DEVELOPMENT OF THE DUTCH JOHNE'S DISEASE CONTROL PROGRAMME SUPPORTED BY A SIMULATION MODEL

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SUMMARY

The development of a simulation model, 'JohneSSim', was part of a research effort in preparation for a national Johne's disease control programme. Initially, the focus was mainly directed on different compulsory 'test and cull' strategies. However, the results from the 'JohneSSim' model showed that eradication with only 'test and cull' strategies would not be possible within 20 years. Better calf management seemed more effective in reducing the prevalence. Overall, control was not an economically attractive option. Simulation of a strategy with an 'ideal test' (80% overall-sensitivity) showed that the usage of this test would result in a significant faster decrease of the prevalence but that this strategy was economically not attractive because of the high number of test-positive, young animals that had to be culled. Therefore, a new potential control programme called, Paratuberculosis Programme Netherlands (PPN), was defined which was based on the stepwise improvement of calf hygiene, with little dependency on 'test and culling' at all. The model indicated that if farmers would consistently carry out the necessary management adaptations, this control programme decreases the prevalence considerably, and is economically more attractive (average benefit-costs ratio, excluding extra labour = 1.58) than previous plans. Based on the results of the 'JohneSSim' model, the new national voluntary Johne's disease control programme, PPN, was started in September 2000. The decision making has been greatly supported by the 'JohneSSim' model.

INTRODUCTION

Paratuberculosis in cattle is an infectious chronic granulomatous enteritis caused by *Mycobacterium avium* subs. *paratuberculosis* (Juste, 1996). In The Netherlands. paratuberculosis has been present for a long time, especially in the low-lying peat moors in the northern part of the country (Benedictus, 1984). Organised disease control started in The Netherlands in the eighteenth century with governmental attempts to eradicate cattle plague (Huygelen, 1997). Since 1919, the Animal Health Service has used faecal cultures from clinical

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affected and suspected animals as a means of detecting *M.a. paratuberculosis*. The first paratuberculosis control programme started in 1942 (Benedictus et al., 1999). Until recently, all control programmes of paratuberculosis were mainly based on early culling of infected animals and improvement of animal husbandry to prevent further spread of *M.a. paratuberculosis* infections within the herd (Kalis et al., 1999). Results of these programmes have been disappointing because diagnostic procedures have been inadequate and because farmers have not consistently carried out husbandry measures aimed at limiting infection transmission (Benedictus, 1984; Benedictus et al., 1985). The lack of progress with an organised control programme based on test and cull, led to a change of focus towards vaccination with a killed vaccine. This strategy has been successful in reducing clinical paratuberculosis and proved to be much cheaper than the subsidised cull-and-slaughter programme (Benedictus et al., 1985). However, even long-term use of a vaccine does not prevent faecal shedding of the bacteria and thus does not lead to elimination of the infection from the herds (Kalis et al., 1999). In 1997, the leading Dutch institutes working on paratuberculosis developed a plan for eradication of paratuberculosis. The plan was initiated to help alleviate the economic losses caused by the disease and also to address the growing awareness of product quality guarantees. This resulted in the 'First global plan for collective control of paratuberculosis'. In 1998, a new preliminary and voluntary paratuberculosis programme was started which was founded on this plan. This programme was based on management improvement and yearly testing of the animals and consisted of two parts: 1)'Unsuspected herds programme' which has as its objective, identifying unsuspected herds and preventing infection of these herds and 2) 'Assisting infected herds', which has the objective of eliminating the infection from known infected herd. A detailed outline of this voluntary programme is available (Benedictus et al. 1999).

The project, 'Preparation of the collective control of paratuberculosis in The Netherlands', was started on July 1, 1998. The objective of this project was to prepare a national control programme for paratuberculosis with the final aim of eradicating the disease. Scientific foundation of this new programme was deemed essential, because previous programmes had not yielded the desired results. A large research effort was initiated that included studies on test characteristics and improvements, prevalence estimates, monitoring and surveillance programmes as well as on the development of a simulation model, called 'JohneSSim' (Groenendaal et al., 2001). The goal of this model was to evaluate different control strategies on their epidemiological effectiveness and their economical attractiveness.

The aim of this paper is to illustrate the results of the 'JohneSSim' model and the subsequent crucial steps in the decision-making process that led to the implementation of the Dutch voluntary national Johne's disease control programme that started in September 2000.

MATERIALS AND METHODS

The 'JohneSSim' model

The simulation model, 'JohneSSim', that was used to evaluate the different Johne's disease control strategies, has been described previously (Groenendaal et al., 2001). This model is a stochastic and dynamic simulation model that simulates the herd dynamics, the disease dynamics, the control of Johne's disease and the economic consequences on a herd level for a default time period of 20 years.

In the herd dynamics, a typical Dutch dairy herd is simulated, including all replacement heifers. Both involuntary and voluntary culling are considered. In the disease dynamics module, five infection routes are considered; (1) fetal infections, (2) infections around birth, (3) infections due to drinking colostrum, (4) infections due to drinking whole milk and (5) infections due to an environment that is contaminated with *M.a. Paratuberculosis*. Control tools that can be simulated with the 'JohneSSim' model can be divided into 'calf hygiene' and 'test and cull' strategies. The benefit-costs ratio (BC-ratio) and the Net Present Value (NPV) are calculated for each control strategy. Both parameters are standard economic measures to value investments that have an extended time component (Dijkhuizen and Morris, 1997) and were calculated for the whole 20 year period, using discounting. However, the NPV should always be the ultimate decision criteria for investments (Brealey and Myers, 2000). The BC-ratio was defined as the total discounted benefits divided by the total discounted costs and the NPV as the total discounted profits minus the total discounted costs. The benefits were calculated as the losses from Johne's disease without control and the losses with the control programme. To discount, the real interest rate (interest rate minus inflation rate) was taken at 5%.

Because of the model's stochastic nature, the model both captures bad and good case scenarios. To represent the difference between dairy farms in the pre-control calf management, eight different herd-profiles were defined. After separately simulating all eight profiles, the model aggregates the different results according to each profile's proportional existence, to determine the results on a national level. A more detailed description of the different herd-profiles is available (Van Roermund et al., 1999).

Input data and control strategies

The strategies that were simulated are shown in Table 1. All strategies were defined by the advisory group 'simulation model Johne's disease control programme', which consisted of eleven experts on Johne's disease. Monthly meetings were held in which the necessary input data and the strategies requiring simulation, were formulated. Input data for the model are extensively described by Groenendaal et al. (2001).

Table 1. Control strategies, simulated with the 'JohneSSim' model

Stage		Test-and-cull	Management
First	a-0	No	No
	a-I	ELISA [a], > 3 yr, once a year	No
	a-II	ELISA [a], > 3 yr, once a year	Improve for calves ≤ 6 months
	a-III	Faecal, > 2 yr, once a year	Improve for calves ≤ 6 months
	a-IV	Faecal, > 2 yr, once a year	Improve for calves ≤ 12 months
Second	b-0	No	No
	b-I	ELISA, > 3 yr, once in first five years	Step 1 of management
	b-II	ELISA, > 3 yr, once in first five years	Step 1 & 2 of management
	b-III	ELISA, > 3 yr, once in first five years	Step 1, 2 & 3 of management

[a] each positive ELISA blood-test was confirmed with a faecal test and, if both tests were positive, the cow was culled

The study was performed in two stages, the first stage was performed from May 1998 to January 1999 and the second stage from January to April 2000.

First stage

The strategies that were simulated in the first stage of the study were mainly focussed on different test strategies for infected herds, combined with a monitoring programme to declare herds as 'unsuspected'. All input data are shown in Groenendaal et al. (2001). However, a few of the differences between stage 1 and 2 are shown in Table 2.

Table 2. The main differences between input parameters in the first and second stage of the 'JohneSSim' simulation study

Parameter	First stage	Second stage
Herd size (number of dairy cows)	50 (constant)	50, growing with 3.5% per year to 100 after 20 years
Introduction of infected animal(s)	Zero or one latently infected replacement heifer per year	Zero to six animals (calves, heifers or cows) per year with variation between farms and years
Costs of separate housing (in Dutch guilders)	2240 per year	1120 increasing to 2240 per year

In addition, an ideal test was defined and simulated with the model. The input parameters that were used for this test are shown in Table 3.

Table 3. Characteristics of both the 'default' ELISA test and the 'ideal test' as simulated in the first stage of the study

		'Default test'	'Ideal test'
Sensitivity	Infection status		
	Latent infected	1%	80%
	Low infectious	10%	80%
	High infectious	60%	80%
	Clinical infected	80%	80%
Specificity (all uninfected animals)		99%	99%
Minimal age of testing		3 year	12 months
Frequency		Once a year	Once a year
Costs (in Dutch guilders)		10.00	4.35

Second stage

In the second stage of this study, the focus changed to management strategies (Table 2). A new potential control strategy was defined called, 'Paratuberculosis Programme Netherlands' (PPN), based on stepwise improvement of calf hygiene (Table 4). In this programme, participating dairy farmers will be strongly encouraged to implement an enhanced three-step calf management programme, with advice being given on suitable management practices. The implementation of these measures was arranged in a logical order that followed the course of development of the calf. In the simulations, it was assumed that participating dairy farmers would implement step 1 in year 1, step 2 in year 2 and step 3 in year 3. Furthermore, it was assumed that all participating farms would test all cows older than 3 years by an ELISA test once in the first five years and cull all cows that were positive by both the ELISA and by a faecal confirmation test.

Table 4. Management adjustments to be made in each of the three PPN steps

Stages/Steps	Practices
Step 1: Calving	• Cleaned cow placed in an individual, clean, calving pen • Separate calf early from dam
Step 2: Calving to weaning	• No whole milk, only milk replacer • Housing, separate from cows >2 years • First two weeks in individual calf-box • Clean drinking water • Clean roughage: hay or dried grass • Only given colostrum from own dam
Step 3: Weaning to year old	• Housing, separate from cows >2 years • Clean roughage, hay, dried grass or silage from clean pasture that had no fresh manure on it • Only on clean pasture (no fresh manure) • Clean drinking water

RESULTS

Stage 1

Figure 1 shows the mean true prevalence of an average Dutch dairy farm (both infected and uninfected farms included) as simulated in the first stage of the study.

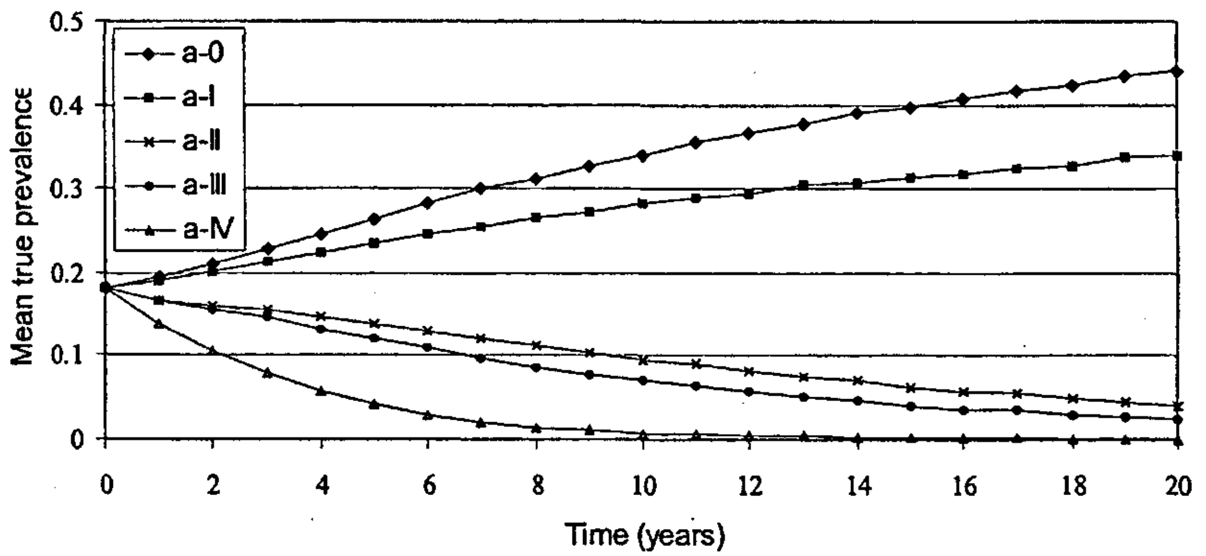

Fig. 1 Mean true animal prevalence over all Dutch dairy farms (infected or uninfected) in the first stage of the study as simulated by the 'JohneSSim' model under no control (a-0) or four different control scenarios (a-I to a-IV)

Without any control (a-0), the prevalence increased gradually. Annual ELISA blood testing with confirmation of positive results by faecal culture with culling if both tests are positive (a-I), resulted in a slower increase, but the prevalence still increased. However, improving the calf hygiene had a much larger impact on the mean prevalence, which can be seen on the difference between strategy a-I and a-II, which is caused only by improved calf rearing management. Furthermore, the difference between strategy a-III and a-IV showed the impact of further improving the calf hygiene, especially using separate housing of 7 – 12 month old calves.

Table 5 shows the economic consequences of the different control strategies, as calculated by the 'JohneSSim' model in the first stage of the study. Without control, the average losses increase considerable because of an increase of the average prevalence in infected herds and an increased of the number of herds infected. For strategy a-II the average BC ratios on farm level were calculated as 0.47 and 0.63 (with or without the costs for extra labour to realise the desired management measures, respectively). There was a large variation around these estimates, the 10% and 90% percentiles of the BC-ratio's were 0.00 and 1.44 for the situation without costs for additional labour. The latter number showed that for 10% of the dairy farms in The Netherlands, control strategy a-II would have a BC-ratio of 1.44 or higher.

Table 5. Losses caused by Johne's disease without control and reduction of the losses (in Dutch guilders), NPV, and BC ratio's of the control strategies as calculated by the 'JohneSSim' model in the first stage of the study

	Losses without control	Reduction of losses with control			
Year	a-0	a-I	a-II	a-III	a-IV
1	1,541	390	395	391	383
10	3,288	1,747	2,783	3,054	3,220
20	4,777	2,653	4,598	4,693	4,772
Total	36,871	18,691	29,070	32,064	33,218
Costs of control		30,054	55,196	66,426	162,610
BC-ratio incl.		0.51	0.47	0.40	0.19
BC-ratio excl.		0.51	0.63	0.50	0.24
10% [a]		0.00	0.00	0.00	0.00
90% [a]		1.15	1.44	1.10	0.57
NPV incl.		-11,362	-26,126	-34,362	-129,392
NPV excl.		-11,362	-11,234	-19,466	-96,664
10% [a]		-23,996	-37,464	-38,979	-120,379
90% [a]		5,670	22,077	6,551	-62,687

[a] 10% and 90% percentiles on farm level

The mean true prevalence under strategy a-II and using the 'ideal test' is shown in Fig. 2. The only differences between the two strategies are the test characteristics as all management measures are the same.

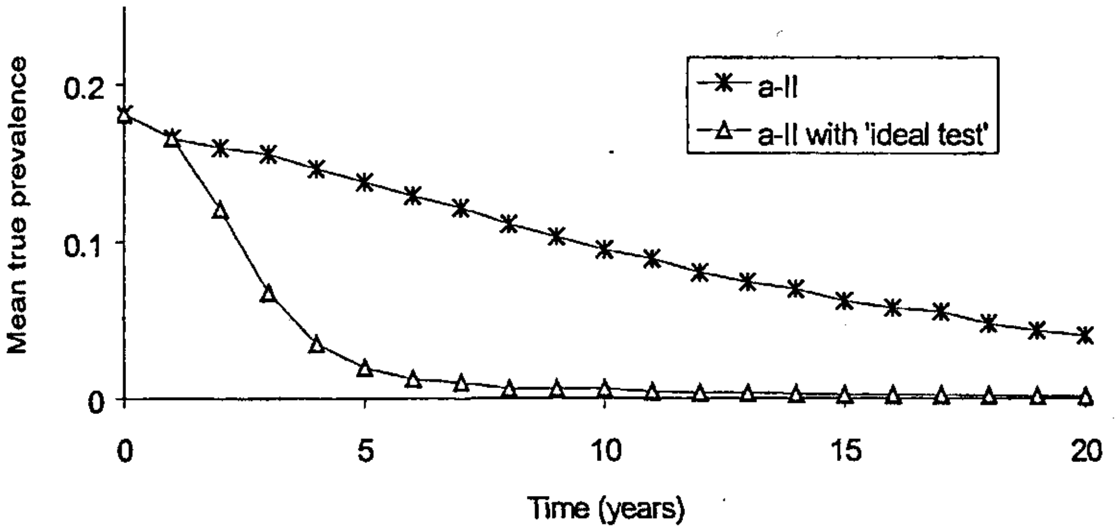

Fig. 2 Mean true animal prevalence over all Dutch dairy farms (infected or uninfected) in the first stage of the study as simulated by the 'JohneSSim' model under strategy a-II with and without an 'ideal test'

It is clear that with an 'ideal test', the prevalence decreased considerably faster but the economic consequences of these two strategies were also quite different (Table 6). A control strategy with an 'ideal test' was economically less attractive because of the much higher costs of culling: the 'ideal test' also found 80% of the latent infected animals (Table 3).

Table 6. Costs of culling test positive animals, total control costs (in Dutch guilders), BC ratio's and NPVs of strategy a-II and the same strategy using an 'ideal test'; calculated by the 'JohneSSim' model in the first stage of the study

	Strategy a-II	'Ideal test'
Costs culling	6,886	34,378
Total costs control	87,615	109,875
Average BC-ratio	0,63	0,44
10% - 90% [a]	0 – 1,44	0 – 0,94
NPV	-11.234	-27.224
10% - 90% [a]	-37,464 – 22.077	-46.026 - -4.481

[a] *the 10% and 90% percentiles on farm level*

Stage 2

Figure 3 shows the mean true prevalence on an average Dutch dairy farm (both infected and uninfected farms included) as simulated in the second stage of the study. It shows a slightly faster increasing average true prevalence without control (Fig. 3, b-0) than in the first stage of the study (Fig. 1, a-I). In addition, fig. 3 shows the additional effect of the three different management steps (see Table 4).

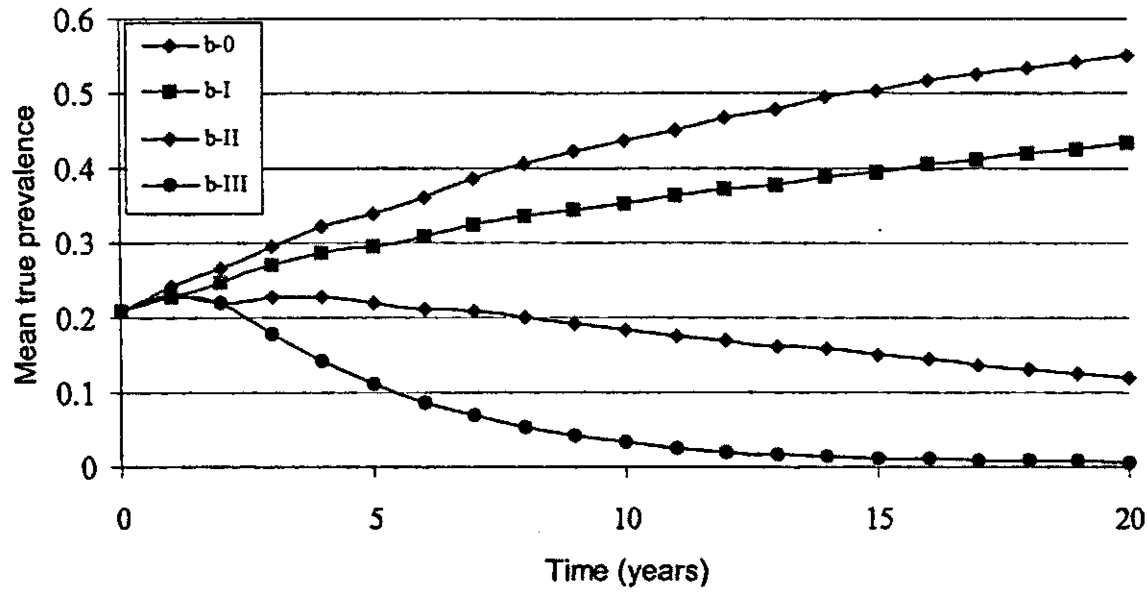

Fig. 3 Mean true animal prevalence over all Dutch dairy farms (infected or uninfected) in the second stage of the study as simulated by the 'JohneSSim' model under no control (b-0) or three different control scenarios (b-I, b-II, b-III)

Table 7 shows the losses due to Johne's disease, without any control measures being taken. Both the prevalence and the losses without control were higher in the second stage compared to the first stage, due to the adaptations of the model in the second stage. A large variation in these losses was observed between different farms. For example, in year 1 the average losses were calculated at Dfl. 1,690, but 10% of the farms had losses higher than Dfl. 5,265. The contribution of the three different categories of losses were decreased milk production (1), decreased slaughter value (2) and losses due to premature or sub-optimal culling (3). The latter accounted for almost 70% of the total losses caused by Johne's disease.

Table 7. Losses caused by Johne's disease without control, reduction of the losses (in Dutch guilders), Net Present Values (NPV) and Benefit Costs (BC) ratio's on an average Dutch dairy farm (infected or uninfected) as calculated by the 'JohneSSim' model. Losses are separated into losses due to decreased production (1), losses due to a decreased slaughter value (2) and losses due to premature culling of clinical or sub-clinical animals (3).

	Total losses				Categories of losses		
Year	Average	10%	50%	90%	(1)	(2)	(3)
1	1.690	0	398	5.265	488	157	1.046
2	2.649	0	750	7.628	616	267	1.767
5	4.304	0	2.166	12.105	1.002	401	2.901
10	7.398	0	4.890	18.561	1.670	640	5.088
15	11.016	0	8.666	26.209	2.384	960	7.673
20	14.808	0	13.797	33.032	3.248	1.268	10.292
Discounted	86.484	0	69.532	200.539	(22%)	(9%)	(69%)

Table 8. Losses caused by Johne's disease without control and reduction of the losses (in Dutch guilders), NPVs, BC ratio's of the control strategies as calculated by the 'JohneSSim' model in the stage phase of the study

	Losses without control	Reduction of losses with control		
Year	b-0	b-I	b-II	b-III
1	1,690	64	64	64
10	7,398	1,277	4,268	6,096
20	14,808	3,457	12,010	14,491
Total	86,484	14,762	49,859	64,340
Costs of control		19,493	40,274	61,732
BC-ratio incl.		0,64	1,10	0.95
BC-ratio excl.		2.22	2.78	1.58
10% - 90%[a]		0.00 - 6.60	0.00 - 5.94	0.00 - 3.32
NPV incl.		-4,731	9,584	- 2,608
NPV excl.		8,701	34,380	27,319
10% - 90%[a]		-8,170 - 36,967	-14,544 - 97,735	- 32,405 - 102,003

[a] 10% and 90% percentiles on farm level

Finally, Table 8 shows the economic consequences of the different control strategies against Johne's disease, as calculated by the 'JohneSSim' model in the second stage. Because of the increase in the reduced losses (=benefits) and the decrease of the control costs, the BC ratio's and the NPV both increased considerably. The average BC-ratio's, with or without the costs of labour, for the programme which included all three management steps were 0.95 and 1.58, respectively. The average NPV, not including the costs of labour, was Dfl. 27,319 for the total 20-year period. Both the BC-ratio's and the NPV's had a large variation, signifying the large difference between the benefits of Johne's disease control per dairy farm.

DISCUSSION

The design of a new Johne's disease control programme was initially mainly focussed on 'test-and-cull' strategies. However, the results of the 'JohneSSim' model showed that eradication was not possible with any of the simulated 'test and cull' strategies. An important reason for this, was the low sensitivity of the available tests for Johne's disease, especially for infected, but not clinically affected animals. In addition, none of the simulated control strategies were on average economically attractive. The results of the first stage of the simulation study indicated that eradication within 20 years was not possible. However, strategies based on improved calf hygiene seemed more promising.

In the second stage of the study, the focus changed to improving the management of calf hygiene. The new programme that was defined was called Paratuberculosis Programme Netherlands (PPN). In PPN, the order of implementation of measures was arranged in a logical order, following the course of life of the calf. Some testing can be performed to get more insight in the Johne's disease status of the farm. However, because PPN is mainly based on the implementation of the necessary management practices, its effect will depend on the farmer's motivation to control Johne's disease. Making PPN a compulsory programme would not be very useful because of the impossibility of monitoring many of the critical management adaptations. Additionally, a compulsory programme might also have a negative effect on the motivation of the farmers, which is the key to the successful control of paratuberculosis. One difficulty is acquiring and maintaining the farmers' motivation to perform all measurements required to effectively reduce the prevalence of Johne's disease (Benedictus, 1984). The epidemiology of the disease and the reasons for the need to implement the measures required are often difficult for farmers to comprehend. It is therefore very important to inform and educate and hence try to change the attitude and behaviour of farmers. An educational instrument, the ParaInformer (ParaWijzer), has been designed as part of PPN. This gives detailed information about the disease, the ways of controlling it and also contains a checklist for designing a control plan which is specific for each farm. A pilot study has been started on 1,500 farms in The Netherlands to determine the implementation rate of the different management practices (Hesselink, 2000).

The average true prevalence in year 0 in the first stage of the study was slightly lower than in the second stage. A reason for this is the more detailed simulation and higher probability of introduction of infected animals. In addition, the stochastic nature of the model can potentially lead to slightly different results. The faster increase in the average prevalence without control in the second stage of the study was caused by the two most important additions to the model (increasing herd-size and the refinement of the introduction of Johne's disease infected animals to the dairy farm). From field data, it is known that the prevalence of Johne's disease is higher in larger herds (Ott et al., 1999; Jackobsen et al., 2000). Furthermore, the more detailed simulation of infected cows is more accurately represented by the practice of animal introduction on dairy farms in The Netherlands.

Simulation of several variants indicated that management adaptations are a more effective and economically more attractive strategy to the control of Johne's disease than test-and-cull only (Table 8). Furthermore, the results indicate that implementation of <u>all</u> necessary management adaptations is critical. For instance, if step 3 is not taken the average true prevalence will not decrease to zero within a 20-year period (Fig. 3).

The results of both stages of the study showed that separation of calves between 7-12 months from adult animals had a significant impact on the average true prevalence. One reason for this is that in The Netherlands the contact between 7-12 months old calves and older cows was found to be high (Muskens et al., 1999). Therefore, a high contact rate was assumed in the model. Separation of the older calves from the animals older than two years reduced this contact rate and therefore resulted in a significant impact on the average true prevalence.

Epidemiologically, the defined 'ideal test' was considerably more effective in reducing the mean Johne's disease prevalence. However, economically, this was a very expensive strategy, caused by the large number of infected animals that had to be culled. A proportion of those infected animals may never have become an excretor of the organism and would never have experienced any production losses. Culling of those animals would therefore lead to high control costs with only small benefits (reduction of losses). It might even result in a lack of replacement heifers, because of the temporary high culling rate caused by the culling of test positive latently infected animals. If a programme was to be based on such an 'ideal test', political decisions would therefore need to be made on which group should suffer the costs associated with the early culling; farmers, consumers or government. In addition, a pool of Johne's disease free herds should be available to provide uninfected replacement heifers. However, a test with the properties as defined for this 'ideal test' will probably not be available within a measurable timescale.

The output of the 'JohneSSim' model depends on the quality of the assumptions and parameters used. Real data were used wherever possible. However, some parameters or distributions had to be based on the best guesses of experts. Validation of the model with field data was difficult because no *M. a. paratuberculosis* infected herds have been monitored intensively for an extended period of 20 years. This extended time periods would be required because of the slow spread of Johne's disease. However, the model has been validated with field data from 21 Dutch dairy herds and by face value validation by Johne's disease experts (Groenendaal et al., 2001).

In conclusion, the 'JohneSSim' model can be considered a flexible, appropriate and useful tool to evaluate different Johne's disease control strategies, combining the current knowledge of Johne's disease in an optimal way. It has proved to be a valuable tool in the process of defining and deciding upon a new national Johne's disease control programme in The Netherlands by predicting the effectiveness and the economical attractiveness of this programme. It has caused a fundamental change in the design of the Dutch paratuberculosis control programme, from a focus on 'test-and-cull' to a focus on 'stepwise improvements of calf hygiene' strategies, which now forms the key of the new national voluntary control programme. This decision making process has been greatly supported by the 'JohneSSim' model.

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