BSE in Northern Ireland: epidemiological patterns past, present and future

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By 30 January 1998, there had been 170 259 confirmed cases of BSE in Great Britain (GB), 1766 confirmed cases in Northern Ireland (NI) (2 January 1998), and 276 confirmed cases in the Republic of Ireland (31 January 1998). Analysis of the epidemiological patterns in the NI epidemic reveals significant clustering of cases in herds and counties. The observed clustering of cases within herds results in lower per capita incidence of BSE in previously unaffected herds, providing support for the introduction of a certified herd scheme in NI. By fitting a backcalculation model to the case data, we can estimate the number of animals infected with the aetiological agent of BSE and project the number of future cases. We predict that the epidemic will decline rapidly, with approximately 99 cases (95% confidence interval: 30, 504) occurring in the five year period 1997–2001.

Keywords: BSE; epidemiology; clustering; backcalculation; mathematical modelling

1. INTRODUCTION

Bovine spongiform encephalopathy (BSE) was first diagnosed in Northern Ireland (NI) on 28 November 1988, by which time there had been over 3000 confirmed cases in Great Britain (GB). By 30 January 1998, there had been 170 259 confirmed cases in GB, 1766 confirmed cases in NI (2 January 1998), and 276 confirmed cases in the Republic of Ireland (31 January 1998). Attention became more intensely focused on BSE in the UK following the announcement in the House of Commons in March 1996 that the most likely explanation for an apparently new variant of Creutzfeldt–Jakob disease (vCJD) in humans (Will *et al.* 1996) was exposure to the aetiological agent of BSE. This announcement triggered a crisis in consumer confidence in beef and beef products throughout Europe.

On 27 March 1996, the export of beef and beef products from GB and NI was banned by the European Union. Since this time, efforts by the UK government to lift the ban have focused on relaxing the export ban of beef and beef products for animals under 30 months of age that have never been in or passed through a herd in which a BSE case has been diagnosed (a certified herd scheme). The Animal Health Computer System, installed in NI in 1988, allows the movement of all cattle in NI to be tracked, thereby facilitating reliable herd certification.

Recent reports of confirmed vCJD cases (23 in total by 31 January 1998), and further evidence connecting BSE and vCJD (Collinge *et al.* 1996; Raymond *et al.* 1997; Bruce *et al.* 1997; Hill *et al.* 1997), have fuelled continuing interest in the course of the BSE epidemic in both GB and NI. Modelling of the BSE epidemic yields information about both past

infections and future trends. The resulting profile of the numbers and incubation stages of infected animals slaughtered for consumption will aid assessment of human exposure to contaminated material from infected cattle. However, additional information about the incubation period distribution (IPD) of vCJD will be required to assess likely future trends in the incidence of vCJD.

Figure 1*a* shows the annual incidence of confirmed BSE cases by year of onset for GB and NI. The epidemic of cases peaked in 1992 in GB and in 1993 in NI. This lag could have resulted from later initial infections in NI compared to GB, but could also reflect the six month interval between the introduction of the bans on the use of ruminant protein in ruminant feed in GB and NI (July 1988 and January 1989, respectively). The epidemiology of BSE in NI has been described in detail in Denny *et al.* (1992) and Denny & Hueston (1997).

In this paper we further characterize epidemiological patterns of BSE incidence in NI and compare them with the trends observed in the GB epidemic. In particular, we focus on the clustering of BSE cases at the herd and county levels. We then report the results of backcalculation models fitted to the case data stratified by birth cohort and age-at-onset. Details of this model are described elsewhere (Anderson *et al.* 1996; Ferguson *et al.* 1997). Using a survival distribution estimated independently from data on the age structure of NI cattle, the model is (i) fitted to the NI data using the maximum-likelihood estimates for the biological parameters obtained from the analysis of GB data and (ii) fitted estimating all model parameters from the NI case data. The fitted model yields estimates of the numbers of animals infected throughout the course of the epidemic (including cases and those animals slaughtered while infected). Predictions obtained using a number of model assumptions indicate that, as in GB, the BSE epidemic in NI will decline rapidly over the coming years.

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Figure 1. (a) Annual per capita incidence of confirmed BSE cases by year of onset for Great Britain and Northern Ireland. (b) Per capita incidence of BSE by onset county and birth cohort.

2. NORTHERN IRELAND CASE DATABASE

From December 1988, all cattle suspected of exhibiting the clinical signs of BSE, either on the farm or in the abattoir, were required to be reported to the Department of Agriculture for Northern Ireland (DANI). A database is maintained by DANI staff containing information on all confirmed BSE cases in NI. In the analyses presented here, data on natal herd, onset herd, date of birth, date of disease onset, natal herd size and country of origin (if not NI born) are used. As in Anderson *et al.* (1996), annual birth cohorts were defined so that, for example, the 1989 cohort consists of cattle born between 1 July 1988 and 30 June 1989.

Herd data are organized into holdings, the unit which most often corresponds to the farm. The NI database includes data on natal herds and this is the unit of analysis. Natal herd data were missing for only 18 confirmed cases which were not known to be imported. In contrast, the analysis of the GB database was limited to the subset of natal holdings for which (biased) estimates of holding size could be obtained, and 21551 (13%) cases were missing data (Donnelly *et al.* 1997b).

3. THE DEMOGRAPHY OF CATTLE IN NI

Data on the age distribution and beef/dairy classification of the national herd are collected in the annual cattle

Figure 2. (a) The observed probability of survival from April 1996 until December 1997 by time of birth (by four-month interval) with the NI maximum-likelihood estimates and the GB survival estimates. (b) Estimated survival probabilities by age for NI and GB.

census, which records at 30 June each year the number of cattle in age classes 0–6, 6–12, 12–24 and over 24 months by county. The size of the NI cattle herd has changed little over the period 1974–1996, in contrast to the decline in the GB cattle herd over the same period. This stability in cattle numbers is also present at the county level. Whilst the size of the NI herd is only approximately 15% of the size of the GB herd in 1995, the total number of BSE cases in NI is roughly 1% of the number in GB.

Sixty-three per cent of confirmed BSE cases in NI are reported to experience the onset of clinical signs in their natal herd, a similar proportion to that in GB. This proportion varies little by county or cohort. The majority of confirmed BSE cases reported in NI are from animals born in NI—84 cases had natal herds in GB and 5 cases had natal herds in the Republic of Ireland.

Data were available on the age structure of the NI herd at April 1996 and December 1997 by time of birth (in four-month intervals). The survival distribution estimated from the National Milk Records data in GB (Donnelly *et al.* 1997b) fit these data poorly (figure 2a) so the survival distribution for NI was estimated using maximum-likelihood methods (figure 2b). Survival probabilities beyond 9.5 years could not be estimated independently for NI, so the conditional survival probabilities estimated for GB were used.

Figure 3. The distribution of confirmed cases by birth cohort and age at disease onset.

4. EPIDEMIOLOGICAL PATTERNS IN INCIDENCE

Between 1988 and 1996, 1745 cases of BSE were diagnosed in 1072 herds in NI. Figure 1*a* shows the temporal pattern in the per capita incidence of BSE in NI compared to GB. Whilst the two temporal trends are similar, the per capita incidence of BSE in NI is approximately 10% of that in GB in the same year.

As in GB, after adjustment for survival, the peak age-at-onset for cattle born in the past 12 years is between five and six years of age (figure 3). This indicates that the peak age at infection is in the first year of life assuming a five-year incubation period (Anderson *et al.* 1996; Donnelly *et al.* 1997*b*).

Analyses of the GB database revealed that BSE cases cluster in herds, counties and regions. Heterogeneity between herds in feed infectivity would contribute to clustering of infections and, consequently, clustering of cases. Variable survival probabilities could also result in the clustering of cases even if infections were randomly distributed. In this section we examine the evidence of clustering of BSE cases in NI.

Figure 1*b* presents the per capita incidence of BSE by onset county. Similar trends are seen in all six counties. However, significant heterogeneity was seen between counties ($\chi^2_5 = 116$, $p < 0.001$), with Antrim and Londonderry having significantly more cases than expected at random and the remainder having significantly fewer cases than expected.

We examined the frequency distribution of cases per herd by herd size (using the herd size categories: 0–29, 30–49, 50–99 and 100 or more adult cattle). Figure 4 shows this distribution with the expected frequency distribution under the assumption that cases were randomly distributed across herds within a herd size category. In each of the three largest herd size categories, there was a significant deviation from the random (Poisson) distribution. In the 0–29 size category, the expected value for two or more cases was too small to test the significance of the observed deviation from the Poisson distribution.

The relationship between the mean and variance of the number of cases by herd and cohort can also be used to identify clustering of cases within herds. If the cases were randomly distributed across herds, the sample mean would

be approximately equal to the sample variance. Figure 5 shows this relationship for the mean number of cases per herd compared to the relationship expected for the Poisson distribution. As previously observed for the GB data (Donnelly *et al.* 1997*b*), over dispersion is more evident in cohort-size category combinations with greater mean numbers of cases. A similar pattern was observed for the mean conditional on having observed at least one case.

The analysis of the GB case database suggested that the per capita incidence was greater in larger natal holdings (Donnelly *et al.* 1997*b*). However, in that analysis we were unable to estimate the holding size for 1/3 of the natal holdings. This resulted in uncertainty in the magnitude of the holding size effect. Similar results were obtained for herds in the Republic of Ireland (Griffin *et al.* 1997). The NI database allows animals to be traced back to their natal herd (rather than their holding). In addition, herd size data were available for 99.6% of the natal herds. A similar trend was obtained for NI using census data (MAFF *et al.* 1995); however, no trend was obtained using herd denominator data from the more detailed cattle tracing system. Further analysis of cattle movements may yield insight into this discrepancy.

Temporal clustering of cases within herds was examined by calculating the correlations within herds between the incidence in year i and year $i + l$, and between the incidence in birth cohort j and $j + l$, where l is the time lag between observations. Complete data are available for years of onset between 1988 and 1995, giving a maximum time lag of seven years, whilst data are available for cohorts between 1981 and 1993, giving a maximum time lag of 12 years. These correlations are shown in figure 6 with confidence intervals calculated using the transformation of the sample correlation, r , to an approximately normally distributed random variable (Snedecor & Cochran 1989). The results show less temporal correlation in all cases than was observed for the GB data (Donnelly *et al.* 1997*b*). In particular, the correlation by cohort lag does not differ for those born prior to the July 1988 compared with those born after. These results suggest that, compared to the GB epidemic, the infection process in NI was more sporadic, both before and after the introduction of the ruminant feed ban in January 1989.

The majority of cases continues to arise from natal herds which have not previously been affected by BSE (figure 7*a*). However, due to the small number of herds affected throughout the epidemic, the clustering of BSE cases is masked by this measure. Figure 7*b* shows the probability that a previously unaffected natal herd will give rise to one or more cases in a given year. The equivalent probability for previously affected natal herds is considerably greater, as shown in figure 7*c*. The probability that a case is reported in a previously unaffected herd is consistently low, so that by 1996 this probability has dropped to 1 in 500 herds. The difference in the risks of BSE cases for affected and previously unaffected herds reflects the clustering of cases within herds.

5. APPLICATION OF BACKCALCULATION MODELS

(a) *Fitting the model*

Backcalculation models were originally developed for application to AIDS data to estimate past trends in HIV

Figure 4. The observed frequency distribution of cases per herd by natal herd size category ((a) 0–29 (b) 30–49, (c) 50–99 and (d) 100+ adult cattle) and the expected frequency assuming cases are randomly (Poisson) distributed.

Figure 5. The mean-variance relationship for the number of cases in given herd and birth cohort. The solid black line denotes the expected relationship under a Poisson distribution.

incidence (Brookmeyer & Gail 1988; Isham 1989; Bacchetti *et al.* 1993). Models of this type were extended for use in the analysis of the GB BSE epidemic to take account of transmission via contaminated feed, maternal and horizontal transmission, as well as age-dependent survival and exposure/susceptibility functions (Anderson *et al.* 1996; Ferguson *et al.* 1997). In this section we use these models to estimate the number of infections and predict the number of future cases in NI.

Full mathematical details of the models are published elsewhere (Anderson *et al.* 1996; Ferguson *et al.* 1997). Two sets of parameter sources were used here. The first uses biological parameter estimates from backcalculation models applied to the GB BSE case data. The second estimates these parameters directly from the NI BSE data. In

Figure 6. The Pearson correlation coefficient for incidence within natal herds (a) for various cohort and year-of-onset lags and (b) for cohort lags stratified by cohorts born before and after the introduction of the ruminant feed ban.

Figure 7. (a) The proportion of total cases reported from previously BSE-unaffected herds. (b) The probability that a case will arise in a previously BSE-unaffected herd. (c) The probability that a case will arise in a previously BSE-affected herd.

both cases, under reporting and the feed risk profile are estimated from the NI BSE data. The birth rate and survival distribution were estimated from independent NI agricultural data, whilst calving seasonality was estimated from independent data from the National Milk Records (Anderson *et al.* 1996; Donnelly *et al.* 1997b). We also use the model to investigate the extent to which the case data are consistent with low-level horizontal transmission independent of transmission via contaminated feed, although it should be emphasized that no biological evidence exists to support such a hypothesis.

For all model fits presented here, an empirically derived age-dependent susceptibility/exposure distribution (ADSED) and a mechanistic IPD were used (model C7 in Ferguson *et al.* 1997). Whilst a wide range of other functional forms were explored for each distribution, these choices provided the best fits to both the GB and NI case data. In general, results were not highly sensitive to the choice of the

IPD functional form. In the case of the ADSED, the functional form used encompassed the range of shapes that could be produced by more limited distributions.

Figure 8 shows the difference between the best-fit estimates of the form of the IPD and ADSED distributions obtained by fitting to the GB and NI case data, respectively. It should be noted that the smaller number of cases in NI reduce our ability to precisely estimate the forms of these distributions. Hence, whilst the distributions shown are the maximum-likelihood estimates, there are a wide range of distributional shapes (albeit with similar basic features to those shown in figure 8) which give very similar deviance values. In particular, the narrowness and exact position of the peak in the ADSED can vary widely and still remain within the 95% confidence interval for its four degrees of freedom. This is unsurprising since it is not possible to precisely estimate both the IPD and ADSED from a single age-structured time-series. However, much uncertainty in the ADSED remains even if one restricts the mean of the IPD to be between 4.5 and 5.5 years. That said, many of the qualitative results and quantitative predictions arising from the backcalculation analysis of the NI data are relatively insensitive to IPD and ADSED uncertainty.

This uncertainty might suggest that it would be prudent to use the GB IPD and ADSED estimates when analysing the NI data. However, there are two main reasons we choose to present results from both: (a) the goodness of fit deviance (G^2) of the model using the GB parameters is $G^2 = 164$ (bootstrap $p = 0.8$), whilst the NI parameters give $G^2 = 90.9$ (bootstrap $p > 0.99$)—significantly better for the seven degrees of freedom involved assuming the G^2 statistics are χ^2 distributed; (b) there may actually be IPD or ADSED differences between GB and NI (e.g. due to different mean infectious doses).

Assuming the necessary asymptotic regularity conditions hold, the null hypothesis that the values of the seven biological parameters estimated from the NI epidemic are equal to those from the GB epidemic is rejected. However, the conditions may not be valid in this instance due to the sparseness of the data. This can result in a deviance statistic that is not χ^2 distributed (in this case, the models appear to fit *better* than one would expect, assuming asymptotic conditions hold). In such cases bootstrap calculation of the hypothesis test p value is desirable. Unfortunately, such a calculation did not prove to be computationally feasible in this instance.

Figure 8c shows the estimated time profile of feed risk (the per capita probability of infection per unit time, for an individual with unit susceptibility) in NI obtained using the GB and NI IPD and ADSED estimates. The higher level of clustering of non-zero feed risk into a few time-points is striking for the NI biological parameter set. The relatively small numbers of cases in NI make it difficult to determine the precise pattern of changes in feed risk through time. As in the GB analysis (Ferguson *et al.* 1997), the estimated feed risk trends exhibit distinct seasonality for both parameters sets. These are broadly consistent with the known seasonality in the use of feed supplements on dairy farms. Also, feed risk peaks in mid-1988 for both parameter sets, and then declines thereafter (although not in a particularly regular manner for the NI biological parameter set)—reflecting

Figure 8. The best-fit forms of (a) the incubation period distribution, (b) the age-dependent susceptibility/exposure distribution and (c) feed risk profile obtained by fitting to the GB and NI case data.

the effect of the introduction of the ruminant feed ban in 1988/1989.

(b) *Pattern of the epidemic*

Figure 9*a,b* shows the overall pattern of the BSE epidemic in NI, using the GB and NI best-fit biological parameters, with no maternal or horizontal transmission. The two sets of results are broadly similar, with the total number of infections prior to 1997 being 12 300 and 11 300 for the GB and NI parameters, respectively. Of these, 10 300 and 9500, respectively, are estimated to have been slaughtered for meat or animal feed, with the remainder surviving to disease onset. Note, however, that the smaller number of cases seen in NI means that the confidence limits on infection estimates are considerably larger than those obtained when analysing the GB case data. Figure 9*c,d* shows the predicted pattern of the epidemic for the GB and NI biological parameter sets, respectively. The effect of survivorship on a long-incubation period disease is seen to be striking—the peak of the *case* epidemic occurs approximately five years after that of *infections*, and with only one fifth the magnitude. In the absence of maternal transmission, the 95% confidence interval for the infection incidence predictions in 1996 is very wide. Estimating infection incidence in this year is

not possible, since no cases arising from those infections have yet been seen. However, for both parameters sets, we predict a continuing rapid decline in BSE case incidence in NI.

There are some subtle differences between figure 9*a* and *b*, most noticeably in the relationship between prevalence and incidence. Since the modal age of infection for the NI biological parameters is some 6–12 months earlier than for the GB parameters, the end of year prevalence ('total infections') is typically larger than the yearly incidence for the former parameter set (figure 9*b*). This is because the major drop in the survivorship curve occurs at two years of age, so that animals infected at, say, six months of age are almost certain to survive for 18 months and hence contribute substantially more to two years of prevalence figures than animals infected, say, at 12–18 months of age.

Figure 10 shows the breakdown of infected animals slaughtered (for meat) by disease incubation stage (for the NI biological parameter set). This represents some of the data required to make preliminary risk assessments for vCJD. However, before accurate assessments can be made, data on both the relative infectiousness of tissue from infected cattle at different incubation stages and the absolute infectiousness of infected tissue for humans are

Figure 9. The overall pattern of the BSE epidemic (*a, b*) and the predicted future pattern (*c, d*) using the GB and NI best-fit biological parameters, respectively. 95% confidence intervals are presented for total infections, new infections and cases.

Figure 10. The distribution of infected animals slaughtered for meat by disease incubation stage.

required. That said, one hypothesis, given indirect support by research on transmissible spongiform encephalopathy pathogenesis in rodents (Dickinson & Outram 1979), is that infectivity increases exponentially throughout the incubation period, rising to the highest levels only close to the time clinical signs of disease are seen in the animal. Under that scenario, figure 10 would indicate that the majority of highly infectious material (animals within one year of onset) only entered the human food chain after the introduction of the specified bovine offal (SBO) ban in 1989. Overall, over 50% of all infected animals entering

the food chain did so before the SBO ban, but the great majority of these were in the early stages of incubation.

(c) Maternal and horizontal transmission

Figure 11 explores model sensitivity to the levels of maternal and horizontal transmission. For the results presented here, we assumed a mean infectious period of the last six months of the incubation period, with exponentially declining infectivity from the time of onset back to the time of infection. However, the results change little if the infectious period is doubled or tripled, providing the maternal or horizontal transmission rates are scaled down by a corresponding factor. The biological parameters were also fitted separately for every combination of horizontal and maternal transmission levels explored.

Figure 11a shows the deviance (G^2) relative to the best-fit choices of the probability of maternal transmission, ϵ , and the basic reproductive rate via the horizontal route, $R_0^{(H)}$. The best fit occurs at zero horizontal transmission and 24% maternal transmission ($\epsilon = 0.24$) over the last six months of the incubation period—effectively equivalent to approximately 10% maternal transmission in the last year of the incubation period. The 95% confidence region is large, however, encompassing (for two degrees of freedom) the region of the graph with $G^2 < 6$. Even when horizontal transmission is ignored, the 95% one degree of freedom confidence interval for ϵ extends from 1% to over 50%. This reflects the difficulty in assessing the significance of such relatively minor transmission routes from a single case notification database, and emphasizes the necessity for independent experimental

Figure 11. Model sensitivity to the rate of maternal transmission (ϵ) and the reproductive rate for horizontal transmission $R_0^{(H)}$. (a) The deviance (G^2), (b) the estimated number of infections prior to 1997, (c) the predicted number of cases between 1997 and 2001, and (d) the cases between 1997 and 2001 predicted to be due to maternal or horizontal transmission.

data on maternal transmission rates. Analyses of the maternal cohort study (Wilesmith *et al.* 1997; Donnelly *et al.* 1997c, 1997d; Gore *et al.* 1997; Curnow *et al.* 1997) and the GB case database (Donnelly *et al.* 1997a) have revealed an enhanced risk of BSE in calves born to infected dams, with the maternal cohort study yielding an estimated maternal transmission rate of approximately 10% over the last five months of the maternal incubation period. An enhanced risk of BSE in calves born up to two years before the onset of clinical signs of BSE in the dam was found in the analysis of dam-calf pairs in the GB case database (Donnelly *et al.* 1997a).

Figure 11b shows how the number of infections estimated to have occurred prior to 1997 varies as a function of the levels of maternal and horizontal transmission. In the absence of horizontal transmission, low-level maternal transmission is seen to have a negligible effect. For moderate values of ϵ , its inclusion slightly reduces the overall size of the epidemic by better-fitting the incidence in animals born after the introduction of the ruminant feed ban than a feed-only scenario and, consequently, driving feed risk to zero slightly earlier than would otherwise be estimated. This is reflected in the slightly reduced numbers of total cases predicted from 1997–2001 (figure 11c). Maternal transmission does extend the long, sporadic tail of the epidemic above what would be expected purely from a feed-based epidemic—although it is incapable of sustaining the infection endemically. Direct horizontal transmission has a more marked effect, and at an $R_0^{(H)}$ level approximately equal to 0.15, it increases total infections prior to 1997 by around 10%. It has a more dramatic effect on predicted future case numbers (and the length of the epidemic tail), increasing predictions for the interval 1997–2001 by up to three-fold.

Figure 11d shows the number of future cases predicted to be due to horizontal or maternal transmission. Even 50% maternal transmission can only account for some 50% of cases over the period 1997–2001, whilst even small levels of horizontal transmission can account for over 90% of cases.

However, despite the dramatic effect even low levels of horizontal transmission can have, such levels are still over five times too small to allow BSE to permanently persist in the NI cattle population—for which $R_0^{(H)} > 1$ is required. It should also be emphasized that at present there is no biological evidence to suggest that horizontal transmission actually occurs—its inclusion here is merely to demonstrate that even in the ‘worst case’ scenario of its presence, its magnitude can only be at a level that is insufficient to sustain the epidemic.

6. CONCLUSIONS

The BSE epidemic in NI provides a unique opportunity to compare the epidemiological patterns of BSE observed in GB with an independently collected data set. The temporal trends of the epidemic in NI closely mirrored those observed in GB but at much lower per capita incidence levels. Similarly, BSE cases were observed to cluster within counties and herds in NI, albeit to a lesser extent than seen in GB. The higher degree of clustering seen in GB may be a result of its greater size and correspondingly larger number of feed mills, which would result in greater feed risk variability.

Despite the difference in the severity of the GB and NI BSE epidemics, the same export ban conditions were imposed by the European Commission on both parts of the UK. A key question for policy makers is to what extent does the lower incidence in NI, together with detailed knowledge of the BSE history of individual herds, allow a ‘BSE-free’ herd certification scheme to be designed in a manner that minimizes the probability of meat from a BSE-infected animal being inadvertently exported. The analyses presented here highlight the difference observed in per capita incidence of BSE between previously affected and unaffected herds, suggesting that previously unaffected herds will fall below any selected incidence threshold well before previously affected herds. Given the detailed information recorded on cattle movement in NI, this result provides a firm scientific underpinning for the introduction of a certified herd scheme in NI.

Insight into the infection processes underlying the observed epidemic of BSE cases requires the use of back-calculation models for the estimation of past temporal trends in infection incidence. The methods developed for analysing the GB BSE epidemic (Ferguson *et al.* 1997) gave statistically good fits when used to model the NI case data. However, the confidence limits on epidemiological estimates were wider than for the GB analysis, due to the much smaller number of NI cases. The sparse nature of the age- and time-structured case data required the use of bootstrap methods for judging goodness of fit, and therefore highlight the need for statistical rigour when analysing complex infectious disease data. Whilst the best fit IPD and ADSED estimated from the NI case data were qualitatively similar in form to those estimated from the GB data, there were significant differences between the two estimates. Interpretation of this observation is difficult, given the broad confidence regions for distributional parameters—particularly since both NI and GB distributional parameter sets both fit the NI case data well ($p > 0.3$). Similarly, the NI case data were found to be consistent with a wide range of maternal and horizontal transmission rates, and the presence of horizontal transmission was found to increase future estimates of NI case numbers by as much as threefold, compared with the zero horizontal transmission scenario. However, the case data were shown to be inconsistent with a level of horizontal transmission sufficient to allow the persistence of BSE in the NI cattle herd.

Our analyses provide estimates of the number of infected cattle in NI which were slaughtered for consumption, stratified by incubation stage. Such information, combined with recent findings suggesting that the aetiological agents of BSE and scrapie may be infectious to humans (Collinge *et al.* 1996; Raymond *et al.* 1997; Bruce *et al.* 1997; Hill *et al.* 1997), is still insufficient to produce reliable estimates of the number of future cases of vCJD. Whilst the incubation period distribution of vCJD remains unknown, models with equally good fits to the data yield widely varied projections of future cases. Thus, whilst the epidemic of BSE in cattle continues to decline in both GB and NI, the future trends in the number of vCJD cases remain uncertain.

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