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A Spatial and Temporal Analysis of Bovine Spongiform Encephalopathy in Irish Cattle Herds, 1996 - 2000

H. Sheridan¹, D. Lynch¹, G. McGrath, P.W. White and W. Martin²

Introduction

Bovine spongiform encephalopathy (BSE) is a subacute, progressive, neurodegenerative disorder of adult cattle which was first recognised in the UK in 1985. Evidence to date supports the thesis that cattle were primarily exposed to the agent through the consumption of meat and bone meal in proprietary concentrates. This feed-borne hypothesis has been used to explain the geographic heterogeneity which has been a constant feature of the UK epidemic, with 20% of farms reportedly responsible for 80% of cases ((Hagenaars et al., 2000; Stevenson et al., 2000). The first case of BSE was diagnosed in Ireland in 1989 (Griffin et al., 1997) and a total of 838 cases had been diagnosed by the end of 2001.

Based on spot maps of Irish cases, a hypothesis that BSE case herds in Ireland tend to cluster geographically and the cause of this clustering was most likely to be heterogeneity in feed exposure, was developed. Hence the principal objective of this study was to test the hypothesis of clustering among so-called herds of putative exposure, or herds in which cases were most likely to have been exposed to the BSE agent.

Materials and Methods

The unit of concern is the bovine herd. Index herds are bovine herds in which at least one case of BSE was notified between January 1, 1996 and January 1, 2001, by passive surveillance and confirmed by laboratory findings. Herds of putative exposure (PE herds) are herds in which the positive animal(s) was most likely to have been exposed to infection, based on the assumption that they were most likely infected in the first 12 months of life. Index herds were the herds in which the case was identified. Control herds are bovine herds from which a BSE suspect, which was subsequently deemed negative, either on the basis of response to treatment or post-mortem analysis, was notified. A total of 469 cases of BSE involving 461 herds were notified by passive surveillance, 541 became control herds.

Information pertaining to case, control and PE herds was obtained from the National BSE Database maintained by DAFRD. This information included location of the home premises in terms both of National Grid UTM Co-ordinates and District Electoral Division (DED, N=2,840), herd size, enterprise type, month and year of clinical onset, and month and year of birth. The number of herds at risk in the population was obtained from the National Tuberculosis Testing Database. Data were aggregated at the DED level and were assigned the centroid location of each DED. The DEDs are organised into 26 larger units called counties. Crude case rates and standardised morbidity ratios (SMRs) were calculated per county per year.

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Detailed statistical testing of clustering was carried out using SaTScan Version 2.1© (Kulldorff et al., 1998). SaTScan© makes use of a likelihood ratio test to identify the most likely cluster, as well as other statistically significant clusters. The programme does this by imposing circles (spatial scan statistic) or cylinders (space-time scanning statistic) of varying size on the spatial data, calculating the likelihood of disease within and without the shape, creating a ratio and assessing the statistical significance of this ratio by comparing it to values obtained by a Monte Carlo simulation carried out under the null hypothesis of random distribution. The starting point for the shapes imposed by SaTScan© can either be supplied in terms of a grid file or assigned automatically by the programme using either the UTM Co-ordinates of case/control herds (Bernoulli model) or the UTM Co-ordinates of the centroid for aggregated count data (Poisson model). In this paper we report on analyses with the centroids being the UTM Map Co-ordinates for the principal feed mills in Ireland. Both Bernoulli and Poisson based approaches were utilised using the PE herd data. Tests for clusters up to 50% of the size of the study area (spatial clusters) and up to 50% of the length of the study period (temporal) were used.

**Results**

The number of cases and controls differed significantly among counties \((P<0.0001)\) with a mean (sd) number of cases per county of 10.6 (3.0) and a mean number of controls per county of 15.1 (2.5). There was significant correlation between the number of case and control herds in each county, with \(r = 0.81\) \((P<0.001)\). 60 per cent of cases were recorded as having been born and reared in the index herd with 36 per cent recorded as purchased. Records that enabled a decision to be made regarding the herd in which the animal had been exposed (PE herds) were available in 123 of the purchased cases.

There was a significant difference in the crude rates per 100 herds between counties \((P=0.004)\) but not between years \((P=0.4)\). Cumulative crude rates were highest in the counties of the Northeast and lowest in the counties of Western Ireland.

Both the Bernoulli and Poisson Models in SaTScan© provided strong evidence of clustering. All models indicated that the most likely cluster \((P=0.0001)\) was present in the Northeast of the country, centred on County Monaghan, though the size and centroid of this cluster depended on the analysis type. The Poisson model indicated that the most likely cluster was a space-time cluster occurring between July 1998 and December 2000 \((P=0.001)\). Based on using feed mill location as the grid, there was some disagreement among models as to the feed mill at the centroid of the most likely cluster. In the case of PE based analyses, there was greater variability when using Bernoulli based approaches regarding the feed mills placed at the centre of the most likely cluster though, interestingly, Poisson based approaches exclusively selected Feed mill C \((P=0.0001)\) as the centroid for the most likely cluster, whether covariates were included or not. The timescale for clustering among PE herds varied with model type, though all selected a timescale in the range January 1989 to December 1995 which corresponds to the time period during which the majority of cases included in the analysis were born.

In addition to the cluster in the Northeast, there was strong evidence of clustering among PE herds both in Cork \((P=0.0024)\) and Wexford \((P=0.001)\). The majority of analyses placed Feed mill D at the centre of the statistically significant cluster in the Wexford region \((P=0.001)\) and placed Feed mill E at the centre of the cluster detected in the Cork area \((P=0.004)\). Neither the Bernoulli nor Poisson model seemed able to detect any true temporal clustering, choosing instead a timescale encompassing the birth of almost all cases included in the analysis.
Discussion
There are many statistical tests available to the researcher interested in searching for clusters of disease in time and space. In this study the statistical package SaTScan® was chosen as the method of choice because of its ease in utilisation, its ability to search for both temporal and spatial clusters, its ability to deal with confounding variables, its ability to facilitate testing independent of artificially imposed administrative boundaries and, finally, its ability to incorporate a set of geographic locations other than the locations of case and control herds, as centroids for potential clusters. At the outset of this study, we favoured the Bernoulli model approach because of its ability to take account of the precise location of herds in testing for clustering thus remaining independent of artificially imposed administrative boundaries. However, it is clear from the results that in this study the Poisson model approach proved to be the more powerful tool - a finding which may have resulted from the relatively small number of case and control herds.

In general, the location and statistical significance of the most likely cluster did not change between index and PE herd analyses. However, as utilisation of PE herds proved the more powerful than using index herds, this leads one to conclude that the clustering observed is caused by factors related to the herds in which the animals were exposed and not just by factors relating to the herds in which the animals become clinically ill.

It is most likely that the clustering in these areas is caused by common exposure of herds to feed cross contaminated with the causal agent of BSE. As the vast majority of rations fed to cattle in Ireland are manufactured in commercial feed mills, it seems reasonable to assume that this common exposure occurred because these herds purchased their feed from the same producer. Circumstantial evidence to support this hypothesis is provided in this study as, of the 61 feed producers included, only 5 were regularly selected as the centroid of statistically significant studies.

References

