Modelling studies on bovine spongiform encephalopathy occurrence to assist in the review of the over 30 months rule in Great Britain

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The objective of this study was to contribute to a risk assessment to review the over 30 months (OTM) scheme in cattle, whereby all cattle aged over 30 months slaughtered in the UK are removed from the human food chain. We use back-calculation methods to estimate the impact of changes to the OTM rule, by using passive and active surveillance data collected between 1 July 2001 and 30 June 2002. There are two types of change considered: increasing the age limit and allowing animals born after a certain date into the food chain. Results indicate that under the OTM rule less than 1 animal in the last 12 months of the incubation period would enter the food chain in 2003. The birth date changes considered and small changes to the upper age limit would increase this number by a relatively small amount.

Keywords: epidemiology; model; bovine spongiform encephalopathy; surveillance

1. INTRODUCTION

The over 30 months (OTM) rule, whereby all animals greater than 30 months of age slaughtered in the UK were proscribed for human consumption, was introduced in May 1996 and became known as the over 30 months scheme (OTMS). It followed advice from the Spongiform Encephalopathy Advisory Committee (SEAC), who advise the government departments on the control of BSE and associated risks to the human population, that all beef from cattle greater than 30 months of age intended for human consumption should be de-boned and all obvious lymphatic tissue and nervous tissue removed under official supervision. This proved to be impractical owing to the lack of appropriate officially supervised facilities for the necessary dissection and excision. As a result, all animals greater than 30 months of age were removed from the human food chain in the UK. The owners of such animals received financial compensation and the carcasses were rendered into greaves, the stores of which are gradually being incinerated. The cost to the tax-payer has been of the order of £400 million per year.

In view of the public health importance of BSE and the related costs of protecting the public's health, the Food Standards Agency (FSA) of the UK included the OTMS in its formal review of the national controls of BSE in December 2000 (FSA 2000), when the FSA recommended that there should not be a change in the OTMS, but that the earliest date after which any revision could be envisioned was January 2002.

The objective of the present study was to contribute to FSA's recommended risk assessment to review the OTM rule. It involved modelling the BSE epidemic to estimate the number of infected animals in the late stage of the incubation period that are likely to enter the human food chain in future years, given that the currently approved EU screening tests are used to test these animals. The

estimates, derived from the modelling, took account of the available evidence of the sensitivity of these current rapid diagnostic tests for BSE.

2. MATERIAL AND METHODS

(a) *Back-calculation model used to estimate the prevalence of infection*

The long incubation period of BSE (with a mean of *ca.* 5 years) means that only a fraction of the total number of infected animals ever live long enough to show clinical signs. Thus, the total number of animals ever infected is much greater than the total number of clinical cases. Back-calculation methods, first used to provide short-term predictions for the AIDS epidemic (Brookmeyer & Gail 1988) and subsequently used in analysing BSE case data (Donnelly & Ferguson 2000) are a way of estimating the number of infections from the number of cases. The basic idea is that if one knows the incubation period distribution, the age at infection and the probability of survival to a given age, then one can estimate the fraction of infections that will result in clinical cases, and also estimate the total number of infections. We used such a method to derive an estimate of the prevalence of infection in each annual birth cohort. In Donnelly *et al.* (2002) back-calculation was used to integrate the results of reported case data and data from a survey of OTM screened animals, to estimate past levels of under-ascertainment of clinical cases. Here, we also integrated the results of reported cases and survey data. However, we used only data from 1 July 2001, from when we assumed that we had the complete ascertainment of clinical cases, as all casualty slaughter and fallen stock animals have been tested since then (see electronic Appendix A available on The Royal Society's Publications Web site for more details of the model and the data used).

(b) *Further assumptions*

We assumed that the total number of clinical cases was the sum of the reported clinical cases (passive surveillance) and the fallen stock and casualty slaughter positives (from active surveillance) using the results from active and passive surveillance between 1 July 2001 and 30 June 2002. In effect this

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Table 1. Expected numbers of infected animals to enter the human food chain, with 95%, 99% and 99.9% upper one-sided confidence intervals, grouped by the length of time before clinical signs for 2003 with the OTMS in place. (These results assume constant level of risk since August 1996.)

months before onset	maximum-likelihood estimate	upper one-sided confidence intervals		
		95%	99%	99.9%
< 6	0.1	0.1	0.1	0.2
6–12	0.4	0.9	1.0	1.2
12–24	5.7	12.5	14.5	17.4
24–36	8.7	41.3	47.7	57.2
> 36	83.2	183.8	212.1	254.5

assumed that the fallen stock and casualty slaughter positives were clinical cases not ascertained through passive surveillance.

We assumed that the sensitivity of the diagnostic test decreased as a logistic function as the time from disease onset increased. We assumed a maximum sensitivity of 99% at disease onset, 50% sensitivity at either three or six months before onset, and 0% at more than either 6 or 12 months before onset, respectively. Further details are contained in electronic Appendix A.

We produced results with two different assumptions regarding the change in risk since August 1996: constant risk of infection from August 1996 onwards, and a constant risk up to the end of the year 2000, and a risk that halved each year from January 2001 (this latter date was chosen as from this time robust feed bans have been introduced throughout the EU).

(c) *Scenarios considered*

We considered scenarios that allowed the following categories of animals into the food chain.

- (i) All animals born from:
 - (1) 1 August 1996;
 - (2) 1 August 1997;
 - (3) 1 October 1998 (date of revised passports);
 - (4) 1 July 2000 (animals will be 30 months old in January 2003).
- (ii) Amend age limits of OTM scheme from 1 January 2003 to:
 - (1) 36 months;
 - (2) 42 months;
 - (3) no age limit.

In each case the estimated number of infected animals entering the food chain was calculated for the calendar years 2003–2010, assuming testing of all animals over 30 months. For the year 2003 under the current OTM restrictions, the expected numbers of infected animals entering the food chain were given for 95%, 99% and 99.9% upper one-sided confidence intervals of the prevalence of infection to indicate the possible range of values due to the sampling error. Confidence intervals were obtained using likelihood ratio tests. For future checking of the model estimates, the number of clinical cases (sum of passive surveillance, casualty slaughter and fallen stock positives) and screen test positives were given for 2003–2010.

3. RESULTS

(a) *With OTM scheme unchanged*

Table 1 shows the estimate of the expected numbers of infected animals that would be slaughtered for human consumption in 2003 aged under 30 months and thereby

Table 2. Expected numbers of infected animals that are predicted to enter the human food chain by stage of incubation period, in the calendar year 2003, with the age limits of 30, 36 and 42 months.

(The results are produced assuming a test sensitivity of 50% six months prior to clinical onset, and constant risk of infection from 1 August 1996.)

months before onset	age limit (months)		
	30	36	42
< 6	0.1	0.1	0.1
6–12	0.4	0.5	0.7
12–24	5.7	6.3	7.0
24–36	18.7	19.7	20.5
> 36	83.4	85.3	86.4

excluded from the OTMS. The expected number in the last 12 months of the incubation period is 0.5, which corresponds to one infected animal every 2 years. The number in the last 12 months before onset rises to 1.4 when the 99.9% upper confidence interval is considered (table 1).

(b) *Age-based cut-offs*

With no age limit, we estimate that there would be approximately 25 infected animals in the last year of the incubation period that would enter the food chain in 2003 (figure 1a). This reduces each year to an ultimate level of approximately 5 per year by 2006, as animals born after August 1996, with a much reduced prevalence of infection compared with earlier born animals, form an increasingly large proportion of the animals entering the food chain. For example, the estimated prevalence at July 2001 (prevalence is a decreasing function of age as infected animals die) was 53 per million for the 1996–1997 cohort, 500 per million for the 1991–1992 cohort and 1200 per million for the 1987–1988 cohort. The estimated number of infected animals is relatively much smaller with the age limits of 42 months and below than in the case of complete abolition (figure 1a). Table 2 shows the expected numbers of infected animals broken down by stage of incubation period for the 30, 36 and 42 month cases in the year 2003. The results indicate that the relative number of infected animals entering the food chain in the last 12 months of the incubation period would increase by less than a factor of 2 if the age limit were increased from 30 to 42 months. If reducing risk from January 2001 is

Figure 1. (a,b) Total numbers of animals in the last year of the incubation period that are predicted to enter the human food chain in each of the calendar years 2003–2010, with (a) different age limits and (b) different birth date cut-offs. (c) The expected numbers of clinical cases and screen test positives in each of the calendar years 2003–2010. The results are produced assuming 50% test sensitivity at six months prior to onset, and constant risk of infection since January 2001.

assumed, then the expected number of infected animals in the food chain reduces each year (figure 2a) and will ultimately be insignificant.

(c) Birth date cut-offs

The earlier birth dates allow more animals into the food chain and would therefore produce a greater risk (figure 1b). The expected number of infected animals would increase each year until it reaches *ca.* 4.7, assuming a test sensitivity of 50% at six months before clinical onset (figure 1b). The results assuming test sensitivity of 50% at three months before clinical onset are qualitatively the

same, but with a final maximum of approximately 7 animals per year. The levelling out of infected animals at a constant number each year is due to the assumption of constant risk from August 1996. If the risk of infection is assumed to halve each year from January 2001 then the estimated number of infected animals that would enter the human food chain reduces to approximately 0.3 by 2010 (figure 2b).

The expected numbers of clinical cases and screen test positives (assuming testing of animals over 30 months) are approximately 400 and 65, respectively, in 2003 (figures 1c and 2c) under the model assumptions. These would fall

Figure 2. (a,b) Total numbers of animals in the last year of the incubation period that are predicted to enter the human food chain in each of the calendar years 2003–2010, with (a) different age limits and (b) different birth date cut-offs. (c) The expected numbers of clinical cases and screen test positives in each of the calendar years 2003–2010. The results are produced assuming 50% test sensitivity at six months prior to onset, and reducing risk of infection since January 2001.

to a level of approximately 50 and 5 per year under the constant risk from 1996 assumption, and to approximately 5 and 0.5 by 2010 under the reducing risk assumption. The total numbers of clinical cases (active and passive surveillance) and the total OTM screen positive confirmed between 1 January and 30 April 2003 were 221 and 9, respectively (not all animals are currently tested). Results will be updated periodically, which should provide more accurate central estimates of clinical case numbers and enable the testing of the assumptions of risk since August 1996. However, updating the results is unlikely to change the main conclusions of the model.

4. DISCUSSION

This analysis represents one component for the ultimate risk assessment to inform policy makers and their advisers of the possibility of changes to the OTM rule, based on date of birth or age of animals. The assumptions used in the modelling were discussed and agreed by a specially formed risk assessment group under the auspices of the SEAC and the FSA. The present study was not concerned with assessing the risks to consumers, but merely the prevalence of infected cattle likely to enter the food chain after screening cattle for BSE using the current

EU-approved tests. It was designed to complement another modelling approach (Ferguson & Donnelly 2003) to provide confidence in the estimates of prevalence ultimately used. The human risk assessment was considered in an additional study and will be reported separately.

In studies such as this there are inevitably uncertainties and therefore the assumptions made can be critical. The most important assumption is the risk of infection for cattle born on or after 1 August 1996. The initial agreed assumption was that this risk remained from August 1996 onwards. This was based on the hypothesis that the cases of BSE in cattle born on or after 1 August (BARB) were as a result of feedborne exposure, possibly from an exogenous source (Wilesmith 2002), such that, from this date, British cattle were exposed to the BSE agent from feed ingredients accidentally contaminated with mammalian meat and bone meal (MMBM) imported from or via countries affected by BSE. The countries of most concern are other Member States of the EU. Although national control measures were instituted in these countries during the late 1990s, active surveillance, using the EU-approved screening tests, was not introduced in all EU Member States until 2001 and the results of passive surveillance previously are clearly unreliable, as they also were in the UK. It is therefore difficult to assess the effects of national control measures. However, in January 2001, the ultimate EU-wide ban on the use of MMBM in feedstuffs for farm animal species came into effect. Therefore, the assumption of constant risk from August 1996 onwards is pessimistic if accidental contamination of feedstuffs has been reduced. The alternative assumption of constant risk until the end of 2000 followed by a halving in risk each year from January 2001 is based on the possibility that risks have reduced owing to the EU-wide ban on MMBM in feedstuffs. The future incidence of BARB cases in the UK will be informative on the validity of the assumptions of risk from August 1996 onwards.

There is also uncertainty about the sensitivity of the screening tests to detect infected animals with respect to the stage of the incubation period. Improvements in our knowledge of the sensitivity of the tests and the development of screening tests that are capable of detecting infected animals in the early stages of the incubation period appear unlikely in the short to medium term. To overcome this uncertainty, two different logistic curves for test sensitivity were used. These had a relatively low effect on the prevalence estimates. However, the ultimate risk to the consumer depends on the amount of infectious material that gets into the food chain. In particular, the less sensitive the test, the more animals in the final stages of the incubation period would be allowed into the food chain, which could result in a significant difference in the amount of infectious material allowed through.

The present study did not include an analysis and modelling of the epidemic of BSE in Northern Ireland or the risks from imported cattle, carcasses or meat products. These aspects are the subject of additional studies and will be reported separately. The results of these are likely to increase the prevalence estimates resulting from the present study, but not to change the overall conclusions.

It was evident at the start of this risk assessment exercise that any relaxation to the OTM rule would result in an increase in the prevalence of infected cattle entering the food chain. The results of this study indicate that the prevalence of cattle currently entering the food chain is low and there is a wide variation in the number of infected animals entering the food chain under the different options considered, depending on the age range of the animals allowed. The most optimistic scenarios arise from the use of a reducing risk of infection after January 2001 and assuming 50% test sensitivity at six months before the onset of clinical signs and employing either a date of birth or an age cut-off. The choice between the two options will depend on the practicalities of confirming either age or date of birth when animals are slaughtered.

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