Epidemiol. Infect. (2009), **137**, 787–791. © Cambridge University Press 2009
doi:10.1017/S0950268809002519 Printed in the United Kingdom

SHORT REPORT
Prevalence of sheep infected with classical scrapie in Great Britain, 1993–2007

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(*Accepted 3 March 2009; first published online 7 April 2009*)

SUMMARY

Extensive surveillance for classical scrapie has been carried out in Great Britain since 1993, the results of which can be used for monitoring the effect of control measures introduced since 2001. A back-calculation approach was used to estimate the prevalence of sheep infected with classical scrapie, which integrates data on reported clinical cases (1993–2007) and the results of fallen stock and abattoir surveys (2002–2007). The prevalence of classical scrapie in GB was fairly constant until 2003, although the estimates depended on assumptions made about the performance of diagnostic tests used in the surveys. If infected animals could be detected in the final quarter of the incubation period, the estimated prevalence was 0·6–0·7%, while if they could be detected in the final half of the incubation period, it was 0·3–0·4%. Between 2003 and 2007 the prevalence declined by around 40%, and the magnitude of the reduction was independent of assumptions made about the diagnostic tests.

Key words: Back-calculation, epidemiology, PrP genotype, scrapie, sheep, transmissible spongiform encephalopathy.

Scrapie, a transmissible spongiform encephalopathy (TSE) which affects sheep and goats, has been present in Great Britain (GB) for several centuries. It became a notifiable disease in GB in 1993, with more extensive information on reported cases, notably prion protein (PrP) genotype, collected routinely since July 1998. In 2002, wide-ranging scrapie surveillance was introduced throughout the European Union (EU), which required sampling apparently healthy animals aged >18 months that were slaughtered for human consumption (abattoir surveys) and testing animals aged >18 months found dead on the farm (fallen stock surveys). These surveillance data make it possible to examine temporal trends in the prevalence of sheep infected with classical scrapie in GB, which is particularly important when monitoring the effect of control measures. Because of the risk to human health posed by the possible presence of bovine spongiform encephalopathy (BSE) in sheep [1, 2], a number of such measures were introduced in GB and the rest of the EU during the same time-period as the surveillance data were collected. These consist of a selective breeding programme (since 2001) and more stringent action within scrapie-affected flocks (since 2004).

Although scrapie surveillance data have been collected from multiple sources and over a number of years, most previous estimates of scrapie prevalence have been based on data collected during a single year, often utilizing only a single source of surveillance data [3–8]. However, there are problems associated with estimating prevalence from a single source of data. For example, scrapie notifications data suffer from under-reporting [9, 10], while abattoir and fallen-stock surveys rely on detection of infected, but preclinical,

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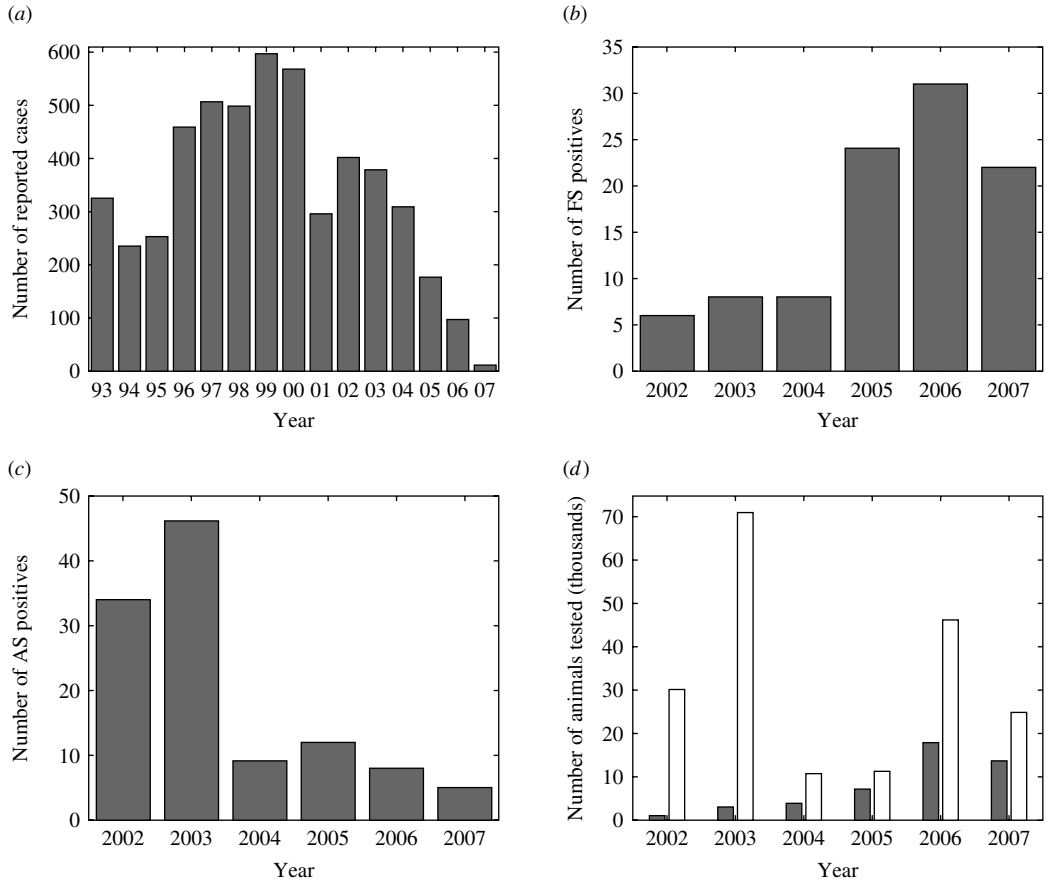

Fig. 1. Surveillance data for classical scrapie in Great Britain, 1993–2007. (*a*) Number of reported cases each year. (*b–d*) Data from active surveillance: (*b*) number of positive samples in the fallen-stock survey (FS) each year; (*c*) number of positive samples in the abattoir survey (AS) each year; and (*d*) number of animals tested each year in the fallen-stock (■) and abattoir (□) surveys.

animals and, moreover, focus on particular sections of the sheep population. By integrating different sources of data it is possible to correct for biases associated with individual sources [8].

In this paper we used a back-calculation approach to examine whether there have been changes in the prevalence of sheep infected with classical scrapie in GB over time. These methods integrated data on reported cases (1993–2007) and the results of fallen-stock and abattoir surveys (2002–2007), which represents virtually all the scrapie surveillance data currently available for GB. The scrapie notifications database (SND), held by the Veterinary Laboratories Agency (VLA) [11] was used to provide the age and, from July 1998, the PrP genotype of confirmed clinical cases for each year from 1993 to 2007 (Fig. 1*a*). Missing values for the ages and PrP genotypes of cases were imputed by assuming that they had the same distribution as reported cases of known age (all years) and PrP genotype (from 1998 onwards). The results of fallen-stock and abattoir surveys (see, e.g. [6, 7]) were used to provide the number and PrP genotype of positive samples and the number of animals tested each year between 2002 and 2007 (Fig. 1*b*, *c*). The PrP genotypes of negative samples were only available for those animals tested in 2002; those for negative samples tested during 2003–2007 were imputed from the population structure of the GB national flock.

The back-calculation methods were based on those developed to estimate the prevalence of sheep infected with classical scrapie for 2002 [8]. However, the approach was extended to incorporate temporal changes in both the risk of infection (to reflect changes in the force of infection) and in the frequencies of PrP genotypes in birth cohorts (to reflect the impact of selective breeding programmes) (see Supplementary online material for details). A number of assumptions were made in the analysis: (i) the risk of infection and the age-at-onset of clinical disease was assumed to differ amongst PrP genotypes; (ii) because there is

https://doi.org/10.1017/S0950268809002519 Published online by Cambridge University Press

evidence for a decrease in susceptibility with age [12], animals were assumed to become infected at, or close to birth; (iii) to allow for an increased risk of mortality in animals close to the onset of disease, it was assumed that a proportion of infected animals which survive to disease onset, die on farm prior to clinical signs becoming apparent [8] and, hence, may be sampled as fallen stock; (iv) there was assumed to be under-reporting of cases, with the level of under-reporting allowed to vary amongst years [9, 10]; and (v) infected animals sampled in the fallen-stock or abattoir surveys were assumed to be detected provided they were in the final proportion (δ) of the incubation period.

The baseline risk of infection for each birth cohort, the relative risk of infection for each PrP genotype, the proportion of infected animals surviving to disease onset which die on farm before clinical signs become apparent, and the probability of reporting each year were estimated from the surveillance data for 1993–2007 using maximum-likelihood methods; independent estimates were obtained for the remaining parameters. The number of lambs of each PrP genotype in a birth cohort was obtained from the number of lambs born each year as reported in June agricultural survey data (1985–2007) and the frequencies of PrP genotypes in animals sampled as part of the National Scrapie Plan (NSP) for GB between 2001 and 2007. Genotype frequencies for cohorts born prior to 2001 were assumed to be the same as 2001, because with few exceptions (e.g. in the Swaledale, Suffolk and Shetland breeds), there was little selection based on PrP genotype in GB prior to 2001. Survival probabilities, the proportion of uninfected animals found dead on farm, and the age-at-onset parameters for each PrP genotype were taken from previously published estimates [8].

To assess the sensitivity of the prevalence estimates to assumptions in the model, a number of scenarios were examined for the baseline risk of infection for each birth cohort and the preclinical detection proportion. Three models were considered for the baseline risk of infection: (1) constant; (2) time-varying, with independent values for each year; and (3) time-varying, with the risk dependent on the prevalence of infection in the national flock that year. In addition, two values were used for the preclinical detection proportion, $\delta = 25\%$ and $\delta = 50\%$, which reflects a plausible range for this parameter [8].

Estimates for the prevalence of sheep infected with classical scrapie in GB indicate that it was approximately constant until 2003, after which it declined (Fig. 2). This decline was gradual if the baseline risk each year was assumed to be constant or explicitly linked to the prevalence of infection, but was more abrupt if the baseline risk was estimated independently for each birth cohort (Fig. 2). The prevalence estimates were similar for all models of the baseline risk of infection in each birth cohort, although the confidence limits for the prevalence in 2005–2007 were much larger for the model in which the baseline risk was estimated independently for each birth cohort. This reflects the relatively small amount of surveillance data available for animals in these cohorts.

Higher prevalence estimates were obtained if the preclinical detection proportion (δ) was assumed to be smaller: between 1993 and 2003, the estimated prevalence was 0·6–0·7% if $\delta = 25\%$ and 0·3–0·4% if $\delta = 50\%$. The estimated ratio of the prevalence in 2007 to that in 2003 was similar for all six scenarios, suggesting that the prevalence of classical scrapie in GB declined by about 40% between 2003 and 2007. This reduction was statistically significant ($P < 0{\cdot}05$) for all models, except that in which the baseline risk was estimated independently for each birth cohort. Again, this is a consequence of the small amount of data on the prevalence in more recent birth cohorts.

Previously, the prevalence of classical scrapie has been estimated for 1997/1998 [3–5], 2002 [6–8] and 2003 [6, 7]. Those based on a single year's abattoir survey data [3–5, 7] yielded estimates lower than those obtained in the present study. However, the small sample size in the 1997/1998 survey means that the 95% confidence intervals (CI) for the prevalence [4, 5] included the present estimates. Moreover, those for 2002 and 2003 [7] are likely to underestimate the prevalence because the analyses did not allow for the effects of PrP genotype. By contrast, those based on multiple sources of surveillance data (reported cases, fallen-stock and abattoir surveys) for 2002 and which allowed for the effect of PrP genotype [8] yielded higher estimates, although the 95% CI (95% CI for $\delta = 25\%$: 0·41–2·35; 95% CI for $\delta = 50\%$: 0·15–0·75) included the prevalence estimates obtained in the present study (cf. Fig. 2).

Our analysis provides evidence that the prevalence of sheep infected with classical scrapie in GB declined by around 40% between 2003 and 2007 (Fig. 2). Over the corresponding time period (2004–2007) various control schemes have been in place in GB, which are likely to have contributed to the decline. The

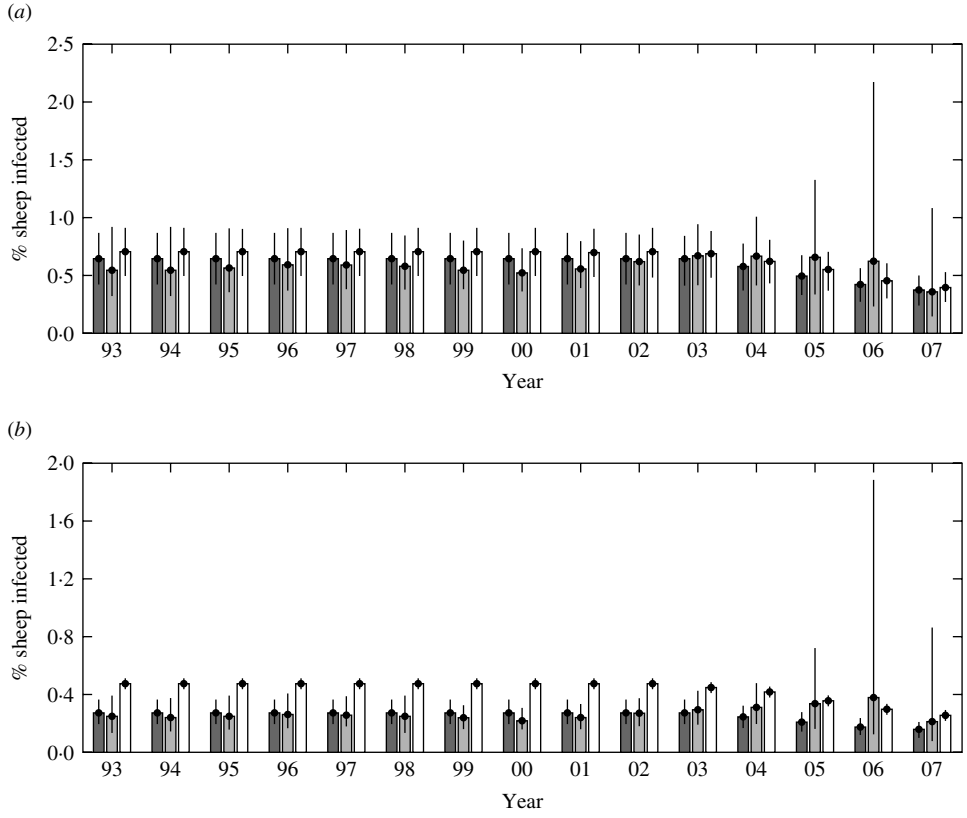

Fig. 2. Estimates and 95% confidence intervals for the prevalence (%) of sheep infected with classical scrapie in the GB national flock, 1993–2007. It was assumed that infected animals could (*a*) be detected in the final quarter of the incubation period, and (*b*) be detected in the final half of the incubation period. Results are shown for the models assuming a constant baseline risk (■), a time-varying baseline risk (▩) or a baseline risk which depends on population prevalence (□).

voluntary and compulsory scrapie flocks schemes will have reduced the force of infection by removing infected animals. By contrast, selective breeding programmes will have reduced the frequency of high-risk PrP genotypes in the GB national flock [13], thus reducing the number of newly infected animals in recent birth cohorts. The back-calculation approach explicitly incorporates this latter effect through changes in the PrP genotype structure of each birth cohort. Moreover, the models which incorporated a time-varying baseline risk of infection for each birth cohort (i.e. allowed for a changing force of infection) yielded better fits than the model which assumed a constant baseline risk (as judged by the Akaike Information Criterion for the fitted models).

The present study has presented the first investigation of temporal trends in the prevalence of sheep infected with classical scrapie in GB, which integrates almost all the available surveillance data and the best available demographic data. It provides a framework for future assessments of prevalence, which will help to strengthen the conclusions of the present paper as additional data are accumulated. Moreover, by integrating multiple sources of data collected over several years the back-calculation methods produce more robust prevalence estimates than those based on a single year or single source of data. The analysis has also highlighted that interpretation of surveillance data requires reliable data on the demography and, in particular, the age and PrP genotype structure of the relevant sheep populations: abattoir, fallen stock and national flock.

Similar surveillance programmes, based on reported cases and fallen-stock and abattoir surveys, have been in place in all member states of the EU since 2002. The results of these surveillance programmes can be used to estimate the prevalence of classical scrapie in each country [14]. The back-calculation approach developed in the present paper could be extended to integrate the various sources of surveillance data for each country and, in addition, indicates what further demographic data are required to do so.

https://doi.org/10.1017/S0950268809002519 Published online by Cambridge University Press

ACKNOWLEDGEMENTS

This work was funded by the Department for Environment, Food and Rural Affairs (Defra) (grant no. SE0243). The authors are grateful to Julia Thomas (VLA), Martin Budd (VLA) and Victor del Rio Vilas (VLA, now Defra) for providing scrapie surveillance data; to Mike Dawson (NSP Advisory Centre, now VLA) for providing NSP genotype data; and to David Schley (IAH) for helpful comments on the manuscript.

NOTE

Supplementary material accompanies this paper on the Journal's website (http://journals.cambridge.org/hyg).

DECLARATION OF INTEREST

None.

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