ABSTRACT

Long-term effects of paratuberculosis on within-herd prevalence and on-farm economy of implementing risk-based control strategies were compared with alternative strategies by using a herd-simulation model. Closing transmission routes is essential for effective control of paratuberculosis. However, many farmers lack the resources to carry out these procedures for all cows in the herd. When using risk-based control strategies 1) all cows are tested quarterly with a milk ELISA, 2) specific cows with a high risk of being infectious are identified, and 3) the farmer can focus only on these infectious animals to close infection routes. In this way the workload can be reduced, making these control strategies more feasible. This study evaluates potential long-term effects of the risk-based approach compared with non-risk-based strategies by simulations conducted with the herd-simulation model PTB-Simherd. Seven control strategies were simulated in herds with initial true herd prevalences of 5, 25, and 50%, respectively. The results predicted the risk-based control strategies to be very efficient and comparable to the best whole-herd strategies in reducing the within-herd prevalence of paratuberculosis with considerably less labor. If infection routes are closed efficiently, prevalence can be reduced to 10% of initial prevalence within 5 to 7 yr. Test-and-cull strategies without closing infection routes were found, by simulation, to be ineffective in reducing prevalence and were not cost-effective methods. The profitability of the various control strategies depends on hourly wages and time spent per cow/calving. Furthermore, simulations show that immediate culling of highly infectious cows is only necessary and cost-effective if infection routes from these cows are not efficiently closed. The risk-based control strategies are recommended in the Danish voluntary control program “Operation Paratuberculosis,” which was initiated in February 2006 and now includes 1,220 dairy farmers in Denmark.

Key words: paratuberculosis, risk-based control, simulation, management

INTRODUCTION

Johne’s disease or paratuberculosis (PTB) is a chronic infection caused by Mycobacterium avium ssp. paratuberculosis (MAP), and the infection is widespread in many species, especially in ruminants (Kennedy and Benedictus, 2001). Infections with MAP can cause animal welfare problems and considerable economic losses due to decreased milk production, diarrhea, weight loss, and death in dairy cattle (Chiodini et al., 1984). Furthermore, transmission of MAP through milk, meat, and surface water is suspected to be a potential risk of causing Crohn’s disease in humans (Feller et al., 2007). The within-herd prevalence in dairy units has been increasing over the last decades, and several countries have initiated individual control programs, but only with limited success (Kennedy and Benedictus, 2001). Two of the major challenges in controlling paratuberculosis are that 1) eradication is slow, requiring the farmer to remain motivated for years while diagnosis is hampered by imperfect tests, and 2) effective control implies labor-intensive procedures, often at inconvenient times of the day (e.g., swift removal of the newborn calves) because efficient closure of transmission routes is necessary for control (Groenendaal et al., 2002; Dorshorst et al., 2006; Kudahl et al., 2007). On busy days and in times with shortage of manpower, such work is often given a low priority.

Risk-based strategies can contribute to reduction of both problems mentioned above. They have been implemented in the Danish voluntary control program, Operation Paratuberculosis (OP), initiated in February 2006 by the Danish Cattle Federation. This program consists of 1) frequent testing that substantially increases the probability of identifying infectious animals and 2)
focusing special management on only infectious animals when closing infection routes and thereby reducing the amount of labor. The median percentage of animals classified as infectious was 16% among 1,065 herds with updated diagnostic test information by February 22, 2008 (Danish Cattle Federation, Aarhus; unpublished data), which suggest that a significant reduction of animals requiring special management is possible. The strategies are based on the “Bang method,” which was used for eradication of bovine tuberculosis in Denmark (Bang, 1908; Bang, 1928). The principle of this method is that all test-positive animals should be managed so that the risk of transmission of the infection is reduced or eliminated (Bang, 1908; Bang, 1928). A prerequisite of the Bang method was frequent testing because the diagnostic test used was imperfect. However, culling of test-positive animals was not a necessity unless the test-positive animals were deemed highly infectious and affected by the infection.

In OP all lactating cows in each herd are tested 4 times per year by using a milk antibody ELISA on milk yield control samples (Nielsen, 2002; Nielsen et al., 2002). The test is optimized to be as sensitive as possible, whereas specificity is of less relevance. Frequent testing enables detection of almost all infected cattle that shed bacteria (Nielsen and Erskboll, 2006). Cows are grouped into 1) repeatedly ELISA-positive cows, called “red cows” in OP (high-risk cows recommended to be culled); 2) one-time ELISA-positive cows, called “yellow cows” (high-risk cows not recommend to be culled); and 3) ELISA-negative cows, called “green cows” (probably noninfectious cows).

Risk-based management can be established using these risk categorizations (Nielsen et al., 2007). The farmer and herd health advisor need to establish a plan for changes in management and housing systems to reduce transmission of MAP from infectious animals. Transmission of bacteria from potentially infectious cows (with at least 1 positive ELISA) to calves should be closed effectively, and the most infectious cows (repeatedly ELISA-positive) should be culled before next calving (Nielsen et al., 2007). The system allows detection of cows at risk of being infectious, and the farmer only has to optimize management of these cows, thereby saving time and money. However, testing implies a cost along with culling of highly infectious cows. An analysis of the total epidemiological and economic effects of implementing these risk-based strategies compared with non-risk-based strategies in different farms is thereby very relevant and demanded by the farmers. It would, however, be extremely expensive, time-consuming, and practically impossible to evaluate all of these different methodologies using field trials. In addition, MAP infections can have many effects on production parameters, and the effects of different control strategies are very complex. Therefore, simulation models are needed for estimation of economic and epidemiologic effects.

Various paratuberculosis models have been developed (e.g., Groenendaal et al., 2002; Dorshorst et al., 2006; Kudahl et al., 2007). These models have all been used for the prediction of long-term effects of different control strategies. Most simulation studies agree that management practices interrupting infection routes are essential to control MAP infections in the herd. However, risk-based approaches have not been thoroughly studied.

The present study was based on the PTB-Simherd model, which reflects both direct effects and indirect effects of PTB related to effects on herd dynamics and herd demographics (Kudahl et al., 2007). The aim of our study was to estimate the total epidemiologic, production-related, and economic effects of risk-based strategies recommended in OP compared with different non-risk-based strategies to control MAP infections in dairy herds.

MATERIALS AND METHODS

Simulations were made with the PTB-Simherd model (Kudahl et al., 2007), which is based on Simherd, a dynamic, stochastic, and mechanicistic Monte Carlo simulation model simulating a dairy herd including young stock (Ostergaard et al., 2003, 2005). The PTB-Simherd model was further developed to simulate the classification system used in OP, where cows are grouped into ELISA-negative, ELISA-oscillating, and repeatedly ELISA-positive groups based on the last 4 milk ELISA results, exactly as practiced in OP. Cows were only classified into the ELISA-negative group if all of the last 4 tests were negative. The repeatedly ELISA-positive group consisted of cows in which at least the last 2 tests were positive. The ELISA-oscillating group consisted of cows with any other combination of positive and negative test results during the last 4 tests. Compared with the sensitivities used in the study of Kudahl et al. (2007), the sensitivities of the milk ELISA were updated based on the study by Nielsen and Toft (2006) (Table 1). Seven scenarios were simulated in a 200-cow dairy herd 10 yr into the future with 500 repetitions. In the PTB-Simherd model both the true infection status and the diagnosed status of each animal is known. Therefore, it is possible to predict the true prevalence of the herd, which is much greater than the apparent (diagnosed) prevalence of the herd. In the results, true prevalences are reported. The 7 scenarios were repeated in 3 herds with initial true prevalences of 5, 25, and 50%, respectively. To compare the effects of risk-based strategies (with different culling strategies)
with alternative strategies used in practice, 7 scenarios were specified as follows:

1. No control: A farm with “average” hygiene level; the calf and dam are together for up to 24 h after calving, colostrum is provided from own dam, and the calves are fed with waste milk or bulk tank milk. No testing is performed.

2. Optimized management: All risks of infection are reduced to 5% of risks of strategy 1 (a risk reduction to 0% is assumed to be impossible). In practice this means that all cows are regarded as high-risk cows and PTB management needs to be optimized for all cows and calves in the herd, because no testing is done. Calving areas are thoroughly cleaned before each calving and calves are removed immediately from their dam. Colostrum is used only from own dam if she seems healthy, otherwise from a colostrum bank. Afterward, calves are fed with milk replacer. Generally, a high hygiene level is required, and calves should be raised separately from cows.

3. Optimized management + culling: Like 2, but, in addition, all cows are tested by milk ELISA once a year and positive cows are culled immediately if confirmed with a positive fecal culture. This strategy was included because many farmers want information about the infection status of the cows even though it might not be essential to stop infection routes.

4. Risk-based management 1: Cows are diagnosed by quarterly milk ELISA and grouped into ELISA-negative, ELISA-oscillating, and repeatedly ELISA-positive groups. Management of calves from all cows with at least 1 positive ELISA is performed to close infection routes; that is, ELISA-oscillating cows calve in thoroughly cleaned calving areas that are not used for ELISA-negative cows. Milk (colostrum and other sources of milk) is not used from ELISA-oscillating cows (only from negative cows), and calves are removed from the dam immediately after birth. Calves should be grouped by age. Repeatedly ELISA-positive cows are culled immediately. However, cows with <8 wk to expected calving are allowed to calve because Danish laws prohibit slaughter of cows in late gestation. All calves from these cows are fattened and slaughtered because they have a high risk of being infected with MAP, either before or after calving.

5. Risk-based management 2: As in strategy 4, but repeatedly ELISA-positive cows are not culled until their daily milk yield drops below 10 kg, but not later than 8 wk before next calving. Cows included in the repeatedly ELISA-positive group are not inseminated. This strategy is represented because sometimes farmers want to keep high-yielding ELISA-positive cows until daily milk yield is low.

6. Test and cull based on testing strategies from OP: Immediate culling of repeatedly ELISA-positive cows. No further management of high-risk cows. This strategy was chosen because it already seems to be practiced by some farmers involved in OP, without priorities to closing infection routes. They only use the test results for culling of infectious cows.

7. Test and cull based on testing strategies from OP, but no culling of repeatedly ELISA-positive cows until daily milk yield drops below 10 kg.

All other parameters in the simulation model were specified to represent typical Danish management of a dairy herd of large breeds with capacity for a maximum of 200 cows plus additional young stock. The specified replacement strategy ensures a minimum of 185
cows, and these limits for the herd size define if heifers are sold or purchased. Culling effects are thereby represented directly by the value of the slaughtered cow and the production of the replacement animal. A set of 2006 Danish prices was used to estimate the economic effects. The price of a milk ELISA was set to be US$6, which is the average price in a commercial lab in both Denmark and the United States. The price of a fecal culture test was set to US$32.

The economic costs also include 1 h (hourly wage of US$35) of extra labor per calving for optimizing management as recommended in OP as described for strategy 4. Milk production is the main economic factor affected by MAP infections, but the calculation of the total economic effect also includes the effect on income from sale of heifers, slaughtered animals, and bull calves together with the effects on expenses: feed, purchased heifers, veterinarian, artificial insemination, PTB tests, and additional labor related to control strategies. Future costs and revenues were discounted.

### RESULTS

#### Effect on True Prevalence

Simulation of the testing used in strategies 4 to 7 using 4 annual tests per cows resulted in the grouping of cows described in Table 2. The simulated effects of the 7 control strategies on true prevalence are illustrated in Figures 1, 2, and 3. The ranking of strategies according to effectiveness in reducing MAP prevalence was independent of initial prevalence.

The curves in Figures 1, 2, and 3 illustrate the importance of closing infection routes by optimizing manage-
ment. This is shown to be equally effective whether management is optimized for all cows (strategies 2 and 3) or only for high-risk cows (strategies 4 and 5). The simulations also demonstrate that if infection routes are not closed and the tests are only used for culling of repeatedly ELISA-positive cows (strategies 6 and 7), the prevalence is kept more or less constant. The prevalence is not reduced, but the results emphasize the importance of immediate culling of infectious cows rather than keeping them until milk yield is low. However, if infection routes are closed, the time of culling is of no importance in relation to effect on prevalence. If

Figure 2. Simulated effects on true herd-prevalence control strategies against paratuberculosis in dairy herds with an initial true herd prevalence of 25%. Risk-based strategies (strategies 4 and 5) were compared with no control (strategy 1) and non-risk-based strategies (2, 3, 6, and 7).

Figure 3. Simulated effects on true herd-prevalence control strategies against paratuberculosis in dairy herds with an initial true herd prevalence of 50%. Risk-based strategies (strategies 4 and 5) were compared with no control (strategy 1) and non-risk-based strategies (2, 3, 6, and 7).
management is carried out as recommended, the prevalence can be reduced to 10% of the initial prevalence within 5 to 7 yr.

**Economic Effects**

The effect on milk production of the different control strategies on a farm with initial true prevalence of 25% is shown in Figure 4 as an example of the main economic factor. Independent of control strategy, it takes 2 to 3 yr before milk production stops decreasing and starts to increase. If no control is performed, milk yield will decrease continuously.

The total economic effect on net annual revenue per cow per year is illustrated in Figures 5, 6, and 7. The economic results of the first 2 yr can be slightly misleading as they are strongly affected by the status of the initial herd. Although true prevalence is still less than 20% (Figure 5, yr 1 to 6) none of the control strategies seem cost effective. However, if no control strategies are implemented after this point (strategy 1), the simulations predict that the losses will increase constantly with increasing prevalence (Figures 6 and 7). If a control strategy is implemented when true prevalence is 25%, costs of all strategies exceed the profit from reducing prevalence in the first 3 to 4 yr, and it will thus be tempting to let things slide. But over a period of 10 yr and with an initial true prevalence above 25%, the risk-based strategies (strategies 4 and 5) seem to be the most favorable economically for control of MAP (Figures 6 and 7). Culling of repeatedly ELISA-positive cows immediately (strategy 4) instead of waiting until their daily milk yield is <10 kg (strategy 5) is of no economic importance as long as infection routes are closed. If routes are not closed, it is important to cull cows as soon as they have their second consecutive positive ELISA (strategies 6 and 7). The best alternative strategy compared with risk-based management is to carry out optimal management on all cows without testing and culling (strategy 2). Supplementing this strategy with testing and culling (strategy 3) is an extra cost that is never recouped and does not make the strategy more effective.

These conclusions are, however, based on the assumption that optimizing management with the aim of closing infection routes takes 1 h (hourly wage of US$35) per calving/calf in total (Figure 8). Herds are, however, different and in some modern herds it may be easier to change management. Figure 9 shows the economic effects in a herd in which the extra management takes only 20 min per calf. In this case, strategy 2 (optimizing management of all cows without testing) is more profitable than the risk-based strategies (4 and 5) the first 3 yr because there are no expenses for tests and culling. From this point, that strategy (with or without using tests once a year) has the same economic effect as risk-based management. This means that if extra labor to optimize management is estimated to take <20 min per calving/calf (or cost <US$12) it is economically favorable to optimize management of all...
cows (strategy 2) without testing and culling (strategy 3) instead of using risk-based management (strategies 4 and 5), which implies costs for tests and culling.

**DISCUSSION**

Our simulations showed that risk-based approaches to control MAP infections are more cost effective than non-risk-based approaches, although the results are highly dependent on the time spent per calving and the hourly wages for management of infectious cows. The resulting simulations predicted risk-based management to be very effective in reducing the prevalence of MAP infection, independent of initial true herd prevalence. Closing infection routes by special management was, however, essential for reducing prevalence effectively.

**Figure 5.** Simulated economic effects (calculated as net annual revenue/cow per year, US$) of control strategies against paratuberculosis in dairy herds with an initial true herd prevalence of 5%. Risk-based strategies (strategies 4 and 5) are compared with no control (strategy 1) and non-risk-based strategies (2, 3, 6, and 7).

**Figure 6.** Simulated economic effects (calculated as net annual revenue/cow per year, US$) of control strategies against paratuberculosis in dairy herds with an initial true herd prevalence of 25%. Risk-based strategies (strategies 4 and 5) are compared with no control (strategy 1) and non-risk-based strategies (2, 3, 6, and 7).
irrespective of the strategy chosen. The importance of closing infection routes was also emphasized by Bang (1908, 1928) and it was predicted by other simulation studies (Groenendaal et al., 2002; Dorshorst et al., 2006, Kudahl et al., 2007). Test and cull strategies were not cost effective in any of the herds simulated in this study.

The results show that, for eradication purposes, the only effective strategies are risk-based management (strategies 4 and 5) and those implying optimized management of the whole herd (strategies 2 and 3). When comparing these strategies, cost effectiveness depends directly on time (wages) and the amount of time necessary for optimizing management for each calf: risk-based management is profitable whenever this special management exceeded US$12 per calving (under Danish conditions).

Available antibody ELISA tests have large variation in their ability to detect infectious animals (Nielsen and Toft, 2008). Moreover, the cut-off values of the

**Figure 7.** Simulated economic effects (calculated as net annual revenue/cow per year, US$) of control strategies against paratuberculosis in dairy herds with an initial true herd prevalence of 50%. Risk-based strategies (strategies 4 and 5) are compared with no control (strategy 1) and non-risk-based strategies (2, 3, 6, and 7).

**Figure 8.** Simulated economic effects of strategies including improvement of management routines where this improvement takes additional 1 h per calving/calf. Thick lines illustrate Operation Paratuberculosis with special management of only infectious cows. Thin lines are strategies in which all cows of the herd are managed to close infection routes using no tests.
individual tests regulate the sensitivity. Choosing a low cut-off value results in high sensitivity and low specificity; the opposite occurs with a high cut-off value. The cut-off value can thereby be adjusted to meet the aims of the control strategy. The cut-off value for the milk ELISA used in our strategies was chosen to obtain a high sensitivity of 50 to 80% for shedding cows (depending on infection stage and parity) and 10% for latently infected cows. Thereby, specificity was reduced to 96% for second-parity and higher parity cows. Other ELISA tests are available on the market, and therefore the simulations were repeated with 2 other levels of sensitivity: 1) for highly infected and clinically ill animals, sensitivity was reduced to 60% and specificity increased to 97%, and 2) for all infectious animals, sensitivity was reduced to 40% and specificity increased to 99.9%. Compared with the high-sensitivity ELISA, the results were that the process of reducing true herd prevalence from 25 to 5% was delayed by 6 mo and 3 yr, respectively. The net annual revenue per year-cow was reduced by US$3 to 5 with a sensitivity of 60%, whereas a sensitivity of 40% actually increased the income in the first 3 yr because fewer animals were culled. However, after 3 yr the net annual revenue was reduced by US$5 to 10 per year-cow.

Another sensitivity analysis was made on the testing intervals. In our strategy, we suggested that all cows were tested quarterly. Testing 2 or 6 times per year was also simulated. By testing 6 times per year a reduction of herd prevalence from 25 to 5% was obtained 4 to 5 mo earlier than when testing quarterly. By testing twice a year, the reduction was delayed by 2 yr. Over a period of 10 yr, there is no economic difference between testing twice a year or quarterly, whereas testing 6 times a year costs an additional US$3 to 5 per cow per year. When considering the effects on both prevalence and economy, we conclude that the optimal test schedule is quarterly.

Earlier studies have shown that herds with poor reproduction and high PTB prevalence react differently to control strategies (Kudahl et al. 2007). Simulations of the 7 control strategies in a herd with a heat detection rate of 40% and an initial prevalence of 50% showed that the culling of repeatedly ELISA-positive cows in such a high-prevalence herd with poor reproduction is very costly because of the scarcity of replacement animals. This made management strategies without testing and culling much more attractive and profitable whenever costs for management were <US$63 per calving. Only above this limit was it attractive to use risk-based strategies and to initiate the culling of repeatedly ELISA-positive cows.

Dorshorst et al. (2006) also suggested control strategies that include special management of infectious groups of animals based on different testing systems and management levels. But they found that testing was profitable under any conditions as long as it was used for managing test-positive cows. They have estimated the total costs for optimizing management to be US$260.50/cow per year, which is about 8 times our estimated cost. The high cost makes detection of risk animals by testing much more profitable. The simulated farming systems are, however, very different from the systems simulated in our study. Dorshorst et al. (2006) included one extra full-time employee to a 100-cow herd for optimizing management and investments in new calf management routines in which this improvement takes only 20 min per calving/calf. Thick lines illustrate Operation Paratuberculosis with special management of only infectious cows. Thin lines are strategies in which all cows of the herd are managed to close infection routes using no tests.

Figure 9. Simulated economic effects of strategies including improvement of management routines in which this improvement takes only 20 min per calving/calf. Thick lines illustrate Operation Paratuberculosis with special management of only infectious cows. Thin lines are strategies in which all cows of the herd are managed to close infection routes using no tests.
lutches. In our studies, we simulated a typical Danish farming system with a new stable (including calf lutches), a high degree of automation, and scarcity of manpower. Under these conditions, costs for the change in management routines to close infection routes are much lower.

In our economic results, all variable costs and income related to the dairy herd and its production are included in the calculations, together with the additional costs for labor when optimizing management. However, there may be farms with other economic effects of controlling MAP infection that we have not included here: investments in additional calving areas, electronic surveillance of calving areas, cleaning equipment, and additional freezing capacity for a colostrum bank. On the other hand, there may also be some positive side effects: 1) closing infection routes for MAP will also close infection routes for several other fecal-orally transmitted infections among the calves, and calf mortality may decrease; body weight gain may increase; and over time, there will be more and better replacement animals in the herd; and 2) the sales value of the herd will increase as the prevalence of paratuberculosis goes down.

The importance of immediate culling of repeatedly ELISA-positive cows has been questioned by the farmers, particularly if there is no apparent effect on milk yield. According to the simulations, immediate culling only seems important if infection routes are not closed. However, the results also show that by postponing the time of slaughter, there is only a minor economic benefit from keeping these cows to the end of lactation (particularly when infection routes are closed), because the majority already exhibit reduced milk production, and some cows lose weight before slaughter. In practice, such a strategy would possibly be very selective, and only high-yielding ELISA-positive cows would be allowed to finish lactation, which is more profitable than keeping all ELISA-positive cows.

Even if a cow is diagnosed as repeatedly ELISA-positive in late pregnancy, Danish law does not allow her to be culled until after calving. It is recommended that her calf is separated from other heifer calves, fattened, and culled. There is a high risk of transplacental infection and probably also a greater risk of shedding bacteria at an early age. This risk of calf-to-calf infection is not included in the simulation model. In scenarios without removal of calves from high-risk cows, the transmission of MAP in the herd is likely underestimated. In practice, however, risk-based strategies recommend that these calves are raised and sold together with bull calves; therefore, the risk of horizontal transmission between heifer-calves is minimized.

In general, the simulations predict the costs of all control strategies against PTB to exceed the increased income (from increased milk production) in the first 3 to 7 yr depending on strategy. Alternatively, the result of not controlling PTB over a longer time span is constantly increasing production losses, and thereby constantly decreasing net annual revenue. This reinforces the point that control of paratuberculosis requires patience and persistence from the farmers.

Operation Paratuberculosis was initiated in February 2006 and there are still only a few results available, and analysis of the effects of using the strategies recommended have not previously been performed. Validation of the simulations is therefore only possible by sensitivity analysis and face validation (Sørensen, 1990). Face validity is obtained by asking people who have insight into the system whether the conceptual model is reasonable by means of flowcharts (Sargent, 1982). One technique in face validation is loop analysis, in which all feedbacks in the model are examined for polarity, gain, and delay. Previous studies have confirmed the importance of closing transmission routes and found poor effects of controlling PTB only by testing and culling (Groenendaal et al., 2002; Dorshorst et al., 2006; Kudahl et al., 2007).

Although these simulations indicate that, under some conditions it is more profitable to use no tests and manage all cows optimally instead of joining OP, experiences from several countries show that this strategy is only practicable for a few farmers (Kennedy and Benedictus, 2001; Groenendaal et al., 2003). The burden of this labor is considered heavy, often occurring at inconvenient hours. Sources for the extra hours of labor are often not available because of the scarcity of manpower. In these cases, the strategies of OP are probably more manageable for effective control of PTB. Furthermore, regular tests can be of important informative and motivational value in control programs because they reflect whether there is an effect on prevalence.

Based on the large economic effects of cullings on farms with poor reproduction, the importance of culling ELISA-positive cows on these farms could be reconsidered and analyzed by further simulations. However, there remain important ethical and biosecurity reasons to quickly cull the most infectious and clinically diseased cows.

Another aspect not included in the simulation model is the communicative learning and motivating process that can be achieved by risk assessments and use of test results for monitoring in collaboration between the farmer and the advisor. The economic value of this process is not included, but the educating and motivating
effect on the farmer is considered to be crucial to the success of the control program.

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