MODELING THE BSE EPIDEMIC AND THE SCREENING FOR BSE IN SWITZERLAND

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The numbers of clinical Bovine Spongiform Encephalopathy (BSE) cases are still increasing in countries in continental Europe. In Switzerland however, the BSE epidemic has peaked several years ago. In addition to the passive reporting of clinical BSE cases initiated in 1990, the post-mortem screening of targeted populations for BSE was implemented in the beginning of 1999[1]. Other European countries like France, Denmark and Ireland are currently developing targeted surveillance systems. The two surveillance methods passive surveillance (since 1990, clinical BSE cases data) and active surveillance (since 1999, new data from screening), may raise two questions:
1) how to describe and analyze the infection trends accounting for the epidemic of clinical cases, and interpret these trends in view of past control measures.
2) how to use these descriptive results to interpret the additional data obtained by the screening, and to evaluate the ascertainment of clinical cases in Switzerland. For this goal, we need to know the numbers of infected cows screened, which depend on the population structure, and on the risk of infection over time (for the cohorts that are screened).
This paper describes ongoing analytical approaches to these questions.

1) Age-cohort analyses of the epidemic of clinical BSE cases

The incidence of clinical BSE cases by birth cohort in Switzerland was estimated by analyzing the numbers of clinical cases with age-cohort models, following the methods that were applied to analyze the BSE and Creutzfeldt-Jakob disease data in the United Kingdom (U.K.)[2,3]. Assuming that the age specific incidence rates were similar for all birth cohorts, the numbers of confirmed clinical BSE cases were analysed by Poisson regression. The BSE-infected cows detected by screening were not considered in this model. The results found in Switzerland were compared to the U.K.[2,4], and to an earlier study of Swiss data[5].

The age-cohort analysis showed that the BSE incidence has increased over birth cohorts until mid-1990 in Switzerland, which is comparable to the increase found in the U.K.'s birth cohorts until mid-1988. Then, the BSE incidence has decreased over cohorts in the U.K., and a similar drop was found in the cohorts 1990/91 and 1991/92 in Switzerland. However, a second rise in incidence over the 1991/92 to 1994/95 birth cohorts was indicated by the model in Switzerland, but not in the U.K. In Switzerland, under the assumption of no new infection after mid-1996 (100% efficiency of the new control measures, and negligible effects of maternal

transmission), the BSE epidemic is likely to last until 2007 (0 to 2 clinical cases predicted in 2007), and the final decrease in the numbers of confirmed clinical BSE cases may start only in 2001.

Our results show that the first cattle feed bans, implemented in 1988 in the U.K. and 1990 in Switzerland, led to a dramatic drop of incidence in the cohorts Born After the cattle feed Ban (BAB), inspite of a lack of full efficiency due to cross-contaminations. In the U.K., the continuous decrease is also explained by additional measures implemented since 1990. As compared to an earlier study of less recent Swiss data[5], which was based on the arbitrary assumption that the numbers of infections in the post-1990 cohorts were linearly decreasing, the rise found over the 1991/92-1994/95 cohorts represents a new result. Because the active surveillance data was not included in the model, this rise is not likely to be an artefact related to the new data from active surveillance. This rise is most likely related to exposure to infected cattle feed, most likely produced in Switzerland. This feed was cross-contaminated with either imported Meat and Bone Meal (MBM), or/and ruminant MBM produced in Switzerland.

2) A Monte-Carlo simulation model of BSE screening in Switzerland

A preliminary study was used to define the parameters required to assess and improve the effectiveness of BSE screening[6]. In particular, the effectiveness of BSE screening depends on the test's sensitivity, which is not known during the pre-clinical period. In fact, for each cow, the test's sensitivity depends on the time to clinical onset. Therefore, the model should simulate the numbers of infected cows screened, and the time to clinical onset for individual cows. Because the numbers of infected cows are small, and the influence of some parameters may depend on the value of others, a stochastic and individual-based approach was adopted, in order to do multivariate sensitivity analyses and to produce Monte Carlo confidence intervals. This model is currently under development but is briefly outlined below.

The following uncertain parameters are to be varied in the sensitivity analysis:
x - the proportion of clinical BSE cases identified by passive surveillance (*a priori* values for this combined case ascertainment and reporting rate: 0 to 1, Uniform distribution);
y - the screening test's sensitivity up to 1 year before clinical onset (*a priori* values: 0 to 1, Uniform distribution).

The following parameters will be fixed in the sensitivity analysis:
(a) the risk of removal for a one-year age cohort for a reason not related to BSE (data from the population age structure);
(b) the risk of removal for a one-year age cohort because of BSE clinical onset (data from the age-cohort analysis);
(c) the risk of infection for each July-June birth cohort (data from the age-cohort analysis).

The animals considered for the screening simulation are those older than 2 years and born after mid-1987. The model's assumptions are listed below: (i) the screening test's specificity is set to 1 (no false positive); (ii) infections occur

before the age of two years; (iii) non-identified clinical BSE cases have the same age distribution as the identified clinical cases; (iv) before clinical onset, BSE-infected cows have the same probability of being removed for other reasons as the non-infected cows; (v) given that the number of BSE-infected cows is small as compared to the population size, the probability of being removed for other reasons is not affected by the number of BSE-infected cows.

In each birth cohort, the number of infected cows is simulated according to the age-cohort analysis' results (the goodness of fit of the model to passive surveillance data is measured by a chi-square criterion).
For each infected cow, the age at removal A_r and the age at clinical onset A_c are randomly sampled from their probability distribution:

If $A_c <= A_r$, the cow is removed at age A_c. Each cow has a probability **x** of being identified with clinical BSE by passive surveillance of clinical cases.
If $A_r < A_c$, the cow is removed at age A_r, (A_c-A_r) years before clinical onset. Depending on the test's sensitivity **y**, this cow may be detected (or missed) by screening (active surveillance).

The simulations are considered as consistent with the observed data when the confidence interval of the predicted number of infected cows detected by screening includes the observed number (25 cows detected in a sample of the population removed in 1999[1]). From the *a priori* **x** and **y** values, the *a posteriori* distributions will be derived from the values that led to simulations consistent with the observed data. Then, the effectiveness of the screening will be assessed by the number of infected cows detected, divided by the number of cows screened.

Acknowledgements: Part of this work is funded by a EU project "Surveillance and diagnosis of ruminant TSE" (FAIRJ-CT98-7021).

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