

CASE-CONTROL STUDIES OF FARM-LEVEL FACTORS ASSOCIATED WITH
ANTIBIOTIC RESIDUES IN MILK: COMPARISON OF USING PREVALENT
VERSUS INCIDENT CASES IN SIMILAR POPULATIONS OF DAIRY FARMS

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The susceptibility of case-control studies to bias is a well recognised problem in epidemiological research. Retrospective studies of drug residue violations in foods of animal origin are perhaps especially prone to bias because of the regulatory/legal implications of residues, the extreme difficulty of masking ("blinding") the subjects and investigators, and because some farmers may wish to deny or hide responsibility. Kaneene and Willeberg (1988) have addressed the problem of information bias in a case-control study of farm-level risk factors of antibiotic residues in milk. A number of seemingly reversed associations between potential risk factors and antibiotic residues in milk were observed and the authors concluded that some of these may have been due to differential information bias created when some of the case farmers reported use of good practices, perhaps in an attempt to give a better, but inaccurate, impression of their management practices. It was mentioned that due to the retrospective nature of the study, some of the case farmers may have changed management/residue prevention practices from the time of residue violation to questionnaire administration, and have answered questions based on their current practices, rather than on those used prior to residue violation. This potential problem has been recognised in case-control studies involving prevalent, or previously diagnosed cases of cancer as opposed to incident, or recently diagnosed cases (Cole, 1980). We have recently conducted two case-control studies of farm-level risk factors for antibiotic residues in bulk milk that differed with respect to the use of prevalent/incident cases. This provided an opportunity to distinguish risk factors for antibiotic residues in bulk milk from the effects of residue detection.

MATERIALS AND METHODS

Details of the studies compared in this report have been published elsewhere (McEwen, Meek & Black, 1991; McEwen, Black & Meek, 1991). Briefly, the sampling frame for the mail survey was the set of dairy farms from which a positive bulk milk antibiotic residue test result was received in a two year period (1987-88) of government monitoring (case farms) and farms that were negative for all tests conducted in the same period (control farms). 350 each of case and control farmers were mailed questionnaires of dairy

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management practices, as well as antibiotic handling and residue prevention methods. Completed questionnaires were received by mail from 248/350 (71%) case and 256 (73%) control farms. As case farmers in the mail survey were asked to complete questionnaires 4 - 28 months after being told that antibiotic residues were detected in bulk milk from their farms, these farms could be called "prevalent" cases.

The dairy farms selected for the personal interview survey were farms test-positive during government monitoring in 1989 (case farms, n=94). Control farms (n=94) were residue-negative and were matched on interviewer and geographical region of the province. Farms in this study were visited one day after antibiotic residues were detected in samples of their bulk milk ("incident" cases), and were administered essentially the same questionnaire used in the mail survey. It was impossible to mask either the interviewer or the subjects with regard to drug residue status of the farms.

Statistical significance ($P \leq .05$) of unconditional associations between case-control status and potential risk factors of interest were determined using Student's t-tests for continuous variables, the chi-square or Fisher's exact test for binary variables and analysis of variance for multiple level categorical variables. Logistic regression was used to perform conditional analysis and to control confounding, but the results of this analysis are not reported here.

RESULTS

The distributions of selected management factors, antibiotic treatment practices, and antibiotic residue prevention methods among the case and control farms of the two studies were compared. Similar results with respect to the first two groups of variables were obtained in the two studies. Risk of residues was increased on larger farms, with the frequent use of part-time employees and with parlour, as opposed to tie stall milking systems. Farmer estimates of the proportion of milking cows treated by various routes of administration tended to be higher for case groups of farms and risk of residues was reduced in both studies when a veterinarian's advice was always sought regarding use of injectable antibiotics.

Reversed associations were observed when the two studies were compared with respect to methods used to prevent residues in milk. Marking of treated cows for the purpose of identification, and use of on-farm antibiotic residue test kits were factors that were observed with increased risk of milk antibiotic residues in the mail survey, but were associated with decreased risk in the personal interview study. In contrast, the use of separate equipment to milk treated cows and the tendency to vary milk withholding times after treatment according to drug label instructions were observed in association with reduced risk of milk antibiotic residues in both studies.

DISCUSSION

Differences in the results of the two studies may be attributed to one or more of the following: use of prevalent versus incident cases; self versus interviewer administration of questionnaires; and method of subject selection. Although it is impossible to separate the effects of these factors when comparing the two studies, it is likely that most of the observed differences were due to the prevalent/incident case factor. Control groups were comparable for most of the factors examined. Interviewer bias could be responsible for some differences, but it would be expected across a range of factors, and management and antibiotic treatment factors were distributed similarly among cases and controls in the two studies. Recall or information bias may well have been present, but should be similar in effect in both studies. Once again, this is supported by the similarity observed in the reporting of antibiotic treatment practices in the two studies.

Marking of treated cows and use of on-farm residue test kits were factors associated with increased risk of residues in the mail survey, but were observed with reduced risk of residues in the personal interview study. These residue prevention methods could easily have been adopted by farmers in the prevalent case group between the time of milk residue violation and questionnaire administration. As the questionnaire was not designed to distinguish past from present practices, these methods may have erroneously appeared to be risk factors in the mail survey. It would have been more difficult for farmers to change management or drug treatment practices, or for some other prevention methods, such as using separate equipment for milking.

Care must be taken that effects of case classification are not confused with risk factors in case-control studies that utilize prevalent rather than incident cases.

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