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Scrapie transmission in Britain: a recipe for a mathematical model

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Responses to an anonymous postal survey concerning scrapie are analysed. Risk factors associated with farms that have had scrapie are identified as size, geographical region, lambing practices and holding of certain breeds. Further analysis of farms that have scrapie only in bought-in animals reveals that such farms tend to breed a smaller proportion of their replacement animals than farms without scrapie. Farms that have had scrapie in home-bred animals have attributes associated with breeding many animals: large numbers of rams bought, few ewes bought, and many animals that are home-bred. The demography of British sheep farms as described by size, breeds, purchasing behaviour, age structure and proportion of animals that are home-bred is summarized. British farms with scrapie reveal certain special features: they have more sheep that are found dead, more elderly ewes and more cases of scab.

Keywords: scrapie; epidemiology; transmission dynamics; sheep demography; mathematical model

1. INTRODUCTION

There have been calls to control scrapie in the UK, with an ultimate aim of eradication (SEAC 1999). One part of planning such a control programme will be a thorough analysis of the structure and dynamics of the UK sheep industry. A mathematical model of the flock-to-flock transmission of scrapie would provide a useful framework for such an analysis. But the British sheep industry, at first glance, presents a morass of trading structures, farm stratification and animal heterogeneities (Pollott 1998). A useful mathematical model will have to make simplifying assumptions concerning these complexities, but which ones?

In November 1998 an anonymous postal survey concerning scrapie was sent to 11 554 farms selected randomly from farms which reported holding more than 30 breeding ewes to the annual census of British sheep farms. The replies to that survey allow an analysis of the farm and flock characteristics associated with scrapie infection. The information gathered is sufficiently detailed that it is possible to differentiate between risk factors for a flock to purchase scrapie cases (but not then progress to develop scrapie in home-bred animals) and risk factors for a flock to actually become infected (in the sense of having scrapie in home-bred animals). As well as identifying the most relevant groupings of farms for a mathematical model of scrapie transmission, we describe distributions of farms across those groups, basic demographic characteristics of British sheep farms and special demographic and epidemiological characteristics of scrapie-affected farms.

2. MATERIAL AND METHODS

The survey, response rates and descriptive epidemiology are described in detail elsewhere (Hoinville *et al.* 1999*a*,*b*). Briefly, a four-page questionnaire was sent to 11 554 farms selected randomly from the census, excluding holdings with fewer than 30 breeding ewes. The overall response rate was 61.4%, but some of these were from farmers who no longer kept sheep, leaving 6362 useful replies, of which 5620 believed they knew whether or not they had ever had scrapie in their flock.

Out of the farms that responded, 15% (95% confidence interval (CI), 14–16%) reported having ever had a case of scrapie whilst 2.7% (95% CI, 2.3–3.2%) reported having had a case of scrapie in the last 12 months. The farms that had ever had scrapie (henceforth referred to as 'scrapie-total') were classified into two groups according to whether or not there had ever been a case in an animal born on the farm. 'Scrapie-challenged' farms are those that have had cases of scrapie, but never in a home-bred animal. 'Scrapie-born' farms are those that have had cases of scrapie in home-bred animals. This distinction recognizes that infection of a flock with scrapie is a two-step process. First the flock must have contact with a source of infection and then that infection must be propagated within the flock. 'Scrapie-challenged' flocks have completed only the first of these two steps and therefore indicate risks for between-flock transmission that is not followed by within-flock transmission. 'Scrapie-born' farms have completed both steps and therefore indicate risks for transmission both between flocks and within flocks.

Binary logistic regression was used to model the relationship between detection of infection on a farm and that farm's attributes. The list of potential attributes and the interpretation of their codings is given in table 1. The analysis was performed using both forwards and backwards stepwise regression through the first ten factors of table 1, followed by the addition of all possible pairwise interactions. After a model based on the

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Table 1. *Potential risk factors considered in binary logistic regressions*

attribute	code	comments on coding
farm size	N_sheep	natural logarithm of the number of ewes and rams over one year old
farm type	L/U/H	lowland, L; upland, U; hill, H
flock type	P/C/PC	pedigree flocks, P; commercial flocks, C; both, PC
region	region	Britain divided into the 11 regions indicated in figure 1
purchasing rams	rams_bt	in the past 12 months bought: 0, 1, 2, or 3 rams, 0, 1, 2, 3, respectively; greater than 3 rams, 4
purchasing ewes	ewes_bt	in the past 12 months bought: no ewes, 0; less than 30 ewes, 1; greater than 30 ewes, 2
purchasing lambs	lambs_bt	in the past 12 months bought: no lambs, 0; less than 100 lambs, 1; greater than 100 lambs, 2
stocking density	SD-qu	quartiles for stocking density calculated as number of animals greater than one year old divided by hectarage used for grazing sheep
lambing practices	lamb_gps	no sheep lambed on the farm last year, 1; in the last year, most sheep lambed: unconfined at pasture, 2; in temporary enclosures at pasture, 3; in a temporary building, 4; in a permanent building in group pens, 5; in a permanent building in individual pens, 6
proportion home-bred	propn hb	no animals home-bred, 1; fewer than 32% home-bred, 2; fewer than 74% home-bred, 3; fewer than 97% home-bred, 4; fewer than 100% home-bred, 5; fully closed flock (i.e. all home-bred), 6. 32%, 74%, and 97% are the quartiles for farms with proportion of home-bred animals greater than zero and less than one
breed	—	for the top 20 breeds and crosses according to the number of animals reported in this study each breed or cross was coded as follows: less than 30 ewes of this breed on the farm, 0; greater than 30 ewes of this breed, 1. Each breed was given a code number and a cross of breed x is denoted x.5

factors in table 1 had been derived, single breeds and crosses from the 20 most popular breeds and crosses were added. The analysis was performed using the statistical package Minitab (Anonymous 1998). This analysis was performed for two different groups of scrapie-related risks: to have ever had scrapie cases or to have had scrapie cases amongst home-bred animals. Each of these groups was compared with the farms that had seen no cases. A third analysis compared the two sub-groups of scrapie-affected farms, to directly analyse the difference between 'scrapie-challenged' and 'scrapie-born' farms. We used adjusted odds ratios significantly different from one as indicators of raised or lowered risks of contracting scrapie for farms in a particular group. Further analysis consists of a series of cross-tabulations and χ^2-analyses of the distribution of farms across risk groups, basic descriptions of the demography of British sheep, and a description of certain demographic and epidemiological characteristics peculiar to scrapie-affected farms.

In the results presented below breeds and crosses are referred to by code number, with x.5 representing breed *x* crossed with some other breed. A breed's status with respect to scrapie infection could have commercial implications and this coding is used to prevent adverse consequences from this study accruing to any sheep breeders.

3. RESULTS

(a) *Risk factors for scrapie affected farms*

(i) *'Scrapie total'*

Farms that have ever had scrapie ($n = 838$) ('scrapie total' in table 2) on average tend to be larger. For every 2.7-fold increase in the number of animals held there is an 80% increase in the odds of having scrapie. Pedigree farms and farms holding both pedigree and commercial flocks tend to have a slightly higher risk of scrapie, and there is strong regional variation, some but not all of which is explained by regional variation in breed. After controlling for other significant factors (e.g. size), Shetland and Yorkshire have more scrapie than average, Scotland, the South-East, Wales and the West Midlands have less. Lambing practices are implicated in the transmission of infection because farms where ewes lamb unconfined at pasture or in individual pens are 25–30% less likely to get a scrapie case than farms where ewes lamb in group pens. Farms that hold more than 30 ewes of breed 7 are twice as likely to have ever had scrapie, but holding breeds 3, 9 or 43 decreases that risk.

The inclusion of each possible pairwise interaction had no effect on the model reported in table 2. However there were significant interactions between size and farm type (upland farms have a greater regression coefficient for farm size), and between size and stock density (the regression coefficient for farm size is greater at higher stock density).

(ii) *'Scrapie born'*

For farms that have had scrapie cases in home-bred animals ($n = 261$) ('scrapie born' in table 2), size and regional effects are similar to those seen in 'scrapie-challenged' farms. In addition, farms with pedigree flocks are more likely to have seen scrapie. 'Scrapie-born' farms tend to buy more rams but fewer ewes and have a larger proportion of their flock bred on the farm. The breed-associated risks are the same as for 'scrapie total', except that there is no breed 9 effect.

When interactions were studied the model reported in table 2 remained valid. In addition, the stock density–size interaction was again revealed. There was, as before, a significant interaction between size and farm type, but this time it was the lowland farms that had a greater regression coefficient for farm size. There was also a significant interaction between the numbers of lambs and

Table 2. *Regression models for different scrapie risks*

(Adjusted odds ratios shown in bold are significantly different from 1.)

	scrapie total				scrapie born				born versus challenged			
predictor	adjusted odds ratio	95% CI lower	95% CI upper	overall *P*	adjusted odds ratio	95% CI lower	95% CI upper	overall *P*	adjusted odds ratio	95% CI lower	95% CI upper	overall *P*
N_sheep	**1.85**	1.68	2.03	—	**1.72**	1.41	2.1	—	—	—	—	—
L/U/H (reference is upland)	—	—	—	—	—	—	—	—	—	—	—	< 0.001
H	—	—	—	—	—	—	—	—	**2.09**	1.16	3.74	—
L	—	—	—	—	—	—	—	—	0.68	0.39	1.2	—
P/C/PC (reference is both)	—	—	—	0.002	—	—	—	0.013	—	—	—	—
C	**0.73**	0.58	0.92	—	0.76	0.52	1.1	—	—	—	—	—
P	1.08	0.78	1.5	—	1.37	0.87	2.16	—	—	—	—	—
region (reference is EM)	—	—	—	< 0.001	—	—	—	< 0.001	—	—	—	—
ER	1.15	0.6	2.21	—	0.73	0.14	3.72	—	—	—	—	—
NE	0.79	0.5	1.25	—	0.9	0.34	2.37	—	—	—	—	—
NW	0.93	0.61	1.44	—	1.52	0.63	3.69	—	—	—	—	—
SC	**0.42**	0.26	0.66	—	0.61	0.24	1.56	—	—	—	—	—
SE	**0.54**	0.31	0.93	—	0.67	0.21	2.1	—	—	—	—	—
Sh	**3.03**	1.57	5.86	—	**3.67**	1.27	10.57	—	—	—	—	—
SW	0.95	0.63	1.43	—	1.45	0.61	3.48	—	—	—	—	—
W	**0.48**	0.31	0.74	—	0.59	0.25	1.41	—	—	—	—	—
WM	**0.58**	0.36	0.92	—	0.66	0.23	1.87	—	—	—	—	—
YH	**1.64**	1.07	2.51	—	1.13	0.44	2.94	—	—	—	—	—
rams_bt (reference is none)	—	—	—	—	—	—	—	0.009	—	—	—	0.045
1	—	—	—	—	1.15	0.66	2	—	1.01	0.5	2.02	—
2	—	—	—	—	**1.96**	1.19	3.23	—	1.66	0.89	3.12	—
3	—	—	—	—	**2.37**	1.34	4.19	—	0.99	0.48	2.04	—
> 3 4	—	—	—	—	**2.16**	1.26	3.7	—	**2.12**	1.16	3.88	—
ewes_bt (reference is none)	—	—	—	—	—	—	—	0.019	—	—	—	0.014
< 30 1	—	—	—	—	0.83	0.51	1.35	—	0.73	0.39	1.36	—
> 30 2	—	—	—	—	**0.52**	0.32	0.82	—	**0.42**	0.24	0.75	—
propn_hb (reference is none)	—	—	—	—	—	—	—	< 0.001	—	—	—	< 0.001
< 32% 2	—	—	—	—	**2.73**	1.13	6.59	—	2.24	0.9	5.57	—
< 74% 3	—	—	—	—	**4.88**	2.12	11.2	—	**4.57**	1.94	10.77	—
< 97% 4	—	—	—	—	**6.63**	2.9	15.13	—	**11.89**	4.97	28.45	—
< 100% 5	—	—	—	—	**6.3**	2.72	14.58	—	**17.21**	6.93	42.75	—
100% 6	—	—	—	—	**5.77**	2	16.63	—	**17.4**	4.92	61.46	—
lamb_gps (reference is gp pens)	—	—	—	0.016	—	—	—	—	—	—	—	—
none 1	0.76	0.29	2.01	—	—	—	—	—	—	—	—	—
confined at pasture 2	**0.74**	0.6	0.91	—	—	—	—	—	—	—	—	—
temporary enclosure at pasture 3	1.13	0.81	1.59	—	—	—	—	—	—	—	—	—
temporary building 4	1.07	0.56	2.05	—	—	—	—	—	—	—	—	—
individual pens 6	**0.68**	0.47	0.98	—	—	—	—	—	—	—	—	—
breed												
breed_7	**1.96**	1.44	2.67	—	**2.09**	1.26	3.47	—	—	—	—	—
breed_3	**0.31**	0.19	0.51	—	**0.22**	0.09	0.5	—	—	—	—	—
breed_9	**0.51**	0.31	0.83	—	—	—	—	—	—	—	—	—
breed_43	**0.79**	0.63	0.99	—	**0.54**	0.33	0.89	—	—	—	—	—
breed_43.5	—	—	—	—	—	—	—	—	**2.62**	1.03	6.62	—
breed_40	—	—	—	—	—	—	—	—	**3.45**	1.26	9.47	—
Hosmer–Lemeshow goodness-of-fit test	$p=0.30$				$p=0.40$				$p=0.45$			

rams bought, farms buying few lambs and lots of rams having the highest odds.

(iii) *'Scrapie born' versus 'scrapie challenged'*

The comparison of 'scrapie-born' and 'scrapie-challenged' ($n=458$) farms differs from the other two analyses in that all farms in this analysis have had scrapie, and the objective is to search for those factors that are special to farms that, once challenged, go on to develop scrapie in home-bred animals (NB the sum of 'scrapie-born' and 'scrapie-challenged' farms is less than the total number of farms with scrapie because some farmers failed to answer the relevant question). The main effects of size and region disappear, as does the impact of holding a pedigree flock. A strong hill farm effect emerges; out of scrapie-affected farms, the hill farms are

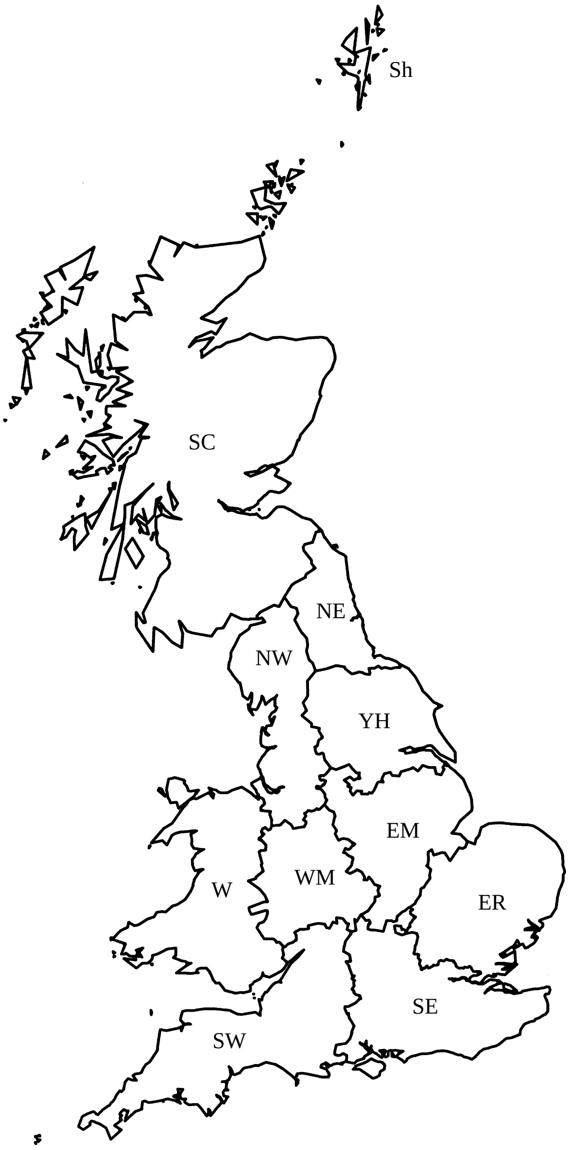

Figure 1. British regions used to code the factor 'region' in tables 1 and 2.

twice as likely to fall into the 'scrapie-born' category. The risk factors concerning buying and breeding replacement animals again emerge as significant. The difference between 'scrapie-challenged' and 'scrapie-born' farms with respect to their proportion of home-bred animals is emphasized by the very large odds ratios for farms that breed more than the median proportion of their replacement animals ($P_{\mathrm{hb}} = 4$, 5 or 6). Finally, holding more than 30 ewes of either of the two breeds 43.5 and 40 increases the risk that a flock that buys a scrapie case progresses to having scrapie in home-bred animals.

When studying interactions the same pattern relating buying of lambs and rams was found as reported above under 'scrapie born'. A possible effect of farm size was revealed by a significantly higher coefficient for farm size in farms buying few lambs.

(iv) *Goodness-of-fit for all three models*

Table 2 shows the Hosmer–Lemeshow goodness-of-fit test for each of the three models. None of the tests are significant, indicating acceptably good fit between models and data.

(b) ***Distribution of farms across risk groups***

This analysis identifies a hierarchy of farm attributes related to the risk of a flock being infected with scrapie. These attributes, or a subset of them, can be used to group farms for a mathematical modelling exercise. However, farms are not randomly distributed across these risk groups. The disposition of farms is described in a series of cross-tabulations in an electronic appendix, which can be viewed at the Royal Society Web site. The general patterns of these cross-tabulations can be described as follows. Larger farms are more likely to be found in hill and upland areas and to have commercial flocks or both commercial and pedigree flocks. There are more large flocks than expected in the North-East, North-West, Scotland and Wales (see figure 1). A large flock is more likely to breed all or nearly all of its replacement animals, but will also buy more rams and ewes. Large farms are more likely to lamb unconfined at pasture, middle-sized farms in group pens and small farms are overrepresented amongst those that lamb in individual pens.

Turning to other regional variation: hill and upland farms tend to be in the North-East and North-West, Scotland, Shetland and Wales. More than expected are mixed commercial and pedigree, except for in Wales, where only pedigree flocks are overrepresented. As expected from the tabulations of size × region and size × proportion of home-bred, Scottish and Welsh farms breed a large proportion of their animals, buying more rams and fewer ewes than expected. But in the North-East and North-West, where there are more large farms than expected, there are more farms breeding only a small proportion of their replacements than expected. These regions are also overrepresented in the group buying large numbers of ewes. The relationship between region and lambing practices is as predicted by their size, farms in the North-East, North-West, Scotland and Wales tending to lamb unconfined at pasture. However, Shetland farms, although small, also tend to lamb unconfined at pasture. The number of farms with a high proportion of home-bred animals is higher than expected amongst hill farms and in pedigree flocks or mixed pedigree and commercial farms. Flocks that are breeding a large proportion of replacement ewes tend, not surprisingly, to buy fewer ewes but more rams. Such flocks will be more likely to lamb unconfined at pasture.

(c) ***Demographic features of British farms***

A description of the underlying demography of a population is an important prerequisite to an understanding of the impact of an infectious disease upon that population. Figure 2 summarizes data on the demographic features of British farms, but is only truly representative of farms that replied to this survey.

Their size is log-normally distributed with an average flock size of 374 (geometric mean 215)—although it must be remembered that this survey specifically excluded flocks with fewer than 30 breeding ewes. The number of rams in a flock is well approximated as one ram for every 40 ewes. A regression of rams against ewes, yields a slope of 0.025 with $R^2 = 67\%$ (data not shown).

There is strong regional variation in the breeds used, figure 2*b* shows the top five breeds in each region. A flock

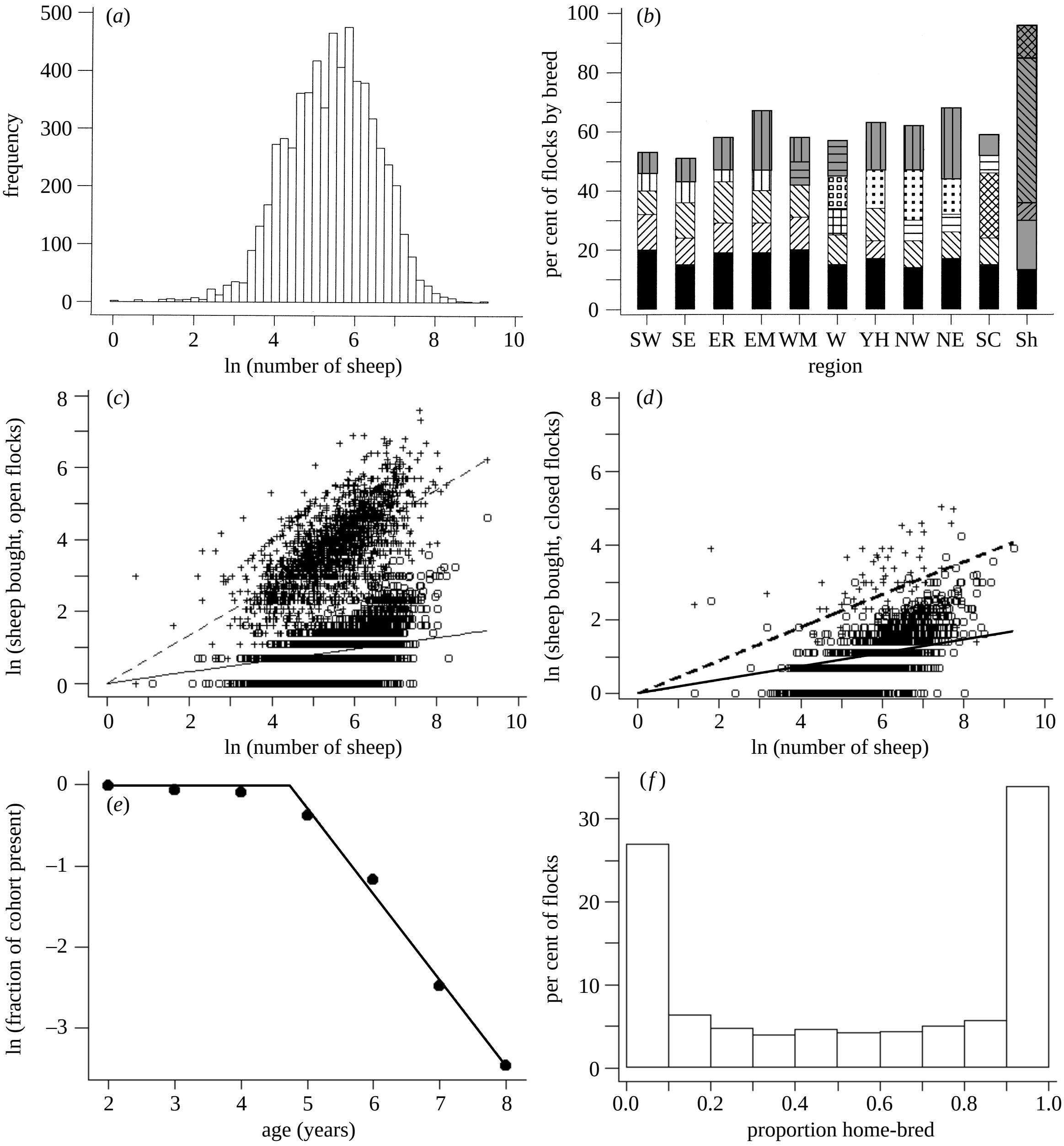

Figure 2. Demography of British sheep farms. (*a*) Size of flocks (rams and ewes greater than one year old) is log-normally distributed. (*b*) There is great diversity and regional variation in the breed make-up of the national flock. In most regions the top five breeds account for fewer than 60% of the flocks present. A flock is defined as a holding of 30 or more ewes of a single breed. Thus, for this analysis, one farm could hold several flocks. (*c*) Sheep purchasing behaviour for open flocks. The number of ewes bought (plus signs) or rams bought (open circles) can be predicted from the number of sheep held. The relationships are: ln(ewes bought) = 0.67 ln(number of sheep), $R^2 = 95\%$, dashed line; and ln(rams bought) = 0.16 ln(number of sheep), $R^2 = 67\%$, solid line. (*d*) Sheep purchasing for quasi-closed flocks, defined as a flock with 95% or more of animals home-bred. Very few such farms buy any ewes (81 out of 1379). Again the number of ewes bought (plus signs) or rams bought (open circles) can be predicted from the number of sheep held. The relationships are: ln(ewes bought) = 0.44 ln(number of sheep), $R^2 = 84\%$, dashed line; and ln(rams bought) = 0.18 ln(number of sheep), $R^2 = 73\%$, solid line. (*e*) Age distribution of the British flock. The average age distribution for the national flock was calculated by summing across all flocks within each age group and then scaling the size of each age cohort by the size of the two-year age cohort. The distribution is well described by an exponential decrease after age 4.7 years at a rate of 1.1 per sheep per year. (*f*) Distribution of farms by the proportion of their animals bred on the farm. In coding the answers to this question no distinction was made between farms that bred none of their own animals, and farms that did not answer the question. This figure therefore includes only those farms that indicated at least one animal bred on the farm and is thus biased to underrepresent farms with a low proportion of home-bred animals.

was defined as a holding of more than 30 ewes of one breed, so one farm could hold more than one flock. Each region was characterized according to the five most popular breeds in that region and the distribution of flocks amongst those five breeds. The country falls into five groups according to the top five breeds farmed. Those five groups are the Southern regions, Wales, the Northern regions, Scotland and Shetland. Of note is the lower diversity in the Shetlands, where five breeds account for 95% of the flocks.

Purchasing of animals is summarized in figure 2*c*,*d*. These show numbers of ewes and rams bought as a function of the number of sheep held. Quasi-closed flocks (here defined as breeding $\geqslant 95\%$ of their own animals) are treated separately. Both types of flock show the same relationship between the number of rams bought and the size of the holding. Most quasi-closed flocks buy no ewes and those few that do buy any, buy fewer in relation to the size of the holding than do open flocks.

Age distribution of sheep, though highly variable between individual farms is remarkably similar across risk groups. Figure 2*e* shows the age distribution of animals aged two years and above across the whole sample. The pattern is one of negligible losses up to four years of age, followed by a constant rate of attrition over the subsequent four years. The rate of loss is $\mu = 1.1$ per animal per year, the intercept is at 4.7 years, giving an average age at leaving the flock of 5.6 years. A good model for sheep age is thus $\mathrm{d}X/\mathrm{d}a = -\mu(a)X(a)$, where $\mu(a) = 0$ for $a \leqslant 4.7$, $\mu(a) = 1.1$ for $a \geqslant 4.7$. Although there is great variability amongst individual farms, there is remarkably little across groups of farms. Thus a test of homogeneity of slopes for the greater than four-years of age data compared across the groups—size, farm type, flock type and proportion of home-bred animals—found no evidence for any differences in age distribution between farms grouped in such ways. When the same analysis was performed grouping the farms by region, there was evidence for a significantly faster loss of sheep from flocks in Scotland. Thus for Scotland $\mu = 1.5$, and for the regions apart from Scotland $\mu = 1.0$, $p = 0.028$ (here p tests the heterogeneity of slopes for Scotland compared to all other regions combined in an analysis of covariance, students $t = 3.37$ with d.f. $= 4$).

Figure 2*f* shows the distribution of farms across the risk factor 'proportion of home-bred animals'. There are more farms with either very few (25% below 10%) or very many (35% above 90%) animals bred on the farm; in between these extremes the distribution is approximately constant.

(d) *Special demographic and epidemiological features of scrapie farms*

Figure 3 summarizes three special features of scrapie-affected farms. They tend to have (i) more animals 'found dead', i.e. dying of unidentified causes, (ii) ewes above seven years of age, and (iii) are more likely to have had cases of scab in the last 12 months. The finding that scrapie-affected farms have more 'found-dead' animals is not simply because they are larger, and survives after controlling for all significant risk factors in table 2. In a recent survey of 'found-dead' animals in the Shetlands (Clark *et al.* 1994) it was found that 28% of the fallen animals had lesions consistent with scrapie upon histopathological post-mortem. An excess of animals found dead on farms that have scrapie may indicate that the economic implications of the disease are greater than had been thought. The elderly ewes effect also survives when the other risk factors from table 2 are included. However, analysis of slopes of total age distributions (as described in the previous section and illustrated in figure 2*e*) reveals no gross difference in age distribution of sheep on scrapie farms, just this subtle excess of elderly animals. The final peculiarity of scrapie-affected farms revealed by this study is that they have more cases of scab. It

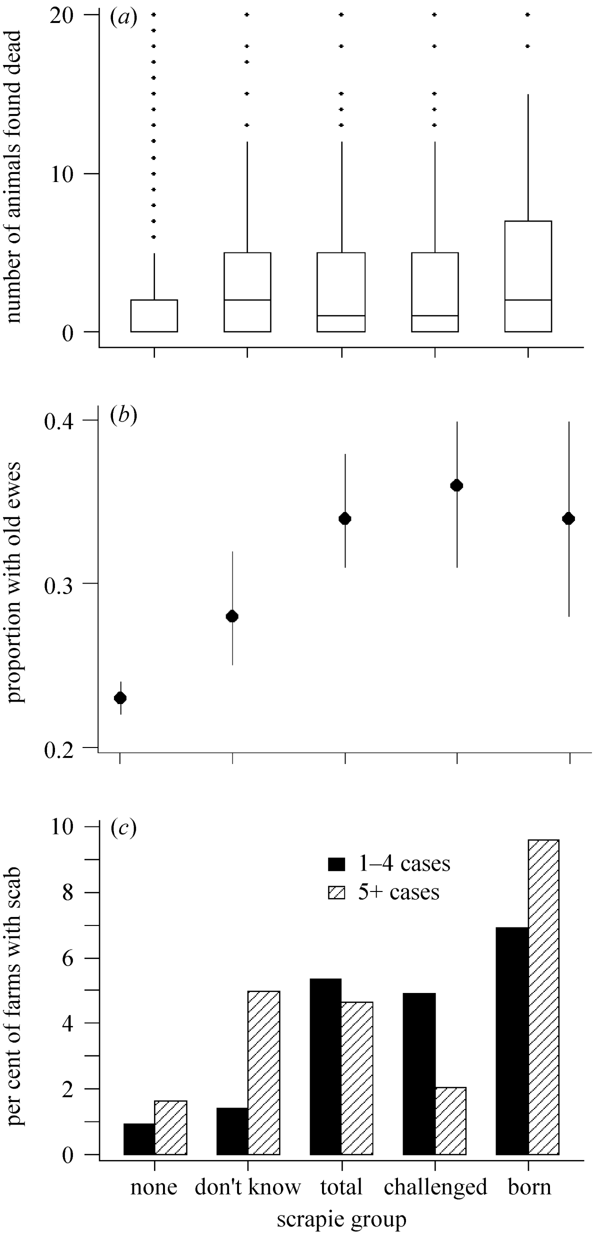

Figure 3. Special demographic and epidemiological characteristics of scrapie farms. According to the answer to the question 'Have you ever had a case of scrapie in your flock?' farms were assigned to one of three groups—no, don't know and yes. The farms that had seen scrapie were further subdivided into 'scrapie challenged' (scrapie only in bought-in animals) and 'scrapie born' (at least one case in animals born on the farm) categories. (*a*) Farms with scrapie have more 'found-dead' sheep. Box-whisker plot of the number of sheep dying of unknown causes in the last 12 months. Outliers extend as high as 200 with no notable differences in outliers between groups. (*b*) Farms with scrapie are more likely to have old ewes. Here old ewes were defined as seven or eight year olds. Farms were coded as having old ewes if they held any animals aged seven or eight years. The proportion of farms with old ewes and 95% CI for that proportion is shown for each group. (*c*) Farms that have ever had scrapie are more likely to report having had cases of scab in the last 12 months.

seems most likely that this is either confusion or ascertainment bias.

4. DISCUSSION

This whole study is based upon farmers' ability to recognize scrapie in their own animals. The disease is thought to be hard to diagnose and there seems to be some confusion between scab and scrapie. However, a large proportion of respondents correctly identified the signs of scrapie. In the question 'Have you ever had a case of scrapie in your flock?' the answer 'Don't know' was specifically offered and farms responding that way were excluded from further study in the search for scrapie risk factors. However, the results presented here are still dependent upon equal recognition and reporting of disease across different groups of farms. Despite this caveat, our understanding of the risks for a flock to acquire scrapie has been substantially enhanced by this study (Hoinville 1996), previous questionnaire surveys about scrapie having been less detailed (Morgan *et al*. 1990; Schreuder *et al*. 1993). However a number of intriguing questions remain. The residual regional variation in the risk of acquiring scrapie needs explaining. Is it just reporting bias or something to do with mixing patterns between farms? In the comparison between 'scrapie-born' and 'scrapie-challenged' farms the regional effect disappears, implying that region determines the risk of acquiring scrapie, but not the risk of propagating it within the flock (or, alternatively, that reporting bias applies equally to both types of scrapie-affected farms). This study has no information on mixing patterns between flocks and highlights the importance of the question 'Who trades with whom (Grenfell & Anderson 1985)?'

This analysis of breeds as risk factors shows that the majority of popular breeds have no impact, in either direction, on scrapie risk. However, one popular breed is significantly overrepresented amongst the scrapie farms whilst others are significantly underrepresented. It is known that there is a strong association between clinical scrapie and certain polymorphisms of the sheep *PrP* gene (Hunter *et al*. 1997). It will be interesting to see if the risks of clinical scrapie revealed by this study predict the prevalence of susceptible genotypes in the relevant breeds. Apart from size the main risks are associated with breeding and acquiring animals. Thus, farms that breed more animals are more likely to progress to seeing scrapie in home bred animals once they have acquired a first case. This may be because they are more likely to propagate scrapie within their flock once a first case has been acquired. This is certainly consistent with long-standing hypotheses about the role of infected reproductive tissues in the spread of scrapie (Pattison *et al*. 1972; Pattison & Millson 1961; Race *et al*. 1998; Ikegami *et al*. 1991; Hourrigan & Klingsporn 1996). However an alternative explanation is simply that farms that breed a large proportion of their flock are more likely to keep infected animals for long enough to see clinical disease.

The demographic data generated by this survey gives important background information that can form the basis of flock-to-flock scrapie transmission models. The special demographic and epidemiological features of scrapie-affected farms all raise interesting new questions. What are the genotypes of the excess 'found-dead' animals on scrapie farms? Are they scrapie susceptible? If they were examined, would they show any signs of scrapie infection (Clark *et al*. 1994)? Why do scrapie-affected farms have more old ewes? Is it because they are attempting to clear their scrapie problem by breeding from elderly ewes? And what of the association of small numbers of cases of scab with scrapie infection—just ascertainment or confusion or could there be a more interesting relationship (Rubenstein *et al*. 1998)? If it is confusion it could act in either direction; farmers may be seeing scrapie and thinking it is scab, or vice versa. Ascertainment bias could equally act in either direction. Whatever mechanism is at the root of it, the effect is large: flocks that are believed to have had scrapie are five times more likely to be reported as having had scab in the previous 12 months and for flocks that are believed to have had scrapie cases in the prior 12 months the increase in reported scab is 12-fold. All these observations generate hypotheses that need further study in more tightly monitored case–control conditions.

At the moment the literature has mathematical models for the spread of scrapie within a flock (Stringer *et al*. 1998; Matthews *et al*. 1999), or for the spread of BSE among herds of cows (Anderson *et al*. 1996; Ferguson *et al*. 1997; Woolhouse & Anderson 1997), but none for the flock-to-flock spread of scrapie. The stated aim of this paper was to identify the heterogeneities most relevant for a mathematical model of the transmission of scrapie from flock to flock. The four factors—size, region, proportion of home-bred animals and lambing practices—are all identified as important by the logistic regressions, so too are a number of breeds. A minimal model could start with size and proportion 'home-bred' and investigate the interplay between within-flock transmission (enhanced by having a high proportion 'home-bred') and between-flock transmission. Other information in the postal survey can give preliminary information on the rate of spread between farms (Gravenor *et al*. 1999).

Scrapie is a reportable disease with stiff penalties for failure to report. Validation of this study's findings by visiting farms at random is therefore extremely difficult. It seems that this survey's anonymity has overcome some of the disincentives for farmers to reveal a suspected scrapie infection. The response rate, at above 60%, is high for this type of study, and that, coupled with the depth of the questionnaire, has generated a database that is a rich source of information about British sheep flocks and their scrapie infections.

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