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Risk Factors for Tuberculosis in Irish Cattle: The Analysis of Secondary Data
S.W. Martin, J. O’Keeffe, P. White, J.D. Collins and V.L. Edge

Introduction

The secondary analysis of disease control programme data can give very useful insight into risk factors for the disease. In the case of bovine tuberculosis, the unit of concern is usually the herd; however, as the initial disease detection process focuses on testing individual animals, it is important to understand the individual-level risk factors before analysing and interpreting herd-level data.

This study focuses on bovine tuberculosis in the individual animal in the years 1989 through 1996. The outcomes of interest included the risk of developing tuberculosis, the magnitude of the skin response to the single intradermal comparative cervical test (SICTT), and the prevalence of lesions in reactors at slaughter. The risk factors of interest included MONTH and animal CLASS. Potential confounders included year, breed, the geographic area (District Veterinary Office (DVO)), the reason for testing the animal or herd (test type), and the factory/slaughter house where the reactors were examined.

The SICTT is the basis for detection of cattle exposed to Mycobacterium bovis in the national control/eradication programme in Ireland. Cattle with a skin change where the bovine response is >4 mm larger than the avian response are denoted as a standard reactor. A veterinary officer, regardless of the skin response, can designate other cattle as a reactor. Reactor cattle are identified and slaughtered under permit; all reactor carcases are examined for evidence of gross lesions consistent with tuberculosis.

Materials and Methods

The herd-test data were obtained from the 28 DVOs and organised into a database. A number of ‘cleaning’ runs were performed to remove duplicates and identify missing data. Approximately 4-6% of the total data were identified as unrecoverable by this process. This data set was merged with the animal level data and checked for errors. Some disagreements between the systems could not be resolved and thus an additional 5% of the data were excluded from analyses.

For risk estimates, the number of standard reactors in a herd was found by cumulating the number of standard reactors from each test within a year. Depending on whether a herd was tested more than once within a year, the denominator was either the actual number tested on a specific test, or the maximum number of animals tested within that year. Animal CLASS and MONTH were entered as indicator variables and the potential confounders were entered as either continuous or indicator variables, whichever was appropriate. The distribution of skin changes was quite skewed; a log transformation was used initially, but later the untransformed data were used. Lesion, defined as a circumscribed tissue lesion consistent with tuberculosis or lymphadenopathy resembling tuberculosis, was entered as a binary variable. For each of the outcomes, the exposure variables MONTH and

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CLASS were examined individually, then a multivariable model containing both variables, and all the 'other' variables, was developed. Skin change was used as a predictor of a lesion but not vice-versa. Selected interactions between exposure variables and confounders were investigated.

Results
The animal database had data on the response of 308,856 cattle deemed to be tuberculin reactors. The original herd database had data on over 2.7 million partial or complete herd tests; in our risk file each active herd was recorded once per year. In testing previously clear herds, cows had the highest risk of being a standard reactor (15.3/10,000), followed closely by steers, with heifers and bulls being between 25% to 30% less likely to be standard reactors. The average annual risk of being a standard reactor was 10.8/10,000. Cattle tested in the February - March period had the lowest risk (odds ratio = 0.75) of being a standard reactor, while cattle tested in July - August (odds ratio = 1.24) had the highest risks. When testing herds where there was a suspicion that bovine tuberculosis was present, cows had the highest risk of being a standard reactor (420/10,000), this risk being approximately 1.4 - 1.5 times higher than the risk in steers and heifers.

The distribution of skin change was markedly right skewed, hence the mean (9.6 mm) was larger than the median (6 mm). The most frequent mean skin changes lay in the 3 - 5 mm range. Approximately 2% of the skin change values were below zero, and approximately 5% were between 30 and 99 mm. The monthly mean skin changes differed by only a very small amount (range of only 0.7 mm). Cows had the smallest skin change responses (7.9 mm) versus the other classes of cattle (11 mm or more). Overall, none of the models fit the skin change data very well; the R² value for the full model was less than 6%. For example, although class of animal had a large impact on the skin response, the prediction intervals for a single animal in a specific test were very wide, with a variation of approximately ± 21 mm (thus, most intervals ranged from negative to very large increases). The confidence intervals were quite narrow because of the large sample size.

Fifty-seven per cent of reactors had no visible lesions. There were large differences in lesion risks amongst months (range = 9.4%). The months of June through November were low lesion risk months, whereas December through April were high lesion risk months. The large CLASS differences in lesion risks (range 14.5%) were almost totally explainable by differences in skin change by CLASS. For example, given adjustment for skin change, cows were expected to have 33% lesions and not the 27% observed; heifers were predicted to have lesion risks of 38%, not the 42% observed.

Discussion
The Irish national tuberculosis database is extensive, thus in modelling the effects of MONTH and CLASS, type II error was of no concern; rather we had to establish 'important' magnitudes and 'changes in coefficient size' to judge the importance of the exposures and the extent of confounding. Thus MONTH and CLASS had to have coefficients that predicted standard reactor risk differences of >2/10,000, skin change differences of >2 mm, and lesion risk differences of >3% to be deemed important. Other variables were deemed to be confounders if they produced more than a 15% change in these coefficients.
With few exceptions, the outcomes were highly confounded, thus it is very important to make inferences based on adjusted as opposed to crude means. This has important ramifications for interpreting aspects of the control programmes as well as when making scientific inferences about the effect of specific exposure factors. For example, the use of standardised responses (morbidity, skin change and lesion risk) should prove very useful; this extends to monitoring changes in standard reactors as distinct from changes in all reactors.

Cows were the highest risk class of cattle for tuberculosis, although, on average, cows had smaller skin changes to the SICTT than other classes of cattle. We believe that age, not type or duration of *M. bovis* exposure, may be the best explanation of the difference in skin change among classes. The higher risk of becoming a standard reactor in cows may relate more to differences in type of exposure, rather than duration of exposure, because even on repeat testing of herd breakdowns, cows have the highest risk of being standard reactors. The seasonal effect in risk may be partially a result of the scheduling of herd tests, in that there is a tendency to schedule testing in areas of ‘concern’ early in the test year that begins in April. This explanation is consistent with the abrupt shift from low-risk to high-risk seasons which centers on April–May. However, it also may be that the management of cows leads them to have a greater exposure to *M. bovis* than the management of younger animals. Badger movement, associated with breeding activity, is most pronounced in the February to April period, although fall peaks also occur (Wilesmith *et al.*, 1986).

Skin change was the best predictor of lesion risk. The effect of MONTH on lesion risk persists even after accounting for all the other factors; recall that there were only minimal differences in skin change among months. Most of the month to month differences in lesion risks was not explainable by the factors included in this study. Given that exposure would likely predate the development of a lesion by at least 6 months, as happened with a small trial after exposing calves to infected badgers (Little, 1982), then peak exposure would be in the summer period. Only very short exposure to lesion times would be consistent with aerosol transmission of *M. bovis* in winter feeding sheds. CLASS effects were due, largely, to skin change, but younger cattle were more likely to have lesions than cows with the same skin change to the SICTT.

Thus, analyses of secondary data can provide a basis for hypothesis generation and testing to answer scientific questions, as well as providing guidance in the manipulation, analysis and interpretation of data as part of a disease control programme.

**References**
