Epidemiologic and Economic Risk Analysis of Johne's Disease Control

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Epidemiologic and Economic Risk Analysis of Johne's Disease Control

Epidemiologisch and Economische Risico Analyse
van de Bestrijding van Paratuberculose

Proefschrift

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Abstract

Johne's disease or paratuberculosis in cattle is a chronic, progressive intestinal disease caused by infection with *Mycobacterium avium* subsp. *paratuberculosis* (*Map*). There is a growing concern about the apparent increase in the prevalence of Johne's disease and the resulting economic and possible trade implications. In addition, although there has not been any definitive proof, Johne's disease may be associated with some forms of Crohn's disease in humans. As a result, there is an increased need for effective and economically attractive control programs against Johne's disease. The main objective of the research described in this thesis was to support decision-making in the design and development of control and certification-and-monitoring programs for Johne's disease by providing insight into the epidemiologic and economic effects of different strategies. To meet this objective, a stochastic simulation model, the 'JohneSSim' model was developed and used to evaluate control and certification-and-monitoring strategies on Dutch and mid-size US cattle herds. According to the model when applied to Dutch dairy farms, test-and-cull strategies alone using the current tests available do not considerably reduce the prevalence of Johne's disease and are economically unattractive. As a consequence, the focus of policy-makers changed to management measures to prevent the spread of *Map* within herds. A new Dutch Johne's disease program was designed, called Paratuberculosis Program Netherlands (PPN), and evaluated with the JohneSSim model. It was found that under PPN, a low true prevalence could be reached within 20 years and that PPN was on average economically attractive. Also, a number of certification-and-monitoring schemes for Johne's disease test-negative dairy herds were evaluated on their costs and effectiveness. Furthermore, control strategies on Dutch *beef* herds were evaluated, and it was concluded that under current practical circumstances no control strategy was economically attractive and realistic. For US mid-size dairy herds, similar results were obtained as for Dutch dairy herds. Vaccination was found to be economically attractive, but not able to reduce the prevalence. Measures to prevent spread of *Map* within herds and contract heifer rearing were found to be better control strategies that both decrease the prevalence and have economic benefits. Both in The Netherlands and in the US, this study greatly supported the decision making process in the development and improvement of Johne's disease control and certification-and-monitoring strategies.

Preface

Many things had to happen for this PhD thesis to be completed. What started in May of 1998 as a 6-month research project on the control of Johne's disease in The Netherlands has resulted in an exciting and life-changing seven years: moving to the US, completing a Masters in Business Administration at the Wharton School of Business, starting 'Vose Consulting US', meeting and marrying my dear Rebecca and finishing this PhD-thesis have been some important highlights. There are many, many family members, friends and colleagues who helped me get to where I am now. Knowing that space is too limited in this preface, I hereby sincerely thank everyone for their important contributions to this PhD-thesis. Thank you! Although mentioning everyone properly would require a thesis in and of itself, in the paragraphs below, I would like to call attention to some specific contributions.

I would first like to thank Aalt Dijkhuizen. Aalt, you sparked and developed my interest in Animal Health Economics and supervised the first part of this thesis. Thank you for your leadership! I would also like to thank Ruud Huirne. Even though we never worked together directly, your enthusiasm for the idea of this PhD, and help during the last stages, have been important and are very much appreciated. Also, I thank you for your inspiring 'people-first' attitude. In addition, during my projects in Wageningen, I have had the pleasure to work with Mirjam Nielen, Suzan Horst and Alien Jalvingh, who all have made significant contributions to this thesis. Mirjam, you not only greatly helped me write several of the papers, but also were immediately supportive of the idea to turn them into this PhD thesis. I appreciate your critical thinking and support. Thank you so much for the evenings you gave to make this possible! Suzan, your enthusiasm in your work and positive attitude truly inspired and motivated me. Alien, I have really learned a lot from you, including the 'science and art' of computer model building and programming. I appreciate all of your patience and guidance.

A special thanks to Dave Galligan. Dave, meeting you in 1998 in Wageningen has changed my life. I truly enjoyed working with you at the Center of Animal Health and Productivity. Your enthusiasm, creativity and inclusive work-style have greatly contributed to my professional career. I have learned at least as much from your generosity and dedication to your family and friends as I have about work. Dear family Galligan, thanks for all. You are the best!

A big 'thank you' to all my Dutch and American colleagues, and especially my roommates; no job is great without you. I truly enjoyed working together with all of you, drinking coffee, having cakes, running, going to the 'Y', wall-climbing, visiting concerts, etc. etc. Also, Jim Beach, Bob Munson and Pandora; I very much enjoyed being roommates with you. A special thank-you to Marian, Anne, Patty, Gay and Lisa, who always were there to help me stay out of trouble, tell the latest gossip or ask me about my latest (crazy) adventure.

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important involvement in this project. Special thanks to Jan Willem Hesselink and Peter Franken, who both were involved in parts of this study, and often ‘translated’ results of this study to policy-makers. Maarten Weber also deserves a ‘thank you’ for his great enthusiasm, healthy criticism, and practical and hard-working attitude during the three months we worked together.

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Thanks to my current colleagues at Vose Consulting. David, Jane, Timour and Inal, thank you for giving me time to finish this thesis during the last year. I very much enjoy working with all of you to make Vose Consulting truly the premier risk analysis consulting firm!

During the time I have worked on this thesis I have been blessed with the support of great friends, both in The Netherlands and the US. My brusjes on Hoevestein 13A and great roommates at the Leeuweriksweide were a second family to me. Eline, Stiek, Peter, Maarten, Annemiek, Jan Willem, Liesbeth, Lei, Karin, Harrold, Bianca, bedankt! Roelof, thanks for our great friendship and your help during the PhD defense. In the US, thank you to my SLKR family who have all made me feel at home in Pennsylvania’s Dutch country.

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This preface would not be complete, however, without thanking my dearest Rebecca. Your encouraging support, enthusiasm and love have truly been critical in finishing this thesis. Rebecca, thank you for making my life complete.

Contents

Chapter 1

1 General introduction

1.1 Introduction

Competitive agricultural commodity markets such as the dairy industry are characterized by producers that have no price control ('price takers') (Pindyck and Rubinfeld, 2000). Therefore, a very important way to improve profit margins for dairy farmers is to reduce costs, specifically, decreasing the marginal production costs. Improving animal health through disease control or eradication programs can play a major role in achieving more efficient production (Dijkhuizen and Morris, 1997). In addition, consumers desire healthy products from healthy animals, and hence the reduction or eradication of a disease could increase quality and hence increase prices. However, as there are numerous diseases in cattle, the choice of which disease or diseases to actively control and to what extent, becomes a decision in which benefits should be weighted against costs and control programs should only be undertaken to the extent that benefits (such as economic and food safety benefits) exceed costs. Also, with more responsibility over animal disease control being transferred from the public to the private sector, the focus on efficiency and return on investment increases. As a result, it is increasingly important to provide appropriate economic justification for animal health measures. This thesis describes an epidemiologic and economic risk analysis which was performed with the aim to support the decision-making process in the design of more effective and economically attractive Johne's disease control programs in cattle.

1.2 *Paratuberculosis* in cattle

Paratuberculosis or Johne's disease in cattle is a chronic, progressive intestinal disease caused by infection with *Mycobacterium avium* subspecies *paratuberculosis* (*Map*; Thorel, 1990). Described for the first time in 1895 (Johne and Frontingham, 1895), Johne's disease has since spread worldwide and is now a common disease in all countries with a significant dairy industry (Office Interational des Epizooties, 2001), except for Sweden that has been officially declared free of Johne's disease (Bölske, 1999).

Worldwide, Johne's disease causes great losses for milk producers (Benedictus et al., 1987; Gill, 1989; Ott et al., 1999). In recent decades, concerns have been raised about the apparent increase in the global prevalence of Johne's disease, the increasing economic costs and potential trade implications (Rideout et al., 2003). In addition, Johne's disease has received increasing attention because of concern (not confirmed nor disproved) over the potential role of *Map* in some cases of Crohn's disease in humans (Collins, 1997; European Commission, 2000). If *Map*, as some fear, becomes widespread in the environment and the food chain, Johne's disease could become a serious public health problem (Rideout et al., 2003). Both the increase of losses and the rising public health concern have caused an increasing need and demand for effective and economically attractive control strategies against Johne's disease.

1.3 Control of Johne's disease

The control of Johne's disease on dairy farms has been difficult for a number of reasons. First, the long subclinical phase often allows the infection to spread in a herd without occurrence of any clinical signs of illness. Second, although a range of diagnostic tests is available (which either detect the organism or assess the host response to infection), all have difficulties that have slowed down the control and eradication of Johne's disease (Rideout et al., 2003). The main difficulty is that current diagnostic tests are often not sensitive enough to detect animals in the subclinical phase of the disease (Whitlock et al., 2000b; Wells, 2003). Third, once an infected animal develops clinical signs, it is often hard to distinguish them from clinical signs of other common ruminant diseases. Finally, although a reduction of the number of cattle with clinical evidence of Johne's disease has been reported, the current vaccines have not yet shown to be effective enough to eradicate Johne's disease (Kormendy, 1992; Wentink et al., 1994). Therefore, vaccination is not considered a viable option for eradication (Rideout et al., 2003).

1.3.1 The Netherlands

Starting on a provincial level as early as 1922 and on a national level in 1952, many different Johne's disease control programs in The Netherlands have been initiated (summarized by Kalis, 2003). However, all of the control programs were discontinued preliminary because of the lack of desired results. The two main factors behind the failures were considered to be the lack of sensitive diagnostics and the fact that producers did not improve calf management sufficiently (Benedictus, 1984; Reinders, 1987; Benedictus et al., 2000).

In 1999, the project 'Preparation for the collective control of paratuberculosis in The Netherlands' was started. Figure 1 gives a schematic overview of the decision-making process within this project. The initial objective of the project was to prepare a national control program for paratuberculosis with the final aim of eradicating the disease. A scientific foundation of this new program was deemed essential as previous programs had not yielded the desired results. Therefore, a large research effort was initiated that included studies on (1) test characteristics and improvement, (2) prevalence estimates, monitoring and surveillance programs as well as (3) on the development of two simulation models to aid the decision making process during the design and development of a Johne's disease control and certification-and-monitoring program. The development and use of a simulation model for the within-herd effects of Johne's disease control are described in this thesis (Chapter 2-5). An analytic model to study the between-herd spread of Johne's disease, is described by Van Roermund et al. (1999; 2002).

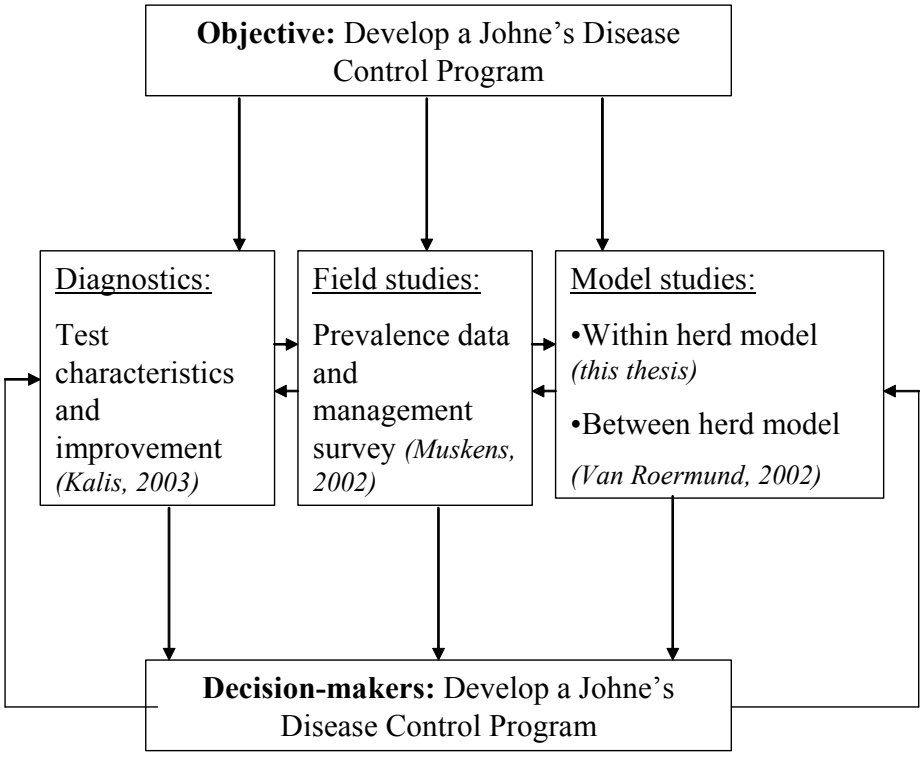

Figure 1. Schematic overview of the decision-making process in the development of a new Dutch Johne's disease control program

1.3.2 United States

The organization and coordination of control programs of Johne's disease in the US has historically been left to the discretion of individual states. Over the years, many states have adopted control programs for Johne's disease test-positive herds and status programs for test-negative herds, each program a bit different in design and state support. The first initiative to establish a U.S. national certification program took place in 1993. After disappointing participation by producers, the more affordable U.S. Voluntary Johne's Disease Herd Status Program for Cattle (VJDHSP) (Whitlock, et al., 2000a) was adopted. The basis of this status program now serves as an example for states and more states are moving to Johne's disease programs that are compatible with national standards (USDA, 2004).

In the U.S., the study described in this thesis was not part of a large national organized 'preparation project' similar to the Dutch preparation project described earlier. Instead, the evaluation of alternative Johne's disease control strategies was performed because of a need for economically more attractive Johne's disease control strategies on dairy farms. Because mandatory control programs against Johne's disease were not considered politically feasible or desired, economic attractiveness from the producer's perspective is required for a producer to invest in the control of Johne's disease. However, to our knowledge, no control strategy in the US had ever been fully evaluated for its on-farm economic consequences.

1.4 Epidemiologic and economic risk analysis to support decision-making in the development of a paratuberculosis control program

To select the most effective and economically attractive control strategy, evaluation and quantification of the economic and epidemiologic effects of the current and alternative strategies, are required (Dijkhuizen and Morris, 1997). Field studies to evaluate the effectiveness of different control strategies would however be very time-consuming and expensive. In such situations, field data can be supplemented and expanded using analytical approaches such as stochastic simulation modeling to aid the decision-making process of complex problems (Dijkhuizen and Morris, 1997). Simulation models have often been used to get better insight in the effects of alternative control strategies and prove to be valuable in evaluating the economic and epidemiologic effects of current and alternative strategies both at an individual farm (e.g. Houben, 1995; Van der Fels-Klerx et al., 2000) and at the regional or national level (e.g. Vonk-Noordergraaf et al.,1998; Jalvingh et al., 1999; Mangen, 2002).

While the main focus of this thesis is on the quantitative evaluation of the risks associated with Johne's disease and Johne's disease control (expressed as epidemiologic and economic consequences), the decision-making process and communication within and after the study are also described. The study in this thesis can therefore be described as a risk analysis process, which is composed of risk assessment, risk management (including decision-making) and risks communication (Ahl et al., 1993). The first step, the risk assessment, involves risk identification and characterization, risk description and a semi-quantitative or quantitative analysis of the risk involved and is mainly described in chapter 2, 3, 5 and 6. The risk management part is mainly addressed in chapter 4, which describes the evaluation of alternative strategies and the decision-making process that resulted in the basis of the new Dutch Johne's disease control program. The risk communication part in this thesis includes the extensive discussions with Johne's disease experts during model development as well as communication of the results and decisions made based on the results to the relevant stakeholders (e.g. veterinarians, dairy producers).

1.5 Objectives of this thesis

The primary objective of the work described in this thesis was to support decision-makers in the design and development of control and certification-and-monitoring programs for Johne's disease. To achieve this primary objective, the following sub-objectives were defined:

1. Development of a computer model that takes into account the latest field and literature knowledge and expert opinions on epidemiologic and economic attributes of Johne's disease and Johne's disease control;

2. Obtain insight in the economic and epidemiologic effects of potential Johne's disease control programs for suspected herds and certification-and-monitoring programs for unsuspected herds;
3. Identify important gaps in knowledge on Johne's disease that greatly impact the expected epidemiologic effectiveness and economic attractiveness of Johne's disease control programs.

1.6 Outline of this thesis

Figure 2 shows the various components of this study and in which chapter they are described.

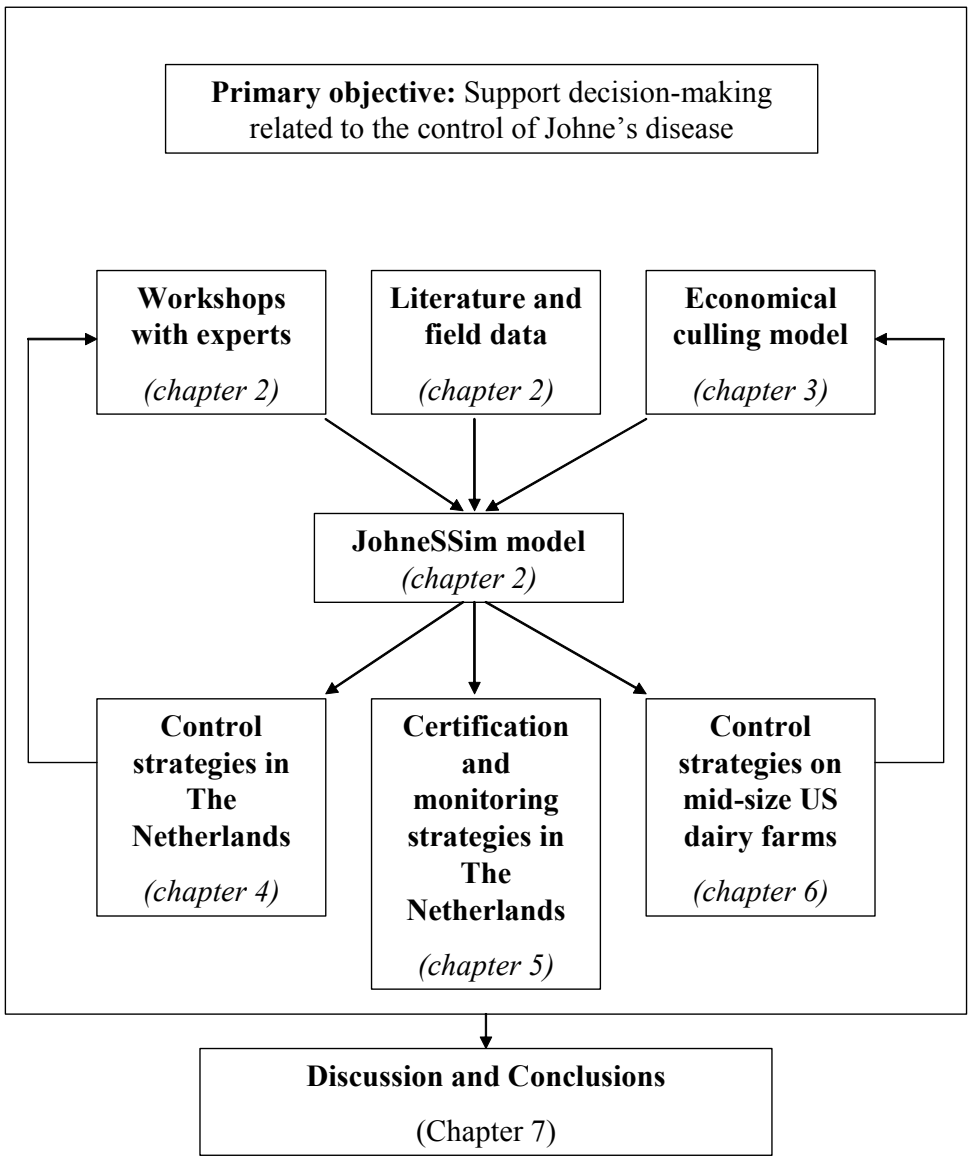

Figure 2. Outline of the thesis

Chapter 2 describes the development and structure of a stochastic simulation model, called the JohneSSim model. In addition, it describes the application of the JohneSSim model to Dutch dairy farms and midsize dairy farms in the U.S. and shows results for both situations to illustrate the model's use.

Chapter 3 then describes an economic model that was used to calculate the costs of sub-optimal culling of dairy cows due to Johne's disease. Because sub-optimal culling causes the majority of losses due to Johne's disease and also is an important component of the costs of test-and-cull strategies, the accurate calculation of these losses is an important part of this thesis.

Chapter 4 describes in detail how results of the JohneSSim model aided in the development of a Johne's disease control program in The Netherlands. The decision-making process took place in three steps which coincided with the development of the JohneSSim model.

While chapter 4 mainly focuses on control strategies for infected Dutch dairy herds, chapter 5 describes the evaluation of different Johne's disease certification-and-monitoring programs for free herds. The currently used Dutch certification-and-monitoring scheme was compared with eleven alternative schemes in which different tests, test frequency, tested age group and number of tested animals, were used.

Chapter 6 describes in detail the adaptation and use of the JohneSSim model to Johne's disease control programs on mid-sized dairy farms in the U.S. A range of possible control strategies are evaluated on the epidemiologic efficacy and economic attractiveness.

Finally, chapter 7 provides a discussion of the approaches used in this thesis, presents the main results as they relate to the objectives of this thesis and discusses how the results of this study supported decision-making in both The Netherlands and the US. A summary that includes the main conclusions of the study is provided at the end of the thesis.

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Chapter 2

2 A simulation of Johne's disease control

Paper by Groenendaal, H., Nielen, M, Jalvingh, A.W., Horst, S.H., Galligan, D.T., Hesselink, J.W., 2002. *Preventive Veterinary Medicine* 54, 225-245.

Abstract

A dynamic and stochastic simulation model (the "JohneSSim model") was developed to evaluate the economic and epidemiological effects of different strategies for control of paratuberculosis in dairy herds. Animals occupy one of the six defined infection states; the spread of Johne's disease is modeled with five infection routes. Many different dairy farm situations can be simulated. Control strategies that can be simulated are: (1) test-and-cull; (2) calf hygiene management; (3) vaccination and (4) grouping of animals. Losses are caused by: (1) reduced milk production; (2) diagnosis and treatment costs; (3) lower slaughter value of cows and (4) sub-optimal culling. The benefits were calculated as reduction in the losses caused by Johne's disease; the costs of each strategy were calculated on the basis of actual costs of each item; and net present value (NPV) was calculated as benefits minus costs. Herd and prevalence data from The Netherlands and Pennsylvania, USA were used. In both situations, a low true mean prevalence within 20 years could be reached only when all calf management tools were applied. The Dutch control program (PPN) was on average economically attractive (with or without labor costs, the average NPV was Euro 1183 and 12,397, respectively). In Pennsylvania, contract heifer rearing and improved calf hygiene reduced the prevalence effectively and had large economic benefits (US$ 43,917 for 20-year period) if the calves were sent to the heifer facility while very young. Validation with data from 21 infected Dutch dairy farms (as well as face-validation: comparison of the results of the JohneSSim model with experiences of Johne's experts) supported the basic assumptions in the model.

2.1 Introduction

Paratuberculosis is a chronic enteritis of cattle and other ruminants, caused by the bacterium Mycobacterium avium subsp. paratuberculosis (herein called "Johne's disease") (Lambert and Borromeo, 1990). Worldwide, Johne's disease has great economic importance for milk producers (Benedictus et al., 1987; Jones, 1990; Ott et al., 1999). Additionally (although there has not been any proof), *M.a. paratuberculosis* might be associated with some forms of Crohn's disease in humans (Lambert and Borromeo, 1990; Brown et al, 1996). One way or the other, the wholesome image of the dairy industry might be threatened by Johne's disease; consumers desire 'healthy products from healthy cows'. All of these factors increase the need for effective and economically attractive control programs against Johne's disease. However, because of the nature of Johne's disease, any field study would be very costly and time-consuming. A simulation model is therefore an appropriate approach to aid the development of control programs.

Most cattle with clinical Johne's disease are infected as young calves because cattle infected as adults are unlikely to develop clinical disease. Infection routes that are considered important for the spread of Johne's disease are: (1) fetal infections, (2) infections via colostrum or milk

and (3) infections due to exposure of calves to a contaminated environment (McCaughan, 1990).

The first organized control program against Johne's disease in The Netherlands started in 1942. Several programs have evolved since, but none of them resulted in the desired reduction of the number of infected herds. In 1997, the leading Dutch institutes working on Johne's disease developed a plan for eradication of Johne's disease, which resulted in a national voluntary control program that started in 1998. In preparation for a compulsory control program, the project 'Preparation for the collective control of paratuberculosis in The Netherlands' was started (Benedictus et al., 1999). The current stochastic and dynamic simulation model (the 'JohneSSim model') was developed as part of this project to evaluate both the epidemiological and economic consequences of different Johne's disease control strategies. The purpose of this paper is to describe the JohneSSim model. To illustrate some of the possible applications, the results of several Johne's disease control strategies for the Dutch and Pennsylvania, USA dairy industries will be shown.

2.2 Material and methods

The JohneSSim model was programmed in Visual Basic for Applications in combination with Microsoft Excel 7.0® spreadsheets. It contained time as a variable (and, therefore, is dynamic) and simulated one dairy herd including youngstock, in which all animals had specific attributes (age, parity, milk production, gestation status, and infection state). The model contained probability distributions to deal with variation in replacement, infections, pathogenesis, mortality, and testing. Repeated runs of the model provided insight into the variation in outcome on the farm level. By simulating different dairy farms, insight could be obtained in the outcomes of different strategies at the state or national level. To accurately reflect the variation in results between farms, for different farms (risk profiles), a number of runs was included (a minimum of 100 runs) that represented the existence of each specific risk profile. Specific input parameters for the Dutch and Pennsylvanian situations are shown in Appendices A–K.

2.2.1 Herd simulation

Because of the slow spread of Johne's disease, a 6-month time step was chosen for the JohneSSim model and the chosen simulated period was 20 years. Heifers calved at a default age of 2 years and the calving interval was 12 months. The calving pattern could be either spread (each half year) or concentrated (once a year).

In the model, the percentage of cows culled involuntarily was specified per lactation (Appendix B); voluntary culling was based on the retention pay-off (RPO) value of the individual cows. The RPO value was defined as the total extra profit to be expected from trying

to keep a cow until her optimal life-span, compared with immediate replacement (taking into account the risk of premature removal of retained animals) (Van Arendonk, 1985).

2.2.2 Spread and control of Johne's disease

Animals occupied one of the six infection states (Table 1). Only susceptible animals could be infected; after 1 year of age, uninfected animals were considered 'not susceptible'. Four statuses were defined to represent the course of infection; age at the time of infection influenced this course (Chiodini et al., 1984; McCaughan, 1990). This was modeled with triangular probability distributions (Appendix C). For example, the most likely age of becoming highly infectious after an in utero infection was 2.5 years, compared to 6 years after an infection that occurred between 7 and 12 months of age (Chiodini et al., 1984; McCaughan, 1990; discussions in the 'Johne's Disease Discussion Group', 1999). Infection between 7 and 12 months of age resulted in a considerably higher age of becoming highly infectious. Infected animals were estimated to become lowly infectious (shedding 2 months after calving) two calvings before becoming highly infectious (discussions in the 'Johne's Disease Discussion Group', 1999).

Table 1. Assumed infection states in the JohneSSim model (of bovine paratuberculosis in dairy farms)

Infection state		Description
Not infected	Susceptible	Uninfected animals < 1 year old
	Not susceptible	Uninfected animals ≥ 1 year old
Infected	Latent	Not shedding
	Lowly infectious	Shedding first 2 months after calving
	Highly infectious	Shedding continuously
	Clinical	Shedding continuously

Susceptible animals could be infected via one of the five infection routes shown in Table 2. All infection probabilities (Appendix F) depended on the number of infectious animals present in the herd. It was assumed that highly infectious or clinical cows always give infectious milk and colostrum, compared to 30% of the lowly infectious cows. If mixed colostrum and raw milk is fed to the calves, the average number of calves drinking colostrum or raw milk from one cow (excluding own calf) is assumed to be, respectively, 2 and 8. If bulk milk is fed to the calves, 20% of the highly infectious and clinical cows can infect 95% of the calves by their infectious milk. In addition, introduction of animals to the dairy herd could result in infection of a herd with Johne's disease. The probabilities that introduced animals of a specific age were in one of the six infection statuses (Table 1) were based on the estimated overall real prevalence in both the Dutch and Pennsylvanian study.

Table 2. Description of the infection routes in the JohneSSim model of bovine paratuberculosis in dairy farms (related input parameters shown in Appendices C–G)

Infection route	Infection probability
Fetal infection	Depending on infection state of the dam, between 0 (latently infected dams) and 50% (clinically infected dams) (Sweeney et al., 1992b)
Infection around birth	Depending on infection states of own dam and cows in the rest of the herd, between 0 (if only latently infected animals in herd) and 90% (if own dam is highly infectious)
Infection via colostrum	Depending on infection state of colostrum-producing cows, between 0% for a latently infected cow and 100% for a highly infectious or clinical cow (Sweeney et al., 1992a)
Infection via spilled milk	Depends on infection state of lactating cows; for probabilities see colostrum.
Infection via bulk milk	Depends on presence of at least one lactating cow that sheds large amounts of M. a. paratuberculosis in her milk (20% for highly infectious cow)
Infection via surroundings	Depends on the number of infectious cows in the herd at the start of each 6-month period, using a modified Reed-Frost method (Abbey, 1952)

Control tools or measures to prevent infection of calves were divided into: (1) 'test-and-cull' tools, (2) measures to prevent the infection of calves by improvement of 'calf hygiene', (3) vaccination and (4) grouping of animals. Test-and-cull tools could be specified in the model by parameters such as the test sensitivity and specificity (per infection state), minimum and maximum age of testing, frequency of testing, and number of cows tested. Different consequences of test results could be simulated such as culling after a positive test (on the animal level) or changing to an 'unsuspected' herd-status if all test results (on the herd level) were negative. In the two studies, a hypothetical ELISA test was the default test and a hypothetical fecal test was used to confirm ELISA-positive animals (personal communication of the Johne's Disease Discussion Group, 1999; Whitlock et al., 2000) (Appendix H). In the model, vaccination only increased the age of becoming infectious. Grouping of animals could be applied on the basis either of test results or age. Results of the last two strategies (vaccination and grouping) are not shown in the current paper.

In the JohneSSim model, 'calf hygiene' tools reduced (standard 90% reduction used) or eliminated certain spread parameters or infection routes. Different control strategies could start in different years, depending on the predicted adoption of the control tools by farmers. All input parameters related to the simulated control program of Johne's disease in The Netherlands and the simulated control strategies in Pennsylvania are shown in Appendix J.

2.2.3 Economics

The economic consequences of the control of Johne's disease were divided into: (1) the losses due to Johne's disease and (2) the costs of the control program. The values of losses due to Johne's disease are shown in Appendix K. Losses were caused by: (1) lower milk production, (2) diagnosis and treatment costs, (3) reduced slaughter value and (4) sub-optimal culling. For clinical animals (involuntary cull), the losses caused by sub-optimal culling (future income foregone) equaled the RPO value. For voluntarily culled cows, the missed future income equaled the difference between the RPO value with and without the reduction in milk production caused by disease.

The net present value (NPV) was calculated for each control strategy for the whole 20-year period. The NPV is a standard economic measure to value investments that have an extended time component (Brealey and Myers, 2000; Dijkhuizen and Morris, 1997). The NPV was defined as the total discounted reductions of the losses minus total discounted costs. Reductions of losses were calculated as losses caused by Johne's disease without a control program minus losses with a control program. To discount, the real interest rate (approximated by interest rate minus inflation rate) was taken as 5%. The costs of the different control tools are shown in Appendix K. Depending on the farm situation, the appropriate costs of control were added for the economic evaluation of each simulated farm. Because of the variation between farms in the opportunity costs of labor, the NPVs were calculated both with and without labor. Furthermore, in the Pennsylvanian study, the direct costs and benefits of contract heifer rearing were not included because the benefits (forgone costs of rearing one's own heifers) are very similar to the costs of contract heifer rearing (Gabler et al., 1999) and the direct costs and benefits were not the main interest of this study.

2.2.4 Initial situation

The risk profile of a farm represented the entire calf management on this farm. Thus, the risk profile influenced the infection routes and, hence, the spread of Johne's disease. The risk profile was also important to calculate the proper costs of additional management measures. On better managed farms (better risk profile), fewer costs had to be made to reach a good calf management. To capture the variation in calf management in the total dairy industry of a region, respectively, eight and three risk profiles were defined in the Dutch and Pennsylvanian examples that were simulated individually (Appendix I, Van Roermund et al., 1999).

The infection status of a dairy herd could be (1) infected and test positive, (2) infected but test negative and (3) uninfected (both test positive and negative). To create initially infected herds, an infected animal was introduced into an uninfected herd, and the herd simulated for a certain time period (so infected animals were distributed among all age groups). In the Dutch study, both infected and uninfected herds were simulated; the distribution of the test prevalence was taken from the study of Muskens et al. (1999). However, based on observations of Kalis et

al. (2000), we assumed that 80% of all dairy herds in The Netherlands were infected. For the Pennsylvanian study, only infected herds were simulated. The distribution of the within-herd test prevalence was according to Ott et al. (1999).

Evaluation of any Johne's disease control program on a state or national level included all possible combinations of calf management ('risk profile') and infection states of the herds. For each combination of risk profile×infection state, a set of 'initial herds' was created prior to initiating control effort. These herds represented the total pre-control situation of calf management and infection states. Once the 'initial herds' were defined, different control strategies could be simulated (each control strategy starting with the same overall situation).

2.2.5 Validation

Validation of the model was carried out with data from 21 dairy farms in The Netherlands, in which the transmission parameter (β) of the disease was estimated by generalized linear modeling (Van Roermund et al., 1999). For Johne's disease, β is the number of calves infected by one infectious animal per unit of time in a susceptible population. The reproduction ratio R_0 (the number of animals infected by one infectious animal) is a key measure to quantify the transmission of an infectious agent per total lifetime infectivity and can be derived from β (e.g. Anderson and De). For the validation procedure, the JohneSSim model simulated the first 3 years after the introduction of an infectious animal in an uninfected herd and calculated the number of new infections per time step of 6 months. A short period of 3 years was chosen to be sure that the number of susceptible individuals was not limiting. The simulated values were compared with the observed transmission parameter (Table 3). Comparison could be imprecise because of different assumptions about the length of the infectious period; however, our focus was on the order of magnitude of β between the two studies (Van Roermund et al., 1999). In addition to the comparison of the β's, the 'face-validity' of the model results was evaluated by showing them to Johne's disease experts.

Table 3. Comparison (by inspection, for validation) of the β's from 21 farms from three geographical areas in The Netherlands and the β's of three different risk profiles (profiles 1, 6 and 8), simulated with the JohneSSim model (500 replications), representing the range of risk seen in all three geographical areas

Data source	N	Profile [a]	β-values				
			Min.	10th percentile	Mean	90th percentile	Max
Farm data							
Middle/West	5	2	0.9	1.3	2.1	3.1	3.8
North	14	4.4	3.4	4.1	5.4	7.2	7.3
South	2	5	7.9	8.3	9.8	11.3	11.7
Simulation (risk profile)							
Low-risk	500	1	0.0	2.7	3.6	4.3	7.5
Most-common	500	6	1.0	3.3	5.2	8.4	9.3
High-risk	500	8	1.0	4.0	5.7	9.0	10.3

[a] *the average risk profile for the farms and the risk profile of the simulated data*

2.2.6 Example simulations

To illustrate the JohneSSim model, the results of different control strategies are shown. In the Dutch situation, the simulated control program (called 'PPN') consisted of three steps. We assumed that farmers improved the management around calving (Step 1) in year 1, from calving until weaning (Step 2) in year 2, and from weaning until the end of a calf's first year (Step 3) in year 3. The implemented control steps were assumed to continue in all future years. Also, all animals >3 years old were tested once in the first 5 years with an ELISA test, with positives confirmed by fecal culture (test characteristics are in Appendix H) and the cow culled if positive in both tests.

In the Pennsylvanian situation, we assumed that all calves were brought to a 'contract heifer facility' at an age of 1 day where they had no contact with cows or heifers older than 2 years. Two situations of calf management on the dairy farm were simulated. The first one had no improvement of the management before the calves were sent to the contract heifer facility (no improvements in the calving pen and mixed colostrum on 45% of the farms). The second situation was a clean calving pen, separation of the calf and cow within one hour of calving, and only colostrum from the calf's own dam fed to calf.

2.2.7 Sensitivity analysis

A sensitivity analysis was performed for the Dutch situation, on the parameters and processes shown in Table 4. In the default situation (PPN, Steps 1–3), we assumed that a reduction of

90% of the infection probabilities was achieved if the proper management tools were implemented. As an alternative (Sens. I), we assumed that in the presence of a highly infectious animal, only a 50% reduction was obtained. Secondly, in scenario "Sens. II", only ELISA-negative animals were introduced to the dairy herd. Finally, to determine the total effect of the spread between herds on the mean true prevalence, a strategy was simulated in which no animals at all were introduced to any herd (Sens. III).

Table 4. Sensitivity analysis of the JohneSSim model for the Dutch situation

Parameter/process	Name	'Default'	'New'
Effect management on reduction infection probability	Sens. I	90%	50%
Introduction ELISA negative animals only	Sens. II	No testing	Test with ELISA
No introduction of animals	Sens. III	0-6 animals/yr	None

2.3 Results

2.3.1 Validation

The simulated values were in relative agreement with the estimated β's for the 14 farms in the north of The Netherlands. The variation in β among simulated farms with the lowest risk profile (most hygienic management) was slightly higher (as was the mean) than the variation among the 21 Dutch farms. We concluded that the epidemiological module of the JohneSSim model simulated an overall transmission parameter similar to those observed on the Dutch dairy farms. For more details about the validation of the JohneSSim model, see Van Roermund et al. (1999). In addition, the JohneSSim models' results were according to expectations of Johne's disease experts. These experts also agreed with the relative importance of underlying processes and the different transmission routes of the JohneSSim model.

2.3.2 Dutch study

The mean Johne's disease true prevalence on an average (infected and uninfected) 50-cow Dutch dairy farm, increasing towards a 100-cow dairy farm in year 20, under different strategies is shown in figure 1. Without any control efforts, the mean herd prevalence gradually increased to >50% after 20 years. The efficacy of the simulated disease control program depended mainly on the number of steps that farmers carried out. Test-and-cull had only a minor effect on the mean herd prevalence, when combined with all control steps (data not shown). In agreement with the increasing prevalence and herd size, the yearly losses due to Johne's disease increased when no control efforts were implemented (Table 5). The mean total discounted benefits for the 20-year period equaled Euro 29,196 (total losses without control

minus total losses with control: Euro 39,245 minus Euro 10,049) (Table 5). The mean NPVs including (Euro 1183) or excluding (Euro 12,397) labor costs equaled the mean benefits (Euro 29,196) minus the mean costs of, respectively, Euro 28,013 and Euro 16,799. The 10th and 90th percentiles of the herd-level NPVs indicated large variation between herds (mainly caused by the difference in the initial herd prevalence and the difference in the initial calf management). Most of the losses (69%) were due to sub-optimal culling and only 9% of the costs were due to a reduction of the slaughter value of cows (Table 6).

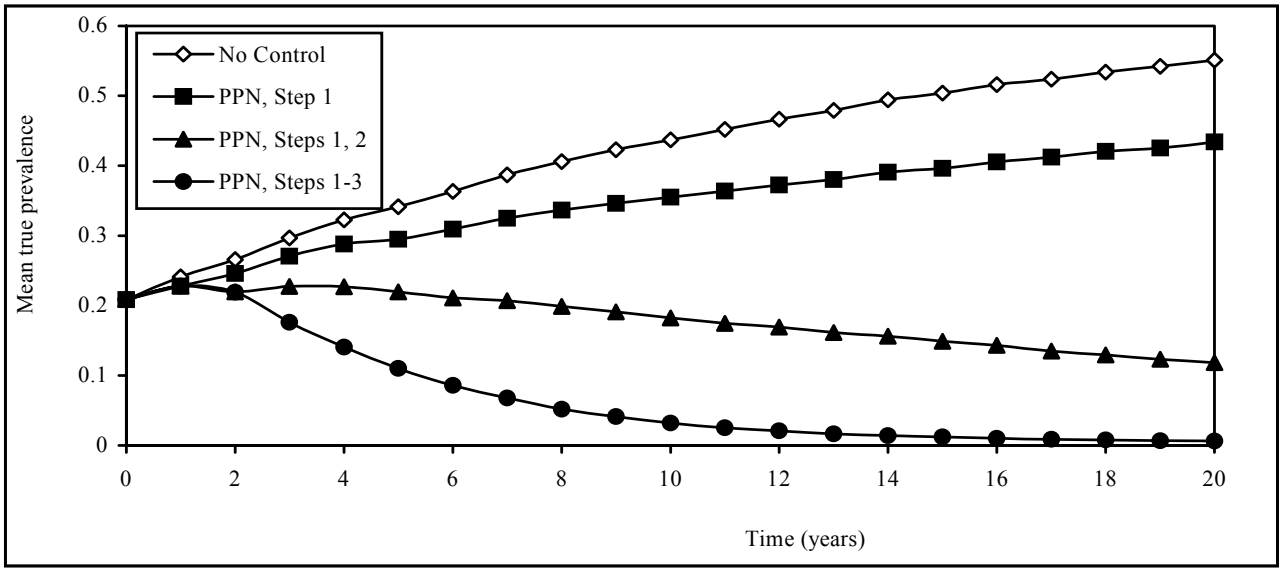

Figure 1. Mean true within-herd prevalence of Johne's disease on an average Dutch 50-cow dairy farm (both infected and uninfected farms), increasing towards a 100-cow dairy farm in year 20, as simulated with the JohneSSim model. The four scenarios that are shown are under no control program (no control) or under the Paratuberculosis Program Netherlands (PPN) with one (PPN, Step 1), two (PPN, Steps 1 and 2) or three (PPN, Steps 1–3) management steps taken

Table 5. Simulated economic consequences of the control of Johne's disease with the three steps in the Dutch voluntary control program on an average Dutch 50-cow dairy farm (both infected and uninfected farms), increasing towards a 100-cow dairy farm in year 20 (in Euro). The NPV equals the reduction in losses of Johne's disease resulted from the control effort, minus the costs of the control effort

	No control effort			With Dutch control program		
	Losses			Losses	Costs	
					Labor included	Labor excluded
	10^{th} percentile	Mean	90^{th} percentile	Mean	Mean	Mean
Year 1	0	767	2,389	738	593	265
Year 2	0	1,202	3,461	1,172	1,149	485
Year 5	0	1,953	5,493	1,409	2,649	1,857
Year 10	0	3,357	8,423	591	2,390	1,433
Year 15	0	4,999	11,893	255	2,799	1,663
Year 20	0	6,720	14,989	143	3,285	1,935
Discounted total	0	39,245	91,001	10,049	28,013	16,799
					NPV	
					Labor included	Labor excluded
				10^{th} percentile	- 25,335	- 14,705
				Mean	1,183	12,397
				90h percentile	32,373	46,287

Table 6. Simulated relative attribution of causes of discounted total losses from Johne's disease on an average Dutch 50-cow dairy farm, increasing towards a 100-cow dairy farm in year 20 (in Euro)

Reason	Losses	Percentage of total
Milk-production losses and treatment costs	8,775	22%
Reduction in slaughter-value	3,444	9%
Missed future income (sub-optimal culling)	27,026	69%
Total (20 years)	39,245	100%

2.3.3 Pennsylvanian study

Without any control efforts, the mean prevalence in infected Pennsylvanian dairy herds gradually increased (Figure 2). However, if heifers were reared from days 1–365 on a contract heifer rearing facility, the mean prevalence decreased. In addition, the calf hygiene on day 1 appeared to be critical. Without control, the total annual losses increased from US$ 3400 to >7200 in year 20; the variation was large (Table 7). The 20-year discounted mean benefits of contract heifer rearing without or with calf hygiene management on the first day were US$

29,905 and 43,917, respectively. There was a large variation in the potential benefits of control for infected dairy farms.

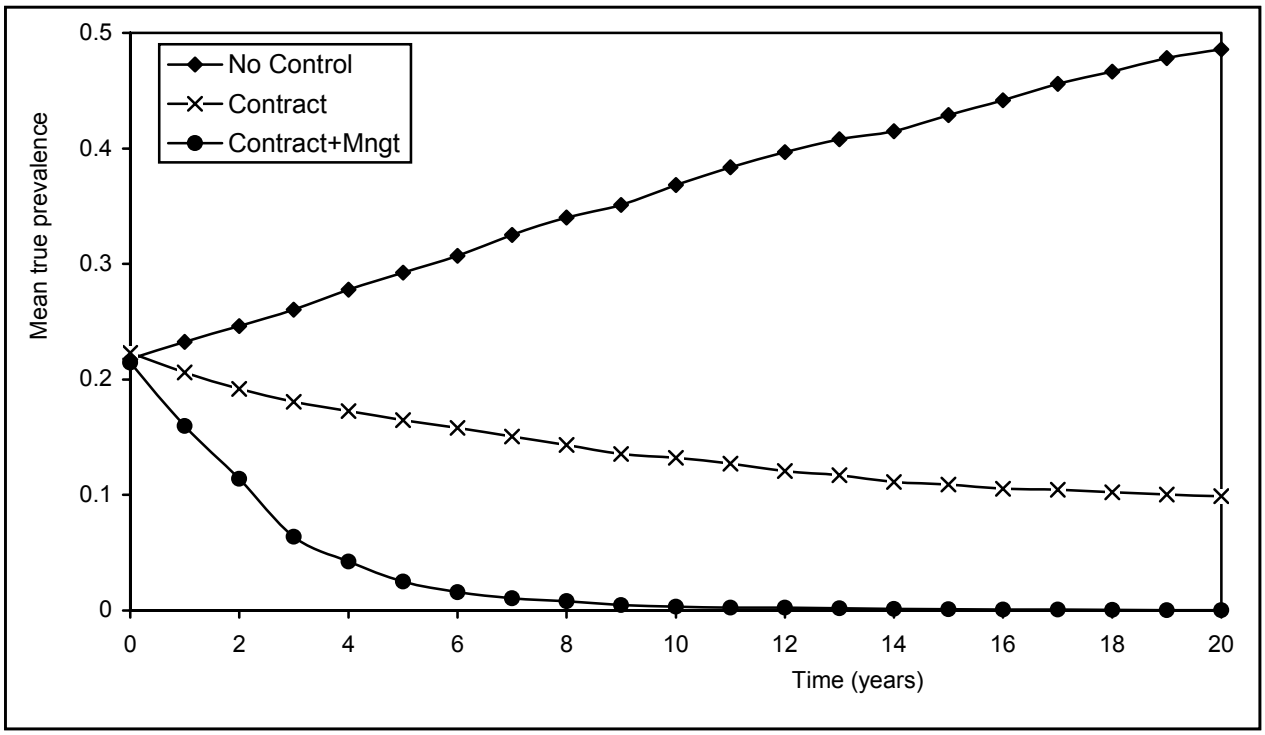

Figure 2. Mean true within-herd prevalence of Johne's disease on infected Pennsylvanian 100-cow dairy farms as simulated with the JohneSSim model. The three scenario's that are simulated are under no control program (no control), under contract heifer rearing of calves from days 1–365 (contract) or under the same contract plus an improved management on day 1 (contract+Mngt) (Appendix C)

Table 7. Simulated economic consequences of the control of Johne's disease by 'contract heifer rearing' with (+Mngt) or without improved calf management at day 1, on an average infected Pennsylvanian 100-cow dairy farm (in US$). The NPV equals the reduction in losses of Johne's disease resulted from the control effort, minus the costs of the control effort (Mngt=improved calf hygiene)

	No control efforts			'Contract heifer rearing'	'Contract heifer rearing + Mngt'
	Losses			Losses	Losses
	10th percentile	Mean	90th percentile	Mean	Mean
Year 1	67	3,434	8,354	3,434	3,434
Year 2	65	2,819	7,836	2,819	2,819
Year 5	80	3,795	9,612	3,079	2,461
Year 10	141	5,239	13,033	2,220	428
Year 15	217	6,234	14,180	1,814	130
Year 20	418	7,202	14,937	1,453	0
Discounted total	10,314	61,310	127,834	31,405	17,393
				NPV	NPV
			10% percentile	4,319	8,233
			Mean	29,905	43,917
			90% percentile	68,485	90,445

2.3.4 Sensitivity analysis

Figure 3 shows the results of the sensitivity analysis for the Dutch example. In the situation that management tools only have a 50% reduction-effect on the infection probabilities (PPN_Sens. I) instead of 90%, the reduction of the mean true prevalence was considerably smaller. Secondly, figure 3 shows that the effect of introducing only ELISA-negative animals has almost no effect on the decline of the mean true prevalence (Sens. II). Finally, the figure shows that not introducing any animals enhances the reduction of the mean true prevalence only slightly (Sens. III).

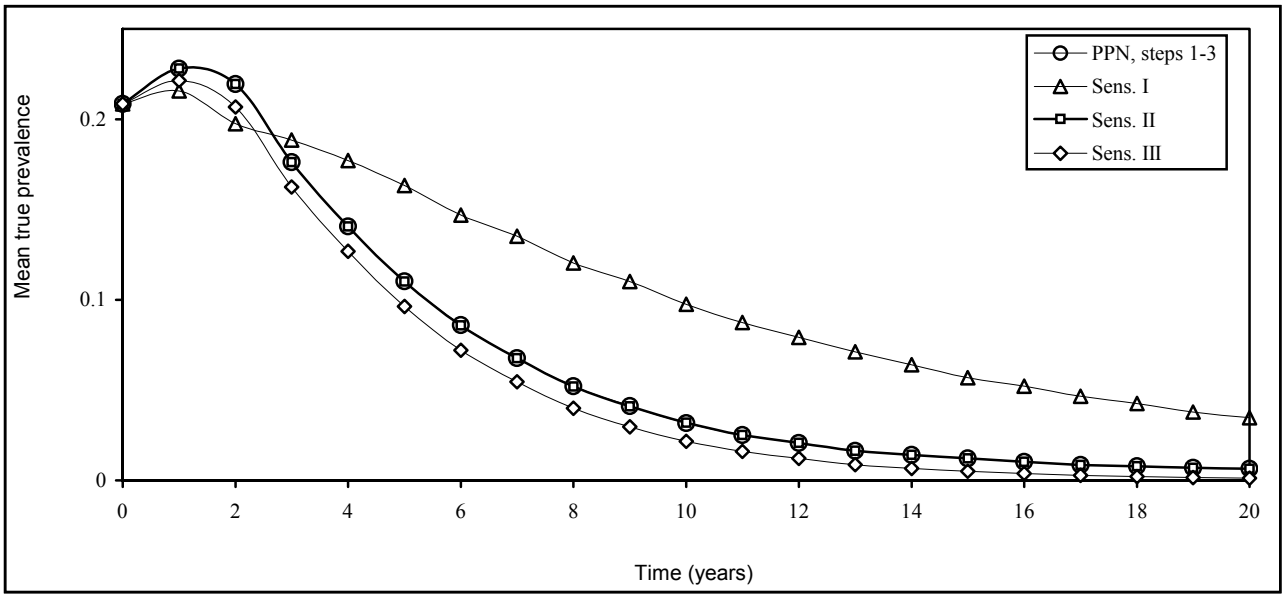

Figure 3. Mean true within-herd prevalence of Johne's disease on an average Dutch 50-cow dairy farm (both infected and uninfected farms), increasing towards a 100-cow dairy farm in year 20, as simulated with the JohneSSim model. Sens. is the sensitivity analysis under the standard PPN program (PPN, Steps 1–3) and three alternative situations (Sens. I–III).

2.4 Discussion and conclusion

2.4.1 Epidemiology

The first simulation model of Johne's disease was developed by Walker and Walker. This model was stochastic and considered many economic parameters, but was not dynamic, lacked flexibility and gave limited epidemiological data. Collins and Collins developed a simpler, more flexible and user-friendlier model, in which they defined factors that were most critical to the spread Johne's disease in a dairy herd. Limitations of their model were the deterministic nature, the inclusion of only one infection route, the fact that all infected animals older than 2 years were considered infectious, the inability to evaluate a large variety of control strategies and the exclusion of the economic aspects of Johne's disease. In the JohneSSim model, both aspects of the model of Walker and Walker (stochastic nature and economic parameters considered) and of Collins and Collins (dynamic and consideration of the nature of spread) were taken into account. Furthermore, control strategies can be modeled in more detail because test characteristics can be specified per each of the four infection states (Table 2 and Appendix H). In the JohneSSim model, infection probabilities were positively correlated with the within-herd prevalence, which is in agreement with the observed close correlation of the environmental contamination with the herd prevalence (Rosenberger et al., 1992).

The Dutch and Pennsylvanian simulations showed that without any control effort, the mean animal prevalence gradually increased (Figure 1 and 2). This was caused by the gradually

increasing within-herd prevalence and the introduction of Johne's disease into uninfected herds. A reason for the increasing within-herd prevalence in the Dutch simulation study is the increasing herd size causing, on average, a higher spread of Johne's disease in the JohneSSim model. This is in agreement with the results of field observations (Ott et al., 1999)—as is the increasing overall prevalence (field: Jackobsen et al., 2000; model: Collins and Morgan, 1992). In contrast to the Collins and Morgan model, no plateau of the prevalence (around 40–60%) was observed in our results.

Improved calf hygiene was critical to control Johne's disease. In the Dutch situation, this meant that all three management improving steps should be taken. In the Pennsylvanian situation, it means that calf hygiene on day 1 should be improved even though the calves leave the farm for contract rearing. According to the model, Johne's disease can be eradicated but only by application of all calf management related measures. Although test-and-cull strategies (ELISA, confirmed with fecal test) did not reduce the prevalence effectively, they might play a role as stimulation for the farmer to improve calf management.

Validation of the model with field data was difficult. No *M.a. paratuberculosis* infected herds have been monitored intensively for an extended period, which is needed because of the slow spread of Johne's disease. Validation with field data from 21 vaccinating Dutch dairy herds (Kalis et al., 1999) showed that the overall spread of Johne's disease in the JohneSSim model was similar to the observed spread (see also Van Roermund et al., 1999). If the spread of Johne's disease in vaccinated herds is slower than in non-vaccinated herds (e.g., because vaccinated and infected animals spread less *M.a. paratuberculosis*), the rate of spread of Johne's disease in the JohneSSim model could be an underestimation. Nevertheless, the model results agreed with expectations of Johne's disease experts (discussions in the 'Johne's Disease Discussion Group', 1999).

There is still a lot of uncertainty about the epidemiology of Johne's disease. Therefore, the input of the JohneSSim model was based mainly on estimates from literature and expert knowledge. Different kinds of quantitative data are needed. First, data are needed about the relative contribution of the different infection routes of Johne's disease within a herd and about the reduction of the infection probabilities of those routes by various control tools. The effects of the management strategies on the prevalence of Johne's disease are sensitive to the assumed reductions (Figure 3). Secondly, data are needed on the age that infected animals become lowly or highly infectious or clinical. Thirdly, data on test sensitivity are needed per infection status. Currently, the tests for Johne's disease mainly detect highly infectious or clinical animals; most infected animals, however, are low-shedders or animals that shed undetectable levels of *M.a. paratuberculosis* (Whitlock et al., 2000). Therefore, test-and-cull strategies and tests before introduction of animals have a relatively small influence on the prevalence (Figure 3). Fourthly, data are needed on the contribution of infected animals <2 years old to the spread of Johne's disease. Wherein the model animals will never become infectious before 2 years of age, it has been suggested that in herds with a high prevalence, animals <2 years of age also could spread *M.a. paratuberculosis* (McCaughan, 1990; Wells et al., 2000). This would reduce the

effectiveness of any Johne's disease control programs based on separation of young and old animals. However, because only a small percentage of herds has a high prevalence (Muskens et al., 1999; Ott et al, 1999), the effect of spread by young animals on a national basis probably will not be large—but it might be important in such high-prevalence herds. Finally, more data are needed on the survivability of *M.a. paratuberculosis*. Johne's disease is very resistant and can survive up to 1 year in the environment (Rosenberger et al., 1992); because in the JohneSSim model the time steps are 6 months, the survivability was assumed to be 6 months.

2.4.2 Economics

Ott et al. (1999) standardized the losses due to Johne's disease for six studies and found that they ranged between US$ 20 and 27 per cow per year on an infected farm except for one study based on only one herd. In our two simulation studies, the losses due to Johne's disease were on average Euro 15 per cow per year on an average (uninfected or infected) Dutch dairy herd (on average 19 Euro per cow per year on an average infected Dutch dairy herd) and US$ 34 per cow per year on an average infected Pennsylvanian 100-cow dairy herd (Table 5 and Table 7). Thus, across all herds, the results were consistent with previous Johne's disease-loss estimates. In addition, Ott et al. (1999) estimated that >75% of the losses due to Johne's disease were caused by reduced milk production. In our study, this accounted for only 10–15% of the losses; missed future income caused ≈70% of the losses (Table 6). However, the losses due to missed future income equal the direct costs of replacing a cow with a heifer plus the reduction of the milk output due to replacement of the cow by a less productive heifer, weighted by the survivability.
The simulated Dutch control program was on average economically attractive; the average farm level NPV was Euro 12,397 (excluding costs of extra labor). Contract heifer rearing had substantial economic benefits in the Pennsylvanian example: on average, about US$ 44,000 for the 20-year period. In the JohneSSim model, reduction of losses due to other diseases was not taken into account. Combination of several disease control programs (also called "integrated disease control") against infectious diseases could make each program economically more attractive because of shared costs (e.g. separate housing of calves from adult cattle). Secondly, no losses were considered for the potential loss of consumers' confidence in milk infected with *M.a. paratuberculosis*. Finally, potential loss of the current export markets because of Johne's disease was not taken into account.

2.5 Conclusion

The JohneSSim model seemed to be a flexible tool to evaluate Johne's disease control strategies. The structure of the model enabled simulation of various dairy situations of current management, herd performance, economics, test attributes, and Johne's disease apparent test

prevalence. The main conclusion from the results of the model is that control of Johne's disease is effective only if calf management is improved drastically. Test-and-cull strategies with the current tests could be seen only as a tool to stimulate the farmer to improve the calf hygiene. Control of Johne's disease is economically attractive for an average herd but there is a large variation between herds. We concluded that in The Netherlands, the optimal control program focuses primarily on improved calf management, in combination with limited testing. In Pennsylvania, contract heifer rearing in combination with on-farm calf hygiene improvement appeared to be an effective and economically attractive Johne's disease control strategy.

In The Netherlands, the model has been used to develop a nationwide voluntary control program that has started in September 2000. In Pennsylvania, the results contributed to the discussion about the attributes of an effective and economically efficient Johne's disease control program. The model also gave several directions to further research.

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Appendices

Appendix A

Input parameters related to the herd simulation of Johne's disease control in dairy herds

Variable	The Netherlands	Pennsylvania
Herd size (dairy cows)	50 cows	100 cows
Yearly increase in herd size	+ 3.5 % per year	0
Age first calving	2 year	2 year
Calving interval	1 year	1 year
Total culling percentage	30%	30%

Appendix B

Input parameters for lactation-specific involuntary dairy cow culling percentage (Van Arendonk, 1985)

Lactation	1	2	3	4	5	6	7	8	9	10	11	12
%	13.6	14.9	17.0	19.8	22.7	24.5	25.9	27.3	29.0	31.0	32.6	34.5

Appendix C

Age (years) of a dairy cow becoming highly infectious for Johne's disease, modeled as a triangular distribution. In addition, an infected cow becomes lowly infectious two calvings before becoming highly infectious

	Age dairy cow becomes highly infectious		
Age of infection	Minimum	Most-likely	Maximum
Congenital infection	1.5 [a]	2.5	20
Around birth (first days)	2	3.5	20
Month 0 – 6	2	4	20
Month 7 – 12	4.5	6	20

[a] minimum age of shedding is 2 years; the age 1.5 year was used in the triangular probability distribution

Appendix D

Intervals between becoming highly infectious for Johne's disease and culling in dairy cows

	Parameters of the triangular distribution		
Interval	Minimum	Most-likely	Maximum
Between becoming highly infectious and becoming clinically ill (years)	0.5	1	2
Between becoming clinically ill and being culled (months)	0.5	1	3

Appendix E

Probability of fetal infection, in relation to status of dam when dam is either highly infectious or clinical

	Number of months before becoming clinical			Clinical cow
	> 12 months	7-12 months	0-6 months	
Probability	0.035	0.07	0.22	0.50

Appendix F

Infection probabilities around birth without extra calf hygiene per calf born

	Herd infection state		
Dam infection status	No infectious cows	One or more lowly infectious cows	One or more highly infectious cows
Not infectious	0.00	0.025	0.10
Lowly infectious			
Two calvings before highly infectious	N.A.	0.20	0.50
One calving before highly infectious	N.A.	0.50	0.50
Highly infectious or clinical	N.A.	N.A.	0.95

Appendix G

Johne's disease infection probability of dairy calves due to environmental contamination = $1-(1-kS/N)^I$ (modified Reed–Frost)

S	Susceptibility of calves to infection with *M. a. paratuberculosis*
k (NL)	Total number of effective cow-calf contacts: 7 (0 – 6 months) and 63 (7 – 12 months)
k (PA)	Total number of effective cow-calf contacts: 5 (0 – 6 months) and 5 (7 – 12 months)
N	Number of dairy cows, determined by the model
I	Number of infectious cows in the last 6 months; lowly infectious cows only spread the first 2 months after calving (Jacobson et al., 2000)

Appendix H

Test characteristics used in the JohneSSim model as a basis for test-and-cull strategies for paratuberculosis control in dairy herds

Infection state	ELISA		Fecal culture	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Latently infected	1	-	0	-
Lowly infectious	10	-	40	-
Highly infectious	60	-	95	-
Clinically infected	80	-	90	-
Uninfected	-	99	-	100

Appendix I

Risk profiles used in the JohneSSim model to represent the variation in current calf management and hygiene on Dutch and Pennsylvanian (PA) dairy farms

	Current calf management and hygiene			
	"+" = Quick calf-cow separation (within 1hr) "-" = Other	"+" = only milk-replacer and colostrum own dam "+/-" = waste milk and colostrum own dam "-" = waste milk and mixed colostrum	"+" = proper separation of calves 0-6 months of age and adult animals "-" = Other	Percentage of farms with risk-profile (Dutch * and US**)
Dutch risk profile				
1	-	+	+	8,2 %
2	-	+	-	10 %
3	+	+/-	+	7,9 %
4	+	+/-	-	12,4 %
5	-	+/-	+	18,0 %
6	-	+/-	-	26,5 %
7	-	-	+	6,4 %
8	-	-	-	10,6%
PA risk profile				
1	-	-	-	45%
2	-	+	-	45%
3	-	+	+	10%

** Personal communications of the Johne's disease discussion group (1999)*

*** Personal communications of D. T. Galligan (2000)*

Appendix J

Effect of management adaptations used in the JohneSSim model

	Management tools	Effect on infection probability
The Netherlands		
Step 1	Better hygiene around birth	90% reduction around birth
	Colostrum from own dam only	100% reduction mixed colostrum
Step 2	Only milk replacement	100 % reduction waste and bulk milk
	Effectively separate calves from adult cows from birth to weaning	90% reduction of k [a]
Step 3	Effectively separate calves from adult cows from weaning to the end first year	90% reduction of k [a]
Pennsylvania		
Contract heifer rearing (1 – 365 days)	Calves to contract heifer facility at day 1	100 % reduction waste and bulk milk 100% reduction of k [a] from day 2 to 365
Management (Mngt.)	Better hygiene around birth	90% reduction around birth
	Colostrum from own dam only	100% reduction mixed colostrum

[a] *k is the total number of effective cow-calf contacts*

Appendix K

Losses caused by Johne's disease or costs of Johne's disease control in dairy cow herds

Category	Loss or cost	Netherlands (Euro)	Pennsylvania (US$)
Milk-production losses	Reduction depends on infection state: 5 % (lowly infectious) – 20 % (clinical)	0.13 / kg	9 / 100 lb
Diagnosis and treatment	Treatment clinical cow (average total)	27	30
Reduction slaughter value	Standard slaughter value (per cow): Reduction depends on infection state: 5 % (lowly infectious) – 30 % (clinical)	516	400
Missed future income: Retention Pay Off (RPO) value	The RPO value of a cow depends on The lactation number, month in lactation and production level	0 – 1900 (average fresh 3rd lactation cow Euro 926	0 – 3600 (average fresh 3rd lactation cow $965

Appendix K (Continued)

Losses caused by Johne's disease or costs of Johne's disease control in dairy cow herds

Category	Loss or cost	Netherlands (Euro)	Pennsylvania (US$)
Costs of testing	Visit veterinarian [a]	17.50 / visit	25 / visit
	Testing (by the veterinarian) [a]	2.30 / test	2 / test
	ELISA test [a]	4.50 / test	5 / test
	Fecal test [a]	16 / test	15 / test
	Additional laboratory costs [a]	6 / delivery	0
Culling test-positive animals	Equal to the RPO value of the animal	0 – 1900 (average fresh 3rd lactation cow Euro 926	0 – 3600 (average fresh 3rd lactation cow $965
Contract heifer rearing [b]		-	0
PPN, general	Animal Health Service costs and once a year visit of veterinarian [a]	89 / year	-
PPN, Step 1	Extra hygiene calving pen [a]	90 / year	-
	Extra labor around calving [c]	7 / calving	-
	Extra labor colostrum own dam [c]	7 / calving	-
PPN, Step 2	Better hygiene first year [a]	90 / year	-
	Milk replacer instead of raw milk [c, d]	3.40 to 9.00 / heifer	-
PPN, Step 3	Separate housing of animals < 1 year from cows > 2 year [c]	547 + 3.5% / year	-

[a] *Discussions in the 'Johne's disease discussion group' (1999)*

[b] *no costs were included for contract heifer rearing because of the large variation between farms*

[c] *Agricultural Information and Knowledge Center and Research Station for Animal Husbandry (1997)*

[d] *these costs depend on the pre-control management on the farm*

Chapter 3

3 An Economic Spreadsheet Model to Determine Optimal Breeding and Replacement Decisions for Dairy Cattle

Paper by Groenendaal, H., Galligan, D.T., Mulder, H.A., 2003. *Journal of Dairy Science* 87, 2146-2157.

Abstract

The aim of this paper is to describe a user-friendly spreadsheet culling model that was constructed to support economical, optimal breeding and replacement decisions on dairy farms. The model was based on the marginal net revenue technique. Inputs for the model can be entered for specific farm conditions, and the output is easily accessible. In the model, the retention pay-off (RPO) value of individual dairy cows was calculated. The RPO value of a cow is equal to the total additional profits that a producer can expect from trying to keep the cow until her optimal age, taking into account the changes of involuntary removal compared with her immediate replacement. To calculate the RPO values, the future production, revenues, and costs of dairy cows at different levels of milk production with different numbers of days open (DO) were determined. Furthermore, the ranges of carcass value, calf revenues, and the range of involuntary disposal rates of cows within and across lactations were taken into account. To illustrate the model, parameters in the model were chosen to represent a typical Holstein dairy herd in Pennsylvania. The results of this model are very comparable with earlier, more complex models that are more difficult to use on the farm. In addition to using the RPO values to evaluate the decision to breed or replace a cow, the costs per additional DO were estimated. Early conception was most profitable with the costs per additional DO varying from $0 to more than $3/d. The model can be used as a decision-supporting tool for producers, extension personnel, veterinarians, and consultants. In addition, researchers, economists, and government organizations can use the model to determine the costs of culling dairy cows in a disease control program. The model and manual are available at http://cahpwww.vet.upenn.edu/software/econcow.html.

3.1 Introduction

An important goal of a commercial dairy farmer is maximization of total farm profits (Renkema and Stelwagen, 1979). Breeding and replacement decisions play an important role in the management of a dairy herd (Van Arendonk, 1985a; Jalvingh, 1993). Several studies found that the replacement policy of dairy cows greatly influences the profitability of the herd (Renkema and Stelwagen, 1979; Congleton and King, 1984). Thus, maximizing farm profits requires optimizing reproduction and replacement decisions (DeLorenzo et al., 1992).

On dairy farms, the most observed reasons for culling cows are reproductive problems, low production, and mastitis (Morris and Marsh, 1985; Van Arendonk, 1988). Although culling decisions are of great economic importance for a dairy farm, they are often made in a non-programmed fashion and based partly on the intuition of the decision-maker (Lehenbauer and Oltjen, 1998). To improve expected future profits on the dairy farm, culling decisions should be based on economic principles rather than on biological considerations (Dijkhuizen, 1983; Lehenbauer and Oltjen, 1998). Economic analysis of the replacement decision should include

the expectation of the cow's future performance as well as that of the potential replacement (Dijkhuizen, 1983).

To evaluate decisions on dairy cattle breeding and replacement, 2 main techniques, marginal net revenue (MNR) and dynamic programming (DP), have been applied Burt (1965) stated that the MNR approach is, in fact, a special case of DP. Both techniques rely on the production function approach in which the economic costs and revenues of a cow are modeled during her life span (Van Arendonk, 1985a). The 2 main differences between the MNR and the DP approach (and limitations of the MNR approach) are 1) the DP approach can take into account the variation in expected performances of both present and subsequent replacement, and 2) DP can take into account genetic improvement. Because DP can overcome both limitations of the MNR approach, many researchers (Giaever, 1966; Van Arendonk, 1985a, DeLorenzo et al., 1992; Jalvingh, 1993; Kristensen, 1993; Houben, 1995) have used DP techniques to provide guidelines for replacement and breeding decisions.

A problem with the DP technique, however, is that DP models can easily become very large and complicated depending on the number of states defined, incurring the risk of limited breadth of application because of intensive resources requirements (Smith et al., 1993). Although more efficient DP models have been developed (Kristensen, 1993), most of the DP models that have been developed so far are relatively complicated and need high computer skills to use. In addition, most DP models are compiled with many fixed parameters, thus limiting the number of parameters that could be changed by the user. Furthermore, most of the existing models are not very user friendly and have interfaces that are unfamiliar to the end users. The majority of effort on decision-supporting models in the dairy industry has been focused on constructing models (Van Arendonk, 1985a; Kristensen, 1993; Houben, 1995) rather than on using models as applied decision-making tools. This fact is illustrated by the observation that, to our knowledge, none of the existing models are directly available. As a consequence, little progress has been made at the farm level in making better culling decisions (Lehenbauer and Oltjen, 1998).

For use as a decision-supporting tool on the dairy farm, a model should be simplified as much as possible without compromising the accuracy of outputs. For that reason (Van Arendonk, 1985a) and for the possibility of structuring a replacement model in a spreadsheet program that is familiar and easily available to the end users, the MNR approach sometimes can be justified. An often-cited limitation of the MNR approach (Van Arendonk, 1985a; Kristensen, 1993) is its inability to easily account for genetic improvement. However, Van Arendonk (1985a) concluded that genetic improvement hardly affected the optimal breeding and replacement policy. A second limitation of the MNR approach is that it does not easily take into account the variation in the expected performance of present animals. However, as the expected performance of a replacement heifer, which is used in the MNR approach, is equal to the average of the probability distributions that are used in the DP model, both models are likely to give very similar results. In other words, although DP takes into account variation, the optimal decisions in both methods are based on the expected performances of the animals in the herd.

The goal of the current paper is to describe a spreadsheet dairy cattle replacement model. With the model, optimal replacement and breeding decisions can be supported for cows with different production characteristics. With the model, the costs per additional day open (DO) for cows with different production characteristics can also be calculated. The model is based on the MNR approach and is user friendly in that it allows users to easily change all input parameters under different production and economic situations on dairy farms.

3.2 Material and Methods

3.2.1 Calculations

The optimum time for replacement of a dairy cow was determined by comparison of the MNR anticipated from the present cow with the economic opportunity of a replacement. The latter value equals the maximal average discounted net revenue anticipated from replacement cows, also reported as annuities (Van Arendonk and Dijkhuizen, 1985; Brealey and Myers, 2000). Figure 1 shows a graphical representation of these calculations for 3 situations.

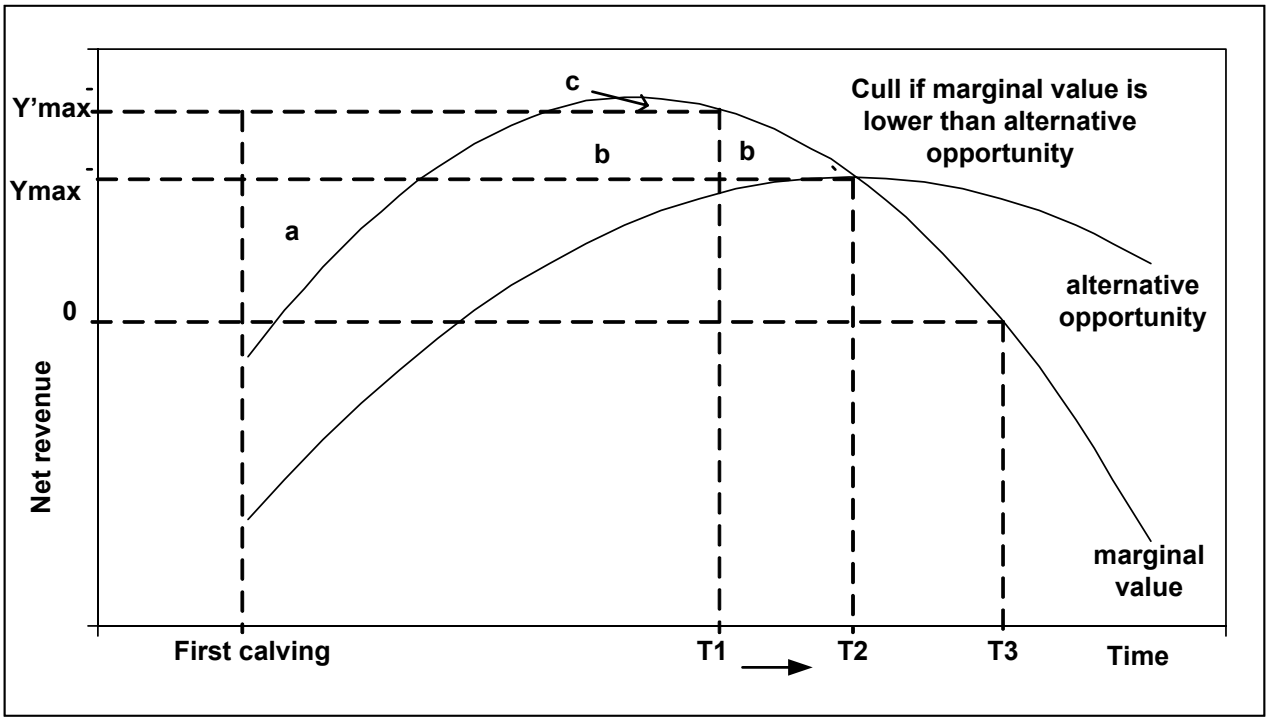


Figure 1. Graphical representation of the way to establish the optimal time for replacement in a situation without an alternative opportunity (T3) and in situations of identical replacement (T2) and non-identical (in this case better) replacement (T1) (modified from Huirne et al., 1997)

For a situation with identical replacement (T2) or non-identical replacement (T1), the optimum time of replacement was defined as the first time period in which the annuity value of the cow

drops below the maximal annuity value of the replacement animal. The maximal annuity calculation of the replacement was based on the average performance of animals present in the herd, assuming this to be the best estimate for expected future net revenue of young replacement animals. For the situation T2, the retention pay-off (RPO) value would be calculated as the area 'b' plus 'c' minus the area 'a,' all shown in Figure 1. For a situation without a replacement animal available (T3; no alternative opportunity), the optimal time of replacement is equal to the time period in which the MNR decreases below zero (Huirne et al., 1997). The RPO value in this situation would be equal to the net area below the marginal value line.

All future revenues and costs were weighted with the probability of animal survival. Animal survival (p_i) was defined as 1 minus the probability on involuntary culling. A formula, modified from Huirne et al. (1997), was used to calculate net revenues as an annuity per month (Brealey and Myers, 2000):

$$ANR_j = \left[\sum_{i=1\ldots j} p_i \times \frac{1}{(1+r)^i} \times MNR_i \right] \times \frac{r}{1-(1+r)^{-\sum_{i=1\ldots j} p_i \times m_i}} \qquad (1)$$

where

ANR_j = annuity of the net revenue of a replacement animal per month;

i = decision moment of replacement ($1 \leq I \leq j$) at the end of period i;

j = period, at the end of which an animal can be replaced;

r = discount rate per month;

p_i = probability of survival until the end of period i, calculated from the moment at which a young animal starts its first production (end of period 0);

m_i = length of period i (mo); and

MNR_i = MNR in period i, including a change in slaughter value and financial loss associated with involuntary disposal.

In the current application of the model in this paper, the replacement animal was assumed to have been bred to an average calving interval (CI) and kept until her maximal annuity value was reached.

The RPO value of a cow is equal to the total additional profits that a producer can expect from trying to keep the cow until her optimal age, taking into account the changes of involuntary premature removal compared with her immediate replacement (Huirne et al., 1997). In other words, the RPO value represents the maximum amount of money that could be spent to try to keep an animal in case of reproductive failure or health problems. The RPO value assumes that the only opportunity, other then keeping the cow, is a replacement heifer. Therefore, the maximization of net revenue per cow-place per year in the long run is the objective, and the

opportunity costs have to be included in the calculation. The RPO value was calculated as follows (Huirne et al., 1997):

$$RPO_i = \sum_{j=j+1\ldots d} p \times \frac{1}{(1+r)^j} \times (MNR_j - ANR_{\max} \times m_j) \quad (2)$$

where

RPO_i = RPO at decision moment i;

d = optimal moment for replacement (when $MNR_j < ANR_{max}$);

r = discount rate per month;

p_j = probability of survival until the end of period j, calculated from decision moment i;

j = period, at the end of which an animal can be replaced;

m_j = length of period j (mo);

MNR_j = MNR in period j; and

ANR_{max} = expected maximum average net revenue per month.

In the model, the RPO values can be calculated for different production levels, which were defined relative to the herd average milk yield. The herd average milk yield in this application was set at 9072 kg (20,000 lb)/yr per cow. In the current model's application, the RPO values of 5 production levels (76, 88, 100, 112, and 124% of average) were calculated, but any level can be used. To capture different reproductive efficiencies, the model calculates the RPO values for cows with CI of 11, 12, ...17 mo. The CI in the following lactations can take on a variety of levels, including the overall herd average (set as default). The herd average CI, without confounding by culling, was calculated by:

$$CI_{aver.} = RND((VWP + 21/(EDR \times CR) + LP)/30.4) \quad (3)$$

where

$CI_{aver.}$ = average CI (mo),

RND = rounding function,

VWP = voluntary waiting period (d),

EDR = estrus detection rate (%),

CR = conception rate (%), and

LP = length of pregnancy (assumed to be 274 d).

In the current application, the average CI ($CI_{aver.}$) was calculated at 15 mo (for input parameters, see Table 1). This average CI was used as the expected CI of replacement heifers.

Table 1. Parameter values used for variables in the example applications of the culling model for a typical dairy herd in Pennsylvania

	Parameter [1]	Value / price	
Prices	Milk price	0.256	$ / kg
	Calf value	50	$ / calf
	Costs replacement heifer	1132	$ / heifer
	Veterinary costs (for an average first calving heifer)	50	$ / cow / year
	Financial losses at disposal	50	$ / case
	Insemination costs	12	$ / breeding
	Feed costs lactation (feeding program based on milk production)	0.20	$ / kg DMI
	Feed costs dry period	0.15	$ / kg DMI
	Price per kg of carcass weight (basis)	0.69	$ / kg
	Risk-free discount rate	5	% / year
Herd data	Average herd milk production per year	9,072	Kg
	Weight at birth	41	Kg
	Weight of an adult dairy cow	612	Kg
	Voluntary waiting period after calving	50	d
	Heat detection rate	40	%
	Conception rate	40	%
	Age first calving	26	Mo
	Dressing percentages within and across lactations	See appendix B	
	Lactation function (See 'Revenues')	Wood (1967), Delorenzo et al. (1992) or Skidmore (1990),	

[1] *for additional parameters, see Table 2, 3, 4 and 5*

After calculating the RPO values, the costs per DO were calculated by the model:

$$CDO_{CI} = (RPO_{CI} - RPO_{CI+1}) / 30.4 \quad (4)$$

where

CDO_{CI} = costs per DO ($),

CI = CI (mo),

RPO_{CI} = RPO value in first month of a lactation with a CI measured in months, and

RPO_{CI+1} = RPO value in first month of a lactation with a CI of CI + 1 mo.

To calculate the effect of a difference in CI on the RPO values, the RPO values in the first month of lactation (between calving and the end of the voluntary waiting period) were used. One could also choose a later month during the lactation (as long as this month is before the month of conception of the shortest CI) to compare RPO values and calculate the costs per extra DO. To keep the model consistent for different CI, the first month of the lactation was chosen. To get more insight in the costs per extra DO both the costs with and without opportunity costs (of a replacement heifer) were calculated. The RPO values without opportunity costs represent a situation where the RPO value is equal to the total net present value of the current cow (representing a situation where no replacement is available), without confounding by voluntary replacement.

3.2.2 Input

3.2.2.1 General

The spreadsheet model (http://cahpwww.vet.upenn.edu/software/econcow.html) was developed using Excel 2002 with Visual Basic for Applications (Microsoft, Redmond, WA). The user can customize the model by changing all input parameters and variables to calculate results for specific herd situations. In the model, the performances, revenues, and costs of individual dairy cows were calculated for each month (30.4 d) to allow replacement at regular intervals within the lactation period. All future costs and revenues were discounted at a 5% discount rate (Brealey and Myers, 2000). Previous work found that milk price, feed price, milk production, replacement costs, and carcass prices have the largest influence on optimal replacement decisions (Van Arendonk, 1985a). Therefore, to keep the number of input parameters low and the model simple, only these and a few other important parameters were included (Table 1). The default parameter values for this paper's application were chosen to represent a typical dairy farm in Pennsylvania.

3.2.2.2 Revenues

Three lactation curves are currently available in the model (the user chooses the curve with a pop-down menu), but other equations can easily be included. The lactation equation used in this paper's application was developed by Oltenacu et al. (1981), adapted by Marsh et al. (1988), and later modified by Skidmore (1990):

$$Y = A(DIM)^b e^{cDIM} e^{gDP} \quad (5)$$

where

Y = daily milk yield (kg),

A = ((GNRHA/100 – a)/2.96),

GNRHA = rolling lactation average (genetic rolling herd average) (kg/yr),

DIM = days in lactation (milk),

DP = days in gestation (days pregnant),

e = base of natural logarithm, and

a, b, c, g = constants that determine the shape of the lactation curves.

For lactation numbers 1, 2, and ≥3, different constants for the coefficients a, b, c, and g (Table 2) were used (Skidmore, 1990). The constant g, which determines the effect of gestation stage on milk yield, was modified to reflect a 200- and 350-kg cumulative milk yield decrease in the 305-d production of first and second and higher lactation animals (Olori et al., 1997). Prediction of future milk production levels was done, assuming a repeatability of 0.55 for the next lactation and 0.50 for all lactations afterward (mean reversion), similar to the method used by Van Arendonk (1985b). Whereas the current application of the model used this formula for generating lactation curves, in other situations other curves might be more applicable.

Table 2. Input parameters used in the example calculations to generate the modified Oltenacu et al. (1981) lactation curve. (Structure and parameters of lactation curve can easily be changed by the user)

Lactation nr.	a	b	c
1	-20	0.08	-0.002
2	14	0.12	-0.004
>2	14	0.16	-0.005

The average calf net revenues (bull or heifer calves) were estimated at $100 and were added to the total revenues during the first month in each lactation. Monthly changes in carcass value were also included in the model. The carcass value was calculated from the following equation (Van Arendonk, 1985b):

$$CV_{i,j} = LW_i D\%_i (p_j + dp_i) \quad (6)$$

where

$CV_{i,j}$ = carcass value of cow i in month j,

$LW_{i,j}$ = live weight (kg) of cow i in month j,

$D\%_j$ = dressing percentage (%) in month j,

P = average price per kilogram of carcass weight for a heifer 210 d in lactation ($/kg), and

dp_j = price in month j as a deviation from the average p_j ($/kg).

The effect of lactation number and stage of lactation on dressing percentage and the price per kilogram of carcass weight is given in Table 3. This price was expressed as a deviation from the price of a heifer at 7 mo in lactation, which was taken at $1.52/kg (Pennsylvanian Agricultural Statistic Service, 1997).

Table 3. Effect of lactation number and stage of lactation on the dressing percentage (D%) and the deviation in price (/kg carcass weight)

	Lactation number at calving											
Trait	1	2	3	4	5	6	7	8	9	10	11	12
D (%)	50.0	49.8	49.6	49.4	49.3	49.2	49.1	49.0	48.9	48.7	48.5	48.2
Price [1] ($)	0.00	-0.01	-0.014	-0.02	-0.03	-0.04	-0.05	-0.06	-0.08	-0.1	-0.12	-0.14

	Month in lactation											
Trait	1	2	3	4	5	6	7	8	9	10	>10	Dry period
D (%)	- 0.6	- 0.6	- 0.6	- 0.6	- 0.4	- 0.2	0.0	+ 0.2	+ 0.4	+ 0.6	+ 0.6	+ 0.2
Price[2] ($)	-0.04	-0.04	-0.04	-0.03	-0.02	-0.01	0.00	0.02	0.02	0.02	0.02	+ 0.01

[1] *as a deviation of the price for a heifer 210 days in lactation*

[2] *as a deviation of the value at 210 days in lactation*

The live weight of each cow in each month of lactation was calculated from the function developed by Korver et al. (1985). This function takes into account age, DIM, number of days pregnant, mature weight, and birth weight. Furthermore, the maximum decrease of live weight during lactation was set at 50 kg at 75 DIM (Van Arendonk, 1985b). Finally, the effect of pregnancy on live weight was excluded, in agreement with Van Arendonk (1985b). Live weight was used in the model to calculate carcass value and to determine DMI.

3.2.2.3 Costs

In the model, the rearing of young stock was isolated from other activities under the assumption that pregnant heifers are purchased from the farm's rearing enterprise or through the market. The costs of replacement heifers for this paper's application were calculated by interpolation data from the Cornell Cattle System 4 model (Van Amburgh and Fox, 1996). These data imply that, between reasonable biological limits, the total costs per kilogram of weight gain are lower

with a lower age at first calving. The total costs of a replacement heifer calving at an age of 26 mo were, therefore, calculated at $1132, which was consistent with the average costs to raise a replacement heifer of $1124 found by Gabler et al. (2000). However, the user can include costs of replacement animals at any price without using the interpolated data.

Feed costs were calculated by multiplying the DMI (kg) of each individual cow with the costs per kilogram of DMI. The DMI was calculated using the following formulas (Galligan et al., 1985).

For lactating cows:

$$DMI_{i,j} = 1.10 + 0.015BW_{i,j} + 0.2185P_{i,j} + 0.0001280BW_{i,j} \times P_{i,j} \quad (7a)$$

For dry cows:

$$DMI_{i,j} = 1.92 + 0.012BW_{i,j} \quad (7b)$$

where

$DMI_{i,j}$ = DMI (kg) for cow i in month j,

$BW_{i,j}$ = mature BW (kg) for cow i in month j, and

$P_{i,j}$ = milk production (kg) for cow i in month j.

Although this model can account for a variety of feeding systems, a one-group TMR was used in this paper's application. The costs of DMI in lactating cows were set at $0.20/kg (US $0.09/lb). The feed costs for growing heifers and dry cows were $0.15/kg of DMI ($0.07/lb) (Galligan et al., 1985).

To calculate the breeding costs for different CI, the estrus detection rate was set at 40%, and the conception rate was set at 40%, close to what has been observed in the field (Smith et al., 1988; Lucy, 2001). The voluntary waiting period was assumed to be 50 d. The breeding costs per month were calculated by multiplying the expected number of breedings per month with the insemination costs per breeding. The expected number of breedings per months was calculated as the potential number of breedings per month (1.45, which was calculated as 30.4 d ÷ estrous cycle of 21 d) multiplied by the estrus detection rate. The minimal number of total breedings per pregnancy was set at one.

Other costs included (Table 4) were the costs associated with morbidity, disposal, and mortality. Typically, yearly veterinarian costs per cow were estimated at $50 for an average first lactation cow (Snow, 1993) and increased $5 each lactation. Van Arendonk (1985b) assigned 33% of these costs to the first month, 11% to the second and third months, and 5% to the later months of each lactation. The direct financial costs associated with mortality were set equal to the slaughter values.

Table 4. Average veterinary costs and mortality and disposal percentages of dairy cows per lactation

	Lactation number											
	1	2	3	4	5	6	7	8	9	10	11	12
Veterinary costs (US$)	50	55	60	65	70	75	80	85	90	95	100	105
Mortality	0.02	0.04	0.05	0.05	0.06	0.06	0.07	0.07	0.08	0.08	0.09	0.09
Disposal	0.14	0.15	0.18	0.20	0.23	0.25	0.27	0.29	0.32	0.35	0.38	0.41[1]

[1] *because the maximum age is set at 12 lactation, the marginal disposal rate in the last month of lactation 12 is 1*

Type of cow disposal not subject to this decision-making was referred to as involuntary culling (Van Arendonk, 1985b). Field data on culling probabilities are biased because of voluntary culling (Giaever, 1966; Dijkhuizen, 1983). Therefore, to obtain marginal probabilities on involuntary culling (Tables 4 and 5), Dijkhuizen (1983) corrected field data on culling probabilities within and across lactations for voluntary culling. Finally, the financial losses caused by idle production factors (lack of immediate replacement) were set equal to $50 and were assigned to the month in lactation during which the cow had to be involuntarily disposed.

Table 5. Allocation of the morbidity, mortality, and disposal in different months of the lactation as a proportion of the total in each lactation

	Month in lactation (12 mo calving interval)																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16[1]	17[1]
Morbidity	0.33	0.11	0.11	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Mortality	0.20	0.20	0.20	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
Disposal	0.15	0.07	0.06	0.07	0.08	0.10	0.11	0.11	0.10	0.09	0.06	0.05	0.04	0.04	0.04	0.03	0.03

[1] *the mo 16 and 17 represent the rates in the dry period*

3.2.3 Application on dairy herds

The calculations of the RPO values of 5 dairy cows are shown to illustrate the way in which the model could be used on a dairy herd or by a researcher or government organization. The input values of the parameters that are needed to obtain the RPO values and, if the cow is not pregnant and replacement of is not the optimal decision, the costs per extra DO of each of these 5 cows are estimated. The cows were assumed to be part of a typical Pennsylvania herd, and, consequently, their economic optimal replacement was determined by comparing the cow's performance with that of an average heifer on such a herd (Table 1).

3.3 Results and discussion

3.3.1 RPO Values

The RPO value is an economic index that makes it possible to rank animals according to their future profitability; the higher the RPO, the more valuable the animal. An RPO value has 2 important and related meanings. First, any RPO value <0 means that immediate replacement is the most profitable choice; there is no extra profit to be expected from trying to keep the cow, compared with replacing her (Figure 1). Second, the RPO represents the cow's economic value beyond the slaughter value, i.e., the total maximum amount of money that could be spent in trying to keep an animal in case of reproductive failure or health problems (Van Arendonk, 1985a; Huirne et al., 1997).

For 5 different milk production levels, the calculated RPO values for typical Pennsylvania conditions are given in Table 6, calculated for cows that have just become pregnant at 6 mo after calving (resulting in a 15-mo CI). The RPO values in Table 6 vary between –$37 and +$1995; variability was mainly caused by the difference in milk production. A first lactation cow with a relative milk production of 76% has an RPO value of –$37, which means that keeping her 1 additional mo instead of replacing her with an average replacement heifer (if available) would cost the producer $37. In contrast, if the producer would have to cull (involuntarily) a first lactation heifer that has a relative production level of 124% and replace her with an average heifer, he would have an economic loss of $1995.

Table 6. Retention pay-off of cows that became pregnant at 6 mo after calving (in $)

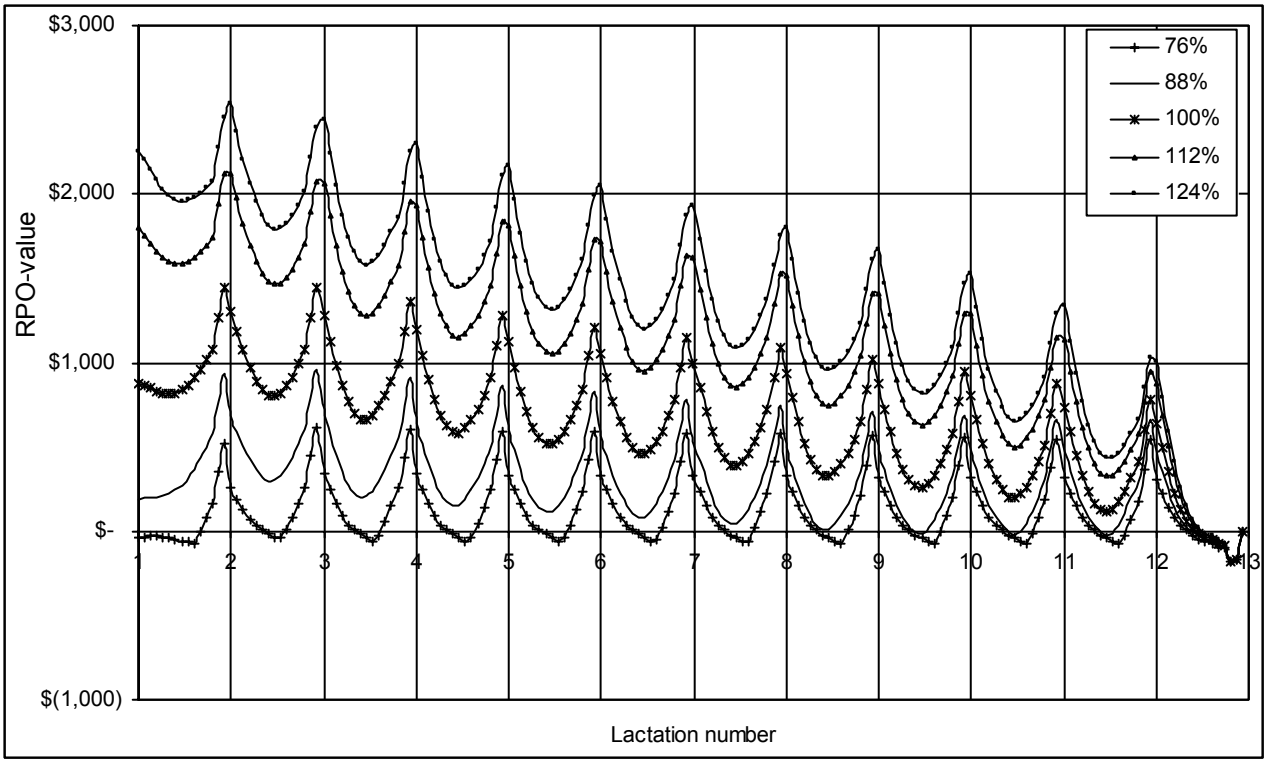
	Relative production level of cow [1]				
Lactation	76%	88%	100%	112%	124%
1	-$37	$224	$814	$1404	$1995
3	$10	$226	$702	$1178	$1654
5	$9	$139	$554	$970	$1385
7	$8	$70	$431	$793	$1154
9	$7	$28	$306	$599	$893
11	$6	$27	$164	$345	$529

[1] *relative to the herd average milk yield (%)*

For cows with a 15-mo (average) CI and under the 5 different production levels (the same production characteristics as Table 5), the sequences of RPO values are shown in Figure 2. As can be seen from Figure 2, a cow's RPO value can be negative temporarily and become positive again because of the high future expected milk and calf revenues from a new lactation. When this cow with a negative RPO value is kept (instead of replaced) and she was successfully bred, her RPO can become positive again during the late stages of gestation. If this is the case, the producer should keep the cow until the RPO becomes negative again. To determine optimal

breeding and replacement decisions, the sequences of RPO values are more useful. Figure 2 shows 4 main attributes of the sequences of the RPO values within and across lactations.

Figure 2. Retention pay-off (RPO) value for different milk production levels (relative to the herd average milk production) for cows with an average 15-mo calving interval. (Vertical lines indicate calving event; a successful breeding occurs 9 mo before)



First, cows having a higher milk production have significantly higher RPO values for a given reproductive efficiency. A large influence of the cow's relative level of milk production on the average monthly net revenues during the lactation period has been previously reported (Van Arendonk, 1985a; Kristensen, 1993). Cows with a 124% milk production level with a 15-mo CI (herd average) have a maximum RPO value at the end of their first lactation (start of the second) of around US $1800. Assuming a normal distribution with the average milk production of 9072 kg (20,000 lb) and a standard deviation of 907 kg (2500 lb) (De Veer and Van Vleck, 1987), only 2.7% of the cows have a milk production ≥124%. Finally, Houben (1995) found that not including within-lactation transitions results in an overestimation of high-producing cows and an underestimation of low-producing cows in the beginning of the lactation. As the current model allows for transitions between different levels of milk production only at the end of the lactation period, the model's effect of milk production on RPO could be slightly overestimated.

Second, the RPO value of a cow is generally the highest just before calving. For cows with a 15-mo CI, the RPO is minimal around 7 to 9 mo after calving, depending on the milk production level. Thereafter, the RPO increases again (Figure 2) because of the decreasing risk

that she is involuntarily culled before calving, the increasing expected revenues of the next lactation, and because during the dry period the costs are becoming sunk cost.

Third, the maximum RPO values across lactations for high-producing cows gradually decline from lactation 1 to 12. An exception is that for lower-than-average-producing cows the maximum RPO values increase from lactation 1 to 2, but after lactation 2, the RPO values are also gradually decreased. The lower RPO value in the first lactation of low-producing animals was caused by the lower production in this lactation compared with later lactations (Equation 5). For average- and higher-than-average-producing cows, lower production in the first lactation was offset by the high relative production level of the cow (≥100%) compared with an average replacement heifer. After reaching the maximum, the RPO value of cows gradually declines with a higher lactation number for 3 reasons. First, the time until optimal culling becomes shorter, and, therefore, the total extra profits of keeping the cow until this optimal time of replacement (= RPO value) decrease. The 2 other reasons for the decreasing RPO values are the higher involuntary culling and higher morbidity rates in later lactations.

Fourth, the RPO of cows with a lower production level decreased <0 around 6 to 7 mo in lactation, depending on lactation number and reproductive efficiency. For example, during the third lactation, under a 15-mo CI, the RPO value of a cow at 76% production goes <0 at 7 mo, which means that this cow should be replaced after 7 mo in milk. If the RPO value of a cow is negative, replacing her is economically more attractive than keeping her. However, if the producer decides to keep the cow and successfully breeds her, her RPO value will increase again >0 around 4 mo before calving. Beyond that point, the cow should be kept again until the next optimal time of replacement when the RPO again goes <0.

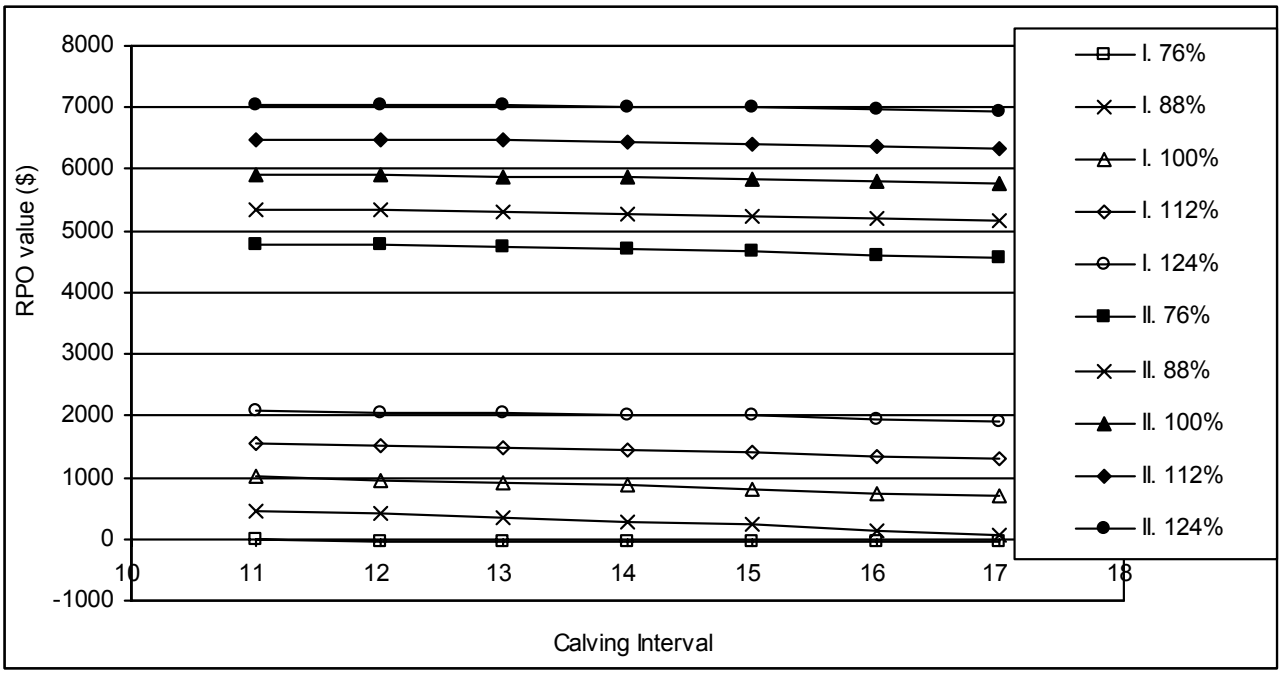
The calculations of the opportunity costs (ANR_{max}; see Equation 1) were based on the average performance of animals present in the herd, assuming this to be the best estimates for future net revenue of young replacement animals. Three underlying assumptions of the results shown above are 1) no genetic gain, 2) unlimited availability of identical replacement heifers, and 3) constant number of cows in the herd. Genetic gain would result in lower RPO values because the opportunity costs are higher (i.e., replacement heifers are on average better than the current average animals). However, Van Arendonk (1985a) showed that genetic gain had only a very small influence on the optimal breeding and replacement decisions. Secondly, opportunity costs are 0 if there are (temporarily) no replacement heifers available. Replacements on dairy farms are often dictated by the calving of new heifers (Kristensen, 1993), and then naturally the least profitable cows should be replaced. Such situations often arise in herds that only use homegrown heifers, which is a very common policy in Pennsylvania. Opportunity costs can also be 0 (temporarily) when circumstances of the dairy farm allow heifers to be added without requiring existing cows to be culled. This situation can occur because of planned long-term expansion or short-term fluctuation in cattle numbers (Lehenbauer and Oltjen, 1998). In both situations when opportunity costs are 0, current cows can be kept as long as her MNR is >0 (Huirne et al., 1997). However, in any situation, the ranking of cows according to their RPO values selects the least profitable cow, and if a heifer is available, this cow is replaced

(Kristensen, 1993). Therefore, the ranking of cows is more important than the absolute RPO values (Kristensen, 1993). In addition, the ranking of RPO values is far less sensitive to changing opportunity costs and changing prices and interest rates than the absolute RPO values.

3.3.2 Costs per Extra DO

The model calculated the RPO value of cows that have different reproductive efficiencies as measured by differences in their CI. First, Figure 3 shows the RPO values of cows in the first month of the third lactation without and with opportunity costs. A comparison of the situation with and without opportunity costs reveals 2 main differences. First, the RPO values without opportunity costs are considerably higher than the RPO values with opportunity costs. This is caused by 2 factors. First, the RPO values with opportunity costs represent the total extra profits of keeping the cow compared with replacement. Therefore, the opportunity costs (expected maximal average revenues of the replacement heifer) are subtracted from the MNR of the present cow (see Equation 2). In contrast, the RPO values without opportunity costs represent the extra profits of keeping the cow compared with an open place in the barn (zero opportunity costs subtracted). Second, the age until optimal replacement will be lower for situations where a replacement heifer is available than for situations where no replacement heifers are available. As a consequence, the total profits of keeping the cow were lower. The second difference between both situations is the slope. In the situation in which no opportunity costs were included, the graphs always had a negative slope (future value of the cow became lower); in the situation with opportunity costs, depending on the milk production, beyond a certain CI, the slope becomes zero. The reason is that if the CI increases, postponing breeding of the cow will not always decrease the RPO value of the cow because of the model's assumption of economical optimal culling. Because the model calculates the total benefits of keeping the current cow until the optimal time of replacement, it does not take into account losses that occur after this optimal time of replacement. As a consequence, a longer CI (beyond the maximum interval that is allowed to still be economically attractive) will not result in a decreased RPO in the model and subsequently will not result in losses per additional DO (in other words, the cow should not be bred at all).

Figure 3. Retention pay-off (RPO) values if replacement heifers are available (bottom: with opportunity costs) and if replacement heifers are not available (top: without opportunity costs) for cows in the first month of the third lactation with 5 different milk production levels for different potential future calving intervals



For the same 2 situations (without and with opportunity costs), the costs per extra DO (set equal to the negative slope of the graphs) were calculated, which are shown in Figures 4 and 5. Figure 4 shows a steady, almost linear increase of the costs per extra DO, increasing from about $0.10 to $1.60 if the number of DO increases from 2 to 8 mo for different milk production levels in a situation without opportunity costs. It shows that, without opportunity costs, the costs per extra DO are slightly higher for lower production levels. This is because during the later stages of lactation, low-producing cows will have a MNR that is lower than that of an average replacement heifer, and an increase of DO will, therefore, result in higher losses than for a high-producing cow. This is in agreement with Strandberg and Oltenacu (1989), who found that a longer CI for high-producing cows does not decrease profitability as much as for low-producing cows.

Figure 4. Costs per extra day open for third lactation cows with 5 production levels (no replacement heifers available and without opportunity costs)

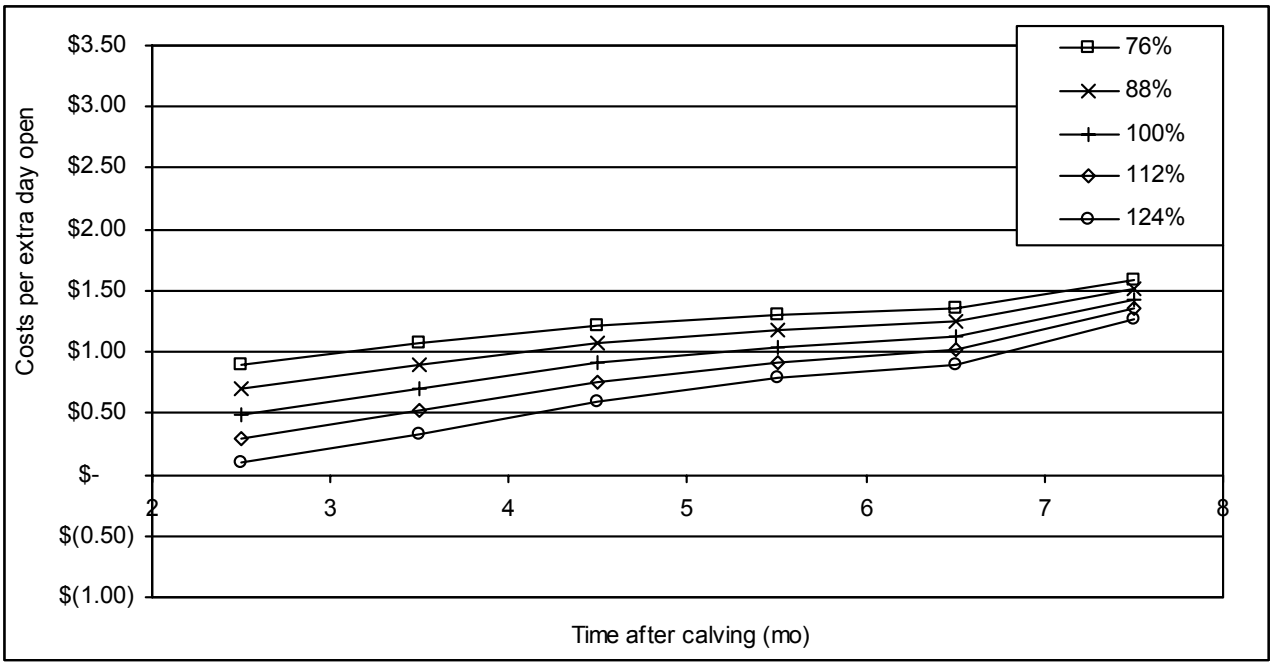


Figure 5. Costs per extra day open for third lactation cows with 5 production levels (with replacement heifers available and with opportunity costs)

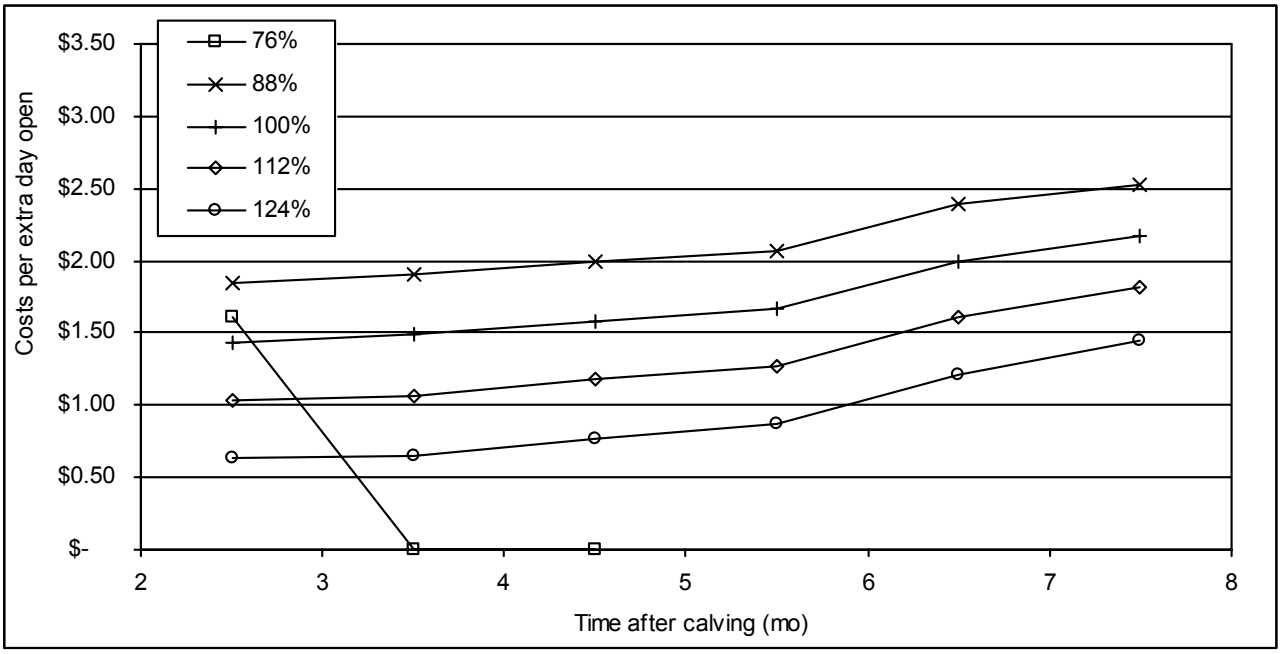
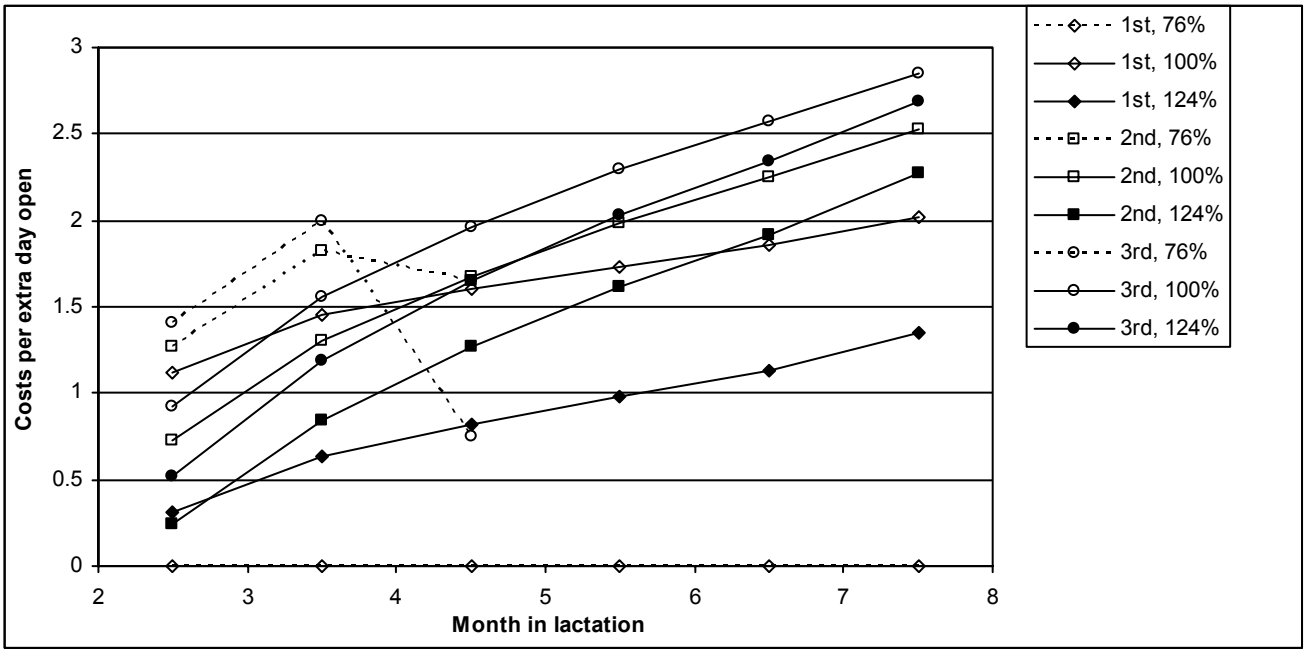


Figure 5 shows the same trend, with costs per extra DO going up when the time after calving gets longer. Also, if a replacement heifer is available, the costs per extra DO are higher for lower-producing animals. However, there are 2 main differences between the situation where replacement heifers are available (Figure 5) or not (Figure 4). First, the costs per extra DO are

considerably higher than in the situation where no replacement heifers are available. In other words, if a heifer can immediately take over the place of the cow, the costs of an extended CI increase substantially. A second difference is that Figure 5 shows a down-sloping line of the low-producing (76%) cow. This represents the period during which a successful insemination will not increase the value of a cow anymore because replacement becomes economically the optimal decision. For a third lactation cow with a current relative milk production of 76%, this occurs between 3 to 4 mo after calving.

Costs per extra DO vary across the lactation for animals in different lactations (first, second, and third) or with a low (76%), average (100%), or high (124%) milk production levels (Figure 6). Costs per extra DO are lower and increase slower for first lactation animals than for animals in the second and higher lactation. This effect is caused by higher persistency of milk production of first lactation animals (Skidmore, 1990). Also, for all 3 lactations, the costs per extra DO are higher for low-producing animals than for higher producing animals. An exception to this, are animals (for example first lactation animals that produce 76% of the average) that should not be bred because breeding would not increase their RPO value and, therefore, is not optimal. Hence, the costs per DO will be calculated as $0 (Equation 4) for these animals (Figure 6). Finally, the difference between an extra DO for average- and high-producing animals in the third lactation is small and smaller than the difference with first lactation animals (Figure 6). This result is in agreement with Dijkhuizen (1983), Van Arendonk (1985b), and Strandberg and Oltenacu (1989).

Figure 6. Costs per extra day open for first, second, and third lactation cows with a low (76% level), average (100% level), or high (124% level) production level with replacement heifers available (with opportunity costs). Breeding does not increase the RPO value of first lactation cows at the 76% production level; hence, the costs per extra day open are shown as $0



Costs of $2 to $3 per extra DO have often been quoted in studies dealing with the economic consequences of reproductive failure (Dijkhuizen, 1983; Strandberg and Oltenacu, 1989). Other studies suggested an advantage of a prolonged DO period for high-producing cows (Arbel et al., 2001). The results of the current model are in general agreement and show that the costs per extra DO vary greatly and are dependent on many factors. Four important factors are 1) availability of replacement heifers, 2) lactation number, 3) milk production level of both the cow and the herd mates, 4) and CI (used as a proxy for reproductive efficiency) of the cow. In the application of this model using typical input parameters for Pennsylvania, the costs per DO vary between $0 and $3.00 for a situation where replacement heifers are available. Therefore, fewer DO or shorter CI's were economically optimal. If the number of DO extends beyond a certain maximum, replacement becomes economically the optimal decision, and breeding is not attractive anymore as illustrated at the 76% production level in Figure 5. In the model, economic costs per extra DO drop because pregnancy will not increase the economic value of the cow.

3.3.3 Application on Dairy Herds

The RPO values of 5 dairy cows are shown in Table 7. In addition to the herd data that are shown in Table 1, the cow data that are needed to calculate individual RPO values include the cow's lactation number, the current milk production per day, the number of DIM, and the number of days pregnant. To determine the cow's milk production level as a percentage of the herd average mature equivalent milk, the inverse of the modified Oltenacu lactation curve (Equation 4; Oltenacu et al., 1981) was used. With these data, the model determines the individual RPO values and, if applicable, costs per additional DO.

Table 7. Determination of the retention pay-off (RPO) values of 5 dairy cows in a typical dairy herd in Pennsylvania

	Input parameters				Output of the model		
Cow	Lact nr.	Milk/day (kg)	DIM	Days pregnant	ME Milk (kg)	RPO-value	Costs/ extra DO
1	1	36	60	0	9,124	$ 419	$1.73/day
2	2	18	350	200	12,377	$ 2,015	NA [1]
3	3	59	100	0	10,785	$ 114	$2.24/day
4	5	36	140	60	7,523	$ 164	NA [1]
5	10	29	210	0	7,958	- $ 7	NA [2]

[1] *no costs per extra day open apply as the cows are already pregnant*

[2] *because the RPO of this cow is below zero, immediate replacement is economically the best*

The first cow (no. 1) was assumed to be 60 DIM with a milk production of 36 kg/d, which is

very close to the average mature equivalent milk production of 9072 kg (20,000 lb)/yr (Table 7). The RPO value for her was $419, but that value was projected to decrease by $1.73/d as she stays open beyond 60 d. However, costs per extra DO will increase gradually if the cow does not get bred as illustrated in general in Figure 5. The current milk production of the second cow was translated into a mature equivalent milk production of 12,377 kg (27,286 lb), and a RPO value of $2015. The costs per extra DO for Cow 3 are higher than for Cow 2 because she has been open for a longer time. Finally, the economical optimal decision for Cow 5 is to replace her (assuming an average replacement heifer is available), and breeding Cow 5 is not optimal; hence no costs of an extra DO were calculated.

3.4 Conclusions

Depending on lactation number, stage of lactation, reproductive status, and milk production level, the RPO value varied from –$181 (for a cow that should be culled 'immediately') to +$2650 (for a second lactation cow just before calving with a relative milk production level of 124%). In addition to calculating RPO values to support replacement decisions, the current model provides a new perspective on the calculation of the costs per extra DO that takes into account the optimal breeding policy. With the current model, we found that the costs per extra DO vary between $0 and $3, depending on the cow and herd characteristics (Figures 4 to 6). In addition, the decision to breed a cow or not and the costs per extra DO were dependent on availability of replacement heifers.

With the current spreadsheet model, based on the MNR approach, the dairy cow breeding and replacement problem was modeled accurately, and optimal replacement and breeding decisions can be supported. The results are in close agreement with former studies (Van Arendonk, 1985a; Jalvingh, 1993; Kristensen, 1993; Houben, 1995). The strength of the currently described model is the integral evaluation of age, production, reproductive efficiency, and survivability in a simple and user-friendly economic computer spreadsheet model to support replacement and insemination decisions on dairy farms. Strandberg and Oltenacu (1989) concluded that there are no magic numbers for the optimal breeding and replacement decisions nor for the losses per marginal DO that apply to all herds and cows. Rather, there is a need of more customized breeding decisions for each (type of) cow that are herd specific. The current model can help in this need by providing user-friendly input and output to customize the calculations for individual herds and cows. On-farm, the model can support optimal decisions regarding voluntary replacement and breeding decisions. In addition, it can determine the on-farm costs associated with involuntarily culling or with additional DO. Other potential users of the current model are researchers, economists, and governmental organizations that wish to calculate the (farm or cow-specific) losses of involuntarily culled dairy cows because of a particular disease (Van Schaik et al., 1996) or as part of a specific disease control program (Groenendaal et al., 2002). Finally, users of the model can obtain estimates on the farm-specific

costs of an extra DO for cows with different production characteristics, which can be useful to calculate the economics of specific insemination policies.

In summary, the current user-friendly model determines the economic value of individual dairy cows under farm-specific circumstances and uses a new approach to calculate the costs per extra DO. The results of the model are very similar to results of more complex models that are more difficult to use. Therefore, we consider the model a valuable tool for dairy farms to support farm and cow-specific optimal breeding and replacement decisions. Although not shown in this paper, the model can also be useful to assess economic costs of involuntary culling under disease control programs.

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Chapter 4

4 Development of the Dutch Johne's disease control program supported by a simulation model

Paper by Groenendaal, H., Nielen, M., Hesselink, J.W., 2003. *Preventive Veterinary Medicine* 60, 69-90.

Abstract

The development of a simulation model, 'JohneSSim', was part of a research program aimed at designing a national Johne's disease control program for The Netherlands. Initially, the focus was mainly directed towards different compulsory 'test-and-cull' strategies. However, the results from the JohneSSim model showed that eradication of Johne's disease based on such strategies would not be possible within 20 years and that it was also economically unattractive. However, improved calf management seemed to be more effective in reducing the prevalence within the same time period. Simulation of a strategy using an 'ideal test' (80% sensitivity in all infected animals) showed a considerably faster decrease in prevalence. However, this strategy proved to be economically unattractive because of the high culling rate of (young) test-positive animals. The simulation model was also adapted to study beef cow herds. However, the results indicated that none of the strategies were able to reduce the mean true prevalence to almost zero for such herds. Only strategies based on 'separation of calves and adult animals' proved to significantly reduce the prevalence but such a strategy is unpractical and uneconomic for Dutch beef cow herds. Due to this finding and the relative low number of Dutch beef cow farms, first priority has been given to the development of a Johne's disease control program for dairy farms.
Based on the results of the 'JohneSSim' model, the new national voluntary Johne's disease control program for dairy, Paratuberculosis Program Netherlands (PPN), started in September 2000. The PPN is based on a stepwise improvement of calf hygiene, with little dependency on 'test and culling'. The model results indicated that, if dairy farmers consistently carried out the necessary management adaptations, PPN considerably decreased prevalence and that it was economically more attractive than any previous plans.

4.1 Introduction

Paratuberculosis in cattle is an infectious chronic granulomatous enteritis caused by *Mycobacterium avium* subsp. *paratuberculosis* (Juste, 1996). In The Netherlands, paratuberculosis has been present for many years, especially in the low-lying peat moors situated to the north of the country (Benedictus, 1984). The first paratuberculosis control program started in 1942 (Benedictus et al., 1985). All previous control programs for paratuberculosis were based mainly on early culling of infected animals (Kalis et al., 1999b). Results from such programs have been disappointing as diagnostic procedures have been inadequate and farmers have not consistently maintained husbandry measures aimed at limiting transmission of infection (Benedictus, 1984 and Benedictus et al., 1985). The lack of progress with a control program based on test and cull led to a change of strategy towards use of vaccination. This strategy has been successful in reducing clinical paratuberculosis and it proved to be considerably cheaper than the subsidized test-and-cull program (Benedictus et al.,

1985). However, even long-term use of a vaccine does not prevent fecal shedding of the bacteria and thus does not lead to elimination of the infection from herds (Kalis et al., 1999a).

In 1997, the Dutch institutes working on paratuberculosis developed a plan for eradication of the condition. The plan was initiated to help alleviate the economic losses caused by the disease and also to cater for the growing public awareness of product quality guarantees. In 1998, this initial plan for control of the disease was integrated into a preliminary and voluntary paratuberculosis program. This program was based on management improvement and yearly testing of the animals and consisted of two parts. The 'unsuspected herds program' (unsuspected was defined as the whole herd being test-negative), had the objective of identifying herds thought not to be infected and prevent the infection of these herds while the 'infected herds program', which had the objective of eliminating the infection from identified infected herds. A detailed outline of this voluntary program is available (Benedictus et al., 1999).

On 1 July 1999, the project 'Preparation for the collective control of paratuberculosis in The Netherlands' was started. The objective of this project was to prepare a national control program for paratuberculosis with the final aim of eradicating the disease. A scientific foundation of this new program was deemed essential, as previous programs 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 programs as well as on the development of a simulation model, called 'JohneSSim' (Groenendaal et al., 2002). The goal of this model was to evaluate the epidemiological effectiveness and economical attractiveness of different control strategies.

This paper illustrates the crucial steps in the decision-making process that were based on results of the JohneSSim model. The final result of this process was the implementation of the Dutch voluntary national Johne's disease control program (Paratuberculosis Program Netherlands, PPN) in September 2000.

4.2 Materials and methods

4.2.1 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., 2002). The model is a stochastic and dynamic simulation model that simulates (a) the herd dynamics, (b) the disease dynamics, (c) the control of Johne's disease and (d) the economic consequences at the herd level for a default time period of 20 years. The herd dynamics of a typical Dutch dairy herd were simulated, including all calves and replacement heifers. Both involuntary and voluntary culling were considered. In the disease dynamics module, five infection routes were considered: (i) fetal infections, (ii) infections around birth, (iii) infections due to drinking colostrum, (iv)

infections due to drinking whole milk and (v) infections due to an environment that is contaminated with *M. a. paratuberculosis*. Control tools that were simulated with the JohneSSim model can be divided into 'calf hygiene' and 'test-and-cull' strategies. Benefits were defined as losses without control minus losses with control. The net present value (NPV) and the benefit–costs ratio (BC-ratio) were calculated for each control strategy. The NPV was defined as the present value of the benefits minus the present value of the costs. The BC-ratio was defined as the present value of the benefits divided by the present value of the total costs. A positive NPV and a BC-ratio larger than 1 represent an economically attractive investment. Both parameters are standard economic measures to value investments that have an extended time component (Brealey and Myers, 2000) and were calculated for the whole 20-year period, using discounting (the process of converting future resources to their present value).

Both infected and non-infected herds were simulated in all strategies. Because of the model's stochastic nature, the model simulated both good and bad case scenarios. To represent the difference between individual farms in the pre-control calf management, different herd profiles were defined and simulated within the JohneSSim model. Each profile and infection status combination was simulated 100 times (stochastic iterations) with the model. After simulating all these profiles separately, the model aggregated the different results according to each profile's proportional presence in the national herd, to determine the results on a national level for The Netherlands.

4.2.2 Stages

The development of the JohneSSim model coincided with the decision-making process that was required for the development of the control program. The study was performed in three stages, the first stage was carried out from May 1998 to January 1999, the second stage from January to May 1999 and the third stage from January to April 2000. Stages one and three both focused on the control of Johne's disease on dairy farms, while stage two focused on Dutch beef cow herds. In this study, a beef cow herd was defined as either a farm where calves normally suckle for several months or where calves were separated from the dams shortly after birth but the milk is only used for the calves. The latter group includes cows of the Belgian Blues and Improved Red-and-White breed (double muscle), where calves are separated from the dam after birth.

4.2.2.1 First stage

In the first stage of the study, eight different herd profiles were defined to represent the differences between individual dairy farms. A more detailed description of the different herd profiles for dairy herds is available (Van Roermund et al., 1999). The strategies that were simulated in the first stage of the study mainly focused on different test strategies for infected

dairy herds, combined with a monitoring program to declare herds 'unsuspected'. All input data are extensively described elsewhere (Groenendaal et al., 2002).

4.2.2.2 Second stage

In the second stage of the study, the focus was on Johne's disease control programs for beef cow herds and the model was modified to represent typical Dutch practices on such farms. The main structure of the JohneSSim model was maintained but several input parameters were changed. Herd profiles were defined as breeding-oriented herds, beef-oriented herds and mixed herds. The main difference between the three herd profiles was the replacement strategy, which also resulted in different age distributions. In essence, in beef-oriented herds, cows were culled at a younger age. In addition to the three herd profiles, 'small' (four adult cows) and 'large' (27 adult cows) herds were simulated separately because of the large number of very small beef cow herds in The Netherlands. A more detailed description of the different herd profiles for beef cow herds is available (Muskens and Jongeneel, 1999).

4.2.2.3 Third stage

After the first two stages, decision-makers changed their focus from test-and-cull strategies to use of management strategies on dairy farms. A voluntary program was considered most appropriate as the importance of farmers' motivation was seen as a crucial factor for a program to be successful. In addition, several differences were made to the input parameters to make the model more realistic (Table 1). In the first stage of the study, the size of the dairy herd was assumed to be constant at 50 cows. In the third stage, herd size was assumed to increase by 3.5% per year to reach 100 after 20 years so as to represent the expected growth of Dutch dairy herds. Furthermore, the introduction of infected animals was simulated in greater detail. Finally, the costs of separate housing of calves under 1-year-old were included in the economical analysis at only 50% since this management strategy could result in reduced losses (additional benefits) relating to other diseases.

Table 1. The main differences between input parameters relating the first and third stages of the JohneSSim simulation study

Parameter	First stage	Third stage
Herd size (number of dairy cows)	50 (constant)	50, growing by 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 of calves < 1 year	1016 Euro per year	508 Euro increasing to 1016 Euro per year

4.2.3 Control strategies

All strategies were defined by the advisory group, which consisted of 11 experts on Johne's disease who also advised the decision-makers. Monthly meetings were held in which the necessary input data and control strategies requiring to be simulated were discussed (Table 2).

Table 2. Control strategies (test-and-cull and management tools) simulated by the JohneSSim model during the three stages of the study

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	Improved for calves ≤ 6 months
	a-III	Faecal, > 2 yr, once a year	Improved for calves ≤ 6 months
	a-IV	Faecal, > 2 yr, once a year	Improved for calves ≤ 12 months
Second	b-0	No	No
	b-I	Faecal-pooled, > 2 yr, once a year	No
	b-II	No	Improved for calves ≤ 6 months
	b-III	ELISA [a], > 3 yr, once a year	Improved for calves ≤ 6 months
	b-IV	ELISA [a], > 3 yr, once a year	Separate young (< 3rd calving) and old cows (3rd calving)
	b-V	Faecal-pooled, > 2 yr, once a year	Separate positive cows from negatives
	b-VI	No	Vaccinate calves at young age
Third	c-0	No	No
	c-I	ELISA, > 3 yr, once in first five years	Step 1 of management [b]
	c-II	ELISA, > 3 yr, once in first five years	Step 1 & 2 of management [b]
	c-III	ELISA, > 3 yr, once in first five years	Step 1, 2 & 3 of management [b]

[a] *each positive ELISA test was confirmed with a faecal test and if both positive, the cow was culled immediately*

[b] *see Figure 1*

Most control strategies in the first stage of the study were focused on different testing scenarios (a-I to a-IV). Stage two control strategies (b-I to b-III) were also based on testing and 'improved management'. Strategies b-IV and b-V were based on separation of adult beef cows (with their calves) in two groups, based on age of the dam (b-IV) or on fecal test-result of the dam (b-V). In the simulation model, it was assumed that no cross-infection occurred between the two separated groups. Finally, the effect of vaccination of all calves at a very young age was simulated in strategy b-VI. Vaccination was assumed to increase the age at which infected animals became 'highly infectious'. The increase was dependent on the infection route and varied from no increase for fetal infections to a maximum increase of 14 years for infections between 6 and 12 months of age.

In the third stage, the focus changed to management strategies for dairy herds (Table 2). A new potential control strategy was defined called, PPN, based on stepwise improvement of calf hygiene (Figure 1). In this program, participating dairy farmers were expected to implement improved calf management practices in three steps. The implementation of these measures was arranged in a chronological order, which followed the development of the calf. In the simulations, it was assumed that participating dairy farmers would implement the steps in sequential years. Furthermore, it was assumed that all participating farmers would test all cows over 3 years old by an ELISA test once in the first 5 years and cull all cows that were positive by both the ELISA and by a fecal confirmation test.

Step 1 - Calving:
- •Cleaned cow places in an individual clean calving pen
- •Separate calf early from dam

Step 2 - Calving to weaning:
- •Only given colostrum from own dam
- •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

Step 3 - Weaning to end first year of age:
- •Housing separate from cows > 2 years
- •Clean roughage: hay, dried grass or silage from clean pasture (no fresh manure)
- •Only in clean pasture (no fresh manure)
- •Clean drinking water

Figure 1. Management adjustments to be made within each of the three steps of the PPN

For the strategies with management changes, 50% of the costs of those changes were attributed to Johne's disease control. In addition, financial analyses were conducted both in the presence and absence of extra labor costs. Excluding the costs of extra labor is valid on many dairy farms because of the low opportunity costs of labor on these farms.

Additionally, in the first stage of the study, an ideal test was defined and simulated with the model and compared to the default test using strategy a-II. The input parameters that were used for the simulated 'default test' (a-II) as well as the 'ideal test' are shown in Table 3.

Table 3. Characteristics of both the 'default' ELISA test and the 'ideal test' as simulated by the JohneSSim model during the first stage of the study

	'Default test'	'Ideal test'
Sensitivity per infection status		
Latent infected	1%	80%
Low infectious	10%	80%
High infectious	60%	80%
Clinically 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 Euro)	4.54	1.97

4.2.4 Sensitivity analysis

A sensitivity analysis was performed in the third stage of the study on the parameters and processes shown in Table 4. In the default situation (PPN_Standard), it was assumed that a reduction of 90% of the infection probabilities would be achievable if the proper management tools were implemented. As an alternative (Sens_A), it was assumed that in the presence of a highly infectious animal, only a 50% reduction was obtained. Secondly (Sens_B), only ELISA-negative animals were introduced to the dairy herd. Finally, to determine the total effect of the spread between herds on the mean true prevalence, a strategy was simulated in which no animals at all were introduced to any herd (Sens_C).

Table 4. Parameters on which sensitivity analysis was performed using the JohneSSim model

Parameter/process	Name	Default	New
Effect of management on reduction of infection probability	Sens_A	90%	50%
Introduction of only ELISA negative animals	Sens_B	No testing	Test with ELISA
No introduction of animals	Sens_C	0-6 animals/yr.	none

4.3 Results

4.3.1 Stage one

The mean true prevalence of an average Dutch dairy farm (both infected and uninfected farms), as simulated in the first stage of the study, is shown in figure 2. Without any control (a-0), the prevalence increased gradually. Annual ELISA blood testing with confirmation of positive results by fecal culture followed by culling if both tests were positive resulted in a slower increase, but the prevalence still increased (a-I). However, improving the calf hygiene had a much larger impact on the mean prevalence, which can be seen from the difference between strategy a-I and a-II. The difference between strategy a-III and a-IV showed the impact of further improvement of the calf hygiene especially separate housing of 7–12-month-old calves (a-IV).

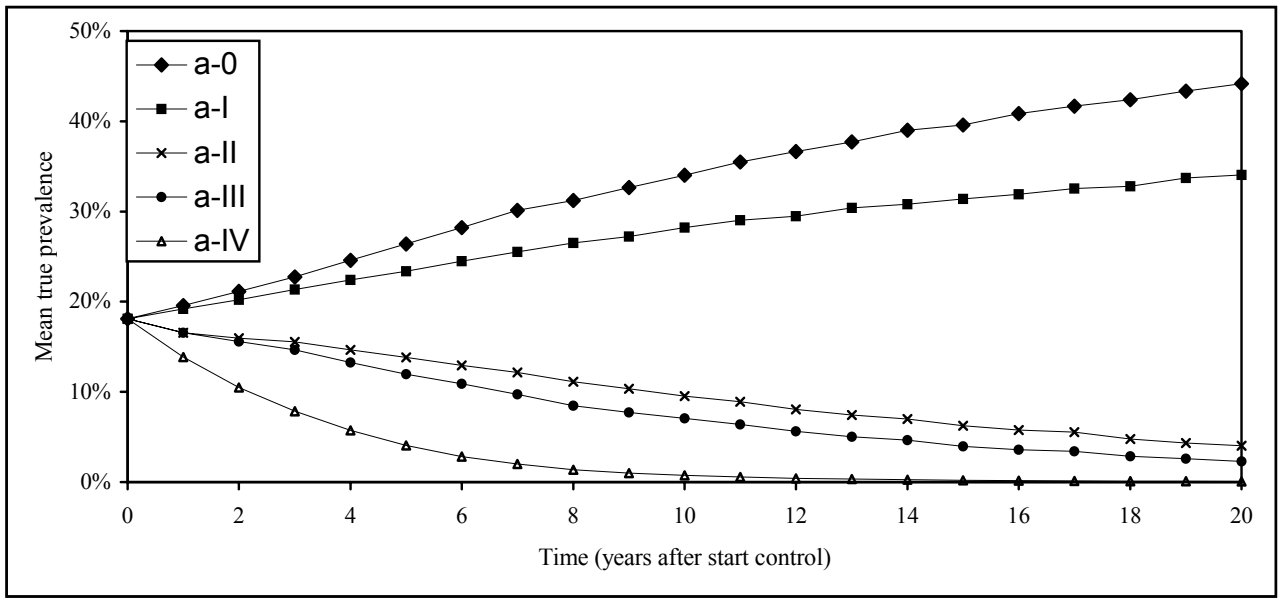

Figure 2. Mean true individual animal prevalence over all Dutch dairy farms (infected and uninfected) in the first stage of the study as simulated by the JohneSSim model with 'no control' (a-0) or with four different control scenarios (a-I to a-IV)

Table 5 shows the economical consequences of the different control strategies, as calculated with the JohneSSim model in the first stage of the study. Without control, the average losses increased considerably because of an increase in the average prevalence within infected herds and also an increase 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 and without labor costs, respectively) to realize the desired management measures (Table 6). Note that the mean BC-ratio is not equal to the mean benefits divided by the mean costs because of the non-symmetrical distribution of the BC-ratio. There was a large variation around the estimates of the BC-ratios with the 10 and 90 percentiles were, respectively, 0.00 and 1.44 for the situation without costs for extra labor. 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. Mean annual and total losses caused by Johne's disease without any control strategy compared with the reduction in losses through using different control methods (in Euros), as calculated by the JohneSSim model during the first stage of the study

	Losses	Reduction of the losses through control			
Year	a-0	a-I	a-II	a-III	a-IV
1	699	177	179	177	174
10	1,492	793	1,263	1,386	1,461
20	2,168	1,204	2,086	2,130	2,165
Total losses [a]	16,731	8,482	13,191	14,550	15,074
Total costs control [a]		13,638	25,047	30,143	73,789

[a] *discounted total from year 1-20*

Table 6. NPV (in Euros) and BC-ratio for the control strategies as simulated using the JohneSSim model during the first stage of the study over a 20-year period (± extra labor costs)

		Control strategy			
	Labor costs	a-I	a-II	a-III	a-IV
Mean NPV	incl.	-5,156	-11,855	-15,593	-58,716
Mean NPV	excl.	-5,156	-5,098	-8,833	-43,864
10% [a]	excl.	-10,889	-17,000	-17,688	-54,626
90% [a]	excl.	2,573	10,018	2,973	-28,446
Mean BC-ratio	incl.	0.51	0.47	0.40	0.19
Mean BC-ratio	excl.	0.51	0.63	0.50	0.24
10% [a]	excl.	0.00	0.00	0.00	0.00
90% [a]	excl.	1.15	1.44	1.10	0.57

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

The mean true prevalence under strategy a-II and using the 'ideal test' is shown in figure 3. The only differences between the two strategies were the test characteristics; all management measures were similar. 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 7). A control strategy with an 'ideal test' was economically less attractive because of the much higher costs of culling caused by the detection of 80% of the latently infected animals (Table 3).

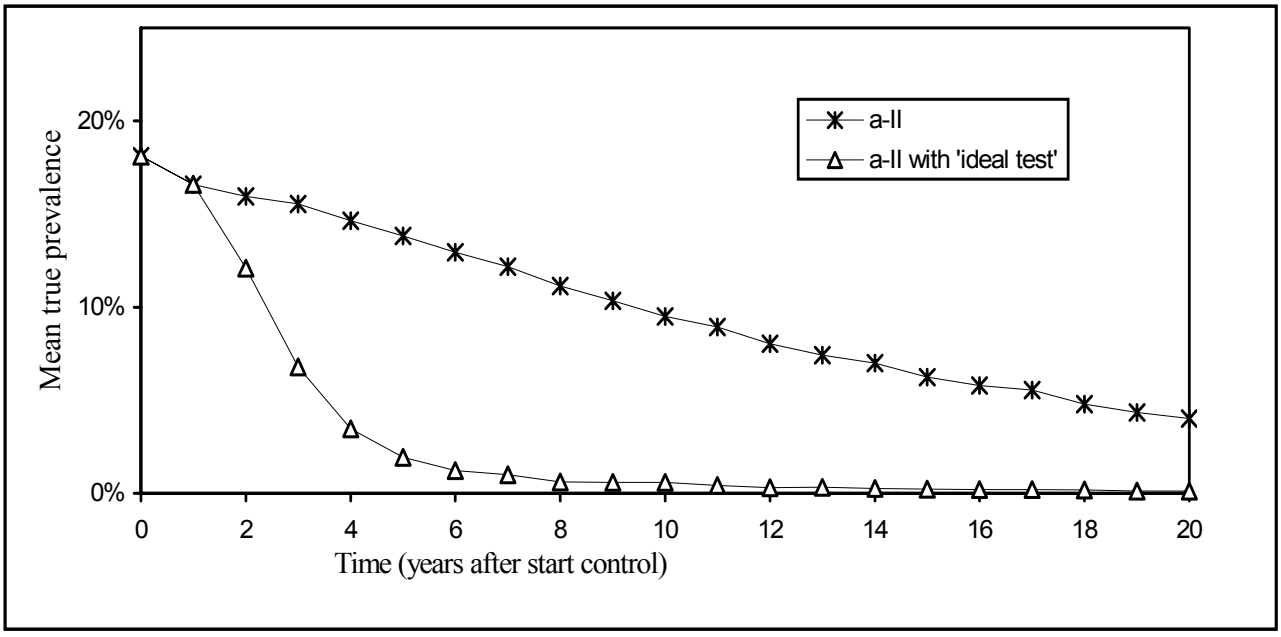

Figure 3. Mean true individual animal prevalence over all Dutch dairy farms (infected and uninfected) in the first stage of the study as simulated by the JohneSSim model under strategy a-II with a standard and with an 'ideal test'

Table 7. Costs of culling test-positive animals, total (discounted) control costs (in Euros), BC-ratios and NPVs of strategy a-II and the same strategy using an 'ideal test' as calculated by the JohneSSim model during the first stage of the study (excludes extra labor costs)

	Control strategy	
	a-II	'Ideal test'
Mean costs culling	3,125	15,600
Mean total costs control	39,758	49,859
Mean NPV	-5,098	-12,354
10% [a]	-17,000	-20,886
90% [a]	10,018	-2,033
Mean BC-ratio	0.63	0.44
10% [a]	0	0
90% [a]	1.44	0.94

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

4.3.2 Stage two

Figure 4 shows the mean true prevalence for the simulation of no control (b-0) for small and large Dutch beef cow herds and for all farms together which indicated that the mean true prevalence in large herds was higher than in small herds.

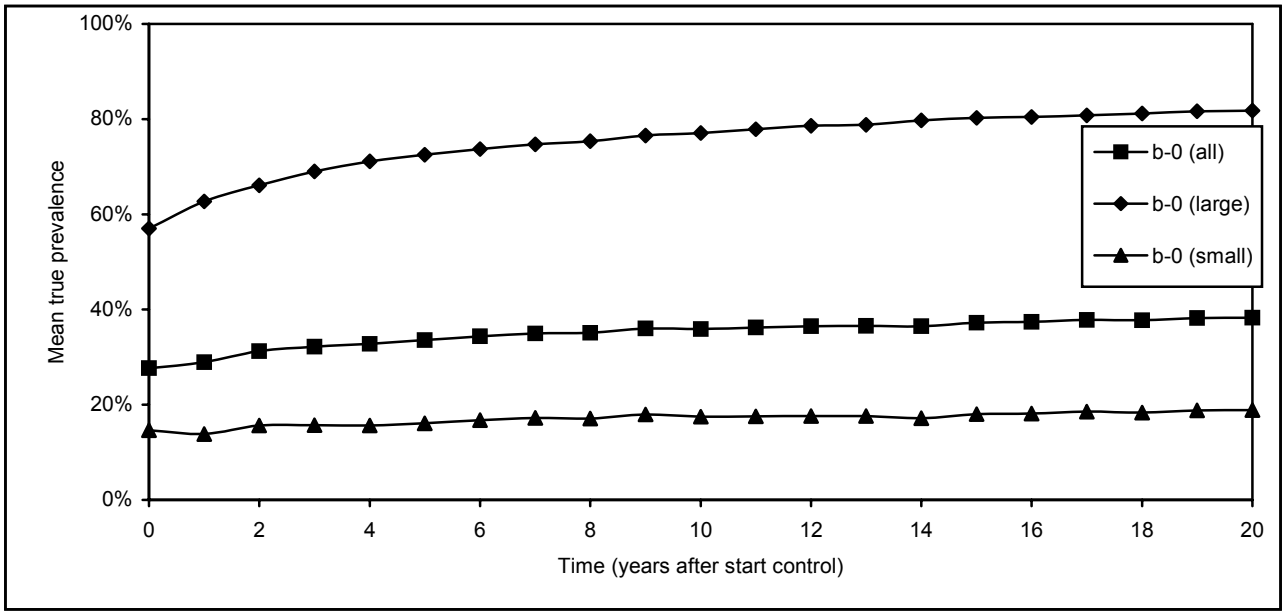

Figure 4. Mean true individual animal prevalence for small and large Dutch beef cow farms (infected and uninfected) in the second stage of the study as simulated by the JohneSSim model under 'no control' (b-0)

Figure 5 shows the mean true prevalence of an average Dutch beef cow herd (both infected and uninfected farms) as simulated with no control (b-0) and six different control strategies (b-I to b-VI). Without any control, the mean true prevalence slowly increased. A control strategy based on an ELISA test once a year for all cows over 3 years old (b-I) was able to slightly decrease the prevalence over the 20-year simulation period compared to no control. Changes of management (b-II) resulted in a greatly decreased prevalence, but did not result in a prevalence that was close to zero. A strategy that combined both testing and management changes (b-III) resulted in a similar decrease, with a very small decrease attributable to the additional test-and-cull control measure. Both strategies, which are based on separation of 'suspected animals' from the 'unsuspected animals', did not result in a relevant decrease in prevalence. Separation based on age (b-IV) was a little more effective than separation based on a fecal culture of all animals older than 2 years of age (b-V). Finally, vaccination of all calves before 1 week of age also did not result in a decreased mean true prevalence (b-VI).

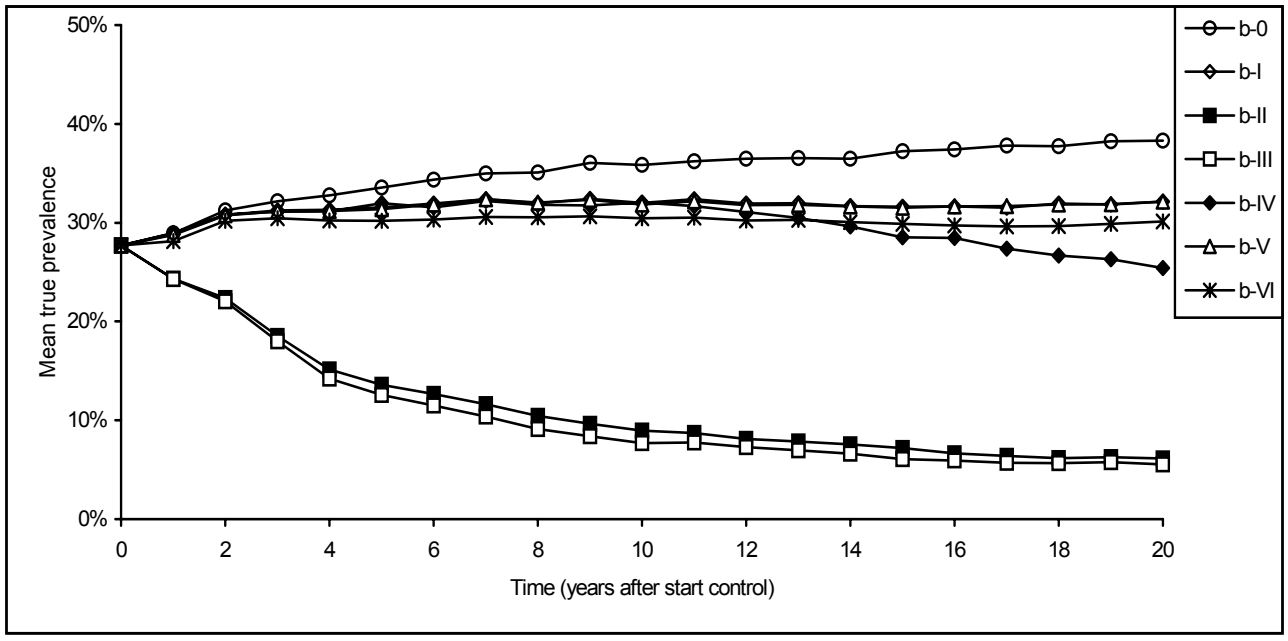

Figure 5. Mean true individual animal prevalence over all Dutch beef cow farms (infected and uninfected) in the second stage of the study as simulated by the JohneSSim model with 'no control' (b-0) or with six different control scenarios (b-I to b-VI)

Table 8 shows the losses due to Johne's disease in an average beef cow herd, without any control measures being taken. In agreement with the increasing mean true prevalence, the losses per year increase. There was large variation in the losses as in year 1 the average losses were 217 Euros, but 10% of the farmers had losses more than 1103 Euros. In addition, the losses per adult cow present in small herds were considerably lower than the losses per adult cow present in larger herds. This is in agreement with the higher prevalence in larger herds.

Table 8. Annual and total losses caused by Johne's disease without any control measures for an average Dutch beef cow farm (infected or uninfected) as calculated by the JohneSSim model (in Euros)

	Total losses caused by Johne's disease				Losses per cow present	
Year	Mean	10%	50%	90%	Small herds	Large herds
1	216	0	0	1,103	16	21
10	465	0	0	1,556	22	49
20	561	0	0	2,004	20	60
Total losses [a]	5,251	0	972	17,673	204	561

[a] *discounted total from year 1-20*

Table 9 shows the losses without control and the reduction of the losses through control with the simulated control strategies for Dutch beef cow herds. None of the control strategies have a BC-ratio that is on average higher than 1 (Table 10). Vaccination (b-VI) has the highest mean BC-ratio of 0.34 and on 10% of the herds vaccination has a BC-ratio of 0.80 or more. Both

strategies based on separation of 'suspected' and 'unsuspected' animals (b-IV and b-V) may result in high losses (negative benefits and therefore negative BC-ratio) as shown by the negative 10% percentiles of the BC-ratios.

Table 9. Mean losses (in Euros) caused by Johne's disease in Dutch beef cow herds with and without control measures, as calculated by the JohneSSim model during the second stage of the study

	Losses	Reduction of losses through control					
Year	b-0	b-I	b-II	b-III	b-IV	b-V	b-VI
1	216	4	0	4	0	0	21
10	465	129	357	403	40	44	336
20	561	167	500	525	187	107	415
Total losses [a]	5,251	1,938	3,193	3,731	958	506	3,453
Total costs control [a]		3,695	11,756	17,014	3,854	3,099	6,293

[a] *discounted total from year 1-20*

Table 10. NPV (in Euros) and BC-ratio for the control strategies as simulated using the JohneSSim model during the second stage of the study over a 20-year period (excludes extra labor costs)

	Control strategy					
	b-I	b-II	b-III	b-IV	b-V	b-VI
Mean NPV	-1,757	-6,744	-8,075	-4,039	-2,592	-2,840
10% [a]	-5,848	-12,038	-15,596	-12,669	-8,065	-8,349
90% [a]	0	-4,041	-4,575	0	0	-68
Mean BC-ratio	0.29	0.18	0.17	0.18	0.19	0.34
10% [a]	0	0	0	-0.15 b	-0.02 b	0
90% [a]	0.80	0.55	0.52	0.61	0.70	0.80

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

[b] *losses are higher with the control strategy than without*

4.3.3 Stage three

The simulated mean true prevalence on an average Dutch dairy farm (infected and uninfected farms) is shown in Figure 6. It shows a slightly faster increasing average true prevalence without control (Figure 6, c-0) than in the first stage of the study (Figure 2, a-0). In addition, the figure shows the effect of the three different management steps.

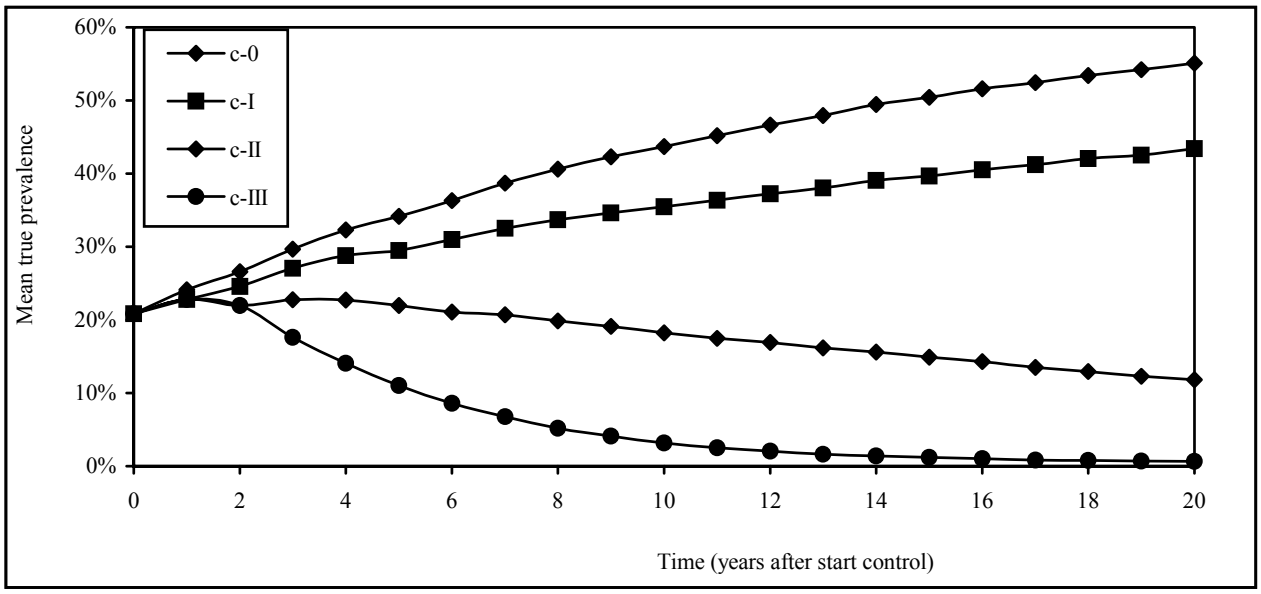

Figure 6. Mean true individual animal prevalence over all Dutch dairy farms (infected or uninfected) in the third stage of the study as simulated by the JohneSSim model with 'no control' (c-0) or three different control scenarios (c-I, c-II, c-III)

Table 11 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 third stage compared to the first stage (Table 5), due to the adaptations of the model in the third stage. Again, large variation in losses was observed between farms. For example, in year 1 the average losses were calculated to be 767 Euros, but 10% of the farms had losses higher than 2389 Euros. Sub-optimal culling accounted for almost 70% of the total losses caused by Johne's disease without control.

Table 11. Losses caused by Johne's disease on an average Dutch dairy farm (infected or uninfected) as calculated with the JohneSSim model where no control measures (c-0) have been implemented (third stage of the study)

	Total losses without control				Categories of losses		
Year	Mean	10%	50%	90%	(I)	(II)	(III)
1	767	0	181	2	221	71	475
10	3,357	0	2,219	8,423	758	290	2,309
20	6,720	0	6,261	14,989	1,474	575	4,670
Total losses [a]	39,245	0	31,552	91,001	8634	3532	27079
Percentage					(22%)	(9%)	(69%)

[a] *discounted total from year 1-20*

Table 12 and Table 13 show the economic consequences of the different control strategies against Johne's disease, as calculated with the JohneSSim model in the third stage. Because of

the increased reduction in losses (increased benefits) and the decreased control costs, the BC-ratios and the NPV both increased considerably compared to the first stage (Table 6). The average BC-ratios, with or without the costs of labor, for the program with all three management steps were 0.95 and 1.58, respectively. The mean NPV, not including the costs of labor, was 12,397 Euros for the total 20-year period. Both the BC-ratios and the NPVs again were very variable, signifying the large difference between the benefits of Johne's disease control per dairy farm.

Table 12. Mean annual and total losses caused by Johne's disease without any control strategy compared with the reduction in losses through using different control methods (in Euros), as calculated by the JohneSSim model during the third stage of the study

	Losses without control	Reduction of losses through control		
Year	c-0	c-I	c-II	c-III
1	767	29	29	29
10	3,357	579	1,937	2,766
20	6,720	1,569	5,450	6,576
Total losses a	39,245	6,699	22,625	29,196
Total costs control [a]		8,846	18,276	28,013

[a] *discounted total from year 1-20*

Table 13. NPV (in Euros) and BC-ratio for the control strategies as simulated using the JohneSSim model during the third stage of the study over a 20-year period (± extra labor costs)

		Control strategy		
	Labor costs	c-I	c-II	c-III
Mean NPV	incl.	-2,147	4,349	-1,183
Mean NPV	excl.	3,948	15,601	12,397
10% [a]	excl.	-3,707	-6,600	-14,705
90% [a]	excl.	16,775	44,350	46,287
Mean BC-ratio	incl.	0.64	1.10	0.95
Mean BC-ratio	excl.	2.22	2.78	1.58
10% [a]	excl.	0.00	0.00	0.00
90% [a]	excl.	6.60	5.94	3.32

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

4.3.4 Sensitivity analysis

The results of the sensitivity analysis within stage three are shown in figure 7. In the situation where management tools had only a 50% reduction-effect on the infection probabilities (PPN_Sens_A) instead of 90%, the reduction of the mean true prevalence was considerably smaller. Secondly, figure 7 shows that the effect of introducing only ELISA-negative animals

has almost no effect on the decline of the mean true prevalence. Finally, the figure shows that not introducing any animals only slightly enhances the reduction of the mean true prevalence.

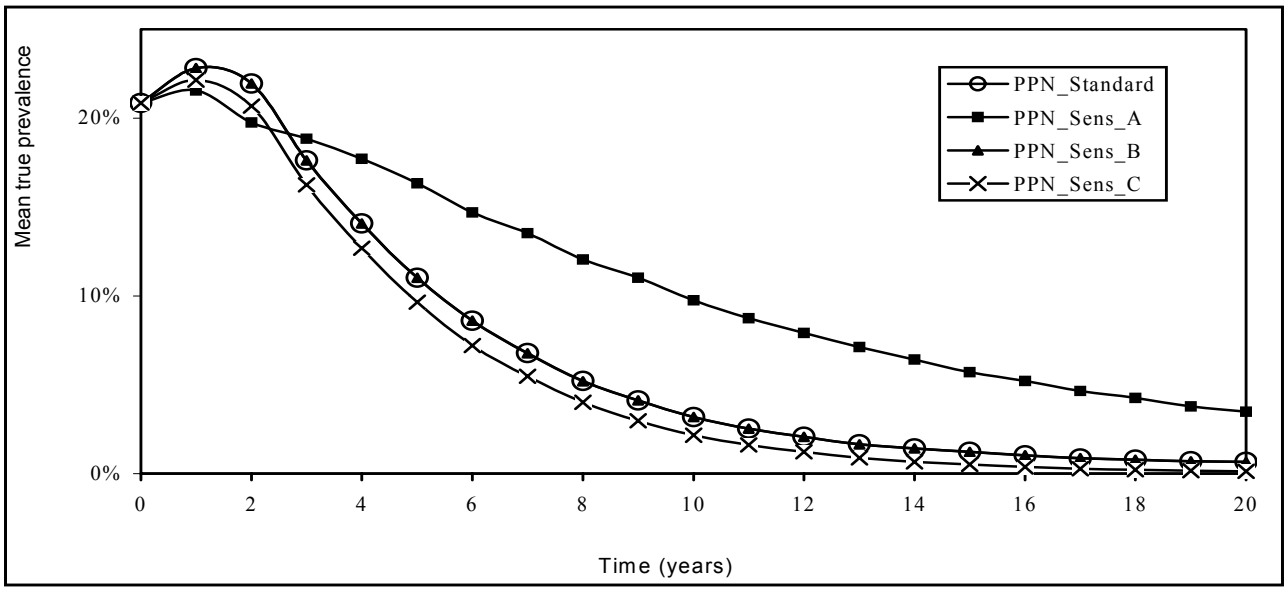

Figure 7. Mean true individual animal prevalence over all Dutch dairy farms (infected of uninfected) from the sensitivity analysis carried out as part of the third stage of the study as simulated by the JohneSSim model under the standard PPN and three alternative situations (Sens_A to Sens_C). Sens_A shows the effect of reducing the probability of infection from 90 to 50% when adequate management control measures are in use. Sens_B indicates the effect of only introducing ELISA-negative animals into the herd compared to any animals (no testing). Sens_C shows the influence of operating a closed herd as opposed to introduction of 0–6 animals each year

4.4 Discussion

The design of a new Dutch Johne's disease control program was initially mainly focused on 'test-and-cull' strategies. However, the results of the JohneSSim model indicated that eradication was not possible within 20 years using only these strategies. The main reason for this was the low sensitivity of the available tests for Johne's disease, especially for animals that were infected, but not clinically diseased. In addition, none of the simulated control strategies were economically attractive. However, strategies based on improved calf hygiene seemed more promising.

In the second stage of the study, Johne's disease control strategies for beef cow herds were evaluated. It was concluded that none of the strategies were able to reduce the mean true prevalence to almost zero. Only strategies based on 'separation of calves and adult animals' (b-II and b-III) significantly reduced the prevalence. However, this industry is highly dependent on calves suckling adult animals which results in very close contact. Therefore, strategies b-II and

b-III were considered impractical in commercial farming systems. Both strategies based on the separation of the 'suspected' and 'unsuspected' animals were not able to significantly reduce the mean true prevalence. Vaccination had the highest BC-ratio (average BC-ratio of 0.34) of all strategies for the suckling herds. In addition, vaccination was not able to significantly reduce the prevalence. This is in agreement with a field study which found no reduction in the spread of disease due to vaccination (Kalis et al., 1999a). The simulations have shown that an effective Johne's disease control for beef cow herds was much harder to achieve than for dairy herds. Indeed, the results yielded no control program for beef herds that was attractive, effective and realistic under current field circumstances.

Due to the results from the first two stages, decision-makers changed their focus to improvement of calf hygiene management on dairy farms. A new program, based on stepwise implementation of measures was defined and called PPN. In PPN, the order of implementation of measures was arranged in a logical order which following the different stages of calf rearing. Since 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. Indeed, motivation is critical and many of the critical management adaptations are impossible to monitor, so making PPN a compulsory program would not have been a pragmatic approach. Moreover, a compulsory program might even have had a negative effect on the motivation of the farmers.

One difficulty is acquiring and maintaining the farmers' motivation to perform all the 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 required measures are often difficult for farmers to comprehend. It is therefore very important to inform and educate, and hence try to change the attitude and behavior of farmers. Communication to and between farmers about Johne's disease control will therefore be the main focus of the organized Johne's disease control program. As an educational instrument within PPN, the ParaInformer (ParaWijzer) has been designed, which gives detailed information about the disease and the ways of controlling it. The ParaInformer also contains a checklist to design a control plan that is specific for each farm. Furthermore, small working groups are organized in which farmers gain knowledge and can exchange experiences about the control of Johne's disease. A pilot study has been started on 1500 Dutch farms to determine the implementation rate of the different management practices as a result of the farmers increased knowledge about Johne's disease control (Hesselink, 2000).

The average true prevalence in year 0 in the first stage of the study was slightly lower than in the third stage. A reason for this was the more detailed simulation along with the 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 third stage of the study was caused by the two most important additions to the model. The refinement of the introduction of animals to the dairy herd more accurately represented the practices of dairy farms in The Netherlands. The prevalence of Johne's disease in the introduced animals was set equal to the animal prevalence on the 'unsuspected' dairy

farms during at that point of time in the 20-year period. The increase in farm size over the 20-year period was another adaptation, and from field data it is known that the prevalence of Johne's disease is higher in larger herds (Ott et al., 1999 and Jackobsen et al., 2000).

Simulation of several control strategies in stages one and three indicated that management adaptations were a more effective and economically more attractive strategy to control Johne's disease than to only test and cull. Furthermore, the results indicated that implementation of all necessary management adaptations was critical. If for instance, step three is not taken, the average true prevalence will not decrease to zero in a 20-year period (Figure 6). Indeed, the results of both dairy stages showed that separation of calves between 7 and 12 months from adult animals had a significant impact on the average true prevalence. A reason for this is that in The Netherlands the contact between 7 and 12 months old calves and older cows was found to be high (Muskens and Jongeneel, 1999). Therefore, a high contact rate was assumed in the model. Separation of the older calves from the animals older than 2 years reduced this contact rate and therefore resulted in a significant impact on the average true prevalence. In beef cow herds, contact between calves and their dams is inherent in the system since calves suckle for several months. The contact rate is therefore very high and as a consequence control of Johne's disease in the current beef cow herd situations did not result in a decrease of the prevalence when calves and dams were not separated. Only with separation (b-II and b-III) did the prevalence decrease considerably.

In epidemiological terms, 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 excretors of the organism and would never have experienced any 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 infected animals. If a program was to be based on such an 'ideal test', political decisions would therefore need to be made on which party 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 the next few years.

The sensitivity analysis showed that the results of the model are very sensitive to the assumed reduction of the infection probability. If the reduction which is achieved on dairy farms is smaller than the assumed 90%, PPN will result in a slower decline of the mean true prevalence. In addition, this analysis showed the importance of maximum effort to reduce infection probabilities within the control program. The sensitivity analysis also showed the relevance of introduction of potentially infected animals. Testing all introduced animals with an ELISA test had only a very small effect due to the low sensitivity of the ELISA test. No

introduction of animals had only a small effect, but this effect was limited because of the effectiveness of PPN to control the within-herd spread of *M. a. paratuberculosis*.

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. Such extended time periods would be required because of the slow spread of Johne's disease. However, the model has been validated both with field data from 21 Dutch dairy herds and by face value validation by Johne's disease experts (Groenendaal et al., 2002).

In the model, it was assumed that the control measurements reduced the infection probabilities with 90%. Furthermore, it was assumed that calves younger than 1 year of age do not shed *M. a. paratuberculosis* and that the bacterium only survives for 6 months in the environment. If the reduction in reality is less than 90% or if animals younger than 1 year of age play a role in the spread of Johne's disease, the effect of the management strategies was over-estimated. Future research should therefore determine the effect of management strategies and the role of young animals in the on-farm spread of Johne's disease. The pilot study on 1500 farms to determine the rate of implementation of management changes may also reveal useful data on the reduction of infection probabilities.

The current economic analysis assumed that the farmers mainly paid the costs of the program and some of the costs were paid by the government through subsidized testing. PPN is a voluntary program, and therefore it was considered important that PPN was not only epidemiologically effective but also economically attractive.

4.5 Conclusion

In conclusion, the model was a valuable tool in the process of defining and deciding upon a new national Johne's disease control program for The Netherlands by predicting the effectiveness and the economical attractiveness of various possible control strategies. It caused a fundamental change in the design of the Dutch paratuberculosis control program, from a focus on 'test and cull' to a focus on 'stepwise improvements of calf hygiene' strategies, which forms the key of the new national voluntary control program. The decision-making process has been greatly supported by the JohneSSim model.

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Chapter 5

5 Simulation of alternatives for the Dutch Johne's disease certification-and-monitoring program

Paper by Weber, M.F., Groenendaal, H., van Roermund, H. J. W., Nielen, M., 2004. *Preventive Veterinary Medicine* 62, 1-17.

Abstract

To identify optimal method(s) for certification and subsequent monitoring of *Mycobacterium avium* subsp. *paratuberculosis* (Map)-unsuspected herds, certification-and-monitoring schemes were studied using a stochastic simulation model ("JohneSSim"). JohneSSim simulated the within-herd transmission and economic aspects of Map in closed Dutch dairy herds. The model was validated with field observations on Map-unsuspected herds. The current Dutch certification-and-monitoring schemes were compared with 11 alternative schemes in which individual and pooled fecal culture, ELISA, Johnin-intradermal test and γ-IFN ELISA were used, varying the test frequency, tested age group and number of tested animals.

On reaching the 'Map-free' status with the standard certification scheme, 11% of the simulated herds were not truly Map-free. Therefore, the designation 'Map-free' should be changed into, for instance, 'low-risk Map'. In the most-attractive alternative certification scheme, the 'Map-free' status was reached after four herd examinations (at 2-year intervals) consisting of serial testing of all cattle ≥2 years of age with a pooled fecal culture and individual fecal culture of positive pools. This scheme resulted in lower total and annual discounted costs and a lower animal-level prevalence at reaching the 'Map-free' status compared to the standard scheme, assuming that there was no new introduction of the infection.

Schemes to monitor the 'Map-free' status were compared, assuming that this status was reached with the standard certification scheme. In comparison to the standard monitoring scheme, none of the alternative monitoring schemes resulted in both a lower animal-level prevalence of undetected pre-existing Map infections in closed herds, and lower median annual discounted costs.

Results of the model were very sensitive to the assumed sensitivity of the fecal culture test and to management measures that prevent within-herd transmission of Map. If these preventive measures were taken, the probability of undetected Map infections in closed 'Map-free' herds was decreased substantially.

5.1 Introduction

In a control program for Johne's disease, certified *Mycobacterium avium* subsp. *paratuberculosis* (Map)-free cattle herds are important as a source of non-infected cattle. Certification programs to identify Map-free (i.e. low-risk) herds have been developed in several countries (Kennedy et al., 2001). In the Netherlands, herds can obtain 'Map-free' status following five annual herd examinations for which all results are negative (Benedictus et al., 1999). The first herd examination consists of serial testing of all cattle≥3 years of age by serology (ELISA) and individual fecal culture of seropositive animals. The second to fifth herd examinations each consist of serial testing of all cattle≥2 years of age with pooled fecal culture and individual-animal fecal culture of positive pools. The status of these certified 'Map-free'

herds is then monitored by annual herd fecal examinations, exactly as the second to fifth herd examination. For the pooled fecal culture, all animals≥2 years of age are stratified by age. A pooled fecal sample is then obtained from each group of five animals and cultured as a single sample (Kalis et al., 2000). If a pooled sample is culture positive, the five animals are re-examined by individual fecal culture. If all individual fecal samples of a previously positive pool are negative, then this pool is regarded as culture negative. To reduce the risk of introduction of a Map infection in 'Map-free' herds, cattle may be added to these herds only if the cattle originate from another 'Map-free' herd. In addition, cattle may be added to herds that are in the process of 'Map-free' certification only if they originate from a herd with an equal or higher number of negative annual herd examinations.

In September 2000, the first Dutch dairy herd obtained the 'Map-free' status, and at the end of 2002 there were 233 'Map-free' certified herds in the Netherlands. However, because the current certification-and-monitoring scheme was felt to be too expensive (especially for closed herds), a study of alternatives was required. Alternative schemes had to fulfill three requirements to be considered for implementation: (1) the prevalence of undetected pre-existing Map infections in closed 'Map-free' herds should not be higher than with the current scheme, (2) the costs of obtaining and monitoring a 'Map-free' status had to be reduced, and (3) transmission of Map infections between 'Map-free' herds had to be limited. (The transmission of Map infections between 'Map-free' herds was studied in a separate study with a mathematical R_0 model by Van Roermund et al. (2002b) In the present study, alternative schemes were simulated to study their effects on the prevalence of pre-existing infections in closed dairy herds, and to study the associated costs.

5.2 Materials and methods

5.2.1 The JohneSSim model

The JohneSSim model 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. The model simulates a period of 20 years with, at the background, time steps of 6 months and generates output-data with time steps of 12 months. The time horizon of 20 years was chosen to support middle-to-long-term decisions. The herd dynamics of a typical Dutch dairy herd are simulated, including calves and replacement heifers. All animals in the herd have various attributes (such as parity, stage of infection, month in lactation, and milk production). The model contains many probability distributions for uncertain events (such as infection, progression of the stage of infection and culling). In the model, five infection routes are considered: (1) intra-uterine infections, (2) infections occurring around birth, (3) infections due to drinking colostrum, (4) infections due to drinking whole milk, and (5) infections due to environmental contamination with Map. Six stages in the infection-and-

disease process are distinguished: (1) susceptible, (2) non-susceptible, (3) latent-infected, (4) lowly infectious, (5) highly infectious and (6) clinical disease. Both voluntary culling and involuntary culling are considered. The probability distributions for uncertain events are used for random sampling; repeated runs of the model provide insight into the variation in outcome at the farm level. Results at a higher aggregation level (e.g. national level) are obtained by simulating different types of dairy herds and aggregating the results according to their relative abundance. Preventive management and prevalence in the simulated herds was set to reflect the distribution of management practices and prevalence in the Dutch dairy industry (Muskens et al., 2000 and Groenendaal et al., 2002). To represent the difference between preventive management on individual dairy farms, eight different herd risk-profiles were defined (Van Roermund et al., 1999) and simulated separately. In total, the aggregation of all risk-profiles consisted of 7805 iterations. In the present study, relevant herd-specific model outcomes were the within-herd true prevalence and test prevalence over time, and costs spent over time on the certification-and-monitoring schemes. The JohneSSim model and assumptions made on parameters (such as herd size, yearly increase in herd size, herd prevalence and distribution of the within-herd seroprevalence at the start of simulations and probability distributions for uncertain events) were described in detail previously (Groenendaal et al., 2002). Resulting from these assumptions, the initial herd-level prevalence of the simulated dairy herd population was 79%, and the initial animal-level prevalence in the total simulated dairy population was 22%.

5.2.2 Assumptions in the JohneSSim model for present study

In the present study, all herds were assumed to be closed, and no new introduction of Map into any herd could occur during the simulations. Assumptions were made by an expert panel on the characteristics of tests (Table 1) and the costs of the programs (Table 2). The estimated sensitivity of the ELISA depends on the stage of infection and the ELISA-kit used, and ranges from 12–24% in low shedders to 68–79% in high-shedders and 87–88% in clinically diseased animals (Sweeney et al., 1995, Dargatz et al., 2001 and Kalis et al., 2002). However, in the JohneSSim model, lowly infectious animals were defined as intermittent-shedders and highly infectious animals as continuous shedders, and therefore sensitivities were estimated to be slightly lower than for low- and high-shedders, respectively. The sensitivity in latent-infected animals arbitrarily was set at 5%. The sensitivity of serial testing with the intradermal test (Johnin skin test) and the gamma interferon (γ-IFN) ELISA was calculated assuming independence of these tests. Combined specificity was based on field data (Kalis, personal communication, 2001). In the model, the minimal age at which infectious animals contribute to the transmission of Map was set to 2 years. Nevertheless, in the present study we assumed that fecal shedders between 1 and 2 years of age could be detected by fecal culture (Table 1). Discounted costs of the certification-and-monitoring program were calculated assuming a real interest rate (approximated by interest rate minus inflation rate) of 5% per year.

Table 1. Assumptions on sensitivity (Se) and specificity (Sp) of different tests in simulations of the certification-and-monitoring of 'Map-free' herds (Johne's disease, The Netherlands)

	Age group (month of age)	Stage of infection	Individual fecal culture	Pooled fecal culture	ELISA	Intradermal test [a]	γ-IFN ELISA	Serial testing with intradermal test [a] and γ-IFN ELISA
Se %	12 – 36	Latent	0	0	–	60	60	36
		Lowly infectious	40	36	–	60	60	36
		Highly infectious	95	95	–	50	50	25
		Clinical disease [b]	90	90	–	30	30	9
	> 36	Latent	0	0	5	60	60	36
		Lowly infectious	40	36	10	60	60	36
		Highly infectious	95	95	60	50	50	25
		Clinical disease	90	90	80	30	30	9
Sp %	*All*	*Not infected*	100 [c]	100	99.7 [d]	88.8 [e]	96.0 [f]	98.6 [f]

[a] Intradermal test = Johnin skin test, at a cut-off value of 2 mm; [b] In JohneSSim simulations, animals do not become clinical diseased before 2 years of age; [c] Reinders (1963); [d] van Maanen et al., (1999); [e] Kalis et al., 2003b. [f] Kalis, personal communication, 2001.

Table 2. Variable costs (€) of participation in the 'Map-free' certification-and-monitoring program for Johne's disease in the Netherlands

Test or action	Veterinarian	Transport	Laboratory (per submission)	Laboratory (per test)
Veterinarian's visit	18.15	–	–	–
Pooled fecal culture	2.72 per animal	7.26	6.81	34.49 per pool (max 5 animals)
Individual fecal culture	2.27 per animal	7.26	6.81	28.13 per animal
ELISA	2.27 per animal	7.26	6.81	5.67 per animal
Intradermal test [a]	3.18 per animal	–	–	–
γ-IFN ELISA	2.27 per animal	7.26	6.81	11.34 per animal

[a] *Two veterinary visits are required for an intradermal test. Yearly subscription costs were € 88.49 per year. Costs do not include Value Added Tax (VAT). VAT for subscription and laboratory tests=6%; VAT on other costs=19%.*

5.2.3 Validation of the model

Results of a simulation of 7805 closed dairy herds were compared with the results of a field study of 90 dairy farms in the North of the Netherlands (Kalis et al., 2003a). In 100 herds entering the field study, herd management had been closed for ≥3 years, while clinical signs of paratuberculosis and positive laboratory results were absent for ≥5 years. Ten herds were withdrawn from the field study (for instance, because farmers ceased farming), and were excluded from the analyses here. In both the simulation and the field study, herds were selected in which a first herd examination of all cattle ≥2 years of age with the pooled fecal culture did not reveal any Map infections. This selection criterion was used to start the comparison with a set of herds that were Map-unsuspected in both the simulation and the field study. The number of selected herds in the simulation was 3995, and in the field study 77. Subsequently, the selected herds were examined a further eight times at half-year intervals by pooled fecal culture of all cattle ≥2 years of age. At each 1-year interval, the simulated proportion of remaining test-negative selected herds was compared with the observed proportion of remaining test-negative selected herds in the field study by Pearson's χ^2. Exact 95% confidence intervals were calculated for the number of remaining test-negative herds as a proportion of the number of herds test-negative at the first herd examination.

5.2.4 Comparison of different 'Map-free' certification schemes

The current (standard; St) and nine alternative schemes for certification of 'Map-free' herds were simulated (Table 3). Herds with a positive individual fecal culture were expelled from the certification program, and could not re-enter the program. For each of the certification schemes, we determined: (1) the within-herd prevalence over time of pre-existing Map infections in the remaining test-negative closed dairy herds, (2) the animal-level prevalence over time in a dairy population consisting of all remaining test-negative iterations (i.e. herds) of the simulation, and (3) the costs from the start of the program until reaching the 'Map-free' status. Because the time from the start of the program to reaching the 'Map-free' status differed between the various certification schemes, both the total discounted costs and annual discounted costs (annuity costs) until the 'Map-free' status were calculated. The animal-level prevalence (i.e. total number of infected animals/total number of animals in the population) at reaching the 'Map-free' status and the total and annual discounted costs until reaching this status were compared for the different certification schemes.

Monitoring test schemes were simulated for herds that had reached the status 'Map-free' by the standard certification scheme. A positive result in the ELISA or pooled fecal culture always was confirmed by individual fecal culture of the animals concerned. If an individual fecal culture was positive, the herd was expelled from the program, and did not achieve the 'Map-free status'.

Table 3. Simulated test schemes for the certification-and-monitoring of 'Map-free' herds for Johne's disease in the Netherlands

Scheme	Certification schemes	Monitoring schemes	First herd examination for certification		Second through fifth herd examination for certification & all herd examinations for monitoring			Year 'Map-free' status achieved if all herd-tests negative
			Test	Animals and age (yr)	Test	Frequency	Animals and age (yr)	
St [a]	x	x	ELISA	All, ≥ 3	PF [b]	Once / yr	All, ≥ 2	5
A [c]	x	x	ELISA	All, ≥ 3	IDT / γIFN	Once / yr	All, 1 – 3	5
B [d]	x	x	ELISA	All, ≥ 3	PF / ELISA	Once / yr	All, ≥2 / ≥3	8
C [e]	x		--	--	PF	Once / yr	All, ≥ 2	4
D	x	x	ELISA	All, ≥ 3	PF	Once / 2 yr	All, ≥ 2	8
E	x		ELISA	All, ≥ 3	PF	Twice / yr	All, ≥ 2	3
F	x	x	ELISA	All, ≥ 3	PF	Once / yr	30 youngest, ≥ 2	5
G		x	--	--	PF	Once / yr	30 oldest, ≥ 2	--
H	x	x	ELISA	All, ≥ 3	PF	Once / yr	All, ≥ 1	5
I		x	--	--	PF	Once / yr	All, 1 - 3	--
CD [e]	x		--	--	PF	Once / 2 yr	All, ≥ 2	7
DH	x	x	ELISA	All, ≥ 3	PF	Once / 2 yr	All, ≥ 1	8

[a] *St = standard (current) scheme,*

[b] *PF = pooled fecal culture (Kalis et al., 2000)*

[c] *Scheme A includes testing of all cattle between 1 and 3 years of age with the Intradermal test (Johnin skin test). Any animal tested positive with the Intradermal test was tested with the γIFN – ELISA, and if positive, all cattle ≥ 2 years of age in the herd were tested with the pooled fecal culture*

[d] *Scheme B includes an annual herd examination with alternating a pooled fecal culture of all cattle ≥ 2 years of age and a serological examination (ELISA) of all cattle ≥ 3 years of age. The 'Map-free status' was obtained after eight herd examinations (four serological and four fecal examinations)*

[e] *In schemes C and CD the 'Map-free' status can be obtained after only four herd examinations*

5.2.5 Comparison of different schemes to monitor 'Map-free' herds

The current scheme to monitor the 'Map-free' status and eight alternative monitoring schemes were simulated (Table 3). In all cases, simulations were started with herds that had reached the 'Map-free' status in year 5 by the standard certification scheme (Table 3). Herds that were detected as infected were expelled from the certification-and-monitoring program and could not re-enter the program. For each monitoring scheme, we calculated: (1) the animal-level prevalence over time of undetected pre-existing Map infections in a dairy population consisting of all remaining test-negative herds and (2) the annual discounted costs for the remaining test-negative herds. To compare different monitoring schemes, the animal-level prevalence at 6 years after reaching the 'Map-free' status and the annual discounted costs to that time were used. This time span was chosen to maximize discrimination between different test schemes with regard to the animal-level prevalence in remaining test-negative herds.

5.2.6 Sensitivity analysis

The influence of several parameters in the model was studied in a sensitivity analysis. The following parameters were changed one at the time:

- The default herd size at the start of the simulations was 50 adult cattle and 46 young stock. However, at the end of 2002, the mean number of adult cattle (±S.D.) in Dutch dairy herds was 65 (±37). Therefore, to study the influence of herd size, an initial herd size of 100 adult cattle and 92 young stock was simulated with test schemes St, B and D.
- The default sensitivity of the pooled fecal culture was 36% for lowly infectious cattle, 95% for highly infectious cattle and 90% for clinically diseased cattle (Table 1). Alternatively, test schemes St, B and D were simulated with a sensitivity of the pooled fecal culture equal to the default values multiplied by an arbitrary 0.75.
- In the current Dutch certification-and-monitoring program, a confirmatory individual fecal culture of all animals in a fecal culture positive pool is allowed. Therefore, this was assumed by default in the present study. However, if all individual fecal samples of such a previously positive pool are negative, then the pool is regarded as culture negative—which means that an infected herd might not be detected. Therefore, as an alternative, test schemes St, B and D were simulated without confirmatory individual fecal culture of a culture positive pool.
- Because field data of the combined sensitivity of serial testing with the intradermal test and the γ-IFN ELISA were lacking, a combined sensitivity was calculated assuming independence of these tests. However, this is considered a worst-case scenario, because it is unlikely that these tests are independent. Therefore, the combined sensitivity was calculated alternatively assuming complete interdependence of the two tests (which means that these tests would be positive in the same infected individuals).
- By default, the results at the national level were calculated by aggregation of the results of the eight risk-profiles of herds. These risk-profiles reflected the wide variation in preventive

measures taken by Dutch dairy farmers (Groenendaal et al., 2002). However, dairy farmers are stimulated to take preventive measures against the transmission of Map. Therefore, the results were calculated alternatively for the standard scheme and the two most-extreme risk-profiles:

- Risk-profile A (rather good preventive management) in which (a) calves were fed colostrum of their own dams and milk replacer only, and (b) calves from 0 to 6 months of age were housed separately from adult cattle.
- Risk-profile B (rather poor preventive management) in which (a) calves were fed mixed colostrum, whole milk and milk withdrawn from human consumption, and (b) calves from 0 to 6 months of age were housed together with the adult cattle.

5.2.7 Data analysis

Animal-level prevalences obtained by different test schemes were compared by Pearsons χ^2. If an overall χ^2 was significant, then each alternative scheme was compared individually with the standard scheme by Yate's continuity-corrected χ_{cc}^2, using Bonferroni's correction of *P* for adjusting for multiple comparisons (Altman, 1999). Costs of different test schemes were compared using the Kruskal–Wallis rank-sum test (adjusted for ties). If significant differences were found, then the alternative test schemes were individually compared two-sided with the standard test scheme using the Mann–Whitney test (adjusted for ties) with Bonferroni's correction of *P*. In all tests, significance was declared at $P \leq 0.05$ (two-sided).

5.3 Results

5.3.1 Validation

Of 90 herds in the field study, 77 were pooled fecal culture negative at the first herd examination (Kalis et al., 2003a). Of these 77 herds, only 46% (35 herds) were still culture negative at the ninth herd examination (Figure 1). No difference was found between the proportion of unsuspected herds in the field study and in the simulation after the third herd examination (χ^2=3.50, d.f.=1,*P*=0.06), the fifth herd examination (χ^2=0.02,d.f.=1,*P*=0.90), the seventh herd examination (χ^2=0.69,d.f.=1,*P*=0.41) and the ninth herd examination (χ^2=0.30,d.f.=1,*P*=0.58). In retrospect, a true difference of >16% between the proportion of unsuspected herds after the ninth herd examination in the field study and in the simulation could have been detected with a power of 80%.

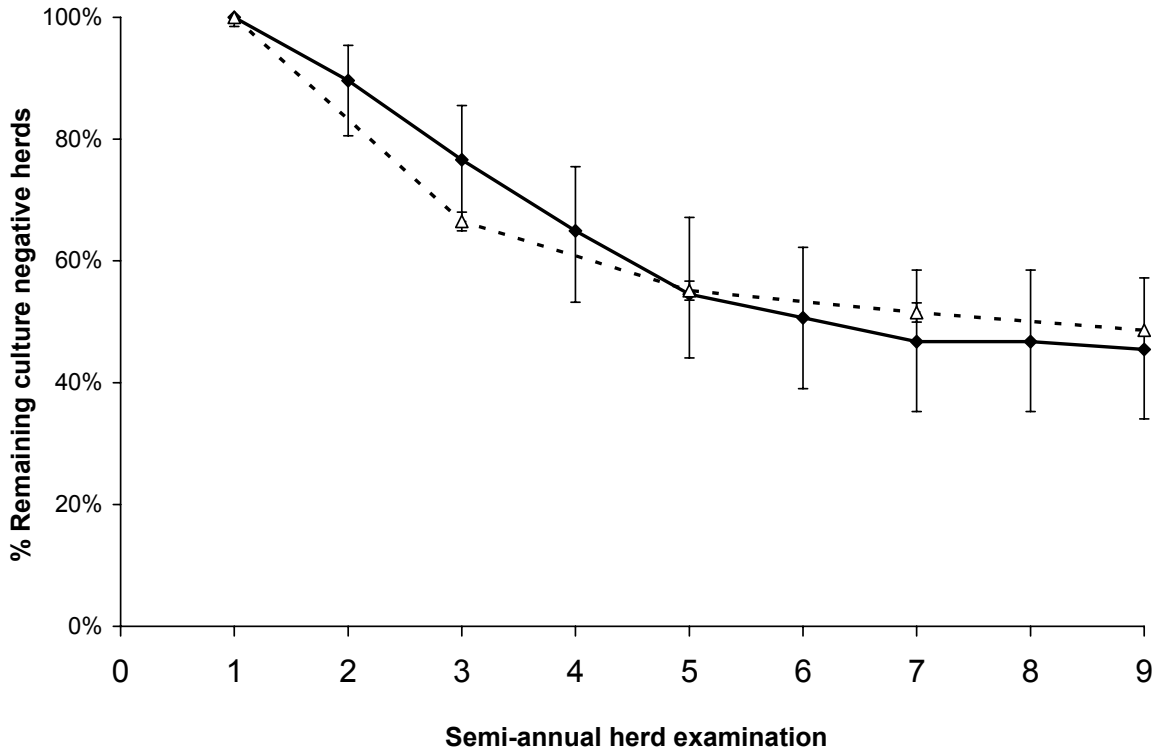


Figure 1. Proportion of remaining test-negative dairy herds examined by semi-annual pooled fecal culture of all cattle≥2 year in a JohneSSim simulation of 3995 herds (△) and a field study on Johne's disease in 77 Dutch herds (♦) ± exact 95% confidence intervals

5.3.2 Comparison of different 'Map-free' certification schemes

Using the standard certification scheme, test-negative herds obtained the 'Map-free' status after 5 years. At that time, 23% of the simulated herds were truly free of Map infection, and 77% of the simulated herds were infected. Using the standard certification scheme, 74% of all simulated of herds had a positive individual fecal culture in any of the first five annual herd examinations, and were expelled from the program. Twenty-six percent of the herds remained test-negative (Figure 2A), and therefore reached the 'Map-free' status at a median cost of € 3412 (Table 4). Thus, with the standard certification scheme, an infection was present but not yet detected in 3% of the simulated herds (i.e. in 11% of the herds that remained test-negative). The initial animal-level prevalence over all simulated herds was 22%. After 5 years, this animal-level prevalence over all simulated herds had increased to 34%. By then, the animal-level prevalence over all remaining test-negative herds was only 0.56% (Figure 2A). The distribution of the within-herd prevalence in herds that were positive in any herd examination and in remaining test-negative herds (i.e. certified 'Map-free' herds) is shown in figure 2B.

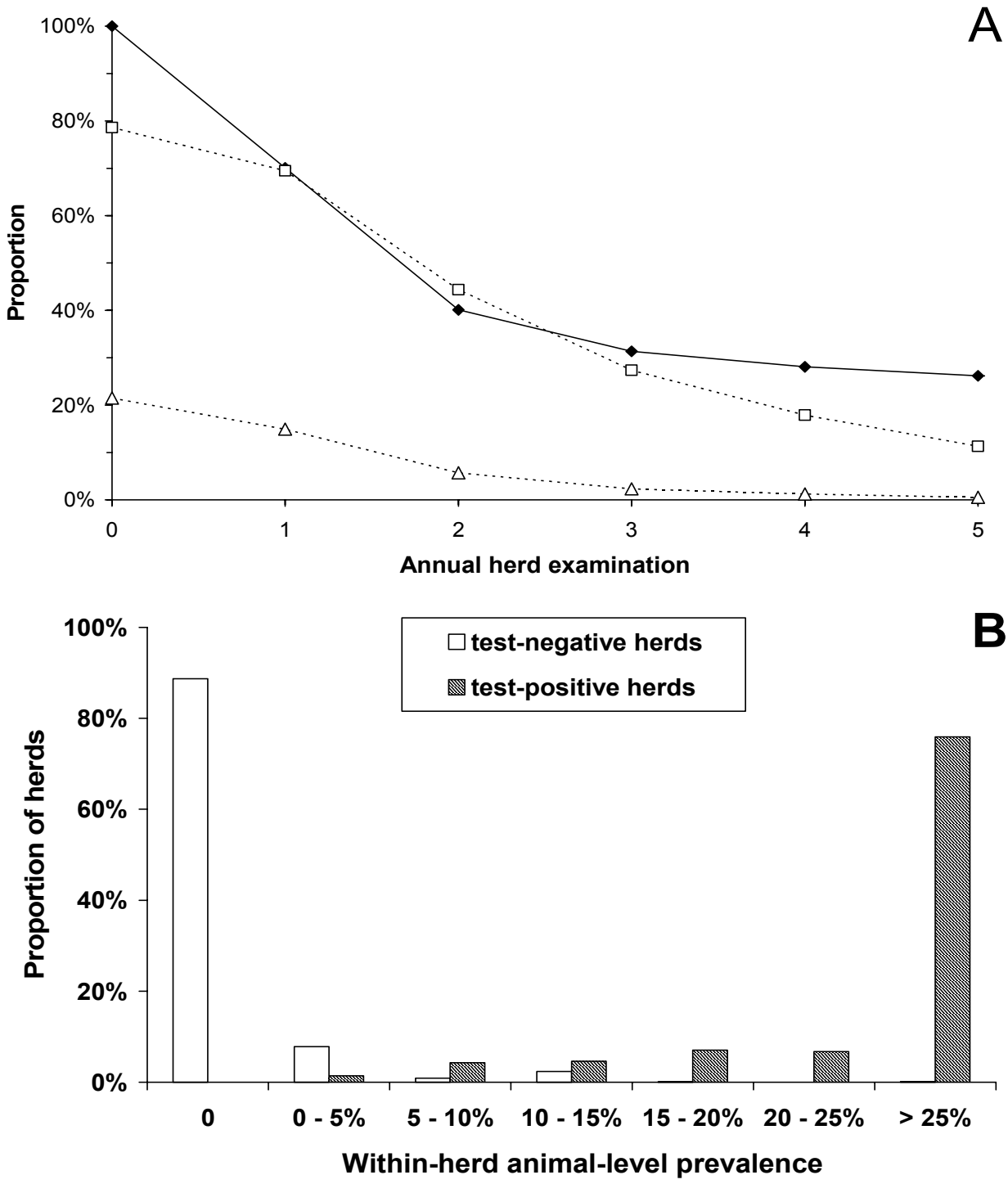


Figure 2. Results of a simulation of the standard certification scheme for Johne's disease in the Netherlands. (A) Proportion of remaining test-negative herds (—◆—), proportion of infected herds in the group of remaining test-negative herds (···□···), and proportion of infected animals in the group of remaining test-negative herds (···△···), at each herd examination. (B) Distribution of within-herd animal-level prevalence after five herd examinations for herds that were test-positive in any of the herd examinations, and in herds that were test-negative in all herd examinations, and therefore reached the status 'Map-free'

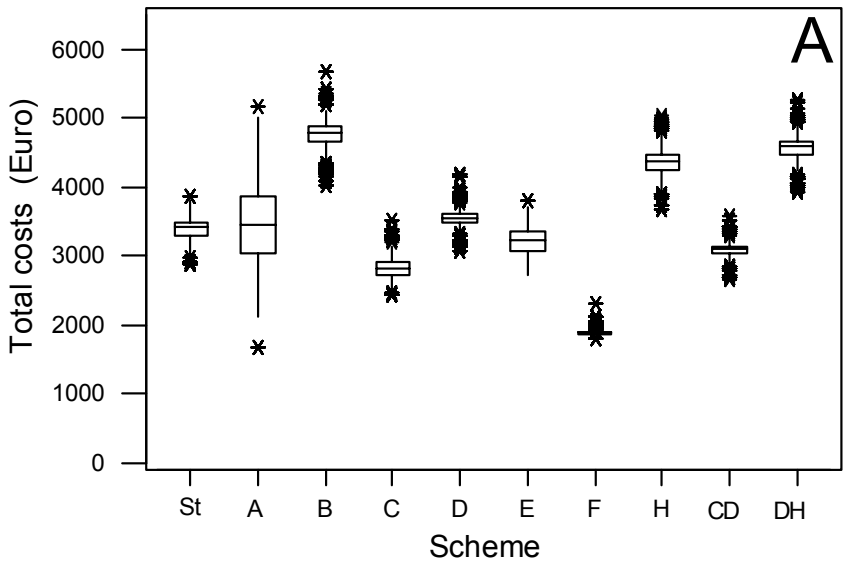
Table 4. Estimated probability and total discounted costs (€) of reaching the 'Map-free' (Mycobacterium avium subsp. paratuberculosis-free) status, and animal-level prevalence upon reaching the 'Map-free' status with various certification schemes

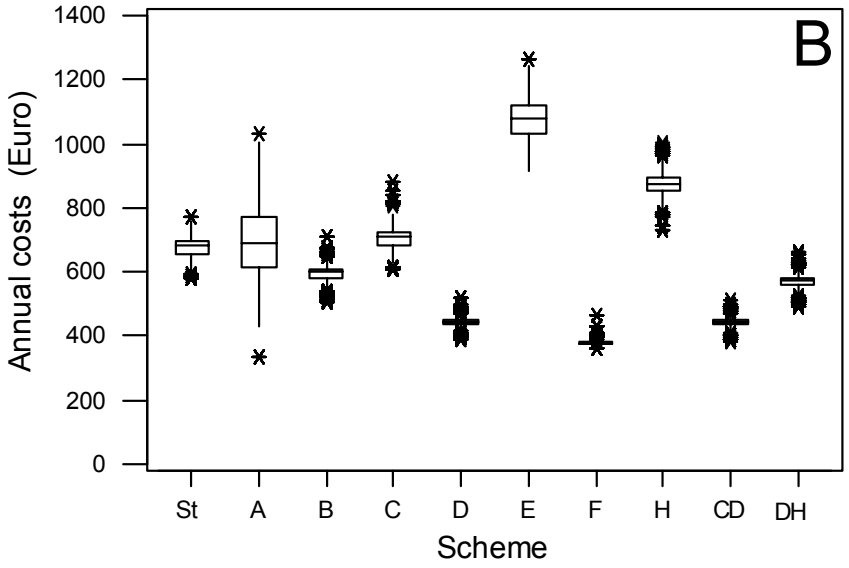
Scheme	Probability of reaching 'Map – free' status	Costs (Euro)					Mann-Whitney		Animal-level prevalence			
										Yates continuity corrected χ^2_{cc}		
		Min	5%	50%	95%	Max	W (*10^6)	p [a]	Prevalence	χ^2_{cc}	df	p [a]
St	26%	2901	3019	3412	3732	3860			0.56%			
A	26%	1670	2380	3447	4603	5162	4.06	0.005	0.61%	8.358	1	0.036
B	25%	4040	4239	4782	5082	5685	2.09	<0.001	0.24%	418.327	1	<0.001
C	27%	2444	2593	2829	3288	3526	6.36	<0.001	1.02%	433.828	1	<0.001
D	27%	3090	3203	3563	3819	4174	3.08	<0.001	0.44%	47.006	1	<0.001
E	27%	2738	2906	3230	3649	3794	5.28	<0.001	0.76%	99.112	1	<0.001
F	27%	1816	1882	1890	2012	2316	6.45	<0.001	1.44%	1254.489	1	<0.001
H	26%	3667	3923	4387	4846	5029	2.09	<0.001	0.58%	1.993	1	>0.5
CD	26%	2667	2813	3106	3428	3570	5.71	<0.001	0.48%	17.609	1	<0.001
DH	27%	3929	4069	4596	4959	5275	2.09	<0.001	0.43%	60.738	1	<0.001

[a] *Bonferroni corrected p*

Overall, the costs for reaching the 'Map-free' status were different (Kruskal–Wallis test: H=17 726.42, d.f.=9, P<0.001) and the animal-level prevalence's were different (χ^2=5539.29,d.f.=9,P<0.001)

With alternative certification schemes, 25–27% of the herds reached the 'Map-free' status at median discounted total costs between € 1890 and 4782 (Table 4). In comparison with the standard certification scheme, schemes C, E, F and CD resulted in lower median *total* discounted costs (P<0.001; Table 4; Figure 3A), and schemes B, D, F, CD and DH resulted in lower median *annual* discounted costs until the 'Map-free' status was reached (P<0.005; Figure 3B). Schemes B, D, CD and DH resulted in a lower overall animal-level prevalence upon reaching the 'Map-free' status (Table 4; Figure 3D). In these four schemes, the pooled fecal culture was used only once every 2 years. Hence, the period until the 'Map-free' status was reached was prolonged (Table 3). Only scheme CD resulted in a combination of both lower total and annual discounted costs until the 'Map-free' status was reached, and a lower overall animal-level prevalence at that point.




B
Annual costs (Euro)
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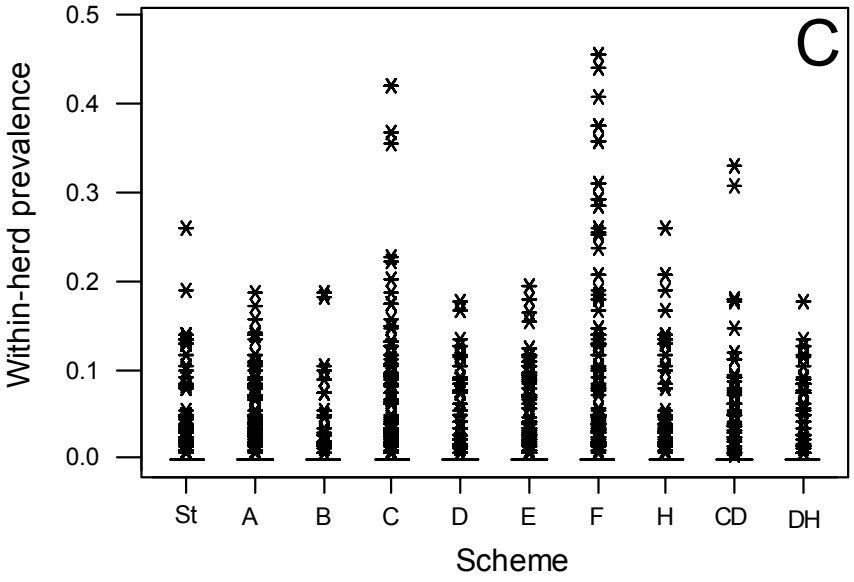
1200
1000
800
600
400
200
0
St
A
B
C
D
E
F
H
CD
DH
Scheme


C
Within-herd prevalence
0.5
0.4
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0.2
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0.0
St
A
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C
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CD
DH
Scheme

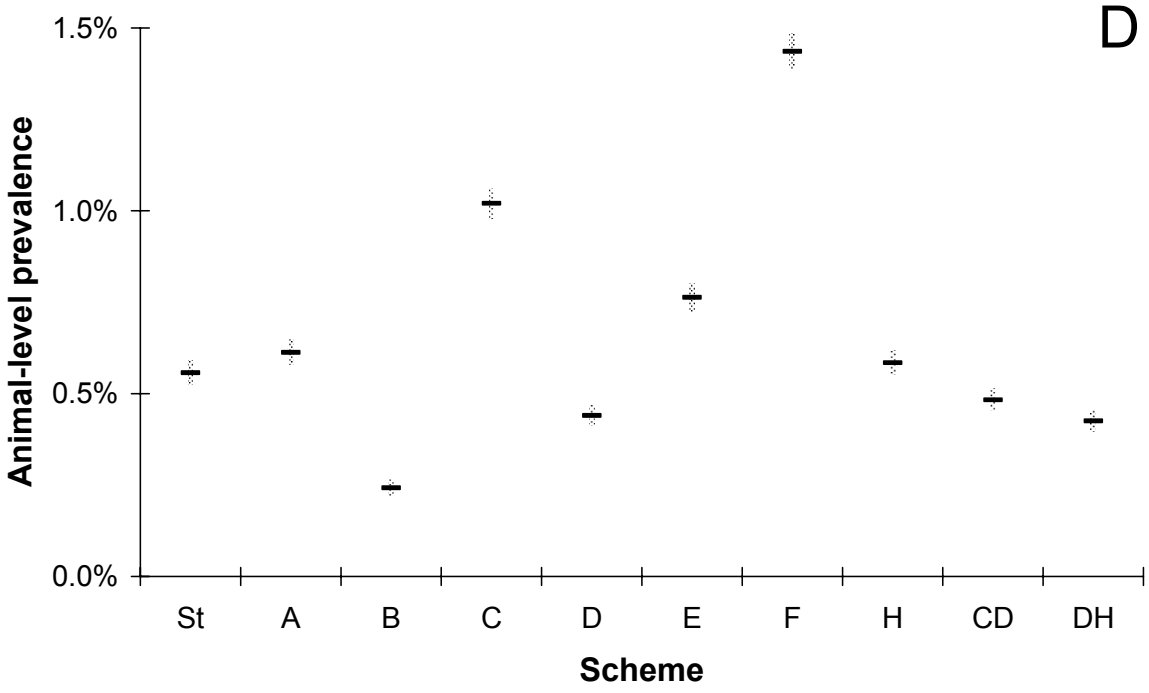

Figure 3. Costs for reaching the 'Map-free' status and prevalence at reaching this status for various simulated certification schemes for Johne's disease in the Netherlands. The certification schemes are defined in Table 3. (A) Boxplot of total discounted costs. (B) Boxplot of annual discounted costs. (C) Boxplot of within-herd animal-level prevalence. (D) Overall animal-level prevalence (i.e. number of infected animals/total number of animals in all herds reaching the 'Map-free' status) with 95% confidence intervals. In the boxplots, the boxes indicate the first, second and third quartile. The whiskers extend from the top and bottom of the box to the lowest and highest observations that are within 1.5 times the inter-quartile range from the first and third quartile. Outliers outside this region are plotted with asterisks

5.3.3 Comparison of different schemes to monitor 'Map-free' herds

After the 'Map-free' status was reached in year 5 with the standard certification scheme, it took an additional 10 years to detect all infected 'Map-free' herds with the standard monitoring scheme. With the alternative monitoring schemes A, B, D, F, H and DH this took 9–15 years. Therefore, with these schemes, the animal-level prevalence over all remaining 'Map-free' herds decreased to zero in year 14–20 (Figure 4). However, monitoring schemes G and I failed to detect all infected 'Map-free' herds within the simulated 20-year period. If the standard monitoring scheme was used, the animal-level prevalence in remaining test-negative herds fell to 0.02% in year 11 (Figure 4). The median annual discounted costs were by then € 708. None of the alternative monitoring schemes resulted in both lower median annual discounted costs up to year 11 and a lower animal-level prevalence in the remaining test-negative herds at the same time. For instance, monitoring scheme DH resulted in a prevalence of 0.04% in year 11, although the median annual discounted costs to that point were only € 596.

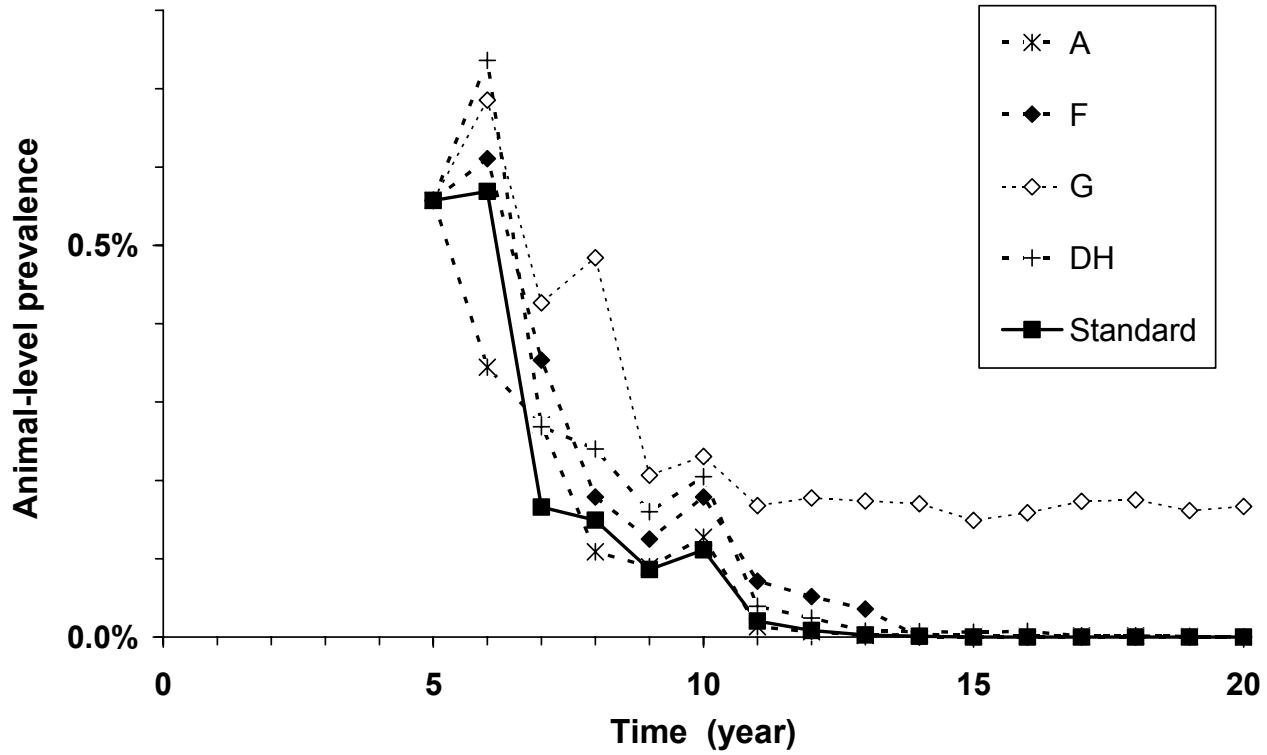

Figure 4. Animal-level prevalence (i.e. total number of infected animals/total number of animals in all 'Map-free' herds) over time when different monitoring schemes are used after reaching the 'Map-free' status in year 5 by the standard certification scheme. The monitoring schemes are defined in Table 3

5.3.4 Sensitivity analysis

The overall animal-level prevalence at reaching the 'Map-free' status was estimated to be 0.1–0.3% lower in herds with 100 adult cattle than in herds with 50 adult cattle, depending on the test scheme used. The animal-level prevalence in 'Map-free' herds at least doubled when the sensitivity of the pooled fecal culture was reduced to 0.75 of the default value (Figure 5). However, if no confirmatory individual fecal culture of a culture positive pool was performed, then the animal-level prevalence upon reaching the 'Map-free' status was reduced by a factor 0.3–0.6. Using alternative certification scheme A, the animal-level prevalence upon reaching the 'Map-free' status was 0.52% if the combined sensitivity of the intradermal test and the γ-IFN ELISA was calculated assuming complete interdependence of these tests, compared to 0.61% if independence of the tests was assumed. If the preventive management practices were rather good (risk-profile A), the prevalence in 'Map-free' herds reached zero the year following the 'Map-free' status. If the management practices were rather poor (risk-profile B), this took approximately 8 years (Figure 6).

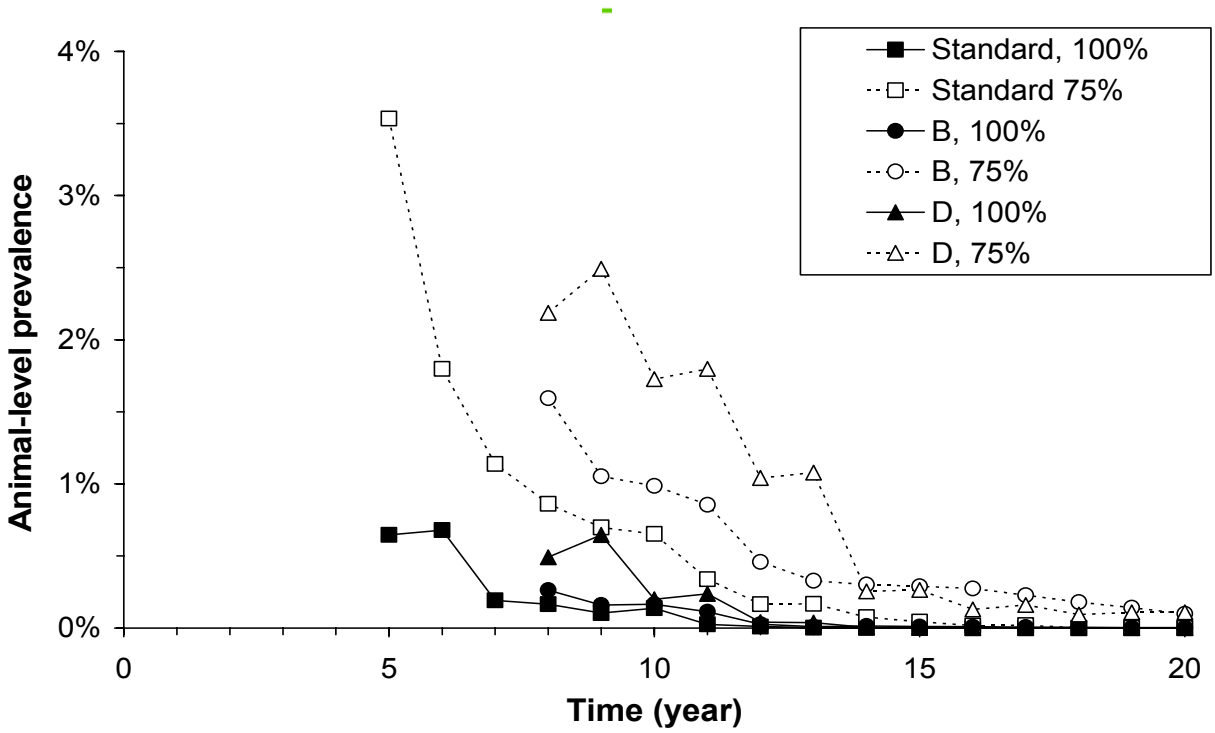

Figure 5. Sensitivity analysis for sensitivity of the pooled fecal culture. Animal-level prevalence in 'Map-free' herds over time at the default sensitivity ("100%") and 25% lower sensitivity for each stage of infection ("75%"). The different schemes are defined in Table 3

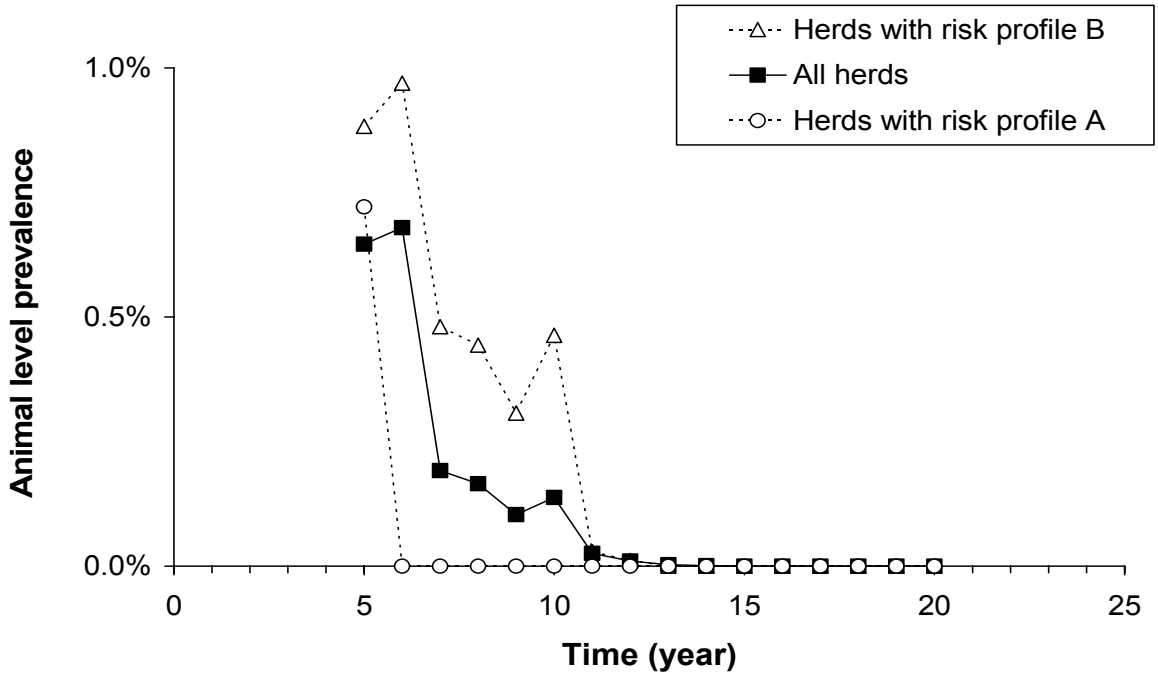

Figure 6. Sensitivity analysis for preventive management measures. Animal-level prevalence over time in all herds, herds with rather good calf management (risk-profile A) and herds with rather poor calf management (risk-profile B). (In all cases, the standard certification-and-monitoring scheme was used; Table 3)

5.4 Discussion

Simulations with the JohneSSim model were considered to be in general agreement with field observations on 77 closed dairy herds over a 4-year period. This does not necessarily mean that a similar agreement would be reached if field data over a longer time frame were available. For instance, the model could overestimate the proportion of remaining test-negative herds on the longer run. However, the results supported the validity of using the model for evaluation of alternative certification-and-monitoring schemes.

The JohneSSim model is a stochastic simulation model; therefore, the outcomes are probability distributions (as shown for within-herd prevalence in figure 2B). However, an individual farmer who buys cattle from a 'Map-free' herd might be interested only in eliminating the risk of buying an infected animal. Because farmers lack information about the true Map infection status of the 'Map-free' herd of origin, the only relevant parameter to purchasing farmers is the overall animal-level prevalence in the population of 'Map-free' herds, which is used as a probability of the animal being infected. Therefore, in the present study, this overall animal-level prevalence of the population of 'Map-free' herds was used to discriminate between alternative test schemes. To estimate this overall animal-level prevalence, the total animal population of 'Map-free' herds was considered to consist of all iterations of a simulation. The resulting proportion (prevalence) is therefore a single point estimate and not a distribution. However, it is important to realize that infected cattle are clustered in a small proportion of 'Map-free' herds—and that most herds truly are negative (Figure 2 and figure 3C). The risk for the buyer is thus not spread evenly over all 'Map-free' herds (in contrast to what might be suggested from our overall animal-level prevalence's).

In the present study, comparisons between the standard and alternative schemes were supported by formal testing of the differences in animal-level prevalence's and costs. However, the value of significance testing in a stochastic simulation is limited. With more iterations of the simulations, small and perhaps irrelevant differences between the standard and alternative schemes may become significant. Therefore, comparisons need to be focused on the practical relevance of the differences between results obtained by different test schemes.

Our results predicted that an estimated 11% of the herds were not truly Map-free on reaching the 'Map-free' status with the standard certification scheme. With the standard monitoring scheme, it took some 10 more years before all pre-existing infections were either extinct or detected. Therefore, the designation 'Map-free' in the Dutch certification program should be changed into, for instance, 'low-risk Map'.

The time from the start of the program to reaching the 'Map-free' status differed between the various *certification* schemes. Therefore, annual as well as total discounted costs were estimated. Alternative certification schemes in which the interval between herd examinations is 2 years lengthened the certification process by 3 years (schemes B, D, CD and DH; see Table 3). However, these alternative certification schemes resulted in both lower estimated annual discounted costs and a lower estimated animal-level Map prevalence at reaching the 'Map-free'

status. This lower prevalence is probably because more individual-animals were tested for a Map infection over the longer period, and thus infected herds were more-likely to be detected. Only certification scheme CD resulted in lower estimated annual and total discounted costs and a lower estimated Map prevalence at reaching the 'Map-free' status, compared to the standard scheme. This might improve the acceptance of the program by participants—although potential benefits of a 'Map-free' status (such as trade and marketing advantages) are postponed by 3 years with this scheme. No data are available to estimate these benefits, but currently the financial benefits for herds that actually have achieved a 'Map-free' status, compared to the benefits for herds that are half-way through the certification trajectory, appear to be limited. Thus, this scheme CD (in which the serologic herd examination was skipped and the 'Map-free' status was reached after four pooled fecal cultures of all cattle≥2 year of age at 2-year intervals) seemed to be the most-attractive alternative, assuming no new introduction of the infection.

Under the assumptions of the model, eventually all infected herds were detected by the standard *monitoring* scheme and the alternative monitoring schemes A, B, D, F, H and DH. However, the assumption that Map is not introduced into closed herds might not be realistic, especially if wildlife would be an important source of infection (Daniels et al., 2003). To our knowledge, field data of long-term (20-year) monitoring of Map-unsuspected herds are not available. However, a monitoring scheme for 'Map-free' herds can be successful, even if introductions of Map into 'Map-free' herds occur, as long as each infected herd is detected before the infection is transmitted to, on average, one other 'Map-free' herd (Van Roermund et al., 2002b).

In comparison to the standard scheme to monitor 'Map-free' herds, none of the alternative *monitoring* schemes resulted in both a lower prevalence of undetected pre-existing Map infections in closed herds and lower median annual discounted costs. Monitoring scheme DH (fecal culture of all cattle≥1 year of age at 2-year intervals) resulted in lower annual costs but a slightly higher prevalence of undetected Map infections in closed herds then the standard scheme. However, this scheme resulted in a sufficiently low between-herd transmission, if it was assumed that cattle could be traded between certified 'Map-free' herds at a rate observed in 87 Dutch herds that were certified or in the process of certification as 'Map-free' (Van Roermund et al., 2002b). Therefore, we consider this scheme to be a suitable alternative for the standard monitoring scheme for maintaining a pool of 'Map-free' herds.

The model was shown to be robust for initial herd size. This is important, because there is considerable variation in the herd size of Dutch dairy herds. If no confirmatory individual fecal culture of positive pools in the pooled fecal culture was allowed, the prevalence in remaining test-negative herds was reduced markedly. Preclusion of the possibility of confirmatory individual fecal culture of positive pools might reduce the costs associated with testing of infected herds in a certification-and-monitoring program and might simplify the program. We assumed no changes in preventive management during the simulations. However, preventive measures against the transmission of Map infections resulted in a substantial lower probability of undetected Map infections in closed 'Map-free' herds. Therefore, if a closed farming system

is combined with preventive management, perhaps the certification-and-monitoring of such 'Map-free' herds could be relaxed and carried out with considerable lower costs. Further studies in this field are needed.

We made important assumptions on the sensitivity of tests for the various stages of infection; published data are generally based on studies with high fecal shedders. The results of the JohneSSim model were very sensitive to the assumed sensitivity of the fecal culture. We assumed that young stock do not contribute to the transmission of Map. However, recently it has been suggested that calves contribute to the transmission of Map immediately after infection (Van Roermund et al., 2002a). Furthermore, we assumed that fecal Map-shedders between 1 and 2 years of age could be detected by fecal culture. The efficacy of inclusion of this age group in herd examinations is expected to depend strongly on the sensitivity of fecal culture of this age group. In herds with clinical cases of Johne's disease, 2.1% of young stock between 1 and 2 years of age were culture positive (Kalis et al., 1999), but it is unknown whether this is similar in low-prevalence herds.

The present study was performed to assist decision-makers in selecting suitable alternatives for the Dutch certification-and-monitoring scheme for Johne's disease. A number of assumptions related specifically to Dutch dairy herds (such as the relative abundance of management risk-profiles, costs and initial (sero)prevalence). However, the mechanisms of transmission of the infection, disease and testing are comparable in other countries. Furthermore, the JohneSSim model has been adapted previously for use in Pennsylvanian dairy herds (Groenendaal et al., 2002) and Dutch beef herds, and thus provides a flexible tool for studying the within-herd transmission and detection of Map infections.

We conclude that the current Dutch certification-and-monitoring scheme for 'Map-free' herds could be optimized by: (1) certification of 'Map-free' herds after four herd examinations at 2-year intervals consisting of pooled fecal culture of all cattle≥2 years of age, (2) monitoring of 'Map-free' herds by pooled fecal culture of all cattle≥1 year of age at 2-year intervals, and (3) vigorous execution of preventive management practices against the transmission of Map infections. In addition, the designation 'Map-free' should be changed into, for instance, 'low-risk Map'.

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Chapter 6

6 Economic consequences of control programs for paratuberculosis in midsize dairy farms in the United States

Paper by Groenendaal, H., Galligan, D.T., 2003. *Journal of the American Veterinary Medical Association* 223:1757–1763.

Abstract

Objective - To evaluate the epidemiologic efficacy and economic efficiency of current and potential future control programs for paratuberculosis (Johne's disease) on midsize dairy herds in the United States.

Design - Stochastic dynamic computer simulation model.

Sample Population - Data on prices and other input variables collected from various sources were used to represent a population of midsize US dairy herds infected with paratuberculosis.

Procedure - The simulation model was modified to reflect management and production characteristics of midsize dairy herds in the United States. The model was validated by use of field data and expert opinion. Various control strategies then were simulated and compared on an epidemiologic basis and on the basis of economic efficiency.

Results - Test-and-cull strategies and vaccination against paratuberculosis were not able to decrease the mean prevalence of disease in the United States. Typically, only vaccination was economically attractive. Improved management strategies decreased the prevalence of paratuberculosis considerably and had high economic benefits.

Conclusions and Clinical Relevance - Analysis of results of this study suggests that test-and-cull strategies alone do not reduce the prevalence of paratuberculosis in cattle and are costly for producers to pursue. Vaccination did not reduce the prevalence but was economically attractive. Finally, improved calf-hygiene strategies were found to be critically important in every paratuberculosis control program and most were economically attractive programs for midsize US dairy farms with the disease.

6.1 Introduction

Paratuberculosis (Johne's disease) causes infectious chronic granulomatous enteritis in cattle. It is attributable to infection with *Mycobacterium avium* subsp *paratuberculosis*. Throughout the world, paratuberculosis causes substantial economic losses on dairy cattle operations as a result of reduced milk yield, reduced slaughter values, and increased culling (Benedictus et al., 1987; Ott et al., 1999). Additionally, although definitive proof is lacking, it has been postulated that *M avium* subsp *paratuberculosis* may be associated with some forms of Crohn's disease in humans (European Commission Directorate, 2000). The image of the dairy industry, including the fact that consumers desire wholesome products from healthy cows, may be threatened by

paratuberculosis. These factors increase the need for effective and economically attractive control strategies aimed against paratuberculosis.

In the past, many attempts have been made to decrease the prevalence of paratuberculosis. These attempts primarily focused on test-and-cull and vaccination strategies. However, none of these strategies has proven effective in controlling paratuberculosis, and the worldwide prevalence of paratuberculosis is still increasing (Jakobson et al., 2000; Collins and Morgan, 1992; Groenendaal et al., 2002). The Voluntary Johne's Disease Herd Status Program (VJDHSP) was developed in the United States in an effort to certify herds that are free of paratuberculosis (Bulaga, 1998; Uniform program standards for the VJDHSP, 2002). The program was intended as a model for control programs within each state, and the guidelines were considered to be minimal requirements to control paratuberculosis on dairy operations. Many states have matched, or are in the process of matching, their paratuberculosis control programs with the national VJDHSP. However, most states put a high emphasis on testing (Comparison of state herd status programs, 2001). In 1 report (Wells et al., 2002), it was concluded that the test strategies in the VJDHSP failed to identify most low-prevalence dairy herds. In addition, we are not aware of any scientific studies that have been performed to evaluate costs and benefits of the VJDHSP. Therefore, better information is needed on the epidemiologic efficacy and economic efficiency of the VJDHSP, as well as alternative control strategies against paratuberculosis, such as vaccination and contract rearing of replacement heifers.

The objective of the study reported here was to use a simulation model to evaluate various paratuberculosis control programs for midsize US dairy herds on the basis of their epidemiologic and economic consequences. Because of the chronic, slow-developing nature of paratuberculosis, field studies would be extremely costly and time consuming. Therefore, a simulation model was considered an appropriate approach to aid in the development of effective and efficient paratuberculosis control programs.

6.2 Materials and Methods

6.2.1 Sample population

A typical midsize US dairy herd was defined as a herd with 100 dairy cows plus additional youngstock, which is common in northeastern states, such as Pennsylvania and New York, and midwestern states, such as Wisconsin. Average milk production was set at 9,072 kg (20,000 lb), milk price was set at $0.287/kg ($13/100 lb) (Ott et al., 1999), and variable feed costs were set at $0.088/kg ($4/100 lb). Slaughter value of a cull dairy cow (Ott et al., 1999) in typical body condition was estimated to be $400; for cows infected with paratuberculosis, we estimated that slaughter value would be decreased 0% to 30%. Test prevalence at the start of the simulations was set equal to the prevalence distribution found in the United States (Ott et al., 1999). A large

study (NAHMS, 1997) of farm management with regard to paratuberculosis served as a basis to assess the level of management prior to implementation of a control program (Appendix 1).

6.2.2 Paratuberculosis simulation model

The simulation model[1] used to evaluate various paratuberculosis control strategies has been described elsewhere (Groenendaal et al., 2002). The model is a stochastic and dynamic simulation model that simulates herd dynamics, disease dynamics, control of paratuberculosis, and economic consequences of the control of paratuberculosis on each herd for a default period of 20 years. The 5 infection routes considered were fetal infections, infections at the time of birth, infections attributable to ingestion of colostrum, infections attributable to consumption of milk (waste milk or pooled milk), and infections attributable to environmental contamination with *M paratuberculosis*. Net present value (NPV), defined as total discounted revenues (i.e., present value) minus total discounted costs, was calculated for each control strategy for the entire 20-year period. Revenues were calculated as the reduction of the losses attributable to paratuberculosis that resulted from implementation of the control program. The real interest rate, which can be approximated as the interest rate minus the inflation rate, was assumed to be 5%.

6.2.3 Control strategies

Control strategies that were simulated can be categorized into test-and-cull, contract heifer-rearing, and improved management with regard to calf-hygiene strategies and various assumptions of the efficacy of vaccination (Appendix 2 and Appendix 3). The testing strategies we simulated reflected the VJDHSP standard- and fast-track testing strategies (Bulaga, 1998; Uniform program standards for the VJDHSP, 2002); both testing strategies have been extensively described elsewhere (US Voluntary Johne's disease Herd Status Program for Cattle, 2002). Test sensitivity for the simulated ELISA ranged between 1% and 80%, whereas test sensitivity for the simulated microbial culture of fecal samples ranged between 0% and 90%; sensitivity was dependent on the infection state of each cow. Test specificity for the simulation was estimated to be 99% and 100% for the ELISA and microbial culture, respectively. Within the contract heifer-rearing strategies, it was assumed that all calves were brought to a contract heifer-rearing facility when calves were 1 day old or 30 days old. At the contract heifer-rearing facility, it was assumed that calves would not have contact with cattle > 2 years old. In addition, it was assumed that each calf was born in a clean calving pen, separated from its dam within 1 hour after birth, and provided colostrum obtained only from its own dam. Finally, direct costs and benefits of contract heifer rearing were not included because the benefits (forgone costs of

[1] JohneSSim, Animal Health Service, Deventer, The Netherlands.

rearing your own heifers) were extremely similar to the costs of contract heifer rearing[2] and the direct costs and benefits were not the main interest of our study.

To document the effect of each of the management strategies for improved calf hygiene, each strategy was simulated for dairy farms with bad management. On farms with fair or good management, some positive measurements were already being implemented; therefore, not all of the various calf-hygiene management strategies would affect the results of the model. Thus, bad management farms were chosen as the starting baseline situation.

In addition, 1 vaccination strategy was simulated. The assumption was that all calves were vaccinated when they were extremely young. Although a reduction in the number of cattle with clinical evidence of paratuberculosis has been reported (Kormendy, 1992; Wentink et al, 1994) after vaccination, the exact mechanism by which vaccination against paratuberculosis protects cattle is not known. Therefore, 2 assumptions were made regarding the specific underlying mechanism of the effect of the vaccine (Appendix 2). Without vaccination, it was assumed that each infected animal would become highly infectious between 2 and 20 years of age, with the most likely age being approximately 4 years (Groenendaal et al., 2002). With vaccination, it was assumed that the age at which an animal became infectious increased or there was a 50% reduction in the number of cattle that became infectious after vaccination. The scenario in which vaccination induced an increase of 1.5 years for the age at which an animal would become infectious was considered the default vaccination effect and represented the estimated effect of vaccination as determined by a group of experts on paratuberculosis[3]. The other simulations represented alternative magnitudes and mechanisms of action. Finally, the costs of vaccination were assumed to be $8/calf.

6.3 Results

6.3.1 Epidemiologic analysis

The mean true prevalence on an infected midsize US dairy farm was estimated by use of the simulation model (Figure 1). Without any control program, prevalence of the disease increased gradually. Implementation of the standard- and fast-track testing strategies resulted in a slower but still increasing true prevalence, compared with results for no control program. The only strategy that resulted in a decrease of the mean true prevalence was to reduce the exposure of calves to *M paratuberculosis* by implementation of contract heifer rearing.

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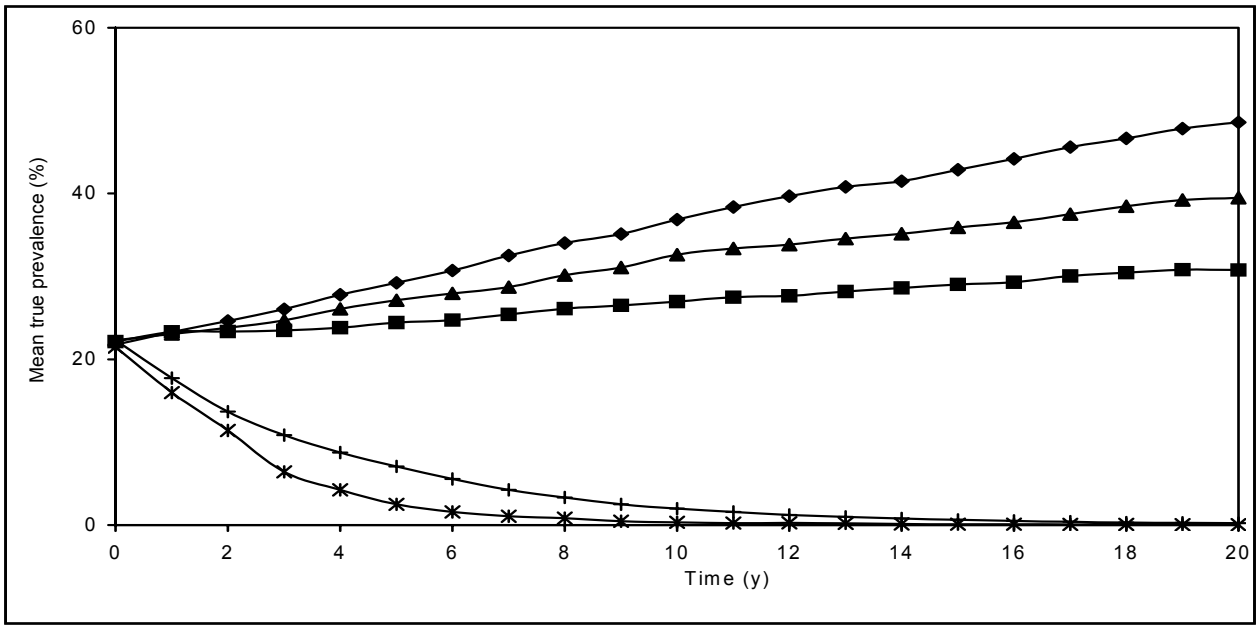

Figure 1—Mean true prevalence on a typical mid-size US dairy farm infected with paratuberculosis (Johne's disease) estimated by use of a simulation model. Estimations were obtained for a herd that did not have a paratuberculosis control program (diamond) and herds that implemented a standard-track testing strategy (square), a fast-track testing strategy (triangle), or 2 contract heifer-rearing strategies that involved taking calves to the rearing facility when they were 1 day old (cross) or when they were 30 days old (plus sign)

The mean true prevalence on US dairy farms with bad management that did not have a paratuberculosis control program or that implemented various calf-hygiene management control strategies was estimated by use of the simulation model (Figure 2). Feeding calves only milk replacer instead of waste milk or pooled milk resulted in a substantial impact on mean true prevalence. In addition, the simulation revealed that only changing all management strategies would result in a decrease of the mean true prevalence toward 0. Implementation of the standard-track testing strategy had a small additive effect when combined with the strategy to change all calf-hygiene management strategies.

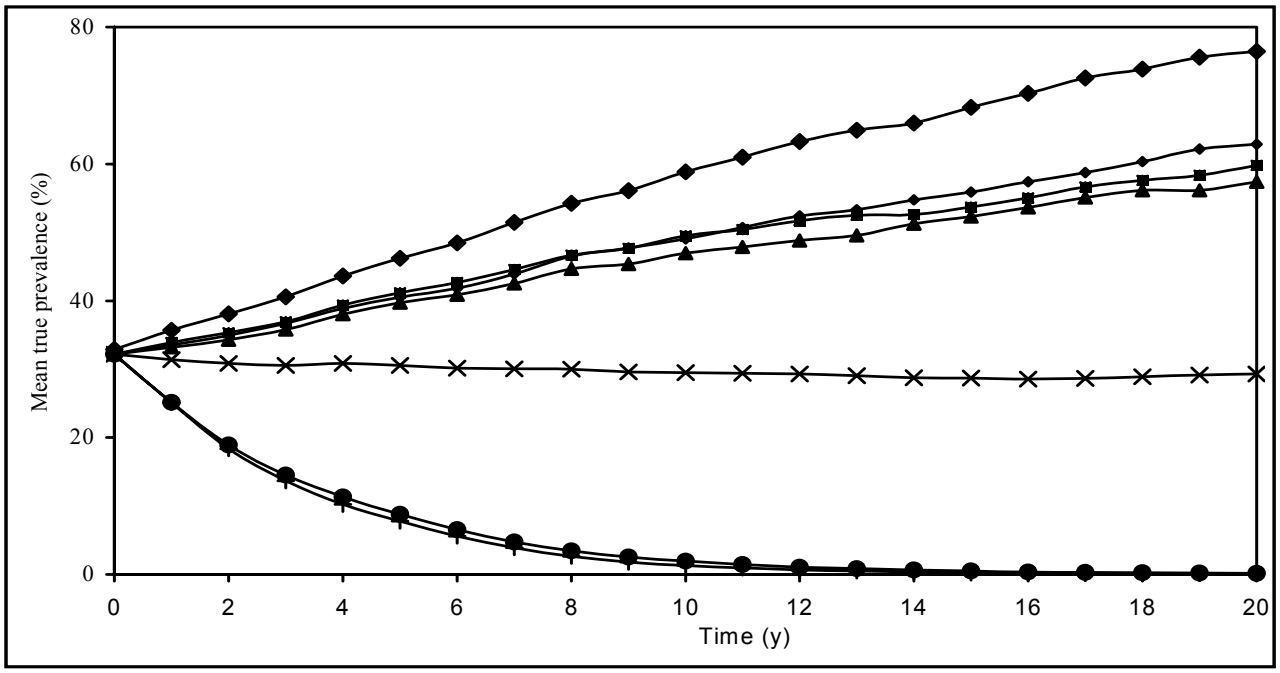

Figure 2—Mean true prevalence on a typical mid-size US dairy farm infected with paratuberculosis with bad management for various paratuberculosis control strategies estimated by use of a simulation model. Estimations were obtained for a herd that did not have a paratuberculosis control program (large diamond) and herds that implemented improvements in calf-hygiene management strategies (calving area is clean, and each calf is quickly separated from its dam and removed from the calving area after parturition (small diamond); each calf is fed colostrum obtained only from its own dam (triangle); only milk replacer is fed to the calves (cross); proper, hygiene for calves and separation of calves and adult cattle (square); all 4 of the calf-hygiene management strategies (circle); and all 4 of the calf-hygiene management strategies and use of a standard-track testing strategy (plus sign)

The mean true prevalence on an average midsize US dairy farm infected with paratuberculosis that opted to implement vaccination of all calves against paratuberculosis was estimated by use of the simulation model (Figure 3). The default scenario (assumption that vaccination would increase the age at which a cow became infectious by 1.5 years) did not have a large effect on mean true prevalence. When it was assumed that vaccination would increase the age at which a cow became infectious by 2.5 years, the effect of vaccination on the prevalence was only slightly larger. Finally, even for the assumption that 50% of the vaccinated cattle would not become infectious, there was only a limited effect on the mean true prevalence.

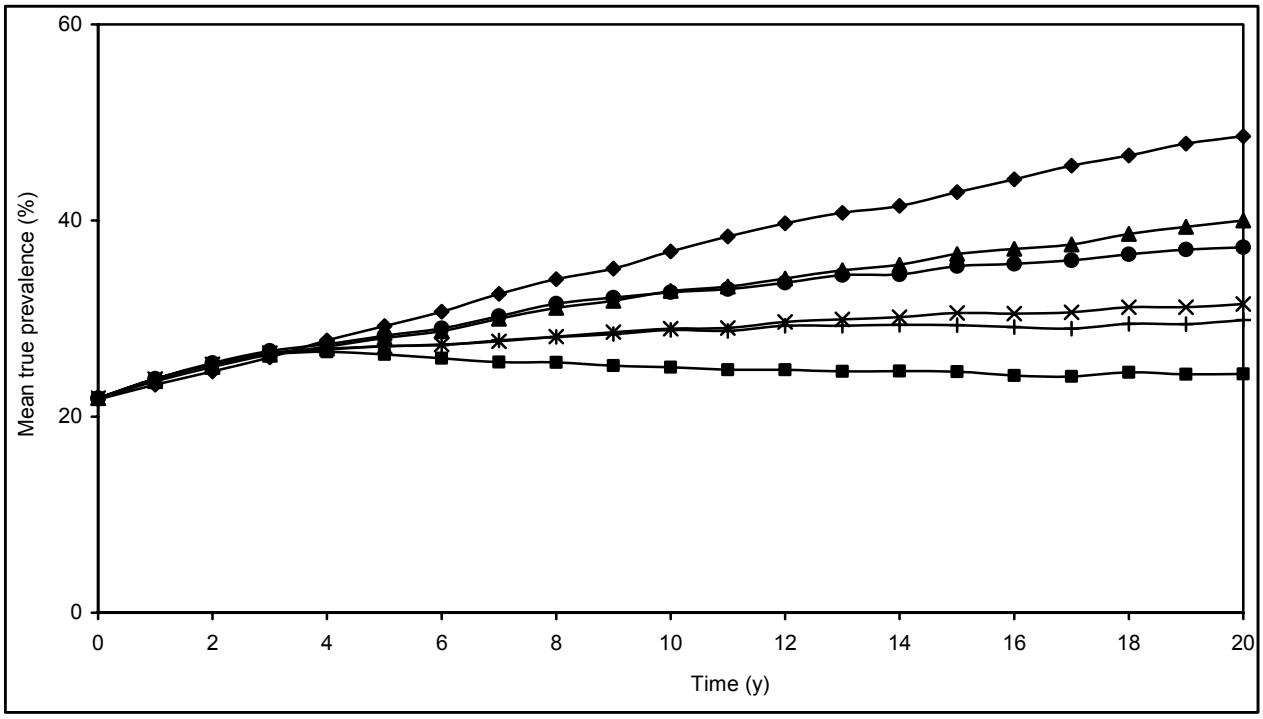

Figure 3—Mean true prevalence on a mid-size US dairy farm infected with paratuberculosis for various vaccination scenarios estimated by use of a simulation model. Estimates were obtained for a herd that did not have a paratuberculosis control program (diamond) or herds that implemented vaccination with the assumption that it would increase the age at which a cow became infectious for paratuberculosis by 0.5 years (triangle), 1.5 years (cross), or 2.5 years (square); reduce by 50% the probability that a cow would become infectious for paratuberculosis (circle); or a combination of increasing the age at which a cow became infectious for paratuberculosis by 1.5 years and reducing by 50% the probability that a cow would become infectious for paratuberculosis (plus sign)

6.3.2 Economic analysis

Economic losses attributed to paratuberculosis in herds with a disease control program were estimated by use of the simulation model (Table 1). Mean loss increased considerably from \$35/cow/y in year 1 to > \$72/cow/y in year 20. There was large variation among farms, as indicated by the 10th and 90th percentiles. This large variation, which was also evident for other economic analyses we conducted, was mainly attributable to the variation among farms in prevalence of disease prior to implementation of a paratuberculosis control program and differences in calf-hygiene management. Lower milk production accounted for 11% of the total loss attributable to paratuberculosis, and 12% of the loss resulted from a lower slaughter value of culled infected cattle and treatment costs of clinically affected cows. Finally, most of the loss (77%) attributable to paratuberculosis was categorized as loss of future income as a result of suboptimal culling.

Table 1—Total and categorized losses attributable to paratuberculosis (Johne's disease) on a typical mid-size US dairy farm infected with paratuberculosis but without a disease control program

	Total loss				Categorized loss		
Year	Mean	Median	10th perc.	90th perc.	Milk production	Suboptimal culling	Reduced slaughter value and treatment costs for clinically affected cows
1	3,434	2,288	67	8,354	308	2,763	363
10	5,239	4,022	141	13,033	556	4,082	602
20	7,202	6,054	418	14,937	750	5,596	856
Discounted total loss	61,310	49,112	10,314	127,834	NA	NA	NA

Results are reported as $/y for a typical 100-cow dairy
Discounted totals represented total costs over the 20-year period
NA = Not applicable

Reduction of the loss of revenues attributable to paratuberculosis and the costs of the standard- and fast-track testing strategies were estimated (Table 2). Both tracks had a mean negative value for NPV. However, the 90th percentiles of the NPV for the standard- and fast-track testing strategies were $7,991 and $9,180, respectively, which indicated that for at least 10% of the infected farms, the standard- and fast-track testing strategies were economically attractive. Contract heifer rearing reduced the economic losses attributable to paratuberculosis. Mean total revenues of contract heifer rearing when calves were taken to the facility at 1 day of age were $43,917/farm. Revenues (i.e., reduction of loss) increased considerably when the heifers were taken to the contract heifer-rearing operation at the youngest age (i.e., 1 day of age vs. 30 days of age). Variation in the total revenues for contract heifer rearing starting at 1 day of age was large (on 10% of the herds, the NPV was ≤ $8,200, but on another 10% of the herds, the NPV was > $90,000).

Table 2—Costs, revenues (reduction of the economic loss attributable to paratuberculosis), and net present value (NPV) for various testing strategies and implementation of contract heifer rearing on a typical mid-size US dairy farm infected with paratuberculosis

	Testing strategy				Contract heifer rearing*	
	Standard track		Fast track			
					Day 1	Day 30
Year	Revenues	Costs	Revenues	Costs	Revenues	Revenues
1	427	916	1,116	2,663	0	0
10	2,820	3,410	1,919	2,246	4,811	4,595
20	4,371	3,659	3,213	2,665	7,205	7,159
Discounted total	31,298	37,418	24,053	28,397	43,917	42,391
Mean NPV		–6,121		–4,344	43,917†	42,391†
10th percentile		–19,374		-17,641	8,233	8,120
90th percentile		7,911		9,180	90,445	87,262

Results are reported as $/y for a typical 100-cow dairy. Net present value represents revenues minus costs

**Contract heifer rearing for calves that are taken to the contract-rearing facility when they are 1 day old or 30 days old*

†Results represent present value for contract heifer-rearing strategies

Reduction of the economic loss attributable to paratuberculosis for the various management strategies was estimated (Table 3). Revenues resulting from feeding milk replacer instead of waste milk or pooled milk were > $36,000 for a typical infected farm with bad management. Mean revenue for implementation of all management strategies was $70,000. Additional revenue when the standard-track testing strategy was added to the implementation of all management strategies was not large.

Mean costs and revenues for the 5 vaccination scenarios were estimated Table 4). Annual revenues for the default scenario increased from extremely low amounts during the first year of vaccination to $1,200 to $4,200 in year 20, depending on the assumed characteristics of the vaccine. Mean NPV was > $0 for all vaccination assumptions, and there was large variation of the NPV among farms for the 10th and 90th percentiles.

Table 3—Revenues (reduction of economic loss) attributable to paratuberculosis on a typical mid-size US dairy farm infected with paratuberculosis for implementation of various improvements in calf-hygiene management

Year	Calving area*	Colostrum management†	Milk management‡	Calf separation§	All improvement	Standard-track testing and all improvements
1	0	0	0	0	0	542
10	1,350	1,476	3,941	1,074	7,749	8,356
20	1,462	2,525	6,737	2,202	11,321	11,336
Mean PV	11,440	13,396	36,217	12,306	69,965	80,975
10th percentile	–794	2,367	15,165	2,370	34,655	40,146
90th percentile	25,337	25,094	55,359	24,241	101,906	117,077

Results are reported as $/y for a typical 100-cow dairy

**Calving area is clean; each calf is quickly separated from its dam and removed from the calving area after parturition*

†Each calf is fed colostrum obtained only from its own dam

‡Only milk replacer is fed to the calves

§Proper, hygienic separation of calves and adult cattle

PV = Present value

Table 4—Costs, revenues (reduction in economic loss), and NPV for various vaccination scenarios implemented on a typical mid-size US dairy farm infected with paratuberculosis

	Costs	Revenues				
Year		Increase in age (years)*				
		0.5	1.5	2.5	50% reduction in probability of an infectious cow†	1.5-year increase in age and 50% reduction in probability of an infectious cow
1	476	19	6	6	–3	17
10	470	420	1,451	616	1,546	2,162
20	473	1,230	3,156	1,836	3,419	4,266
Total	5,977	6,936	17,521	8,933	18,345	24,073
Mean NPV	NA	959	11,702	3,112	12,525	18,257
10th percentile	NA	–9,707	–5,763	–9,213	–5,727	–5,205
90th percentile	NA	14,842	37,502	19,607	39,111	50,547

Results are reported as $/y for a typical 100-cow dairy

**Increase in age at which a cow becomes infectious for paratuberculosis*

†Reduction in the probability that a cow will become infectious for paratuberculosis

6.4 Discussion

Analysis of results of the simulation model revealed that the mean prevalence of paratuberculosis as well as the economic loss attributable to the disease will slowly increase in a typical midsize US dairy herd that does not implement a control program. Neither the standard- nor fast-track testing strategy alone was capable of decreasing the mean true prevalence of paratuberculosis. Two important reasons for this are the extremely low sensitivity of the available tests for detection of paratuberculosis, especially for subclinically infected cattle, and the limited number of cattle tested. This is in agreement with results of another study (Wells et al., 2002). In contrast, contract heifer rearing appeared to be effective in reducing the mean true prevalence, especially when the calves were taken to the contract rearing facility at an extremely young age (Figure 1). Also, improving calf-hygiene management resulted in a considerable decrease in the mean true prevalence (Figure 2). However, if some routes of infection are not eliminated, *M. paratuberculosis* will still spread within a herd, and mean true prevalence close to 0 was only reached when a dairy farmer implemented all necessary management improvements. Finally, the model results revealed that none of the vaccination scenarios was able to reduce the mean true prevalence to < 20% after 20 years of vaccination.

Without a control program, mean loss per cow per year on an infected midsize US dairy farm increased from $35/cow/y in year 1 to > $70/cow/y in year 20 (Table 1). Mean losses for each infected animal were fairly constant (approx $140 to $150). However, because only a small percentage of the infected cows become clinical cases, the total loss per clinically affected cow is much higher. One of the reasons to start a control program is to reduce the direct (on-farm) losses attributable to paratuberculosis. Analysis of the results revealed that the management strategies were extremely effective in reducing the direct losses attributable to paratuberculosis (Table 2 and Table 3). The simulation model did not account for reduction of economic losses attributable to other diseases. A combination of the implementation of several disease control programs (i.e., integrated disease control) against infectious diseases could make each program economically more attractive because of shared costs (e.g., separating calves from adult cattle has benefits for paratuberculosis as well as other diseases). In addition, potential loss of current export markets because of paratuberculosis was not taken into account. Finally, we did not consider losses attributable to the potential loss of consumers' confidence in the wholesomeness of milk from cows infected with *M. paratuberculosis*. These latter costs could potentially be quite large, as has been seen with the decrease in beef consumption attributable to bovine spongiform encephalopathy, thereby making paratuberculosis control programs much more attractive.

In the simulation model reported here, it was assumed that vaccination would not prevent infections; however, vaccination would decrease shedding and the development of clinical signs. Although assumptions regarding the efficacy of vaccination were uncertain, none of the assumed scenarios involving vaccination was considered capable of decreasing the mean prevalence on infected farms. However, vaccination was able to greatly reduce economic losses

attributable to paratuberculosis and, on average, was economically attractive for infected dairy farms (NPV > $0), which is consistent with findings in another study (Van Schaik et al., 1996). Results reported here were also consistent with results of other studies (Kormendy, 1992; Wentink et al., 1994) in which vaccination with heat-killed or modified-live preparations of *M. paratuberculosis* effectively reduced the incidence of clinical disease in dairy herds but did not reduce the prevalence. Finally, vaccination could potentially result in additional benefits, such as decreased spread of disease among or within herds, which were not taken into account in the model.

Although the focus of paratuberculosis control programs has often been on test-and-cull strategies, results of the study reported here indicate that calf-hygiene management strategies are most effective in reducing the mean true prevalence of paratuberculosis on midsize US dairy farms. These basic results held true for high-, medium-, and low-prevalence herds (results not shown). Therefore, calf-hygiene management strategies should be emphasized as being a crucial component in any paratuberculosis control program. Attempts to make improvements in management a compulsory requirement for paratuberculosis control programs would probably not be extremely useful because of the impossibility of monitoring many of the critical management adaptations. However, farmers could be motivated to implement these strategies by documenting to them the long-term economic benefits for the control of paratuberculosis and use of that incentive to change the attitude and behavior of farmers. Finally, contract heifer rearing has seen dramatic growth in the past few years. Results reported here document that there are considerable revenues associated with contract heifer rearing through its effect of reducing the prevalence of paratuberculosis.

Output of a simulation model depends on the quality of the assumptions and inputs used. Field data were used wherever possible. However, some inputs or distributions had to be based on expert opinion. It would be difficult to validate our model by use of field data because *M paratuberculosis*-infected herds have not been monitored intensively for an extended period of 20 years, which would be needed because of the slow, chronic nature of paratuberculosis. The model has been validated with field data obtained from 21 Dutch dairy herds (Groenendaal et al., 2002) and through examination by experts on paratuberculosis in the Netherlands and Pennsylvania.

Although the study reported here focused on mid-size US dairy farms, we believe that the conclusions regarding the control of paratuberculosis are applicable for many situations. For example, application of the simulation model to the Dutch dairy industry resulted in similar conclusions (Groenendaal et al., 2002). Other areas of the United States or other countries may have other mixtures of risk factors, and prices may differ, but the same potential routes of infection exist, and the tests that are used have approximately the same sensitivity and specificity.

Analysis of results from use of the simulation model revealed that test-and-cull strategies alone were not able to reduce the mean true prevalence of paratuberculosis in infected midsize US dairy herds. Management improvements were more effective in reducing the mean true

prevalence and the economic loss attributable to paratuberculosis and therefore must be considered critically important in every paratuberculosis control program. Finally, vaccination was able to considerably reduce the economic loss attributable to paratuberculosis but was unable to reduce the mean true prevalence.

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Appendices

Appendix 1

Classification of mid-size US dairy farms on the basis of management with regard to paratuberculosis (Johne's disease)

Farm management	Calving area*	Colostrum management†	Milk management‡	Calf separation§	Percentage of farms
Bad	-	-	-	-	45
Fair	-	+	+	-	45
Good	-	+	+	+	10

**Calving area is clean; each calf is quickly separated from its dam and removed from the calving area after parturition*

†Each calf is fed colostrum obtained only from its own dam

‡Only milk replacer is fed to the calves

§Proper, hygienic separation of calves and adult cattle

Appendix 2

Assumptions of the effects of various vaccination scenarios for control of paratuberculosis evaluated by use of the simulation model

Increase in age at which cow becomes infectious for paratuberculosis (y)	Reduction of probability that cow becomes infectious for paratuberculosis
0.5	No change
1.5*	No change*
2.5	No change
No change	50%
1.5	50%

**Considered default scenario for vaccination*

Appendix 3

Test-and-cull and management-improvement strategies for control of paratuberculosis that were evaluated by use of the simulation model

Herd management	Test-and-cull strategy	Management-improvement strategy
All farms		
	Not implemented	Not implemented
	Standard track*	Not implemented
	Fast track*	Not implemented
	Not implemented	Contract heifer rearing beginning when calves are 1 day old and continuing until calves are 360 days old plus better calf-hygiene management
	Not implemented	Contract heifer rearing beginning when calves are 30 days old and continuing until calves are 360 days old plus better calf-hygiene management
Bad farms		
	Not implemented	Implementation of a calving lot
	Not implemented	Each calf fed colostrum obtained only from its own dam
	Not implemented	Calves only fed milk replacer
	Not implemented	Proper hygiene and calves < 1 year old reared separately from adult cattle
	Not implemented	Implementation of all 4 calf-management strategies
	Standard track	Implementation of all 4 calf-management strategies

**The standard and fast-track testing strategies have been extensively described elsewhere (U.S. Voluntary Johne's Disease Herd Status Program for Cattle, 2002)*

Chapter 7

7 General discussion

7.1 Introduction

The overall objective of the work described in this thesis was to support decision-makers in the design and development of control and certification-and-monitoring programs for Johne's disease by providing a better understanding into the epidemiologic and economic effects of Johne's disease strategies. The three sub-objectives to reach this primary objective are:

1. Development of a computer model that takes into account the latest field and literature knowledge and expert opinions on epidemiologic and economic attributes of Johne's disease and Johne's disease control;
2. Obtain insight in the economic and epidemiologic effects of potential Johne's disease control for suspected herds and certification-and-monitoring programs for unsuspected herds;
3. Identify important gaps in knowledge on Johne's disease that greatly impact the expected epidemiologic effectiveness and economic attractiveness of Johne's disease control programs.

This general discussion focuses on how the primary and the three sub-objectives were met. Section 7.2 discusses the research approach taken. Section 7.3 then discusses the main insights the study provided into the effects of possible Johne's disease control and certification-and-monitoring strategies. In this section, recommendations for future research are also provided. Section 7.3 covers the support this study provided to decision-makers and thus focuses on the primary objective of this study. Finally, the main conclusions of this thesis are summarized in section 7.4.

7.2 Research approach

Risk analysis entails the process of identifying a risk, describing it, performing a qualitative or quantitative assessment, making decisions (risk management), implementing the approved risk management strategy and communicating the decision to the various stakeholders. The study described in this thesis mostly focuses on an epidemiologic and economic quantitative risk assessment of Johne's disease control. Stochastic simulation (also called Monte Carlo simulation) modeling was used as a technique to assess the risk of Johne's disease and its on-farm losses and control. The paragraphs below will discuss three important attributes of the research approach taken and will draw lessons from them.

7.2.1 Uncertainty and variability

Two important issues to consider when studying Johne's disease control programs are uncertainty and variability.

Uncertainty concerns our lack of knowledge about fixed, but imprecisely known parameters or processes in nature. Uncertainty exists in, for example, our knowledge of the true prevalence of Johne's disease and of the transmission of Johne's disease within and between farms. Where possible, the input of the JohneSSim model was based on field data and literature. However, as there still is much uncertainty about the epidemiology of Johne's disease, Johne's disease experts provided input variables for which no historical or experimental data were available. Although it is hard (if not impossible) to judge how close these estimates are to the 'true' values, until historical data and/or experimental research data are able to provide better results, estimates based on expert knowledge are considered the best information available (Horst, 1997). A risk assessment can therefore be seen as a structured and quantitative process of combining the latest field, experimental and expert data into a decision-support format. In addition, risk analysis has the ability to direct further research by identifying areas where improved knowledge (reduced uncertainty) or better technology will have the greatest impact. The combination of these two attributes makes risk analysis a powerful tool to support decision-making under uncertainty.

Variability includes two separate concepts (Vose, 2001). First, it concerns the variability between individuals in a population, also known as inter-individual-variability. Two examples of inter-individual-variability within this thesis are the variability of the prevalence between herds in a country and the variability of milk production between cows within a herd. Secondly, variability concerns the effects of change or randomness, also known as stochastic variability. An example of stochastic variability within this thesis is the process of testing animals with tests that have a sensitivity or specificity < 100%.

A stochastic simulation approach that takes into account uncertainty and both forms of variability was considered an appropriate method to use for this study. The inclusion of uncertainty and variability within the JohneSSim model not only gives a more realistic picture, but also allows decision-makers to appreciate, for example, the large variation between farms of the epidemiologic and economic consequences of Johne's disease control. For instance, the model showed that costs and benefits of disease control programs are not always evenly distributed among farmers. While the results show that the Dutch voluntary control program was on average economically attractive (see Chapter 2, table 5), for many farms, the control program results in higher costs than benefits. For those who make decisions on a national level, it is very important to be aware of this great variation between farms.

7.2.2 Integrated approach

In this study, many areas related to Johne's disease and its control, such as microbiology, laboratory diagnostics, epidemiology and economics, were taken into account simultaneously. Evaluating different impacts of a strategy at the same time is more useful than examination of the individual impacts separately (Horst, 1997; Van der Gaag, 2004). In this study, two important advantages of taking such an integrated approach surfaces.

First, focusing on the individual impacts of a control strategy separately may not always lead to the optimal situation if there is a trade-off between epidemiologic effectiveness and economic attractiveness. For example, an epidemiologically effective program such "improved calf management combined with annual fecal testing" is often too expensive to be justified for low prevalence herd, even though it would control the disease relatively rapidly. On the other hand, results from different vaccination strategies showed vaccination to be on average economically attractive but not able to considerably reduce the prevalence of Johne's disease. Thus, the decision regarding the appropriate portfolio of Johne's disease control tools often involves trade-offs between epidemiologic efficiency and economic costs and simultaneous consideration is important when supporting disease control decisions.

Second, an integrated approach can provide insights that may be difficult or impossible to obtain when studying individual aspects separately. Below, three examples of such insights are highlighted.

1. Full economic evaluation: Many field studies on the economic implications of Johne's disease only estimate the current losses caused by Johne's disease (e.g. Gill, 1989; Ott et al., 1999). However, while these numbers may describe the current situation regarding Johne's disease, they do not necessarily aid in making decisions about what to do about these losses. To economically evaluate alternative control strategies against Johne's disease, one needs three components: (1) the losses without the control program, (2) the losses with the control program and (3) the costs of the control program. As illustrated in the figure below, the current losses caused by Johne's disease represent only one single data-point of one of the three economic components.

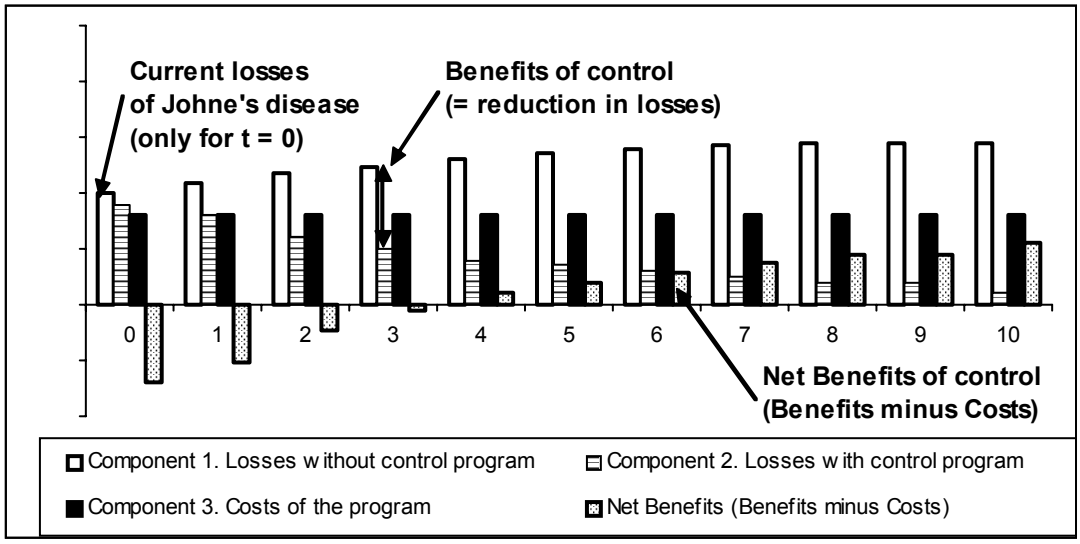

Figure 1. Illustration of required data for an economic evaluation of a Johne's disease control program (data in the figure are for illustration purpose only)

The economic evaluation of Johne's disease control programs in this thesis were performed as illustrated in Figure 1. The losses due to Johne's disease were estimated in two situations: without the control program (Component 1) and with the control program (Component 2). The reduction of the losses due to the control program (Component 1 minus Component 2, a.k.a. the Benefits of the program) was compared to the costs of the program (Component 3) to come to a Net Benefit of control (Benefits minus Costs), expressed in today's economic value as, for example, a Net Present Value (NPV) or Benefit-Cost ratio (BC-ratio). The economic evaluation of alternative Johne's disease control programs therefore required simultaneous consideration of the epidemiologic and economic effects of the control program. Therefore, loss estimates from field studies alone are not adequate to perform economic analyses of alternative control programs.

2. Suboptimal culling: Lower milk production and a decreased slaughter value of infected cows are easily observed and quantified losses of Johne's disease and are often reported to be the main losses caused by Johne's disease. In contrast, results in this thesis show that suboptimal culling (due to the loss of future milk production) causes about 70% of all losses of Johne's disease. The estimates in this thesis required the simultaneous use of epidemiologic aspects of the JohneSSim model and the use and results of an economic model (Chapter 3). While the reduced milk production of an infected animal and the suboptimal culling of an infected animal both result in a lower herd-level milk production, it is important to consider both losses separately when evaluating different control programs.

3. The perfect test: A 'perfect test' is often considered to have a very high sensitivity and specificity, while still being inexpensive. An annual test-and-cull strategy with such a test (sensitivity = 80%, specificity = 99%, cost ~2 Euro) for Dutch dairy farms was, as expected,

much more effective than the currently available diagnostic tests in reducing the mean Johne's disease prevalence. However, when evaluating this strategy on its overall economic effects, the control option was found to be economically unattractive (Chapter 4). The main reason for this was that many subclinical animals needed to be culled because they were found to be test-positive. A proportion of these subclinical infected animals would more than likely never become shedders of *Map* and thus never infect other animals and also never experience large milk production losses. Therefore, this control strategy actually results in costs exceeding its benefits over a 20-year period.

7.2.3 Validity

For any simulation model to truly add value and to be decision-supporting, it has to meet two important requirements. First, it has to be an accurate representation of the situation being studied ('valid') and, second, is needs to be credible and understandable (i.e. decision-makers have to accept it as 'correct') (Law and Kelton, 2000). The section below sheds light on the first issue, while paragraph 7.3.3 discusses the latter.

No matter how much effort is spent on creating a model, a simulation model of a complex system such as Johne's disease control, can only be a simplified approximation of the actual system. As there is no such thing as an absolutely valid model, a simulation model should be developed for a particular set of purposes (a similar argument can, in fact, be made about any field-study). The validation of a model should therefore focus on the aspects that the decision-maker will use for evaluating the system. The validation of the JohneSSim model consisted of a 'technical validation' and a 'practical validation':

- Technical validation: The JohneSSim model was validated by comparing the transmission parameter (β) of the disease calculated from field data with simulated β-values (Chapter 2). Also, field data from a Johne's disease certification-scheme was compared to results of the simulation of herds in similar circumstances (Chapter 5). In both situations, no great differences were found between the field and model results.
- Practical validation: Face validation by Johne's disease experts was used both in The Netherlands and the U.S. to confirm that the results of the JohneSSim model were in general agreement with what is seen in the field (Chapter 2 and 6). Great involvement and close cooperation with Johne's disease experts enabled the face-validation of individual components of the model, as well as the overall results. In addition, the successful adaptation of the model to both countries, and later to New Zealand dairy farms (Soons et al., 2002, Norton et al., 2004) give reason to believe that the JohneSSim model provides a flexible and valid tool for studying the epidemiologic and economic consequences of Johne's disease control.

A related question to the above is how much detail a model such as JohneSSim should include. Two comments can be made to address this question.

First, while the JohneSSim model was kept fairly simple in its early stages, its complexity increased as additional questions were asked (see Chapter 4) and as the model was applied to different situations (see Chapter 6). This increased complexity provided challenges, such as the difficulty of using the model and the greater possibility of making mistakes. To minimize the latter, verification of the correctness of the JohneSSim model was performed during every step of its development and by critical examination of its results. It is thus important to keep a simulation model "as simple as possible, but no simpler." [4]

Second, in addition to the JohneSSim model, a second model was developed (Van Roermund et al., 2002) to model the spread of Johne's disease *between* herds under a range of monitoring schemes. The between-herd model was an analytic model (and not a simulation model), built with mathematical expressions for several processes and which calculated the average transmission between-herds (R_h). As similar as possible input data was chosen for both models and output of the JohneSSim model was used as input into the between-herd model (Van Roermund, 2002). The two different modeling approaches were used to benefit from the strengths of both approaches. For example, the JohneSSim model allowed for the calculation of the economic consequences of Johne's disease control (which would not be possible with an analytical model). An analytical approach on the other hand is appropriate to evaluate if the average number of new infected herds by one initially infected herd is below one (see also Graat et al., 2001).

7.3 Discussion of results and their use in policy-making

In this study, a wide range of control and certification-and-monitoring strategies for Johne's disease in The Netherlands and the U.S. were studied. In the next paragraph, results of these strategies are discussed shortly, followed by paragraph 7.3.2 that discusses how these research findings were used in policy-making. Paragraph 7.3.3 finally lists some critical knowledge gaps related to these strategies and provides some guidance for future research.

7.3.1 Strategies

Johne's disease control programs can be designed for either Johne's disease positive or Johne's disease negative farms. Strategies on both farms have different goals and often use different control tools. The goal of control programs for positive herds is to reduce the spread and losses due to Johne's disease and to prevent any future introductions, eventually resulting in a free (and test negative) status. For Johne's disease negative herds, it is important to prevent the introduction of Johne's disease into the herd, and within a certification-and-monitoring program to obtain a high likelihood of being truly free of the disease.

[4] *Albert Einstein*

To calculate the economic benefits (equal to the reduction of losses) of any of the control strategies evaluated in this study, the 'default' or 'no control' situation was assumed to be the same as the current situation (no changes made related to Johne's disease). The results of the JohneSSim model in both The Netherlands and the U.S. indicated an increase in the average animal prevalence of the disease in the default case. Current losses due to Johne's disease are also rising and estimated to be, on average, €19 and US$34 per cow on infected dairy herds in, respectively, The Netherlands and in the U.S., which is also consistent with past findings in the field.

Both in The Netherlands and in the U.S., results of the JohneSSim model showed that eradication of Johne's disease based on 'test-and-cull' strategies alone would not be possible within 20 years and that test-and-cull strategies were economically unattractive. The main reason for this ineffectiveness is the very low sensitivity of the test for subclinical animals. As a consequence, in The Netherlands decision makers changed their focus towards 'calf hygiene management' strategies. These strategies include quick separation of calf and cow after birth, feeding only milk replacer and raising calves separately from adult animals. For both Dutch and U.S. dairy farms, the results of the model showed that these strategies were much more effective in reducing the prevalence of Johne's disease and were economically more attractive. In addition, in the U.S., contract heifer-rearing showed to be a promising strategy to control Johne's disease, assuming that bio-security risks upon return of the calves to the herd of origin are well managed.

Vaccination was also simulated as a possible Johne's disease control strategy in both The Netherlands and the U.S. Although a reduction of the number of cattle with clinical evidence of paratuberculosis has been reported after vaccination (Kormendy, 1992; Wentink et al., 1994), the exact mechanism by which vaccination against paratuberculosis protects cattle is not well understood. Therefore, different assumptions were made within the JohneSSim model regarding this mechanism. None of these assumed mechanisms resulted in a decrease of the mean prevalence on infected farms. However, in all scenarios, vaccination was able to considerably reduce economic losses due to Johne's disease and was, on average, economically attractive for infected dairy herds. The results of the vaccination scenarios in the JohneSSim model were consistent with a costs-benefit analysis of vaccination against Johne's disease in dairy cattle (Van Schaik et al., 1996) and with field observations that vaccination effectively reduces the incidence of the clinical disease but does not reduce the prevalence (Kormendy, 1992; Wentink et al., 1994).

Certified Johne's disease free cattle herds are important as a source of non-infected cattle in a control program against Johne's disease. This study considered twelve alternative certification and monitoring programs for Dutch dairy farms, varying in tests used, test frequency, age of tested animals and the number of animals tested (Chapter 4). A distinction was made between the testing scheme to reach a 'Johne's disease free status' ("certification scheme"), and the testing scheme to monitor the 'Johne's disease free status' ("monitoring scheme"). The results first showed that, in the current scheme, 11% of the simulated 'Johne's disease free' status

herds were not truly Johne's disease free. This led us to conclude that the designation 'Johne's disease free' should be changed to, for example, 'low-risk Johne's disease'. Secondly, the results showed that, compared to the current scheme, only one alternative scheme (four pooled fecal cultures of all cattle ≥ 2 years of age at 2-year intervals) resulted in lower estimated costs and a lower Johne's disease prevalence when reaching the 'Johne's disease free' status.

After a farm reaches the 'low-risk Johne's disease' herd designation, it enters a monitoring scheme. The results showed that none of the alternative monitoring schemes resulted in both a lower animal prevalence of undetected pre-existing Johne's disease infections and lower median annual costs than the current program (annual pooled fecal test of all animals ≥2 year). However, a monitoring scheme with fecal culture of all cattle ≥ 1 years of age at 2-year intervals may be a valuable alternative as it resulted in lower annual costs and only a slightly higher prevalence of undetected Johne's disease compared to the standard scheme.

7.3.2 Knowledge gaps and future research

The third sub-objective of this thesis was to identify important knowledge gaps that need to be addressed to design more effective and economically attractive programs against Johne's disease. In the following section, several important knowledge gaps and areas of future research are discussed.

- *Effect and costs of improved calf hygiene management:*
  Over the last decade, considerable research in Johne's disease has focused on improving diagnostic tests and many different test-and-cull strategies have been developed and implemented. However, in general, these efforts have not yet yielded the results that were hoped for. Based on the results of the current study on the effects and economic consequences of a variety of control strategies, more research should focus on determining the effects of calf hygiene management on the prevalence of Johne's disease. In addition, better estimates of the costs of all of the strategies are needed in order to make better assessments of the economic attractiveness of the various strategies.

- *Epidemiology of Johne's disease within herds:*
  In the JohneSSim model, five separate transmission routes of Johne's disease within a herd were distinguished. The contribution of these routes to the overall spread of *Map* within a herd was partly based on field data and literature and partly on expert opinion. Although the modeling of all routes would benefit from better data, the route with the most uncertainty was the environmental route. More research is therefore needed on the survival of *Map* within the environment, the exposure of animals to *Map* and the age-dependent dose-response relationship. This, and research on shedding levels of animals < 2 years of age, would also provide useful insight into the possibility of horizontal transmission between young animals.

- *Effect of vaccination:*
  The true underlying mechanism of vaccination against Johne's disease is not well known. In the current study, a range of assumptions was made regarding the effects of vaccination on the disease dynamics. However, to better estimate the epidemiologic and economic effects of vaccination strategies, improved knowledge is needed regarding the underlying mechanism and efficacy of vaccines against Johne's disease.

- *How to change producers' behavior:*
  While in the past, Johne's disease control programs to a large extent depended on test-and-cull programs, future programs should focus more on improved calf hygiene. A difficulty with improved calf hygiene management strategies, however, is acquiring and maintaining the farmers' motivation to perform all the steps required to effectively reduce the prevalence of Johne's disease (Benedictus, 1984). Currently, in The Netherlands, an important focus of the new voluntary control program (PPN) will be on education and motivating producers to make critical management changes. In the U.S., the attempt to change the attitude and behavior of producers is an area that was given high priority by the National Research Council (Rideout et al., 2003) in a review of the diagnosis and control of Johne's disease. To date, there has been very low adoption of external and internal bio-security practices to control Johne's disease spread between and within farms. Although the failure to adopt internal bio-security measures is not limited to Johne's disease (also mastitis control measures are not adopted by a considerable proportion of producers), education to increase producer awareness about preventable losses of Johne's disease is considered an essential component of Johne's disease control. It is therefore very important to understand what incentives best motivate producers to make sufficient management changes to control Johne's disease.

- *Determine economic effects of Johne's disease control (not just losses):*
  As discussed in paragraph 7.2.2, many past research studies have tried to estimate the current losses caused by Johne's disease. However, these estimates alone are not useful to support decision-making regarding the control of Johne's disease. Instead, one needs to determine the reduction of the losses due to the control program and compare this to the costs of the program. Already in 1991, Schepers and Dijkhuizen criticized the practice of just considering the costs of disease and recommended that the focus should be on estimating the net benefits of control. This will not only be useful for policy-makers on a regional or national level, but also will provide valuable insight to producers who most likely only invest in Johne's disease control programs if they expect a sufficient (economic) return on their investment. Thus, especially in studies on Johne's disease, more focus must be put on determining the economic effects of control programs.

- *Determine economic effects of Johne's disease certification-and-monitoring programs:*
  To enter a voluntary Johne's disease certification-and-monitoring program, a producer will need sufficient incentives to do so. Although there may be additional incentives, the economic consequences will likely be an important consideration for a producer to enter a certification-and-monitoring scheme. However, very little research has been performed on the economic benefits of Johne's disease certification-and-monitoring programs. In one recent example, Wells (2004) showed that on a few Minnesotan dairy farms, the 'Johne's disease test-negative' status resulted in higher calf prices. These economic 'market-signals' could directly encourage producers to enter a certification-and-monitoring program resulting in a successful voluntary program. Better insight in the economic incentives from the producers' perspective is thus important.

- *Link between Johne's disease and Crohn's disease:*
  An obviously important question is if there really is a causal link between Johne's disease and Crohn's disease in humans. Out of all the issues considered within this study, the answer to this question (and what the public perception is about the answer), will mostly determine the goal and design of control programs against Johne's disease.

7.3.3 Decision-support

The main goal of this thesis was to support decision-making (i.e. support risk-management) by providing better insight into Johne's disease control and certification-and-monitoring programs. Results of this study greatly influenced the decision-making process during the development and improvement of Johne's disease control and certification-and-monitoring strategies, especially in the Netherlands. Two important considerations related to the decision-making process, which was supported by this study, are discussed below.

First, there was a clear difference between the acceptance and use of the results of this model study in The Netherlands and in the U.S. Chapter 4 describes in detail the crucial steps in the decision-making process towards a new collective program for Johne's disease in The Netherlands. The model's results caused a fundamental change in the design of the Dutch Johne's disease control program, from a focus on 'test-and-cull' to a focus on 'stepwise improvement of calf hygiene' strategies. This stepwise improvement now forms the basis of the new national voluntary Johne's disease control program for infected herds.

In contrast, in the U.S., the results of this study contributed to discussions about Johne's disease control, and only gradually caused more emphasis on calf management but no immediate changes in the design of the U.S. Johne's program were made. An important difference between the Dutch and the U.S. study was the level of cooperation between the researchers, the decision-makers and other stakeholders. In The Netherlands, this cooperation was much closer than in the U.S. In addition, regular meetings between the model researchers and Dutch decision-makers assured that the right questions were answered with the model to

optimally support decision-making. The closer cooperation in The Netherlands also resulted in a better understanding of the JohneSSim model and its assumptions. The resulting ownership of and involvement in the project by stakeholders and decision-makers was most likely one of the main reasons why the JohneSSim model had a greater influence in The Netherlands than in the U.S. This difference illustrates the great importance of cooperation and close interaction between model researchers and all stakeholders and decision-makers during the course of a risk analysis to increase the likelihood that the results will be used to support decision-making.

Second, while policy-makers need to make decisions on a national level, all benefits and costs in the economic analysis in this study were seen from the point of view of individual producers. This level of analysis was chosen because currently none of the economic benefits are on a more aggregate level and all costs of the program are paid by individual producers. The great variation between the economic results of individual farms shows that the costs and benefits of Johne's disease control programs are not evenly distributed among producers. A Dutch control program based on improved calf-hygiene management would only be economically attractive for a proportion of the herds (in general, the higher prevalence herds). Thus, in the current situation, only a voluntary control and certification program is considered feasible. This could change if, in the future, it becomes more likely that there are additional benefits of controlling Johne's disease (for example, if it becomes more likely that Johne's disease is in fact a zoonosis or when stricter trade restrictions are likely). In that situation, a collective national program against Johne's disease would likely become more attractive.

7.4 Main conclusions

The research described in the current thesis has helped decision makers in designing Johne's disease control strategies by increasing the understanding of the epidemiologic and economic consequences of different Johne's disease control and certification-and-monitoring programs. The following conclusions were drawn:

- Most losses of Johne's disease are caused by suboptimal culling of clinical and subclinical infected animals.
- Results from the JohneSSim model indicate that due to the low sensitivity of available tests of subclinical infected animals, test-and-cull strategies alone do not decrease the prevalence of Johne's disease and are economically unattractive.
- Control strategies based on separation of calves and adult animals are more effective than test-and-cull strategies in reducing the prevalence of Johne's disease and are economically more attractive.
- The Dutch Paratuberculosis Program Netherlands (PPN), based on stepwise improvement of calf hygiene, is, on average, economically attractive. However, for a proportion of the herds, the costs of control will be higher than the benefits.

- For an average infected midsize U.S. herd, a control strategy based on improved calf hygiene provides large economic benefits. In addition, the model results show contract heifer rearing to be a promising control strategy that does decrease the Johne's disease prevalence effectively and has great economic benefits.
- Within monitoring-and-certification schemes, it is better to speak about 'low-risk Johne's disease herds' than it is to speak about 'Johne's-free herds'.
- The epidemiologic and economic risk analysis approach used in this study proved to be a useful and flexible approach to gain better insight into the effects of Johne's disease control and to support decision-making.

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Summary

Introduction

Paratuberculosis or Johne's disease in cattle is a chronic, progressive intestinal disease caused by infection with *Mycobacterium avium* subspecies *paratuberculosis* (*Map*). Johne's disease is now a common disease in all countries with a significant dairy industry and causes great economic losses for milk producers. In recent decades, concerns have been raised about the apparent increase in the global prevalence of Johne's disease, the increasing economic losses and potential trade implications. In addition, Johne's disease has received increasing attention because of concern (not confirmed nor disproved) over the potential role of *Map* in some cases of Crohn's disease in humans. Both issues have caused an increasing need and demand for effective and economically attractive control strategies against Johne's disease.

The control of Johne's disease on dairy farms is difficult for a variety of reasons. First, the long subclinical phase often allows the infection to spread without occurrence of any clinical signs of illness. Also, although a range of diagnostic tests is available, they are often not sensitive enough to detect animals in the subclinical phase of the disease. Furthermore, the current vaccines have not yet shown to be effective enough to eradicate Johne's disease. Many different Johne's disease control programs in The Netherlands have been initiated during the last century, but all of the control programs were discontinued preliminary because of the lack of desired results.

In 1999, a project was started with the goal to prepare a national control program for paratuberculosis with the final aim of eradicating the disease. A scientific foundation of this new program was deemed essential as previous programs had not yielded the desired results. Therefore, a large research effort was initiated that included studies on test characteristics and improvement, prevalence estimates, monitoring and surveillance programs as well as on the development of two simulation models to aid the decision making process during the design and development of a Johne's disease control program. This thesis is the result of some of that effort and describes an epidemiologic and economic risk analysis which was performed with the aim to support the decision-making process in the design of more effective and economically attractive Johne's disease control and certification-and-monitoring programs in cattle in The Netherlands.

In the U.S., the study described in this thesis was not part of a large national organized 'preparation project' as in the Dutch situation described above. Instead, the evaluation of alternative Johne's disease control strategies was performed as there was a need for economically more attractive Johne's disease control strategies on dairy farms. Since mandatory control programs against Johne's disease were not considered politically feasible or desired, economic attractiveness from the producer's perspective is an important incentive for a

producer to invest in the control of Johne's disease. To our knowledge, no control strategy in the U.S. had ever been fully evaluated on its economic consequences.

The main objective of this thesis was to support decision-makers in the design and development of control and certification-and-monitoring programs for Johne's disease. To achieve this primary objective, the following sub-objectives were defined:

1. Development of a computer model that takes into account the latest field and literature knowledge and expert opinions on epidemiologic and economic attributes of Johne's disease and Johne's disease control;
2. Obtain insight in the economic and epidemiologic effects of potential Johne's disease control for suspected herds and certification-and-monitoring programs for unsuspected herds;
3. Identify important gaps in knowledge on Johne's disease that greatly impact the expected epidemiologic effectiveness and economic attractiveness of Johne's disease control programs.

Results and decision-support

To select the most effective and economically attractive control strategy, evaluation and quantification of the economic and epidemiologic effects of the current and alternative programs, are required. Field studies would however be time-consuming and expensive. Therefore an analytical approach was considered an appropriate tool to aid the decision-making process.

A simulation model, called the JohneSSim model, was developed and is described in Chapter 2. The JohneSSim model is a stochastic and dynamic simulation model that simulates the herd dynamics, the disease dynamics within the herd, the control of Johne's disease and the economic consequences at the herd-level. The model simulates all individual animals within a herd for a 20-year period with time-steps of 6 months. Animals in the model can be in six distinct infection-and-disease statuses, (1) susceptible, (2) non-susceptible, (3) latent-infected, (4) lowly infectious, (5) highly infectious and (6) clinical disease. In addition, five infection routes are considered, (1) intra-uterine infections, (2) infections occurring around birth, (3) infections due to drinking colostrum, (4) infections due to drinking whole milk, and (5) infections due to environment contamination with *Map*. Economic benefits of control programs were defined as the reduction in the economic losses due to Johne's disease and costs of control programs were considered diagnosis, management changes, vaccination and removal of test positive animals. The many probability distributions in the model require the model to be run repeatedly to provide insight into the variation in the outcomes at the farm level. Results at a more aggregate level (e.g. national level) were obtained by aggregating the results of certain herd profiles according to their relative abundance.

An important and often underestimated loss due to Johne's disease is the loss due to suboptimal culling of clinical and subclinical cows. While reduced milk production and

slaughter value during the presence of an infected cow on a farm is a clear loss, the suboptimal removal of animals due to an infection of Johne's disease is harder to observe and quantify. However, missing the future profits a producer could have expected from a particular cow can cause substantial losses. Chapter 3 describes an economic model that estimates these losses for the US study. In the Dutch study, results of a similar model were used with the main difference being that, in the Dutch situation, the effects of the milk-quotum were taken into account. The economic model described in chapter 3 can also be used as a stand-alone model to support optimal breeding and replacement decisions on dairy farms.

Chapter 4 describes in detail how results of the JohneSSim model aided in the development of a Johne's disease control program in The Netherlands. The decision-making process took place in three stages which coincided with the development of the JohneSSim model. The first stage mainly focused on 'test-and-cull' strategies. However, the results of this study indicated that eradication was not possible within 20-years using only 'test-and-cull' strategies and that none of the simulated strategies was economically attractive. In the second stage, control strategies for beef cow herds were evaluated and it was concluded that none of the strategies were able to reduce the prevalence to close to zero. In addition, no control programs were found to be economically attractive, effective and realistic under current field circumstances for Dutch beef farms.

Due to the results in the first two stages, policy-makers changed their focus to improvement of calf hygiene management strategies on dairy farms. A new program, called Paratuberculosis Program Netherlands (PPN), was designed and based on the stepwise implementation of management improvements. The results of the JohneSSim model showed that the program was found to be able to reduce the prevalence to close to zero if all calf management tools were applied. In addition, PPN was found to be economically attractive with an average net present value per farm of respectively Euro 1183 and 12,397 if labor costs were included or excluded.

While chapter 4 focused on control strategies for infected Dutch dairy herds, Chapter 5 describes the evaluation of different Johne's disease certification-and-monitoring programs for unsuspected herds. The Dutch certification-and-monitoring scheme that was used at the time of the study was compared with eleven alternative schemes in which different tests were used along with varying test frequency, tested age group and number of tested animals. Two important observations were made. First, upon reaching the 'Johne's disease free' status with the current program, 11% of the simulated herds were estimated to still be infected. Therefore, it was concluded that the designation 'Johne's disease free' should be changed to, for example, 'low-risk Johne's disease'. Secondly, only one alternative certification scheme (four herd examinations at 2-year intervals, consisting of serial testing of all cattle $\geq$ 2 years of age with a pooled fecal culture and individual fecal culture of positive tests) yielded lower discounted costs and a lower animal-level prevalence at the time of reaching the 'low-risk Johne's disease' status. None of the testing schemes to monitor the 'low-risk Johne's disease' status resulted in both a lower animal-level prevalence of undetected pre-existing Map infections and lower median annual discounted costs.

Chapter 6 describes in detail the adaptation to the JohneSSim for evaluation of Johne's disease control programs on mid-sized dairy farms in the U.S. Also in the U.S., 'test-and-cull' programs were unable to reduce the average true prevalence on infected herds, and were economically unattractive. A low prevalence was however reached with control strategies based on separation of calves and adult animals. Contract heifer rearing in which calves are raised off-farm in specialized heifer raising facilities also appeared to be an effective strategy in reducing the Johne's disease prevalence. The last two strategies also had large economic benefits assuming that no extra losses due to introduction of other diseases would occur because of the contract heifer rearing.

Discussion and conclusions

Chapter 7 is a general discussion of some important steps in the development of the JohneSSim model and the decision-support this study provided in the design of Johne's disease control and monitoring-and-certification programs. It was concluded that the stochastic simulation model used in this risk analysis proved to be a useful and flexible manner to get better insight into the effects of Johne's disease control. To support decision-making regarding Johne's disease control, it is furthermore important to simultaneously consider the epidemiologic and economic consequences. Also, economic assessments of Johne's disease should focus on determining the benefits and costs of control programs, and not only on the estimate of the current losses. Chapter 7 furthermore gives recommendations for additional research on (1) the epidemiologic effects of calf hygiene and vaccination strategies, (2) ways to change farmers' behavior to control Johne's disease, (3) the economic costs and benefits (not just current losses) of Johne's disease control programs and (4) the possible link between Johne's disease and Crohn's disease in humans.

Based on the research described within this thesis, the following conclusions can be drawn:

- Most losses of Johne's disease are caused by suboptimal culling of clinical and subclinical infected animals.
- Results from the JohneSSim model indicate that, due to the low sensitivity of available tests of subclinical infected animals, test-and-cull strategies alone do not decrease the prevalence of Johne's disease and are economically unattractive.
- Control strategies based on separation of calves and adult animals are more effective than test-and-cull strategies in reducing the prevalence of Johne's disease and are economically more attractive.
- The Dutch Paratuberculosis Program Netherlands (PPN), based on stepwise improvement of calf hygiene, is, on average, economically attractive. However, for a proportion of the herds, the costs of control will be higher than the benefits.
- For an average infected midsize U.S. herd, a control strategy based on improved calf hygiene provides large economic benefits. In addition, the model results show contract

heifer rearing to be a promising control strategy that does decrease the Johne's disease prevalence effectively and has great economic benefits.

- Within monitoring-and-certification schemes, it is better to speak about 'low-risk Johne's disease herds' than it is to speak about 'Johne's-free herds'.
- The epidemiologic and economic risk analysis approach used in this study proved to be a useful and flexible approach to gain better insight into the effects of Johne's disease control and to support decision-making.

Samenvatting

Inleiding

Paratuberculose (ook wel paratbc of de ziekte van Johne) bij rundvee is een chronische besmettelijke darmontsteking veroorzaakt door *Mycobacterium avium* subspecies *paratuberculosis* (*Map*). Paratuberculose binnen de melkveehouderij komt wereldwijd voor (met uitzondering van Zweden) en veroorzaakt grote schade vanwege een lagere melkproductie en het vermageren van geïnfecteerde dieren. Er bestaat een vermoeden dat in de afgelopen decenia de wereldwijde prevalentie en economische schade van paratuberculosis is toegenomen. Ook zou paratuberculose in de toekomst mogelijk voor handelsbeperkingen kunnen zorgen. Daarnaast is er een mogelijk (maar niet bewezen) causaal verband tussen paratuberculose in runderen en de ziekte van Crohn bij de mens. Al deze ontwikkelingen hebben geleid tot een grotere interesse naar effectieve en economisch aantrekkelijke bestrijdings-, certificerings- en bewakingsprogramma's voor paratuberculose bij rundvee.

De bestrijding van paratuberculosis is niet gemakkelijk vanwege een aantal redenen. Ten eerste wordt paratuberculose gekenmerkt door een erg lange incubatietijd waardoor *Map* zich kan verspreiden voordat enige klinische verschijnselen van paratuberculose optreden. Verder zijn de huidige testen veelal niet gevoelig genoeg om geïnfecteerde dieren in de subklinische fase te indentificeren. Tevens lijkt vaccinatie niet effectief genoeg voor eradicatie van paratuberculose. Gedurende de afgelopen eeuw zijn er in Nederland een groot aantal verschillende bestrijdingsprogramma's tegen paratuberculose ontwikkeld en gestart. Al deze programma's zijn wegens gebrek aan gewenste resultaten voortijdig gestopt. In 1999 werd een project opgestart om een bestrijdingsprogramma te ontwikkelen met als uiteindelijke doel de eradicatie van paratuberculose. Een wetenschappelijke onderbouwing van dit nieuwe programma werd noodzakelijk geacht. Om deze reden werd een groot nationaal onderzoeksproject gestart met studies naar de karateristieken en mogelijke verbeteringen van diagnostische testen, de schatting van de prevalentie en het huidige management van kalveren. Ter ondersteuning van het nationale beleid inzake de bestrijding, certificering en bewaking van paratuberculose werden tevens twee computer modellen ontwikkeld. Dit proefschrift beschrijft één van deze twee modellen. Het model beschreven in dit proefschrift is gericht op de verspreiding van paratuberculose binnen bedrijven terwijl het andere model gericht is op de verspreiding van paratuberculose tussen bedrijven.

In Amerika is deze studie geen onderdeel van een groot nationaal onderzoeksproject zoals in Nederland. Het voornaamste doel van de simulatiestudie in Amerika is het identificeren van economisch aantrekkelijke bestrijdingsprogramma's. Juist voor vrijwillige bestrijdingsprogramma's zijn de bedrijfseconomische gevolgen van groot belang voor veehouders in de overweging om te investeren in het programma of niet. Zover bekend heeft

men in Amerika echter nog nooit de economische gevolgen van paratuberculose bestrijdingprogramma's geëvalueerd.

De hoofddoelstelling van dit onderzoek was 'de ondersteuning van het besluitvormingsproces van beleidsmakers inzake de bestrijding, certificering en bewaking van paratuberculose'. Om dit doel te bereiken, werden de volgende subdoelstellingen geformuleerd:

1. Ontwikkeling van een simulatiemodel, gebaseerd op de meest recente veld- en literatuurgegevens en kennis van deskundigen, omtrent epidemiologische en economische gevolgen van paratuberculose en paratuberculosebestrijding;
2. Verkrijgen van beter inzicht in de epidemiologische en economische gevolgen van mogelijke bestrijdingsprogramma's voor verdachte bedrijven en certificering- en bewakingsprogramma's voor onverdachte bedrijven;
3. Identificeren van belangrijke onzekerheden die van grote invloed zijn op de verwachte epidemiologische en economische gevolgen van paratuberculose programma's.

Resultaten en beslissingsondersteuning

Om het meest effectieve en aantrekkelijke bestrijdingsprogramma voor paratuberculose te kunnen selecteren, dient het huidige programma en verschillende alternatieve programma's te worden geëvalueerd. Veldonderzoek zou echter erg veel tijd en geld kosten. De ontwikkeling en het gebruik van simulatiemodellen is een goede manier om economische en epidemiologische kennis te combineren ter ondersteuning van beslissingen omtrent de bestrijding van dierziekten.

Een stochastisch en dynamisch computer simulatiemodel, genaamd JohneSSim, is ontwikkeld om de verspreiding en bestrijding van paratuberculose te simuleren, inclusief de economische gevolgend voor de veehouder, over een periode van 20 jaar (Hoofdstuk 2). In het model worden alle dieren op het bedrijf individueel gesimuleerd, met tijdstappen van 6 maanden. Bij elke tijdstap wordt van elk dier het infectiestadium (gevoelig, ongevoelig, latent geïnfecteerd, laag infectieus, hoog infectieus of klinisch ziek) bepaald. De verspreiding van paratuberculose binnen de veestapel wordt gesimuleerd met vijf verschillende infectie-routes; (1) intra-uterine infecties, (2) infecties rondom afkalven, (3) infecties veroorzaakt door het drinken van biest, (4) infecties veroorzaakt door het drinken van rauwe melk en (5) infecties door contact van jongvee met besmette mest. De economische baten van een bestrijdingsprogramma zijn gedefinieerd als de vermindering van de economische schade als gevolg van paratuberculose. Deze baten werden vervolgens vergeleken met de kosten van het programma, zoals de kosten van het testen, het verbeterde management, de vaccinaties en het afvoeren van test-positieve dieren. In het model wordt door loting de uitkomst bepaald van onzekere gebeurtenissen, zoals het optreden van infecties. Om een goed inzicht te krijgen in de variatie van de uitkomsten op bedrijfsniveau is het model een groot aantal keren gesimuleerd.

Een belangrijke schadepost van paratuberculose is suboptimale afvoer van subklinisch en klinisch geïnfecteerde dieren. In tegenstelling tot de schade veroorzaakt door een lagere melkproduktie of door vermagering van geïnfecteerde dieren, is de schade door een

suboptimale afvoer vaak moeilijker te zien en te kwantificeren en wordt zodoende vaak onderschat. Hoofdstuk 3 beschrijft een economisch model dat is gebruikt in de amerikaanse studie (hoofdstuk 6) voor het kwantificeren van de schade die wordt veroorzaakt door suboptimale afvoer vanwege besmetting met paratuberculose. Voor het berekenen van de schade door suboptimale afvoer op Nederlandse melkveebedrijven zijn uitkomsten van een soortgelijk model gebruikt met als verschil dat in de Nederlandse situatie rekening is gehouden met de economische effecten van het melkquotum. Het in hoofdstuk 3 beschreven economisch model kan verder ook worden gebruikt om afvoer- en inseminatiebeslissingen op melkveebedrijven te ondersteunen.

Hoofdstuk 4 beschrijft in detail hoe de resultaten van het JohneSSim model hebben geholpen tijdens de ontwikkeling van, en besluitsvorming omtrent, een bestrijdingsprogramma voor paratuberculose in Nederland. Drie fases kunnen worden onderscheiden in de besluitsvorming en de ontwikkeling van het JohneSSim model in Nederland. De eerste fase was voornamelijk gericht op test-en-afvoer strategieën. De resultaten van deze studie gaven echter aan dat eradicatie van paratuberculose met deze strategieën niet mogelijk was en dat geen van deze strategieën gemiddeld economisch aantrekkelijk was. In de tweede fase van de studie werden bestrijdingsstrategieën voor vleesveebedrijven geëvalueerd. Er werden geen bestrijdingsstrategieën gevonden die de prevalentie van paratuberculose voldoende zouden reduceren en tevens economisch haalbaar zouden zijn onder de huidige omstandigheden op vleesveebedrijven in Nederland. Gebaseerd op de uitkomsten van de eerste en tweede fase, richtten de beleidsmakers zich in de derde fase van het onderzoek in Nederland op preventieve managementmaatregelen op melkveebedrijven. Een nieuw bestrijdingsprogramma, voornamelijk gebaseerd op stapsgewijze implementatie van preventieve managementmaatregelen, Paratuberculose Programma Nederland (PPN), werd ontwikkeld en geëvalueerd met het JohneSSim model. De resultaten gaven aan dat PPN in staat was de prevalentie sterk te reduceren. Tevens bleek PPN gemiddeld economisch aantrekkelijk te zijn met een gemiddelde economisch voordeel per melkveebedrijf van €1.183 of €12.397 met of zonder toerekening van extra arbeidskosten.

Hoofdstuk 5 beschrijft de evaluatie van verschillende certificering- en bewakingsprogramma's voor onverdachte bedrijven. Het Nederlandse certificering- en bewakingsprogramma dat werd gebruikt op het moment van deze studie, werd vergeleken met elf alternatieve programma's. Er werden drie belangrijke resultaten gevonden. Ten eerste gaven de resultaten aan dat 11% van de bedrijven die de hoogste 'onverdacht status' in het *certificerings*programma bereikten, in werkelijkheid toch nog geïnfecteerd waren. Hieruit werd geconcludeerd dat de naam 'paratuberculose vrij' veranderd moet worden naar bijvoorbeeld 'paratuberculose laag risico'. Ten tweede leidde slechts één alternatief *certificerings*programma (tweejaarlijkse gepoolde faeceskweek van alle runderen ≥2 jaar) tot een lagere prevalentie op dierniveau bij het bereiken van de hoogste onverdacht status (status 1) en lagere totale verdisconteerde kosten dan het huidige programma. Ten derde resulteerde geen van de

alternatieve *bewakings*programma's in een lagere prevalentie van paratuberculose gecombineerd met lagere jaarlijkse kosten.

In hoofdstuk 6 wordt de aanpassing van het JohneSSim model beschreven voor paratuberculose bestrijdingsprogramma's op middelgrote amerikaanse melkveebedrijven. Ook in Amerika bleken test-en-afvoer strategieën niet in staat om de prevalentie van paratuberculose voldoende te reduceren. Bovendien waren test-en-afvoer programma's gemiddeld economisch onaantrekkelijk. Strategieën gebaseerd op preventief management resulteerden wel in een lagere prevalentie en economische baten. Voorts bleek de opfok van jongvee op gespecialiseerde jongvee-opfokbedrijven een mogelijk aantrekkelijke optie voor de bestrijding van paratuberculose.

Discussie en conclusies

In hoofdstuk 7 worden een aantal belangrijke aspecten besproken omtrent de ontwikkeling en toepassing van het JohneSSim model. Geconcludeerd werd dat het stochastische simulatie model een nuttige en flexibele manier was om een beter inzicht te krijgen in de gevolgen van de bestrijding van paratuberculose. Het werd tevens van belang geacht dat de epidemiologische en economische gevolgen van de bestrijding van paratuberculose tegelijk en niet apart worden bepaald. Ook werd nadruk gelegd op het belang van economische evaluaties van paratuberculose bestrijdingsprogramma's. Veder geeft Hoofdstruk 7 aanbevelingen voor aanvullend onderzoek naar (1) de epidemiologische effecten van preventief management en vaccinatie, (2) methoden op veehouders gemotiveerd te houden om preventief management toe te passen, (3) de economische kosten en baten van paratuberculose bestrijding (en niet alleen de huidige schade) en (4) het mogelijke verband tussen paratuberculose bij rundvee en de ziekte van Crohn bij de mens.

Gebaseerd op de model-resultaten in dit proefschrift kunnen de volgende conclusies worden getrokken:

- De meeste van de schade door paratuberculose wordt veroorzaakt door suboptimale afvoer van klinisch en subklinisch geïnfecteerde dieren;
- Vanwege de lage gevoeligheid van de momenteel beschikbare diagnostische testen voor subklinisch geïnfecteerde dieren zijn test-en-afvoer strategieën niet in staat de prevalentie van paratuberculose voldoende te reduceren en bovendien zijn deze strategieën economisch niet aantrekkelijk;
- Bestrijdingsstrategieën gebaseerd op scheiding van jongvee en rundvee ≥2 jaar zijn effectiever dan test-en-afvoer strategieën voor de reductie van de prevalentie en schade van paratuberculose;
- Het nieuwe Paratuberculose Programma Nederland (PPN), dat gebaseerd is op stapsgewijze verbetering van jongvee-management ter bestrijding van paratuberculose, is gemiddeld economisch aantrekkelijk voor melkveebedrijven. Voor een deel van de bedrijven zullen de kosten echter groter zijn dan de baten;

- Voor een gemiddeld geïnfecteerd middelgroot amerikaans melkveebedrijf resulteren bestrijdingsstrategieën gebaseerd op scheiding van jongvee en rundvee ≥2 jaar in grote economische baten. Tevens is opfok van jongvee op gespecialiseerde jongvee opfokbedrijven een mogelijk aantrekkelijke optie voor de bestrijding van paratuberculose;
- Binnen certificerings- en bewakingsprogramma's voor paratuberculose is het beter te spreken van 'paratuberculose laag risico bedrijven', dan van 'paratuberculose vrije bedrijven';
- De beschreven epidemiologische en economische risico-analyse bleek een nuttige en flexibele manier om beter inzicht te verkrijgen in de gevolgen van verschillende bestrijdings-, certificerings- en bewakingsprogramma voor paratuberculose. Deze studie heeft een belangrijke rol gespeeld bij de ondersteuning van beleidsontwikkeling aangaande de bestrijding van paratuberculose in Nederland en Amerika.

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Curriculum vitae

Huybert Groenendaal was born on September 29, 1975 in Amstelveen, The Netherlands. In 1993 he received his secondary high school degree from the Hermann Wesselink College in Amstelveen and started his MSc study Animal Science at the Wageningen Agricultural University (now Wageningen University). During his time at Wageningen, he performed a study and wrote a thesis on the efficacy of Tilmicosin against respiratory diseases in veal calves and a study on the economic consequences of the control of Bovine Virus Diarrhea (BVD) virus in dairy. During his practical period in Uppsala, Sweden (1997), he studied the performance of a diagnostic test to find dairy cows pregnant with a persistently infected BVD fetus. In 1998, he graduated with a specialization in Animal Husbandry and started a research project on the epidemiologic and economic consequences of Johne's disease control in dairy cows at the Farm Management group at Wageningen University. This, three additional projects and 1.5 years of work at the Center of Animal Health and Productivity at the University of Pennsylvania, resulted in this thesis. An intermediate two-year study at the Wharton School of Business, University of Pennsylvania, resulted in a Masters of Business Administration (MBA) with specialization in Corporate Finance in 2003. Also in 2003, Huybert founded Vose Consulting US LLC together with David Vose, and currently works as a risk analysis consultant and trainer to help clients make informed, justifiable and realistic decisions in the face of uncertainty.

Curriculum vitae

Huybert Groenendaal werd op 29 September 1975 geboren in Amstelveen. In 1993 behaalde hij zijn VWO diploma aan het Hermann Wesselink College in Amstelveen. In hetzelfde jaar begon hij met de studie Zoőtechniek aan de Landbouwuniversiteit Wageningen (tegenwoordig Wageningen Universiteit). Tijdens de studie deed hij een afstudeervak Epidemiologie over de efficacy van Tilmicosin tegen luchtweg aandoeningen in vleeskalveren, een afstudeervak Economie over de economische gevolgen van bestrijding van Bovine Virus Diaree (BVD) virus in melkvee en een stageopdracht over een test voor het identificeren van koeien drachtig met een persistent geïnfecteerde BVD foetus. In 1998 studeerde hij af in de richting Veehouderij en trad hij in dienst als toegevoegd onderzoeker bij de vakgroup Agrarische bedrijfseconomie en begon aan een project naar de epidemiologisch en economisch consequenties van paratuberculose bestrijding op melkveebedrijven in Nederland. Dit, een drietal vervolg projecten en ruim anderhalf jaar werk aan het Center of Animal Health and Productivity van de Universiteit van Pennsylvania, resulteerde in dit proefschrift. Een tussentijdse tweejarige studie aan de Wharton School of Business, Universiteit van Pennsylvania, resulteerde in 2003 in een Masters of Business Administration (MBA) met een specialisatie in bedrijfsfinancieën. Tevens richtte Huybert samen met David Vose in 2003 Vose Consulting US LLC op. Huybert werkt momenteel als een adviseur en trainer in risico analyse en helpt klanten met het maken van onderbouwde, verdedigbare en realistische beslissingen in onzekere situaties.

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