Development of a milk quality assurance program for paratuberculosis: from within- and between herd dynamics to economic decision analysis

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ABSTRACT

A new surveillance program was modelled that focuses on limiting the concentration of Mycobacterium avium subsp. paratuberculosis (MAP) to a certain maximum number of bacteria per litre of bulk milk. In this new program dairy herds are distinguished in two categories, ‘Green’ and ‘Red’, where Green stands for the pool of certified herds that produce milk with a MAP concentration of <1,000 litre and Red herds with milk concentrations > 1,000 litre. The program is based on 3 parts: (1) an intake procedure (certification), (2) a surveillance procedure to monitor Green herds, and (3) infection control procedures for Red herds. Models were developed to predict the progress over time of Green and Red herds for certain herd factors (size, prevalence, MAP in bulk milk). Data from several test regimens based on blood or faecal tests were combined with information on herd sanitation measures and animal purchase policies. Results of epidemiological models were used in an economic decision analyses.

Keywords: Certification, surveillance, control, modelling, Mycobacterium avium subsp. paratuberculosis.

INTRODUCTION

In the Netherlands a certification and surveillance program for Mycobacterium avium subsp. paratuberculosis (MAP) has been developed, aiming at eradication of MAP at the herd level. In the program, herds can obtain a MAP ‘free’ status following five annual herd examinations, provided all faecal culture results are negative. The first herd examination is done by ELISA and faecal culture of ELISA-positive animals; the 2nd through 5th by pooled faecal culture (Benedictus et al., 1999). A program such as this that aims at eradication of MAP at the herd level is inherently expensive and there are no incentives for farmers to participate. Therefore, few farmers participate. However, the most important goal from a food safety point of view is to reduce the number of MAP bacteria per litre of bulk milk. Thus, an important research question is can we design a new program that limits the number of MAP bacteria per litre of bulk milk? Can the program be simple, cheap and give farmers enough incentives to join and stay with the program for many years?

In the present study a new certification and surveillance program was developed for farms with ‘low-risk’ or ‘low-MAP’ bulk milk. These farms will guarantee a certain component of their bulk milk, that is, to contain fewer than a preset number of MAP bacteria per litre. In the certification and surveillance program dairy herds are distinguished in two categories, ‘Green’ and ‘Red’, where Green stands for the certified herds that guarantee milk with MAP concentration below the preset quantity. An intake diagnostic test scheme determines which farms will receive a Green or Red status. Green herds are monitored regularly with a surveillance test scheme. Management improvements and trade restriction may help to improve the milk quality in the Green pool, and may help Green herds retain their Green status in the future (vs. moving to the pool of Red herds). A control program assists Red herds to progress to receive a Green status (perhaps again) after a certain time. The control program consists of test and cull of positive animals, whether or not combined with management improvements (step 1, 2 and 3 of PPN, the Paratuberculosis Program in the Netherlands, see Groenendaal et al., 2002 and 2003) and/or trade restrictions (here: purchase of live animals from Green farms only).
MATERIALS AND METHODS

Various alternative programs for certification-and-surveillance-and-control of MAP on low-prevalence Dutch dairy herds were evaluated in this study, assuming an initial herd-level prevalence in the country of 30%, i.e. at the start (before the intake procedure) we assume that 30% of the dairy herds is infected with MAP, and 70% is free from MAP. This prevalence was recently found in the Netherlands (van Weering et al., 2004).

Evaluated test schemes are based on sampling individual animals for blood or faeces (individual faeces test, pooled faeces test, serum ELISA). Testing of bulk milk samples for MAP on a large scale is not yet possible, so this test method was not evaluated. Through modeling we make the step from the number of test-positive animals in a herd to the number of MAP bacteria in milk. To evaluate the effectiveness of the various programs three models were used in this study:

(1) The simulation model JohnnSSim for within-herd transmission of MAP in a closed herd. This is a stochastic and dynamic simulation model that simulates (a) the herd dynamics, (b) the disease dynamics within the herd, (c) the control of Johne’s disease and (d) the economic consequences at the herd level. Details and input parameter values can be found in Groenendaal et al. (2002) and in Weber et al. (2005). With this model the effectiveness of the intake and surveillance procedures in closed herds were determined, as well as the infection control procedures in Red herds. The economic and epidemiologic output of this simulation model served as input for the other two models (see below).

Preventive management in the simulated herds was set to reflect management practices in the Dutch dairy industry (background management, see Groenendaal et al., 2002). An additional simulation assumed that all herds took the following preventive management measures: improved hygiene around birth (step 1 of PP, colostrum from own dam only, and feeding of milk replacer only (step 2), and effective separation of young stock from adult cows from birth to the end of the first year (step 3). Because these measures also affect other animal diseases, only 50 % of all costs of these management measures were attributed to the control of paratuberculosis in this study. Some of these input parameters were updated in February 2004 and are presented in van Roermund et al. (2004) and Weber et al. (2005).

The expected number of MAP bacteria per quantity of bulk milk was the sum of MAP shed directly into milk, and the numbers added through contamination of milk by faeces from faecal shedders. Faecal contamination of milk was estimated to amount on average to 40 mg per litre (Stadhouders and Jørgensen, 1990. For an extensive overview of MAP bacteria and/or CFU’s in milk and in faeces, see van Roermund et al., 2004). Based on these data, assumptions were made on the on-farm MAP contamination of bulk milk (Table 1). Faecal contamination was considered the prime source of MAP in milk. The expected concentration $C_{\text{Map}}$ of MAP bacteria in bulk milk was approximated by the average concentration of MAP in milk in all animals in the herd.
what may be considered an acceptable concentration of MAP bacteria in on-farm bulk milk is not known. in the present study a maximum concentration of 1000 MAP bacteria per litre bulk milk was decided as acceptable by experts from Dutch dairy organisations (NZO/NIZO), based on their knowledge of the effect of pasteurisation.

intake, surveillance and control schemes were first studied separately and then integrated in simulations with JohneSSim. those selected can be found in Table 2. in the integrated simulations, herds were permitted to migrate between the statuses Green and Red. at intake, test-negative herds were designated as Green while test-positive herds were designated as Red. thereafter, Green herds were re-classified as Red if a test-positive animal was found in the herd during surveillance. Red herds were re-classified as Green following the required number of annual test-negative herd examinations, as determined in the separate analyses of the intake and control schemes.

Table 2. Intake and surveillance of Green herds and control in Red herds simulated with the JohneSSim model. A positive result of the ELISA or pooled faecal culture (PFC) during intake and surveillance was confirmed by individual faecal culture (IFC). During control in Red herds IFC-positive animals and their lastborn calf were culled. However, results of ELISA during control in Red herds were not confirmed by another test; ELISA-positive individuals and their lastborn calf in Red herds were culled.

(2) The analytical model. For the total population of dairy herds that interact with each other by trade of living animals, a new model was developed. This mathematical model describes a large group of herds (divided in Green herds and Red herds). The model is deterministic, and variation among herds is modelled by statistical distributions. Input parameters of this model were aligned with those used in JohneSSim, such as the distribution of initial infection prevalences within herds, life expectancy of animals (infected or not), relative infectiousness in various stages of infection, test sensitivity in various stages of infection, and the within-herd transmission rate of MAP. For the within-herd dynamics of paratuberculosis in each herd, the transmission is described by one parameter (beta), with a default value based on simulation results with
Animal trade, i.e. here purchase of live animals from Green herds, is based on actual data of the Netherlands of the year 2000. In that year 37% of all dairy herds purchased cattle, and 63% did not. The average number of purchased life animals by open cattle herds was 7 per herd per year (Velthuis, 2004). In the model for the ‘open herds’ scenario (animal trade allowed), 63% of the herds was treated as closed, and 37% of the herds purchased animals (7 per herd per year). Of course for the ‘closed herds’ scenario (no animal trade), no animals were purchased by any herds.

(3) The economic decision analysis determines the preferred decision for a farmer: should I join the new program or not? The decision of an individual farmer whether to join the program or not will be based on many different aspects (e.g. former experiences with other programs, the amount of labour, the time it will take, the yearly costs, the investments, the benefits and the chances of receiving these benefits, beliefs, etc.). A way to determine the economically preferred decision of a farmer, given the set of alternatives he has, is by analysing a decision tree. A decision tree includes three aspects of the decision making process, namely the costs, the benefits and the risks. In a decision tree all alternative actions available for the decision maker and the outcomes determined by chance are structured in a chronological order. The producer’s goal that drives a decision is the highest Expected Monetary Value (EMV). More background information on decision analysis and decision trees can be found in Hardaker et al (2004), Clemen (1991) and TreeAge (1999).

The decision tree analysis models the costs, losses and the probabilities to change status: Green to Red or Red to Green. The decision tree weighs the economic elements with the risks and shows the preferred decision based on this. When the preferred decision is not to join the program the decision tree estimates the milk price differentiation for Green farms that is needed to change the preferred decision to joining the program. This milk price differentiation serves as an incentive for farmers to join the program.

A decision tree has three elements: 1) decisions to make; 2) outcomes based on probabilities, and 3) the value of the specific outcomes. Each element is explained below. A farmer has to make several decisions in time considering a new MAP program: (1) Should I join the program at the start? (2) Should I continue the program given the test results of the intake procedure?, (3) Should I continue the program during surveillance given the test results of the jth test round? (This decision can be repeated for each test round). It is assumed that a farmer has no prior information on the true infection status of his herd. After the intake procedure a farmer knows more about the infection status of the herd and uses this information when the next decision is made. This new information is also considered in the decision tree. Another scenario that has been modelled is that once he has decided to join, it is not possible for a farmer to leave the program before the sixth test round.

The uncertain events within the MAP program included in the decision analysis as probabilities are: (1) the chance that the farm is infected with MAP at the start of the program, (2) the chance of being classified as Green at the intake given that the farm is infected with MAP, (3) the chance of being classified as Green at the intake given that the farm is free of MAP, (4) the chance of becoming free of MAP within the period between two tests given that the farm is infected at the start of this period, and (5) the chance of becoming infected with MAP within the period between two tests given that the farm is free at the start of the period. The input for the decision analysis (probabilities) is the output of JohneSSim and of the analytical model.

These two elements, that is decisions and chances, influence the value of the specific outcome (pay-off function): profit, costs and losses. The values of the specific outcomes are calculated in a profit function that includes the net present value (i.e. the value in today’s prices) of the following costs and benefits: (1) yearly program costs, (2) test costs, (3) costs for management improvements, (4) losses due to MAP, and (5) milk price differential between Green farms and all other farms. The higher price per litre of milk produced by Green farms compared to other farms is a premium that serves as an incentive to encourage farmers to comply with the program and to compensate them for the costs incurred to earn a “Green” status.

The 36 alternative scenarios for paratuberculosis that have been evaluated in this study are the 9 test schemes of Table 2, each with and without management measures and with and without animal trade (9x2x2).
RESULTS

Epidemiology. We assumed an initial overall prevalence of paratuberculosis in participating herds of 30%, i.e. 30% of the herds were considered infected and 70% were considered to be free. As a result, 90% and 83% of the herds receive a Green status after intake I1 (ELISA) and I5 (faecal culture) respectively. After that, the number of Green herds drops during the first 10 years. This is due to the Green status but truly infected herds that are detected later and reclassified as Red herds. Only with management measures can increase in number of Green herds be seen, as control methods (C1=ELISA or C7=faecal culture) permit Red herds to reach Green status. As an example the percentage of Green herds after 8 years is given in Table 3 (recall that there were 90% at the start in Year 0 after Intake I1). (For codes I, S and C, see Table 2.)

As noted, the pool of Green herds decreases during the first years. As Green herds found to be infected are removed from the pool, the prevalence of infected animals and the MAP bacteria per litre bulk milk in the pool of Green herds falls, showing an improvement in Green herds’ milk quality in time (not shown here; see van Roermund et al, 2004).

Immediately after the intake procedure, the PVN (predictive value negative) is very high: about 97.8% and 99.7% of the Green herds produces milk with MAP<1000 bacteria/litre after intake I1 (ELISA) and I5 (faecal culture) respectively. However, the small fraction of Green herds producing milk with MAP>1000 bacteria/litre have a significant effect on the average MAP content of milk of all Green herds combined, keeping the overall concentration above the limit. The MAP concentration is above the limit for the first 5 years when ELISA is used as the intake assay (I1). This is due to the very skewed distribution of MAP bacteria in milk per herd. After intake procedure I5 (faecal culture) however, the average MAP content of milk in the pool of Green herds drops immediately to the level of 1000 bacteria/litre (see van Roermund et al, 2004).

Figure 1. MAP bacteria per litre bulk milk in the pool of Green herds versus fraction of farms in the Green pool, 8 years after the start of the program. Open dots or squares represent open farms, closed dots or squares represent closed farms. Squares represent farms with management measures (=step123), dots represent farms without management measures.

Figure 1 shows MAP bacteria in bulk milk for Green herds in year 8. The best programs are in the lower-right corner of this figure: these programs result in a higher fraction of participating herds receiving a Green designation, and a low average bulk milk MAP content (after 8 years). From this figure it becomes clear that
acquiring replacements outside of the home herd (purchase from Green herds: open farms: open dots) has a strong negative effect on both outputs. Programs with better outcomes are in the lower-right corner (I5-S1-C7, I1-S1-C7, I5-S2-C7, I1-S2-C7, and I5-S5-C7); they all require management measures and a closed herd. Just one test scheme permits an open herd and does not require management measures yet still keeps the average Green herd MAP concentration below the limit. This scheme is I5-S5-C7, the only one using only faecal culture for all three program components: intake, surveillance and control.

<table>
<thead>
<tr>
<th>Test scheme</th>
<th>Management: yes</th>
<th>Management: no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake-Surva.-Control</td>
<td>Herd: closed</td>
<td>Herd: closed</td>
</tr>
<tr>
<td>I1-S1-C1</td>
<td>77</td>
<td>73</td>
</tr>
<tr>
<td>I1-S2-C1</td>
<td>81</td>
<td>77</td>
</tr>
<tr>
<td>I1-S2-C7</td>
<td>85</td>
<td>74</td>
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The intake procedure (I) and the surveillance procedures (S) appear to have less effect than the type of control procedure on Red herds (all faecal culture C7), and the presence of management measures plus the absence of animal trade. With the fecal culture control scheme C7 Red herds go back to the pool of Green herds sooner (after two negative test rounds) than C1 (ELISA control), explaining the larger size of that pool. In the absence of animal trade, the effect of management measures seems relatively minor (compare closed squares with closed circles), but this may be due to the short analysis period of 8 years.

When found test-positive, a Green herd shifts to the pool of Red herds and is treated as if it had never been classified otherwise (i.e. status is based on the PVN value discussed above). For the pool of Red herds it was found that 6 ELISA or 2 faecal culture test-negative herd examinations are needed to reach a PVN value of 97.8-99.7% (depending on intake I1 or I5).

For the Red herds management measures are very important (see van Roermund et al., 2004) in controlling the percent of infected animals and MAP content of milk. Animal trade is less important for a Red herd, since purchase of an infected animal has a marginal effect on the prevalence of an already infected herd. Except for a short time immediately after culling faecal culture-positive animals (control C7) when management measures are applied on the farm, the average MAP content of milk in the group of Red herds is always above 1000 bacteria/litre. In fact within one year of culling the MAP content rises to at least 7000 bacteria/litre (see van Roermund et al., 2004).

**Decision analysis.** The model predicts that without the milk price incentive, farmers will not join the program. A farmer will drop out if classified as a Red herd (at the intake procedure or after a test round during the surveillance procedure) even if the milk price differentiation is € 0.01 per litre milk. Higher milk price differentiations were not studied here. The one exception is program I1-S1-C7 (without management measures). For this program the optimal decision for a Red farm after testing positive at intake procedure is to join the control procedure for another test round (at a milk price differentiation of at least € 0.003). If the herd tested positive again, the optimal economic decision is to quit the program.

The minimal milk price differentiation needed to change the decision from ‘no’ to ‘yes’ to join the intake-procedure is between € 0.0005 and € 0.0051. If a program is designed in such a way that a farmer cannot stop joining the program before the 6th test round of the surveillance procedure, the milk price differentiation is higher and should be between € 0.0009 and € 0.0080, depending the program. The higher milk price differentiation is needed to balance the higher program costs during 6 test periods. The programs I1-S2-C1, I1-S1-C1 and I1-S2-C7 (without management measures) have the lowest costs for participants. The average yearly costs for Green and for Red farms are € 388 and € 1065 for program I1-S2-C1, € 609 and € 1085 for program I1-S1-C1 and € 386 and € 1647 for program I1-S2-C7. With management measures these costs are much higher: € 2110 and € 2538 for program I1-S2-C1, € 2332 and € 2529 for program I1-S1-C1 and € 3183 for program I1-S2-C7. For a more extensive overview and for benefits, see van Roermund et al. (2004).

A cost-effectiveness analysis is presented in Figure 2. In this figure the milk price differentiation between Green and Red farms (needed to give a farmer enough incentive to join a quality assurance program voluntarily) is set out against the fraction of participating farmers that will have a Green status after 8 years.
Two clusters can be distinguished in this figure: the programs with management measures (step123, right upper corner) and the programs without management measures (left). This shows that management measures result in a higher milk price differentiation and in a more effective program (defined here as the percent of herds classified as Green). The difference in the upper and lower end of each line indicates the effect of animal trade. All programs perform better when no trade is allowed. However, the ban on trade has a greater impact when no management measures are included. The ‘cheapest’ programs that are most effective (where the fraction is higher than 70%) require closed herds but do not require management measures.

**Figure 2.** Milk price differentiation needed to give a farmer enough incentive to join a quality assurance program voluntarily vs. the fraction of participating herds that will have a Green status after 8 years. The milk price differentiation is based on the assumption that a farmer joins the program for the intake procedure and remains for at least 6 infection control. The upper end of each line (closed dots or squares) represents closed farms in a program where no trade is allowed, whereas the lower end (open dots or squares) represents open farms where trading is allowed.

The average concentration of MAP bacteria per litre of Green herd milk is given in Figure 3 in relation to the milk price differentiation. As in Figure 2 two clusters can be seen: the programs with management measures (step123, to the right) and the programs without management measures (to the left).

In setting a target concentration level of less than 1000 MAP bacteria per litre for Green farms on average, the models show that open herds and no management measures are not optimal with one exception (as mentioned above for the scenario that a farmer remains in the program before the sixth test round of the surveillance and control procedures). When management measures are applied almost all programs (with or without animal trade) are provide milk that meets or is below the MAP target concentration.
Figure 3. Milk price differentiation needed to give a farmer enough incentive to join a quality assurance program voluntarily for MAP vs. the average number of MAP per litre of milk of Green farms per year. The milk price differentiation is based on the assumption that a farmer joins the program for the intake procedure and remains for at least 6 test rounds during the control procedure. The lower end of each line (closed dots or squares) represents closed farms in a program where no trade is allowed, whereas the upper end (open dots or squares) represents open farms where trading is allowed.

Management improvements on farms can be costly, and based on this study are less important than reducing animal trade (see Figure 2). However, the positive effect of management measures increases if animal trade is allowed. Furthermore, management measures are important on Red farms, and if they are not taken, the pool of Green farms will never increase in size.

DISCUSSION AND CONCLUSIONS

According to the models, Green herds must be closed to animal trade. The choice of intake and surveillance policies themselves is less important than the effect of animal trade and of management measures. Management measures have less effect when animal trade is restricted (during the first 8 years), but are always very important on Red herds. The control component C7 (individual faecal culture) for Red herds increases the number of herds in Green herd pool due to the shorter lag time of becoming Green again (2 negative test rounds), and C7 is effective at lowering the concentration of MAP in Red herd milk. If there is no milk price differentiation for milk produced by Green farms the preferred decision for a farmer is not to join any program. If a milk price differential is introduced, the Green farms will join. The majority of all dairy farms in the Netherlands will be certified as Green. When a farmer receives a Red status (at the intake procedure or after a test round during the surveillance procedure) the preferred decision is to stop the program immediately even if the milk price differentiation is € 0.01 per litre milk. This will happen with 10-14% of initially participating farms.
As for any modelling study, the reliability of results depends on the accuracy of the model’s assumptions. The most uncertainty in these models concerns the lack of data on the amount of MAP bacteria in milk and the effect of management measures on the within-herd transmission of the infection. Both factors’ assumptions were tested in a sensitivity analysis (see van Roermund et al., 2004 and Weber et al., 2005). In the models MAP in milk is contributed by a small fraction of highly infectious animals plus by the clinical animals (see Table 1). This skewed distribution shown by the model should be verified in the field. It is also important to realise that prevalence impacts of management measures in the program are still based on expert opinions (see Groenendaal et al., 2002) that have yet to be proven. They are now being studied on 17 heavily infected farms in the Netherlands during 2001-2005.

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