.
Jan 1, 1995	94/382/EC	Alternative heat treatment systems for processing animal waste of ruminant origin, with a view to the inactivation of spongiform encephalopathy agents
Mar 6, 1995	95/60/EC	Lifted the restriction in Commission Decision 94/381 on the use of milk, gelatin, amino acids, dicalcium phosphate and dried plasma and other blood products from mammalian tissues in feedingstuffs for ruminants.
Apr 1, 1995	Fresh Meat (Hygiene and Inspection) Regulations 1995 (SI 1995/539)	Implemented Commission Decision 94/474/EC as amended by Commission Decision 94/794/EC by requiring, in meat cutting premises, the removal of spinal cord from bovines >6 months and the removal and collection of obvious nervous and lymphatic tissue and the prohibition of its use for human consumption.
Jul 18, 1995	95/287/EC	Introduced new measures on beef exports. The previous requirement to exempt beef from cattle born after January 1, 1992 from certification requirements was replaced with provision to exempt beef from cattle less than 2½ years of age at slaughter. It also introduced requirement for routine monitoring in feed mills.
Aug 15, 1995	Specified Bovine Offal Order 1995 (SI 1995/1928)	Consolidated and streamlined the old rules on SBO. The main changes introduced were tighter controls on record keeping; dedicated lines for rendering plants processing SBO; a prohibition on the removal of brains and eyes so that the whole skull must be disposed of as SBO and a prohibition

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Table 3 (*continued*)

Implemented	Policy	Measures
		on the removal of the spinal cord from the vertebral column apart from in slaughterhouses.
Dec 15, 1995	Specified Bovine Offal (Amendment) Order 1995 (SI 1995/3246)	Prohibited the export of bovine mechanically recovered meat (MRM) made from the vertebral column for human consumption.
Jan 1, 1996	Fresh Meat (Hygiene and Inspection) (Amendment) Regulations 1995 (SI 1995/3189)	Implemented Commission Decision 95/287/EC by imposing, in meat cutting premises, the requirement to remove specific lymph nodes from meat intended for export or consignment to an EEA State and derived from bovines over 2½ years at slaughter.
Mar 27, 1996	96/239/EC	Prohibited the export from the UK of live bovine animals, their semen and embryos; meat of bovine animals and products obtained from bovine animals slaughtered in the UK which were liable to enter the animal feed or human food chain, and materials destined for use in medicinal products, cosmetics or pharmaceutical products; and mammalian derived meat and bone meal.
Mar 29, 1996	Bovine Spongiform Encephalopathy (Amendment) Order 1996 (SI 1996/962)	Prohibited the sale or supply of any mammalian meat and bone meal, or any feeding stuff known to include mammalian meat and bone meal, for the purpose of feeding to farm animals, including horses and farmed fish.
Mar 29, 1996	Specified Bovine Material Order 1996 (SI 1996/963)	Replaced the Specified Bovine Offal Order 1995 and introduced a requirement that the whole head of all cattle over six months, except for the tongue (provided it was able to be removed without contamination), must be treated in the same way as material designated as 'specified bovine offal'.
Mar 29, 1996	Beef (Emergency Control) Order 1996 (SI 1996/961)	Prohibited the sale for human consumption of any meat from bovine animals showing more than two permanent incisors. Amended on April 4, 1996 to provide for the use of Cattle Identification Documents to identify the age of animals if they had more than two permanent incisors erupted, on April 13, 1996 to exempt meat derived from animals slaughtered in certain third countries where no cases of BSE had been recorded, on April 29, 1996 to provide for a document which could demonstrate the age of cattle in which more than two permanent incisors had erupted and which were not issued with a national identification document. Revoked on July 5, 1996.
Apr 3, 1996	Changes to the Beef (Emergency Control) Order	Introduction of a 30 month slaughter scheme to ensure that all bovine animals over the age of 30 months at the time of slaughter did not enter the human food or animal feed chain.
Apr 4, 1996	The Beef (Emergency Control) (Amendment) Order 1996 (SI 1996/1043)	Provided for the use of Cattle Identification Documents to identify the age of animals if they had more than two permanent incisors erupted
Apr, 1996	Support schemes	Over 30 month scheme; Calf processing Aid scheme; Selective culling scheme
May 1, 1996	Specified Bovine Materials (No 2) Order 1996 (SI 1996/1192)	Amended and replaced the Specified Bovine Material Order 1996. Its effect was to amend the way in which existing controls applied to specified material from animals slaughtered under Commission Regulation 716/96. It required specified bovine material (SBM) to be removed from carcases and to be handled separately. The carcase meat from cattle slaughtered under the Commission Regulation had to be dyed a different colour from SBM. The Order also brought the existing rules on rendering and disposal into line with EU requirements.
Jun 10, 1996	Voluntary animal feed recall scheme	Voluntary recall of MMBM and feed-containing MMBM from farms, feed merchants and feed mills.
Jun 24, 1996	96/385/EC	EU approval of UK BSE control and eradication plan
Jul 1, 1996	The Cattle Passports Order 1996 (SI 1996/1686)	Introduction of mandatory cattle movement documents ('cattle passports') in GB for all cattle born from July 1, 1996. This gave way to the development of a computerised system for recording of birth, deaths and movements (the Cattle Tracing System) which was implemented in 1998.
Aug 1, 1996	Bovine Spongiform EFSA-BIOHAZ-Panel EFSA Panel on Biological Hazards, 2014 (SI 1996/2007)	Revoked and remade the BSE 1991 Order. New provisions included requirements on animals exposed to BSE, the prohibition on the possession of MBM on premises where livestock feeding stuffs were kept, the disposal and recall of MBM and the cleansing and disinfecting of places, vehicles and equipment where MBMs had been produced, stored or used.
Sep 1, 1996	The Fresh Meat (Beef Controls) (No. 2) Regulations 1996 (SI 1996/2097)	Ban of cattle over 30 months of age for human consumption (Over 30 month rule)

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Implemented	Policy	Measures
Dec 16, 1996	Support scheme	The selective cull of cattle most at risk of BSE was announced.
Jan 24, 1997	BSE order 1996 (SI 1996/3183)	Ban of mammalian MBM to livestock, horses and farmed fish Cleaning and disinfection of producers and transporters of mammalian MBM Records keeping requirement for people dealing with mammalian MBM
Mar 15, 1997	Bovine Products (Production and Despatch) Regulations 1997 (SI 1997/389)	Implemented Commission Decision 96/362/EC, consolidated existing regulations and contained registration provisions for by-products and meat products production, production controls and end-use restrictions.
Dec 16, 1997	The Beef Bones Regulations 1997 (SI 1997/2959)	Beef on the bone and all beef-bone derived products were prohibited from sale
Jan 1, 1998	97/534/EC	The destruction and prohibition of the use of Specified Risk Materials
Jan 1, 1998	The Specified Risk Material Regulations 1997 (SI 1997/2965)	Provided for controls on specified risk material (SRM)
Mar 16, 1998	96/239/EC	EU laid down the conditions to allow UK export of beef, veal and other bovine products falling within the Date-Based Export Scheme.
Nov 25, 1998	98/692/EC	Amended Decision 98/256/EC to provide for the Date-based Export Scheme.
Jan 4, 1999	The BSE Offspring Slaughter Regulations 1998 (SI 1998/3070)	Provision for implementing a compulsory cull of offspring born on or after August 1, 1996 to BSE cases confirmed before November 25, 1998.
Apr 15, 1999	The BSE (Feeding Stuffs and Surveillance) Regulations 1999 (SI 1999/882)	Implemented EU obligations on feed sampling and epidemiological surveillance.
May 1, 1999	The Bovines and Bovine Products (Trade) Regulations 1999 (SI 1999/1103)	Implemented Council Decision 98/256/EC (as amended) and replaced the 1998 Regulations (SI 1998/1135). New provisions for the setting up and operation of the Date-based Export Scheme.
Jul 31, 1999	Lift of calf processing Aid Scheme	Lift of calf processing Aid Scheme.
Aug 1, 1999	Lift of EU export ban on boneless products	Relaxation of EU export ban for boneless British beef products from animals aged between six and 30 months.
Aug 1, 1999	Launch of DBES	Date Based Export Scheme launched.
Dec 17, 1999	The Beef Bones (Amendment) (England) Regulations 1999 (SI 1999/3371)	Lift of ban on sale of beef on the bone.
Dec 1, 2000	The Cattle (Identification of Older Animals) Regulations 2000 (SI 2000/2976)	Implemented the provisions of Council Regulation 1760/2000 in relation to older cattle. They required cattle born before July 1, 1996 on a voluntary basis to be registered; they required the location of all cattle with passports without movement cards not already registered with the Minister to be notified; provided for the issue of movement cards to cattle born before September 28, 1998 and required notification to the Minister when these animals were moved; and provided for the use of electronic notification of movement as an alternative to notification using movement cards, and for a register of approved users of electronic notification.
Dec 4, 2000	2000/766/EC	Temporary EU-wide ban on the feeding of processed animal proteins to farmed animals kept for the production of food.
Dec 18, 2000	2777/2000/EC	Required the UK to ensure that any meat from animals aged over thirty months can only be released for human consumption in the Community or third countries if tested negative for BSE. The Regulation also laid out the rules for the purchase for destruction schemes in other Member States.
Jan 1, 2001	2000/766/EC	Ban of all processed animal protein in feed for farmed animals, with exception of fishmeal to animals other than ruminants, gelatine of non-ruminants, dicalcium phosphate and milk and milk products.
Jan 1, 2001	EFSA-BIOHAZ-Panel EFSA Panel on Biological Hazards, 2014/764	Start of Active surveillance, with testing of a sample of cattle over 30 months old that are culled, slaughtered, and that have died (fallen stock surveillance scheme). Not implemented in UK due to Foot-and-Mouth outbreak.
Jun 22, 2001	EC 1248/2001	Surveillance programme expanded to include all cattle over 24 months of age that are, fallen stock, emergency slaughter and clinical signs at post-mortem, and all healthy cattle over 30 months of age slaughtered for human consumption.
Jul 1, 2001	EC 999/2001 ("the EU TSE Regulation")	Rules for the prevention, control and eradication of certain transmissible spongiform encephalopathies. This sets for all EU countries the 1) Classification criteria of BSE status, 2) Start of active surveillance, 3) Total feed ban, 4) Specified risk materials.
Jul 1, 2001	The BSE Monitoring (England) Regulations 2001 (SI 2001/1644)	Implemented the requirements of Commission Decisions 2000/764/EC and 2001/233/EC and required the person in possession or in charge of a notifiable bovine animal (a dead or culled bovine animal aged over 30 months) to notify its death.

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Table 3 (*continued*)

Implemented	Policy	Measures
Aug 1, 2001	The Processed Animal Protein (England) Regulations 2001 (SI 2001/2376).	Council Decision 2000/766/EFSA-BIOHAZ-Panel EFSA Panel on Biological Hazards, 2014/9/EC fully implemented in the UK.
Apr 19, 2002	The TSE (England) Regulations 2002	First consolidated TSE Regulations in GB.
May, 2003	1774/2002/EC	SRM become ABP category 1. Prohibition to bury dead animals on farm.
Jul 1, 2003	Animal By-Products Regulations 2003	Laid down health rules for animal by-products not intended for human consumption and included updated controls on the transport, processing and disposal of SRM.
Sep 1, 2003	EC Regulation 1234/2003	Amended 999/2001, EC) No 999/2001, making permanent the previously transitional measures relating to EU-wide feed controls.
Jul 15, 2005	The TSE Road Map 1	Considering of changes in SRMs, some relaxation in feed ban (i.e. low levels of fishmeal in ruminants); reduction in number of test for surveillance by increasing age at slaughter; relaxation of culling requirement for birth cohorts and feed cohorts of positive animals; and lifting additional export restrictions to live cattle from the UK.
Nov 7, 2005	The Bovine Products (Restriction on Placing on the Market)) Regulations 2005 (SI 2005/1979)	. Remove ban on cattle over 30 month to enter the food chain. The OTM Rule was replaced with a robust testing system for cattle born or reared in the UK after July 1996. Prohibition to sell products from cows born before August 1, 1996 The Beef Assurance Scheme closed.
Jan 23, 2006	End of OTMS	The OTM Scheme closed. The Older Cattle Disposal Scheme (OCDS) commenced for cattle born or reared in the United Kingdom before August 1996.
Mar 8, 2006	End of EU export ban proposed	The EU Standing Committee on the Food Chain and Animal Health (SCoFCAH) adopted unanimously a favourable opinion on the European Commission proposal to lift the embargo on UK exports of live cattle born after August 1, 1996, beef and beef products.
May 2, 2006	657/2006/EC	Lifted the ban on the export of cattle and beef products from the UK.
May 3, 2006	The TSE (No. 2) Regulations 2006 (S.I. 2006/1228), the TSE (Wales) Regulations 2006 (S.I. 2006/1226 W.117)) and the TSE (Northern Ireland) Regulations 2006 (S.R. 2006/202)	Domestic legislation came into force, implementing Commission Regulation (EC) No.657/2006. The Date Based Export Scheme (DBES) and the Export Approved Scheme (XAP) closed with immediate effect and SRM controls were harmonised with other EU countries.
Jan 26, 2007	1923/2006/EC	Allow the feeding of fish derive protein to young (unweaned) ruminants
Jun 29, 2007	2007/453/EC	Established the BSE status of Member States or third countries or regions thereof according to their BSE risk
Apr 26, 2008	357/2008/EC	Amended Annex V to Regulation (EC) No 999/2001, increasing the age limit for removing vertebral column, including dorsal root ganglia of bovine animals, as specified risk material from 24 to 30 months, and amending the definition of specified risk material in Annex V to Regulation (EC) No 999/2001 accordingly.
Jul 17, 2008	571/2008/EC	Amended Annex III to Regulation (EC) No 999/2001, laying down the criteria for Member States to apply for revision of their annual BSE monitoring programmes.
Dec 5, 2008	2008/908/EC	Authorised fifteen Member States, including the United Kingdom, to revise their annual BSE monitoring programme by raising the lower age limit for BSE testing from >24/30 months to >48 months. Implemented in UK on Jan. 1, 2009.
Jul 16, 2010	TSE roadmap 2	Considering relaxation of the feedban for non-ruminants; further increase in age of animals tested in BSE surveillance and sample size requirements; and to stop systematic culling of cohorts in BSE affect herds.
Jul, 2011	2009/719/EC	EC authorizes the UK to raise the age of cattle to be tested for BSE for the active surveillance to over 72 month of age for cattle slaughter for human consumption, and risk animals of 48 month of age for cattle (fallen stock, emergency slaughter and clinical signs at post-mortem).
Mar 1, 2013	Change in BSE testing	Risk animals aged >48 months to be tested (>24 months if born in Romania, Bulgaria, Croatia or third countries). Healthy slaughtered animals no longer required to be tested unless born in Romania, Bulgaria, Croatia or third countries.
Jul 1, 2017	Com. Reg. (EU) 893/2017:	Allow the export of ruminant and non-ruminant PAP, under certain conditions.

Table 4
Cost structure of the BSE epidemic in the UK.

	Cost type
Disease control	Losses due to animals death or culled
	Cost of compensations given
	Cost of cleaning and disinfection of affected premises
	Testing of suspected animals (passive surveillance) – including veterinary visit, sample collection and shipment, testing and processing
	Losses due to not being able to sell beef on bones or beef on bone products
	Losses from not selling cattle over 30 month age
	Cost of the feed recall program
	Cost of the testing feed
	Revenue forgone from SRM
	Cost on enforcement of controls in abattoirs and other premises (meat inspectors, vet, auditers)
	Cost of removing SRM (including training, staff time and facilities)
	Cost of rendering systems for the destruction of SRM and positive cattle
	Cost of epidemiological investigation of positive animals
	Cost on policy development
	Cost on disease communication and reporting
	Revenue forgone from EU ban to UK cattle and cattle products
	Cost of the Beef Marketing Payment Schemes, the Slaughtering Industry (emergency aid) scheme, The Rendering Industry Support scheme, The Beef and Beef Product scheme, The Movement of Hide scheme, The Beef Special Premium Scheme and the Suckler Cow Premium Scheme
Surveillance cost	Cost of testing animals in slaughterhouses (including cost of logistics, setting contracts, etc.)
	Cost of testing animals in the fallen stock scheme
	Cost associated to data management, epidemiological analysis and reporting
Human health costs	Losses due to human death and illnesses
	Losses due to psychological impact on farmers (reduce performance, consultations, etc.)
	Cost of treatments and medical consultations (including travelling)
	Cost of cleaning and disinfections in hospitals and human health centres
Indirect costs	Reduce price in beef products
	Losses due to reduce production of affected farms during following years
	Revenue forgone from exporting live beef (as not free BSE status)
	Reduce productivity in poultry and pigs due feedban on MMBM
	Loss in UK comparative advantage in beef production
	Cost of surveillance and control of Scrapie and Chronic Wasting Disease
Fixed costs	Cost of BSE reference centre and other laboratories
	Research funding on BSE (by government, universities, industry and others)

Table 5
Positive developments that followed the BSE epidemic.

Benefits
Changes in feeding and husbandry practices that reflect the natural need of animals (cow eating their natural food) (O'Brien, 2000)
Triggered the development of an independent organism for food safety control (Food standards agency)
Increased capacity in prions research
Increased prevention and control of other TSEs
Increased collaboration activities between animal and human health sectors for novel emerging disease
Development of novel tools for the diagnosis of prions
Triggered the need for better electronic traceability and recording system
Employment generated for the control of the epidemic and other epidemic diseases
Increased consumption of alternative products (other industry benefited)
Helped generate people awareness on food production and controls
Increased preparedness to major shocks to disease emergence, in particular to zoonotic diseases

1995/1928).

In 1996 cattle over 30 months of age were banned from human consumption, a restriction that remained until 2005 (known as the OTM rule). The policy was implemented together with the introduction of the Over 30 months scheme, which provided farmers the opportunity to voluntarily sell their old animals to the government (to the Intervention Board for Agricultural Produce) for slaughter and destruction, and receive financial compensation at market values. Given the large number of these animals to be slaughtered and disposed of in a short period of time, the scheme also included a payment fee to selected abattoirs and renderers facilities (NAO National Audit Office, 1998). In response to the EU ban on the export of calves from the UK, a calf processing aid scheme was implemented, under which farmers sold male calves to the government for slaughtering in order to help reduce the beef cattle population. The scheme was heavily criticized under welfare grounds (Hansard, 1997). About 1.7 million calves were slaughtered until the termination of the scheme in November 1999 (Hansard, 1999). A Selective Cull scheme (EC 1484/96) was also implemented in 1996, which aimed at identifying and culling animals most at risk of contracting BSE, which were those of the same cohort as confirmed BSE cases born before June 1993. Further schemes were also implemented to provide support to different the sectors within the industry, such as the Beef Marketing Payment Schemes (to support beef finishers from fall in prices), the Slaughtering Industry (emergency aid) scheme (to support abattoirs and cutting plants from potential collapse of the value chain), The Rendering Industry Support scheme (to support renderers from loss of income and increase in prices), The Beef and Beef Product scheme (to support business storing unsellable beef products), The Movement of Hide scheme (to support tanneries on the control and loss of their products), The Beef Special Premium Scheme and the Suckler Cow Premium Scheme (representing an increase subsidy to farmers based on number of animals produced). The details of these schemes and their costs are presented in the report produced in 1998 by the National Audit Office (NAO National Audit Office, 1998).

The Beef Bones Regulations 1997 (SI 1997/2959) required the deboning of all beef derived from cattle both home-produced and imported aged over 6 months at slaughter before it was sold to consumers. This ban was lifted in 1999. In 1997 the European Commission Decision 97/534, implemented in domestic law by the Specified Risk Material Order 1997 (SI 1997/2964), created the classification of Specified Risk Materials, which comprised the skull, brain, eyes, tonsils and spinal cord of bovine animals over 12-month-old and ovine and caprine animals over 12 months of age (the spleen was also a SRM for small-ruminants). These materials had to be stained and destroyed. The classification of SRM has changed over time. In Annex V of Regulation (EC) No. 999/2001, as retained at EU Exit, the SRM list comprises:

(i) the skull excluding the mandible and including the brain and eyes, and the spinal cord of animals aged over 12 months;
(ii) the vertebral column excluding the vertebrae of the tail, the spinous and transverse processes of the cervical, thoracic and lumbar vertebrae and the median sacral crest and wings of the sacrum, but including the dorsal root ganglia, of animals aged over 30 months; and
(iii) the tonsils, the last 4 m of the small intestine, the caecum and the mesentery of animals of all ages.

Only point (i) above is mandatory if the risk status is changed from controlled to negligeable in the future.

On November 7, 2005, the UK replaced the OTM rule, with the pre-1996 rule, which permanently excluded bovines born before August 1, 1996 from the food and feed chain. The export of such animals remains prohibited by Regulation (EC) No. 999/2001, as retained following EU exit.

Two TSE policy strategies were formulated in the EU as TSE roadmap One (covering the 2005–2009 period) and TSE roadmap Two (covering 2010–2015). These Roadmaps provided an outline of possible future changes to EU measures on TSEs in the short, medium and long-term while still making food safety and consumer protection the highest priority. Amendments to the TSE rules, including relaxation of surveillance, feed bans and control measures, were to be taken following a stepwise approach supported by a solid scientific basis. Since 2015, no strategic plan has been published on TSE in the EU or the UK. The full chronology of BSE in GB until the period 2010 is presented in the Annexes. This chronology is an internal document produced by the Department of Environment, Food and Rural affairs (DEFRA, 2010). Earlier versions were published on the Defra website and in the GB Progress Report on BSE published by Defra, which ceased publication in December 2001, but the document was regularly updated internally until 2010.

3.5. BSE impact in Great Britain

The impact of BSE in the United Kingdom has not comprehensively been calculated, but it has affected numerous sectors. On the year that BSE was recognized as zoonotic, the disease was calculated to have a cost of £1.5 billion, of which half of it (£0.8 billion) was associated to the over 30 months scheme (£640 million was used to compensate farmers under this scheme) (NAO National Audit Office, 1998). By April 2000, the BSE inquiry report estimated that the total UK expenditure on BSE control measures was £4.2 billion (BSE Inquiry, 2000). Cunningham (2003) calculated the cost of the epidemic in Europe as the loss of 10% of the annual output of the beef sector, totalling to €92 billion for the epidemic period. These were crude calculations and more detailed analyses are needed to understand the past impact of disease and the current impact of control and emerging BARB cases. For instance, the early crisis not only had an impact on supply losses, but also a negative effect on prices (Turner & Leeming, 2004). A drop of 40% in the consumption of beef occurred when the zoonotic link of the BSE prion was established, with meat consumers switching to pork or poultry. This precipitated a fall of 25% in beef prices, but with farm gate prices falling more than double than retail prices (Lloyd et al., 2006; Sanjuán & Dawson, 2003). As a consequence, by 1999 59% of beef abattoirs operating in the 1990s exited the industry in the UK (Lloyd et al., 2006).

The United Kingdom was also affected through an EU ban in 1989 on export of live cattle born before July 1988 (Legislation), and subsequently an export ban of all cattle older than six month in 1990 (EC, 1990). In 1996 a worldwide export ban of animals and products was imposed (Legislation). Prior to the ban in 1996 the UK was exporting around 39,000 calves and 23,000 tonnes of fresh and frozen carcass beef per month. (Lloyd et al., 2006). The UK export trade in beef and live cattle was worth about $800 million per year (Carter & Huie, 2001). The ban was relaxed in 1999 to allow de-boned beef and beef products from the UK from those animals with less than 30 months of age born after August 1, 1996. Yet, this measure did not increase significantly the exports of UK beef (legislation). France and Germany refused to lift the ban, which triggered legal actions from the UK government. Germany allowed UK exports in 2000, while France only allowed these in 2002. The worldwide ban, for animals born after August 1, 1996, was finally lifted by the EU in 2006 after confirmation that BSE incidence was below 200 cases per million. However, the ban for UK beef animals and products persisted in other third countries, with the United States of America only lifting the ban in 2020. China agreed to lift the ban in 2019, yet after the discovery of the new cBSE BARB case in 2021, the ban has been re-established. The impact of trade has been calculated for the US and Canada, using partial equilibrium models, which estimated a loss of $6.1 billion and $1.7 billion, respectively, for the period 2004–2013 (Peterson et al., 2017). Apart from the losses in exports, the disease has been reported to generate an important damage in US comparative advantage through long term loss in competitiveness (Chen et al., 2020). It is very likely that the same conclusions could be drawn for the UK.

There are other numerous major costs associated with the BSE epidemic. A report on EU state aids estimated costs on TSE testing in the UK at around £3.628 million per year, with testing on cattle fallen stock accounting for 76% of total costs (DEFRA, 2013). In addition to these costs, the cost of the 178 human cases of vCJD in the UK (EuroCJD, 2020), and other associated vCJD costs (e.g. cost of extra cleaning and disinfection in surgeries), have not yet been estimated. Up to date, there is a lack of studies estimating the burden of vCJD. Furthermore, the disease has important socio-economic and psychological impacts on society (Lemyre et al., 2009). In the UK, BSE also had an impact on public trust in the government, after the minister of agriculture claimed in 1999 that beef was safe to eat and the government was viewed to defend the industry at the expense of consumers. The confidence crisis triggered the development of a governmental-independent office in 2000, the Food Standards Agency. This agency has the role to protect public health and consumers' wider interests in food.

The emergence of BSE and its threat to human health has had numerous indirect impacts on other sectors. The establishment of intensive Scrapie surveillance and control programs in small ruminants is a result of the BSE epidemic. The reduction in beef consumption resulted in increased demand and prices for lamb and, to a lesser extent, of pork and poultry (Chopra & Bessler, 2005). On the other hand, lack of access to mammalian protein for pig and poultry producers meant that farmers had to use less efficient protein sources for their production. There were several other impacts on the feed industry, human health system, trade organizations, etc. Table 4 provides suggestions of potential costs that need to be considered to accurately estimate the impact of BSE. The costs presented are not persistent over time, but many of these are only incurred for a small period of time, while others will still be incurred in future years.

Yet, despite the enormous impact of the BSE epidemic, its occurrence generated several benefits which are highlighted in Table 5. Technological advancement, such as novel diagnostic capacity (e.g. protein misfolding cyclic amplification and real-time quaking-induced conversion (RT-QuIC), has improved diagnosis in animals and humans (Saborio et al., 2001). Many of the policies and programs implemented have increased the capacity to control most infectious disease transmission.

Examples of such policies include the implementation of the cattle passport in 1996 or the cattle tracing system in 1998 or the establishment of the Food Standards Agency. Many of the measures were also designed to improve consumers trust and awareness of the food system. The implementation of active surveillance of Scrapie and Chronic Wasting Disease allow better prevention and control of these diseases. In addition, there are numerous lessons learnt from the epidemic, as reported by the BSE inquire report (2000), O'Brien (2000), Cummings (2010) and Hueston (2013), which should help increase preparedness to future major epidemics. Hueston (2013) indicated that the epidemic re-enforced the importance of the precautionary principles, which was one of the reasons for the implementation of major drastic policy decisions. Another key lesson learnt was recognising the need to use a macro-epidemiological perspective or system approach to address these complex problems. Other lessons learnt stressed the importance of promoting timely research, adequate usage of expert committees by government, interdepartmental collaboration, surveillance mechanisms for novel pathogens, separation of responsibility between trade and public health, and adequate husbandry practices. As a consequence, large numbers of interdepartmental bodies were created focussing on areas of zoonoses and disease surveillance (BSE Inquiry, 2000). This, combined with increased research funding and changes in the use of expert committees, has contributed to a change in our approach and preparedness to novel diseases. It is likely that this experience may have enhanced society's awareness of food production.

4. Discussion

The epidemiological analysis of the disease does indeed provide clear indications that feedban measures implemented have been successful in controlling the disease. The emergence of cBSE BARB cases remains an important conundrum to the scientific community. To date, at an individual level there has not been any direct evidence to show prion contamination in feed resulted in the BSE cases. The spatio-temporal analysis did not provide strong evidence of a clear spatial pattern in the occurrence of cBSE BARB cases. Only one small highly localized spatial cluster composed of three cases was found, which could potentially be explained by a point source exposure to the prion. Yet, the spatial analysis did not provide any evidence of a source of infection for the other 98% of cases. Arnold et al. (2017) used BSE BARB case data from different EU countries between 1997 and 2016 and estimated a 33% decline rate in BSE prevalence. The findings of this study, suggest that if spontaneous occurrence does happen it will only explain a minority of cases. Since 2016, the number of cases observed remains consistent with a continuous rate of decline. Moreover, other studies, with smaller sample sizes, have rejected the hypothesis of spontaneous generation based on the existence of spatial clusters in some countries (Ryan et al., 2012). The review of risk factors does not provide evidence of potential causes for the emergence of cBSE BARB cases, although most authors argued that potential residual contamination of feed is likely to be the main causal factor. This hypothesis will be consistent with the declining incidence of the epidemic, as degradation of residual prions in the environment (such as in food storage) progresses. A study that investigated the capacity of field furniture to act as vectors showed evidence of a decline of scrapie prion infectivity over time. It was argued that this may be caused by the weathering process (repeated exposure to wet and dry conditions); processes that may be less severe in food containers (Konold et al., 2015). Yet, prions have been reported to remain extremely resistant to the environment. In a farm in Iceland, a second case of scrapie was detected 18 years after the first case. The cause of infection was speculated to be the residual contamination in one of the animal houses that was not properly cleaned (Georgsson et al., 2006). There may however be differences in environmental persistence between different types of prions, and there is currently insufficient evidence to indicate that BSE prion activity declines through the years. On the other hand, there is likely to be an important dilution effect taking place over time, as adding concentrated feed over time, particularly since PAP was prohibited, will eventually reduce the presence of infectious food clusters in the feed storage units. The detailed field epidemiology reports of the 2015 and 2021 cases noted the possibility that a small amount of contaminated feed may have remained attached to the side walls of the silo from before the restricted feed ban, in the absence of any other explanation for the source of infection. However, these were described as a very low to negligible possibility, with significant uncertainty due to the length of time that contaminated feed would have needed to have remained in the silo (13 years). Given the uncertainty of effective BSE prion degradation and the experience reported with scrapie, it is possible that infective BSE prion material may still persist over many years in some farms.

The hypothesis for exogenous (non-GB) sources of contaminated feed as a potential cause of cBSE BARB cases still remains plausible. It can be argued that if this hypothesis was true, it would be expected to find higher number of BSE cases in Europe and other countries. Yet, since 2016 only three cases of classical BSE have been detected in Europe, one in France and two in the UK (EFSA European Food Safety Authority, 2021). Arnold et al. (2017) suggest that the difference in BSE prevalence between the UK and EU members may just be due to the higher prevalence in the UK at the start of the re-enforced feed ban. Furthermore, in that study no evidence was found of a different rate of decline of BSE BARB cases between EU countries. The difference in surveillance sensitivities between some countries may also affect the prevalence observed (Adkin et al., 2016).

Analysis of the investigation reports conducted by APHA revealed that four of the 13 recent BARB cases were raised on a farm which used homemix within their first six months of life, which was found by Ortiz-Pelaez et al. (2012) in their case control study to be a statistically significant risk factor. Overall, no obvious epidemiological links were identified between farms that experienced BARB cases since July 31, 2009. Assessing the cause of BARB cases remains a very difficult challenge, possibly due to the long incubation period of the disease, which makes it almost impossible to test the environment as it was during the time of infection.

In this study, a difference in detection route and age of cases over time was observed. This difference in age is likely due in part to the increased age of testing of healthy animals over the years, but also the fact that the age upper bound of BARB cases increases each year (e.g. four years for cows in 2000, while nine years for cows in 2005). Interestingly however, five of the nine cBSE BARB cases detected since 2012 have a relatively young age of approximately six years. If the incubation period is proportional to the dose of infection, as suggested by Konold et al. (2012), the low age of these animals (hence short incubation period) indicates that these were likely exposed to material with high concentration of prions. This may have been present in old lumps of feed in silos. It is however expected, as mentioned above, that over time a dilution effect is likely to occur, and persistence of such material to become scarcer on farms. The fact that many young cases were detected in the last decade suggests that high levels of contamination may still be present in some farms. In terms of route of detection, reports of BSE suspected cases through passive surveillance have reduced drastically. This could be attributed to a reduced sensitisation of farmers as the epidemic entered its lowest tail section. Yet most recent BARB cases were detected through the fallen stock active surveillance scheme, which indicates that animals were potentially considered to be unwell by the farmer and culled. Furthermore, the high proportion of case farms which had experienced more than one BARB case may be explained by increased awareness amongst farmers that have experienced a BSE case before, and may therefore be more likely to report a clinical suspicion.

The policy review highlights major drastic policies needed to control the epidemic and protect consumers. The magnitude of the reaction to this disease was due to political, market, health and biological factors, particularly due to the fear of unknown consequences given the novelty of the pathogen and the massive population exposure. Policy makers had to operate under a high level of uncertainty and under extreme pressure, particularly in 1996 when the link to human health was established. Several reports and papers have provided a wide insight into the major problems from handling the epidemic, including the multiple delays in reaction, lack of adequate diagnostics (e.g. there was a lack of tests to detect MBM in food and feed products), logistical barriers to policy implementation, conflicts amongst scientists and between public health and commerce, rapidly evolving scientific facts and discoveries, difficulty in assessing risk, communication problems to consumers and inappropriate action, such as the delay in feed recalls (Inquiry, 2000; O'Brien, 2000; Cummings, 2010; Hueston, 2013). The management of the epidemic has in turn generated several positive impacts and lessons learnt to the industry and society, which have helped generate a more robust and healthy food system. Furthermore, these polices have been proven effective to control BSE.

Several limitations are present in the analysis of data in this study. The CPH number is not always an accurate indicator of a discrete geographical farm holding as, for historical reasons, there may be farm buildings at the same location but with different CPH numbers (or potentially farms at different locations with the same CPH). However, it is currently the standard identifier for farm holdings used in GB and, when herd mark data (which indicates ownership) are also available, it is usually possible to deduce on a case-by-case basis which farms should be considered as a single epidemiological unit. Furthermore, as shown in the analysis of the investigation reports, several cBSE BARB cases may have been raised in more than one holding, but only the CPH of the last holding was used for the spatial analysis. A more complete spatial analysis that takes into account all the holdings where BSE cases have lived may provide different results.

In this study, it was decided to remove atypical BSE cases from the analysis. These were removed because they are likely to have a different aetiology to classical BSE and, while it is still largely unclear, it is likely that atypical BSE arises spontaneously, i.e. without any exposure to the infectious agent (Seuberlich et al., 2010).

5. Conclusion

The analysis and review presented here provides a perspective on the tremendous shock that a novel disease such as BSE had on the industry and society, and the substantial efforts needed to control it. The episode of BSE had indeed a damaging impact to the reputation of the UK industry and its agricultural sector, representing a potent alarm for the need to cautiously re-consider livestock farming practices, such as feeding, and our approach to novel diseases. Yet, the impact of BSE continues with the emergence of new cases, triggering trade bans and justifying the continuation of expensive surveillance measures. There is still much uncertainty remaining on the causes of cBSE BARB cases. There is also much uncertainty of what the health and economic impact of BSE would have been if these aggressive measures were not implemented. Yet, as we are currently on track towards eradication, the story of BSE can be seen as an example of successful disease control under considerable uncertainty which enhanced country preparedness for the control of novel diseases.

Conflicts of interest

None.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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Appendix A. Supplementary data

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