THREE ESSAYS ON THE ECONOMICS OF DAIRY NUTRITION AND DISEASE CONTROL

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This dissertation consists of three essays on the economics of dairy nutrition and disease control, in particular, productivity and profitability associated with the dairy industry. The first essay examines the effect of a dairy feed supplement on milk production and profitability of dairy operations. The second essay develops a conceptual model for examining infectious disease control in livestock using *Mycobacterium avium* ssp. *paratuberculosis* (MAP) and Johne's disease (JD) control in dairy herds as an example. The third essay looks into the economic and epidemiological consequences of current and next generation vaccines for MAP and JD in dairy herds.

Chapter 1 examines the profitability of rumen-protected methionine (RPMet) supplement on milk protein production. The additional daily profit per cow potentially earned by adding various amounts of RPMet supplement to the diet of lactating cows is analyzed and reported. The optimal amount of RPMet reported to maximize daily profit per cow is compared to the RPMet required to maximize milk protein production. These optimal quantities are very similar given current prices for RPMet and milk protein.

Chapter 2 presents a conceptual framework for evaluating the economics of infectious disease control for livestock. An animal compartment model is used to develop a conceptual model that incorporates the complexity inherent in disease-specific epidemiology in livestock. This conceptual model is empirically applied with a discrete optimal control model maximizing

net present value to evaluate the economic and epidemiological consequences of various control strategies for MAP, the pathogen causing Johne's disease in dairy herds.

Chapter 3 investigates the epidemiological impacts and economic values of hypothetical MAP vaccines in dairy herds. Scenarios for the potential epidemiological impacts of MAP vaccines are created, and then economically justifiable values are estimated at which they would be cost-effective to dairy producers. The estimated economic values of MAP vaccines suggest that some vaccinations can be an economically attractive method of MAP control for dairy producers.

BIOGRAPHICAL SKETCH

Jaesung Cho was born in South Korea on September 27, 1977. He has studied livestock management and applied economics at various institutions worldwide, first at Konkuk University in Seoul, South Korea, from 1996-7, where he was awarded several scholarships. After completing 26 months of compulsory military service in South Korea, he attended IPC Barneveld in the Netherlands for one year (2000-2001) to attain technical skills and practical knowledge integral to animal production. While at IPC he completed two programs, pig husbandry and animal feed training, in which he conducted two pilot projects: creating plans for the establishment of a small feed mill, and increasing profits for a medium-scale pig farm. From August 2002 to May 2003, he attended the University of Illinois at Urbana-Champaign as an exchange student in order to study the American agricultural market system. This educational experience encouraged him to further his studies in the U.S. After he graduated from Konkuk University with a bachelor's degree in livestock management in 2003, he entered Cornell University as a M.S. student in Applied Economics. There he focused his M.S. studies on quantitative methods and economic theory especially as related to farm management, production economics, and the dairy industry. He completed his M.S. program in 2007, and joined the Ph.D. program at the Charles H. Dyson School of Applied Economics and Management, Cornell University. His Ph.D. research has comprised a multidisciplinary investigation into animal diseases, production economics, technical efficiency, farm management and agribusiness. His recent research is focused on the impact of domestic animal disease on the livestock industry via a cost and benefit analysis of disease control methods based on the dynamics of pathogens and an animal movement model.

I dedicate this dissertation to my family. Without my parents' undying support and sacrifice, it would not have been possible for me to complete my studies at Cornell University. Especially, I must thank my loving wife, Ina, who has remained patiently and proudly by my side throughout these many years of research.

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Though only my name appears on the cover of this dissertation, I could not have completed it without the support of a great many people. I would like to thank them all for their contributions, in particular, my committee members, Professor Loren W. Tauer, Professor Ynte H. Schukken, and Professor Miguel I. Gomez. It was their invaluable support which has ultimately led me to the completion of my Ph.D. study and this dissertation.

First of all, my deepest and sincerest thanks go to my advisor, Professor Loren W. Tauer. Without his sage guidance, understanding, patience, and support throughout every stage of my studies at Cornell University, I could not have completed this dissertation and my Ph.D. studies. There are simply too many things to thank him for. It is almost unnecessary to mention his academic excellence as a scholar, advisor, and mentor since this is unquestionably obvious to anyone who has worked with him. I do need to point out, however, that he is the one person who has most profoundly contributed to the last five years of my life and the one who opened up for me the path for my future. I am sincerely honored to have had the opportunity to have worked with him at Cornell University.

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insight. Professor Miguel I. Gomez's excellent knowledge and indispensable advice regarding economic value assessment allowed me to effectively conduct my research on economic valuation of potential vaccines in Johne's disease control. Although he only recently joined my committee, his enthusiastic efforts and support for my research allowed me to complete my Ph.D. program earlier than expected.

I would also like to thank to Professor Yjro T. Grohn, who allowed me to join his excellent team in the Johne's disease control program. This opportunity provided me the impetus to start this dissertation and all of the team members have made important contributions to this dissertation in many aspects.

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CHAPTER 1

AN OPTIMAL APPLICATION OF RUMEN-PROTECTED METHIONINE SUPPLEMENT FOR MAXIMIZING MILK PROTEIN PRODUCTION AND PROFIT IN DAIRY HERDS

Abstract

The profitability of feeding rumen-protected Met (RPMet) sources to produce milk protein is estimated using a two-step procedure: First, the effect of Met in metabolizable protein (MP) on milk protein production is estimated by using a quadratic Box-Cox functional form. Then, utilizing these estimation results, the amounts of RPMet supplement that corresponds to the optimal levels of Met in MP for maximizing milk protein production and profit on dairy farms are determined.

The data used in this study are modified from data used to determine the optimal level of Met in MP for lactating cows in the National Research Council publication *Nutrient Requirements of Dairy Cattle* (NRC, 2001). The data used in this study differ from that in the NRC (2001) in two ways. First, as dairy feed generally contains 1.80-1.90% Met in MP, this study adjusts the reference production value (RPV) from 2.06 to 1.80 or 1.90%. Consequently, the milk protein production response is also modified to a RPV of 1.80 or 1.90% Met in MP. Second, as this study is especially interested in how much additional Met, beyond the 1.80 or 1.90% already contained in the basal diet is required to maximize farm profits, the data used are limited to concentrations of Met in MP above 1.80 or 1.90%. This allowed us to calculate any additional cost to farmers based solely on the price of an RPMet supplement, and eliminates the need to estimate the dollar value of each gram of Met already contained in the basal diet.

Results indicate that the optimal level of Met in MP for maximizing milk protein production is 2.40 percent and 2.42%, where the RPV is 1.80 and 1.90%, respectively. These optimal levels are almost identical to the recommended level of Met in MP of 2.40% in the NRC (2001). The amounts of RPMet required to increase the percentage of Met in MP from each RPV to the 2.40 and 2.42% are 21.6 and 18.5 g/d, respectively. On the other hand, the optimal level of Met in MP for maximizing profit is 2.32 and 2.34%, respectively. The amounts of RPMet required to increase the percentage of Met in MP from each RPV to the 2.32 and 2.34% are 18.7 and 15.6 g/d, respectively. In each case, the additional daily profit per cow is estimated to be $0.38 and $0.29. These additional profit estimates are $0.02 higher than the additional profit estimates for maximizing milk protein production.

Introduction

Dairy farmers in New York State (NYS) and most regions of the U.S. presently receive payment for their milk under the Federal Milk Marketing Order multiple-component pricing system. Payment is based on the quantities of milk components such as butterfat, protein, and other solids. Of these components, milk protein is the most valuable for dairy farmers. Its price is the highest of all other milk components, having significantly increased over the last seven years (Figure 1.1). This has led to great interest among dairy farmers in increasing milk protein production in order to increase profits.

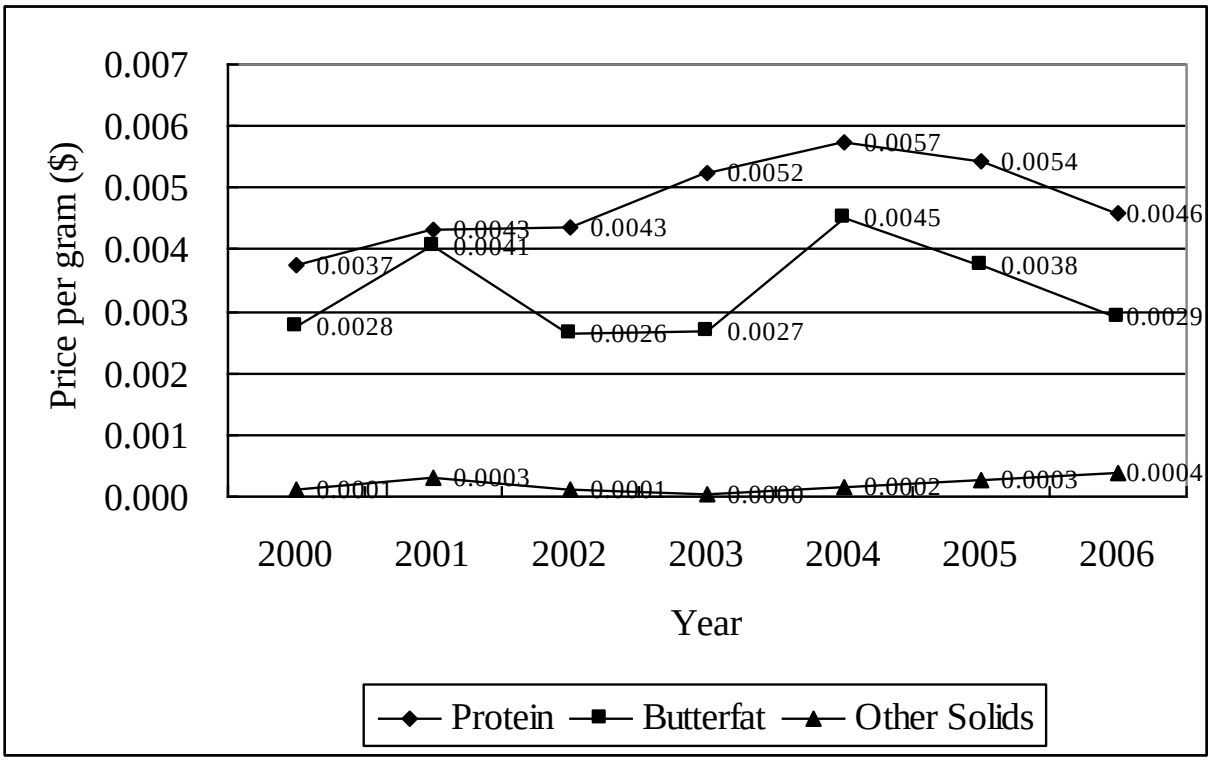

Figure 1.1. Average producer prices for milk components over the last seven years (2000-2006) based on the producer component price data provided by the northeast marketing area of agricultural marketing service, U.S. Department of Agriculture

There are several possible ways to increase milk protein production. These include genetic improvement (Gibson, 1989; McAllister et al., 1990; Hansen et al., 2002), switching breeds (Elbehri et al., 1994; Bailey et al., 2005), and modifying the diets of lactating dairy cows. As genetic improvement of cows is a lengthy and difficult process for individual farmers, and switching breeds is expensive, increasing milk protein output through dietary means is the most

practical short-term option. Of the various ways to do this, balancing amino acids (AA) in the dairy cows' diet is the most convenient way to enhance milk protein production because it can be simply accomplished by providing additional AA supplements to cows.

Of the essential AA in lactating dairy cows, Lysine (Lys) and Methionine (Met) are the two most limiting for the synthesis of milk and milk protein (Schwab et al., 1976), and Lys and Met are often deficient in diets fed to lactating dairy cattle. Thus, several studies summarized in the National Research Council publication *Nutrient Requirements of Dairy Cattle* (NRC, 2001) have examined the relationship between post-ruminal supply of Lys or Met and milk protein production, and found that increasing the post-ruminal supply of Lys or Met increases milk protein production (NRC, 2001). Although the different effect of Lys or Met on milk production reported in several studies depends on the differences in the status of Lys, Met, other AA, genetic traits, or the lactation status of the cows, many studies also reported that providing a dietary supplement of rumen-protected Lys (RPLys) or rumen-protected Met (RPMet) increases milk protein production (NRC, 2001; Misciattelli et al., 2003; Socha et al., 2005; Rulquin et al., 2006). This increase is mainly accomplished by increasing casein in milk, the main ingredient of cheese (Donkin et al., 1989; Chow et al., 1990; Armentano et al., 1993). Thus, increasing milk

protein production by adding an RPMet supplement to the diet of lactating cows is beneficial for not only dairy farmers but also cheese manufacturers.

According to the NRC (2001), the estimated optimal level of concentration of Lys and Met in metabolizable protein (MP) for the combined functions of maintenance and milk protein production is approximately 7.2 and 2.4%, respectively. However, typical dairy lactating feed in NYS contains > 6.65 percent Lys and 1.8-1.9 percent Met, more than 92% of the Lys levels but only 75%-79% of the Met levels suggested by the NRC (2001). Thus, dairy farmers may be able to increase milk protein production simply by adding an RPMet supplement to the diet of lactating cows. However, dairy farmers are reluctant to do this because there are presently no studies available on the economic benefits associated with providing this supplement. Therefore, this study examines the profitability of RPMet supplement on milk protein production using the following two-step procedure: First, the effect of Met in MP on milk protein production is estimated using a quadratic Box-Cox functional form (QBC). Then, utilizing these estimation results, the amounts of RPMet supplement which correspond to the optimal levels of Met in MP for maximizing milk protein production and profit on dairy farms are determined.

Materials and methods

Quadratic Box-Cox functional form

The choice of functional form is not a trivial task in applied economic data analysis. Although there are some popular forms, such as translog, quadratic, and Cobb-Douglas, which are frequently used in production analyses, there is no straightforward statistical test to determine which functional form is superior. Thus, in many cases, researchers choose a functional form according to their research purposes and statistical limitations imposed by their data.

Because this research entails a single-output and single-input production relationship, the Box-Cox transformation (Box and Cox, 1964) with a quadratic functional form is particularly useful to determine the most appropriate functional form. There are several reasons for this. First, the Box-Cox transformation requires no prior restrictions on estimating such a production relationship, so the estimated value of the transformation parameters describes the functional form that best fits the data. Second, this transformation results in less heteroscedastic residuals than those from the untransformed data (Box and Cox, 1964). Third, the QBC incorporates first-order and second-order effects of an input on output. Thus, the QBC has great flexibility. Finally, the QBC contains several traditional functions such as quadratic, translog, and inverse quadratic as special embedded parametric cases, and the validity of these functions can be tested by the likelihood ratio test. This reduces the effort in selecting the underlying functional form for a

given set of data. Thus, this study utilized the following QBC to estimate the relationship between the percentage of milk protein and Met in MP.

The QBC used in this study can be expressed as:

$$y_i^{(\lambda)} = \beta_0 + \beta_1 x_i^{(\lambda)} + \beta_2 x_i^{(\lambda)} x_i^{(\lambda)} + \varepsilon_i \quad (1.1)$$

where the subscript *i* indexes individual observation, y_i is the milk protein content response[1], x_i is the percentage of Met in MP, β_0, β_1, and β_2 are parameters to be estimated, λ is the Box-Cox transformation parameter to be estimated, and ε_i is the residual which is assumed to be normally distributed with zero mean and constant variance σ^2. The term $y_i^{(\lambda)}$ is the Box-Cox transformation $(y_i^{\lambda} - 1)/\lambda$, and $x_i^{(\lambda)}$ is the Box-Cox transformation $(x_i^{\lambda} - 1)/\lambda$, which are transformed with the common parameter λ that can assume any value. Specifically, when the estimated value of λ approaches one, Equation (1.1) is reduced to the quadratic function, when λ approaches zero, Equation (1.1) is reduced to the translog function, and when λ approaches minus one, Equation (1.1) is reduced to the quadratic function with inverse specification.

In this study, the amount of feed consumed by each treatment group varied from experiment to experiment. Thus, if the selected dependent and independent variables in the QBC are those expressed on a quantity basis (g/d), the estimation result of the effect of Met in MP on

[1] Production response expressed as a percentage at each level of Met in MP relative to a reference production value.

milk production will be over estimated. Therefore, this study measured the response effect using variables expressed as percentage of milk protein, and the percentage of Met in MP, as was done in the NRC (2001). This specification minimizes the effects of other nutritional factors on milk protein production caused by the different level of feed consumption in each experiment.

The transformation parameter λ in the QBC was estimated by the maximum likelihood estimation technique using the computer software STATA because the QBC is non-linear in its parameters. However, in the presence of heteroscedastic residuals, estimating the Box-Cox regression model can generate misleading results (Seaks and Layson, 1983; Blaylock and Smallwood, 1985). Due to the complexity of the maximum likelihood estimation technique for estimating the Box-Cox-type models, the majority of empirical analyses employing this estimation technique did not test significantly for heteroscedasticity, and the majority of statistical software programs also do not provide any test for identifying such an econometric problem. Therefore, in this study, the QCB was re-estimated by the ordinary least square estimator after modifying the data with the estimated parameter λ in order to test heteroscedasticity by the Breusch-Pagan test.

If heteroscedasticity exists, the models should be either modified as the QBC with a Just-Pope risk specification in a mean-variance framework (Just and Pope, 1978), or re-estimated by

using alternative estimation techniques such as the Box-Cox with a weighted-least-squares correction for heteroscedasticity (Seaks and Layson, 1983). A Just-Pope specification would be especially useful since it allows formulating the heteroscedastic residuals as an inherent risk in the production function.

Optimal RPMet application

When a single-output and single-input are measured on a quantity basis such as grams per day, and output is represented as a continuously differentiable function of input, the producer's strategy for maximizing profit is simply a matter of choosing the appropriate input level. If such a function is concave, the optimal level of input is determined to be the point at which the marginal product of input equals the ratio of a given input price and output price. However, this producer's strategy for maximizing profit described above cannot be directly applied to this study because the selected output and input in Equation (1.1) are expressed as percentages. Therefore, this study used a different profit maximization method to determine the optimal application levels of RPMet supplement corresponding to the optimal levels of Met in MP for maximizing milk protein production and profit on dairy farms.

The first derivative of the quadratic Box-Cox functional form is

$$dy_i / dx_i = \lambda^{-(1/\lambda)} x_i^{\lambda-1}(2\beta_2 x_i^{\lambda} - 2\beta_2 + \beta_1\lambda) \\ [\beta_2 x^{2\cdot\lambda} + x_i^{\lambda}(\beta_1\lambda - 2\beta_2) + \beta_2 - \lambda(\beta_1 - \beta_0\lambda - 1)]^{(1-\lambda)/\lambda} \quad (1.2)$$

In this study, this derivative represents the elasticity of protein production at a certain percentage of Met in MP (x_i), that is, how much the percentage of milk protein increased or decreased when small changes were made in a certain percentage of Met in MP (x_i). Thus, the optimal percentage of Met in MP for maximizing milk protein production is simply the point where the output elasticity, the first derivative of the estimated QBC, equals zero and begins to be negative.

The optimal level of Met in MP for maximizing profit is calculated according to the following steps: i) define the reference production value (RPV) of Met in MP (x_0) according to the general level of Met in MP in typical dairy lactating rations in NYS such as 1.80 or 1.90, ii) set the base production and input level corresponding to the RPV (x_0) as the amount (g/d) of base milk protein (y_{x_0}) and the amount (g/d) of base Met (Met_{x_0}), iii) calculate the amount (g/d) of additional milk protein (y_{x_i}) when the percentage of Met in MP changes from the RPV (x_0) to a certain percentage of Met in MP (x_i). To obtain the amount (g/d) of additional milk protein (y_{x_i}), first, rearrange the deterministic part of the QBC in Equation (1.1), and multiply this by the amount (g/d) of base milk protein (y_{x_0}) as

$$y_{x_i} = [\{(c + b((x_i^{\lambda} - 1)/\lambda) + a((x_i^{\lambda} - 1)/\lambda)^2)\lambda + 1\}]^{1/\lambda} \times y_{x_0} \quad (1.3)$$

iv) calculate the amount (g/d) of additional Met required (Met_{x_i}) when the percentage of Met in

MP changes from the RPV (x_0) to a certain percentage of Met in MP (x_i). Because the difference between a certain percentage of Met in MP (x_i) and the RPV (x_0) is [$x_i - x_0 = \{(Met_{x_0} + Met_{x_i})/(MP_{x_0} + Met_{x_i}) - (Met_{x_0} / MP_{x_0})\} \times 100$], the amount (g/d) of additional Met required (Met_{x_i}) can be written as

$$Met_{x_i} = \{(x_i - x_0)MP_{x_0}^2\} / \{(x_i - x_0)MP_{x_0} + 100(Met_{x_0} - MP_{x_0})\} \quad (1.4)$$

where $MP_{x_0} = Met_{x_0} / x_0$ is the amount (g/d) of total MP at the RPV (x_0).

v) calculate the amount (g/d) of RPMet required ($RPMet_{x_i}$) when the percentage of Met in MP changes from the RPV (x_0) to a certain percentage of Met in MP (x_i) as

$$RPMet_{x_i} = Met_{x_i} / TIAMet \quad (1.5)$$

where $TIAMet$ is the total intestinal availability of an RPMet supplement, which is calculated as the ruminal escape rate multiplied by the intestinal digestibility of the RPMet supplement.

vi) calculate the additional (cumulative) daily revenue per cow (R_{x_i}) when the percentage of Met in MP changes from the RPV (x_0) to a certain percentage of Met in MP (x_i) as

$$R_{x_i} = y_{x_i} \times P_{\mathrm{Prot}} \quad (1.6)$$

where P_{Prot} is a milk protein price per gram.

vii) calculate the additional (cumulative) daily cost per cow (C_{x_i}) when the percentage of Met in MP changes from the RPV (x_0) to a certain percentage of Met in MP (x_i) as

$$C_{x_i} = RPMet_{x_i} \times P_{Met} \quad (1.7)$$

where P_{Met} is a milk protein price per gram.

viii) calculate the additional (cumulative) daily profit per cow (π_{x_i}) when the percentage of Met in MP changes from the RPV (x_0) to a certain percentage of Met in MP (x_i) as

$$\pi_{x_i} = R_{x_i} - C_{x_i} \quad (1.8)$$

ix) determine the amount (g/d) of RPMet required when the percentage of Met in MP changes from the RPV (x_0) to the percentage of Met in MP where the calculated additional (cumulative) daily profit per cow is the maximum by incrementally changing the input using the spread sheet software Excel.

Data

The data used in this study were modified from the database used to determine the optimal level of Met in MP for lactating cows in the NRC (2001). These data were collected from several existing studies and contain 28 experiments, conducted solely on the Holstein breed, with 87 treatments in which Met was infused continuously into the cow's abomasum or duodenum, or fed in ruminally protected form (Table 1.1). The data used in this study differ from that in the NRC (2001) in two ways. First, as NYS dairy feed generally contains 1.80-1.90

percent Met in MP, this study adjusted the RPV from 2.06 to 1.80 or 1.90 percent. Consequently, the milk protein production response is also modified to a RPV of 1.80 or 1.90 Met in MP. Second, as this study is especially interested in how much additional Met, beyond the 1.80 or 1.90 percent already contained in the basal diet is required to maximize farm profits, the data used were limited to concentrations of Met in MP above 1.80 (48 observations) or 1.90 (40 observations) percent. Because the data used in the NRC (2001) contain observations which have significantly less Met in MP percent than RPV of 1.90, these observations (8 observations) are deleted when estimating the QBC where RPV is 1.90 percent. This allows us to calculate any additional cost to farmers based solely on the price of an RPMet supplement, and eliminates the need to estimate the dollar value of each gram of Met already contained in the basal diet.

Table 1.1. Studies used to determine the dose-response relationships for Lysine and Methionine in Metabolizable Protein (Source: National Research Council. 2001. Nutrient Requirements of Dairy Cattle. 7th rev. ed. National Academies Press, Washington, DC)

Armentano et al. (1997)	Rulquin and Delaby (1994)
Casper et al. (1987)	Rulquin et al. (1994)
Casper and Schingoethe (1988)	Schingoethe et al. (1988)
Illg et al. (1987)	Schwab et al. (1976)
Munneke et al. (1991)	Schwab et al. (1992a)
Papas et al. (1984a)	Schwab et al. (1992b)
Papas et al. (1984b)	Socha (1994)
Pisulewski et al. (1996)	Socha et al. (1994a)
Polan et al. (1991)	Socha et al. (1994b)
Rogers et al. (1987)	Yang et al. (1986)
Rulquin and Delaby (1997)	

As in the NRC (2001), this study also used only the restricted Met experiment data in which Lys was 6.50 percent or more of MP in order to examine the production relationship between milk protein and Met in MP because low concentrations of Lys in MP limited milk protein responses to Met in MP. Total intestinal availability of Met (TIAMet), which is calculated as the ruminal escape rate multiplied by the intestinal digestibility of supplemental

Met, was used to represent the contribution of supplemental Met to predicted flows of digestible Met originating from the basal diet. In the NRC (2001), the TIAMet of infused Met is considered to be 100 percent, and the TIAMet of all RPMet products is calculated to be 81 percent (0.90×0.90).

In this study, the final data set (containing 48 observations) where the RPV is 1.80 percent showed an average Met_{x_0} is 41.55 grams per day per cow, an average MP_{x_0} is 2308.23 grams per day, and an average y_0 is 1052.25 grams per day. On the other hand, the final data set (containing 40 observations) in which the RPV is 1.90 percent showed an average Met_{x_0} is 43.27 grams per day, an average MP_{x_0} is 2277.56 grams per day, and an average y_0 is 1047.46 grams per day.

Results and discussion

Tables 1.2 and 1.3 report the estimated QBCs where the RPV is 1.80 percent and 1.90 percent, respectively. The values of the estimated parameters are different because the RPV and the number of observations in each model are different. After estimating both of the QBCs by the ordinary least square estimator with data modified by each estimated λ, this study tested heteroscedasticity by employing the Breusch-Pagan test. Because the null hypothesis

(homoscedastic residual) of the Breusch-Pagan test was not rejected at the significance level of 0.05, it was concluded that no heteroscedastic residuals are present in either of the QBC equations.

Table 1.2. Estimation results for the quadratic Box-Cox functional form with the reference production value of 1.80 Met in MP

	Dependent variable: Milk protein content responses (g/100g)			
	No. of Observation = 48, LR chi2(2) = 43.17, P > chi2 = 0			
	Estimate	Standard error	z-value	P > z
λ	0.3451	0.05	6.82	0.00
Test H_0	Restricted log likelihood	LR statistic chi2	P-value Prob > chi2	
λ = -1	-413.6801	1038.67	0.00	
λ = 0	57.3194	96.67	0.00	
λ = 1	71.8203	67.67	0.00	
	Dependent variable: Transformed milk protein content responses (g/100g)			
	No. of Observation = 48, P > F = 0.00, R^2 = 0.59, Adj. R^2 = 0.58			
	Estimate	Standard error	t-value	P > t
β_0	-9.0356	1.41	-6.43	0.00
β_1	14.8872	3.23	4.61	0.00
β_2	-7.2902	1.80	-4.06	0.00

Table 1.3. Estimation results for the quadratic Box-Cox functional form with the reference production value of 1.90 Met in MP

	Dependent variable: Milk protein content responses (g/100g)			
	No. of Observation = 40, LR chi2(2) = 34.78, P > chi2 = 0			
	Estimate	Standard error	z-value	P > z
λ	0.4129	0.06	6.46	0.00
Test H_0	Restricted log likelihood	LR statistic chi2	P-value P > chi2	
λ = -1	-332.3985	850.90	0.00	
λ = 0	53.6245	78.85	0.00	
λ = 1	70.1678	45.77	0.00	
	Dependent variable: Transformed milk protein content responses (g/100g)			
	No. of Observation = 40, P > F = 0.00, R^2 = 0.58, Adj. R^2 = 0.56			
	Estimate	Standard error	t-value	P > t
β_0	-8.9451	1.55	-5.79	0.00
β_1	14.0465	3.29	4.28	0.00
β_2	-6.5771	1.71	-3.85	0.00

In this study, the RPMet price is assumed to be \$0.0141 per gram[2], the TIAMet of an RPMet supplement is assumed to be 65.6%[3], and the milk protein price is assumed to be \$0.0046

[2] This price was arrived at by taking the base price of a commercially available RPMet supplement which contains 85% of RPMet, sold to feed companies \$0.012 per gram of RPMet and adjusting for profit after being added to feed and resold to farmers.

per gram, which was the average producer price for milk protein in 2006. Based on these assumptions, the estimated output elasticity and additional profit at various levels of the percentage of Met in MP are reported in Figures 1.2 and 1.3. These estimation results indicate that the optimal level of Met in MP for maximizing milk protein production is 2.40 percent and 2.42%[4], where the RPV is 1.80 and 1.90%, respectively. These optimal levels are almost identical to the recommended level of Met in MP of 2.40% in the NRC (2001). According to Equation (1.5), the amounts of RPMet required to increase the percentage of Met in MP from each RPV to the 2.40 and 2.42% are 21.6 and 18.5 g/d, respectively. On the other hand, the optimal level of Met in MP for maximizing profit is 2.32 and 2.34%, respectively. Again, according to Equation (1.5), the amounts of RPMet required to increase the percentage of Met in MP from each RPV to the 2.32 and 2.34% are 18.7 and 15.6 g/d, respectively. In each case, the additional daily profit per cow is estimated to be $0.38 and $0.29. These additional profit estimates are $0.02 higher than the additional profit estimates for maximizing milk protein production. Over a 300 day lactation period this is $6.00 per cow; with a herd of 1,000 cows this

[3] This is the TIAMet of the same commercial RPMet supplement whose price was assumed to be $0.0141 per gram in this study.

[4] The optimal percentage of Met in MP for maximizing milk protein production is the point where the output elasticity equals zero and begins to be negative.

amounts to $6,000 cost savings per year using economic optimal rather than output maximum use of Met in MP.

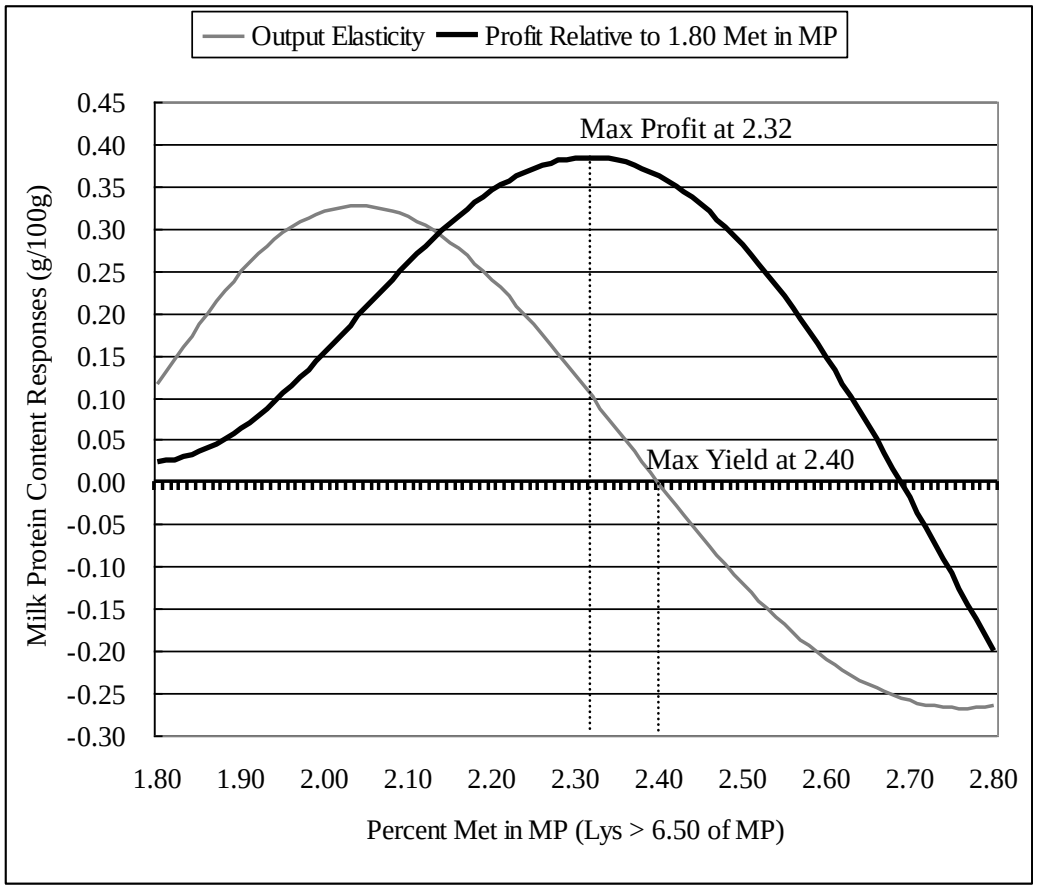

Figure 1.2. The estimated output elasticity and additional profit at various levels of the percentage of Met in MP where the reference production value of 1.80 Met in MP

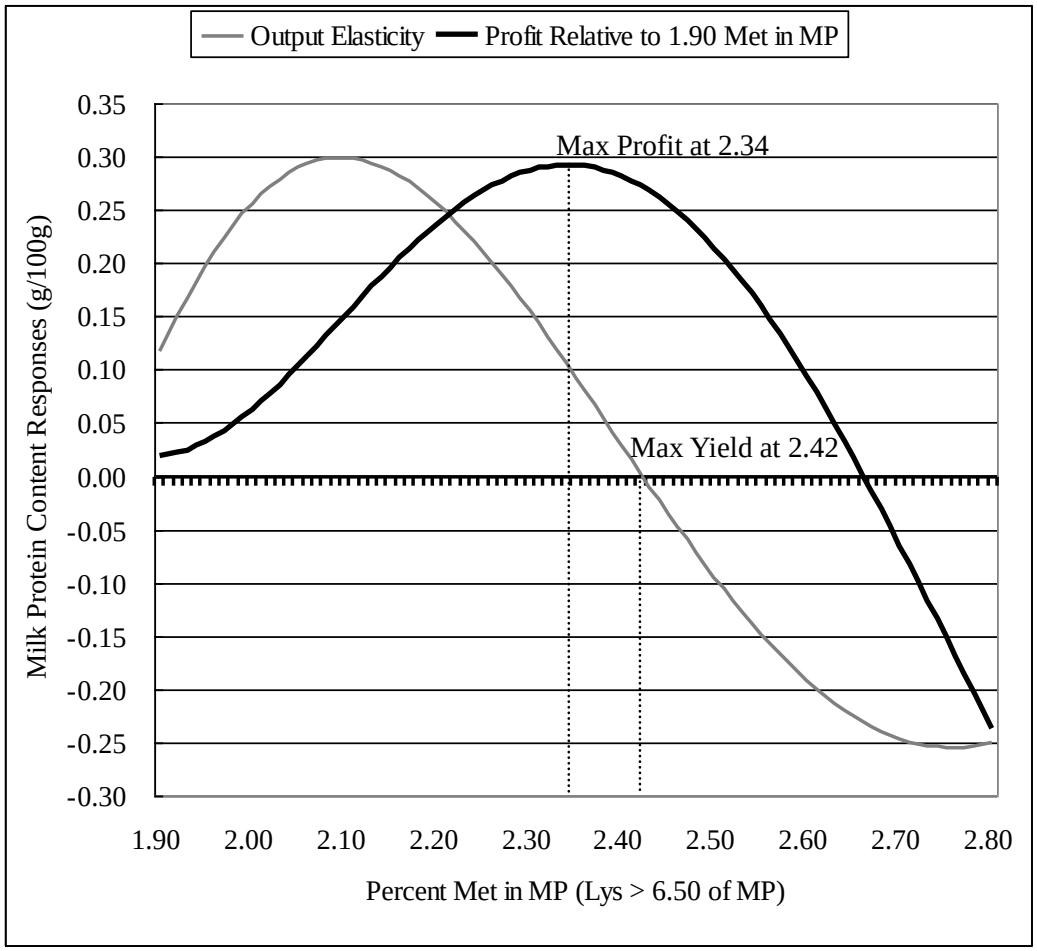

Figure 1.3. The estimated output elasticity and additional profit at various levels of the percentage of Met in MP where the reference production value of 1.90 Met in MP

If any initial assumptions on the milk protein price, the RPMet price or the TIAMet of an RPMet supplement are changed, the new optimal levels of Met in MP for maximizing milk protein production and profit, and the associated amounts of RPMet required to each optimal levels of Met in MP, can be computed by inserting the new assumptions into the profit analysis

formula provided in this study. This is because these initial assumptions do not affect the estimated parameters of the QBC in this study. For example, if we change the milk protein price of $0.0046 per gram in 2006 to $0.0037 per gram in 2000[5], the optimal level of Met in MP for maximizing milk protein production and the amounts of RPMet required to increase the percentage of Met in MP from each RPV to the optimal level of Met in MP for maximizing milk protein production will not be changed. This is because the milk protein price only affects the additional revenue formula (Equation 1.6) without affecting the estimated parameters of the QBC in this study. Thus, the optimal level of Met in MP for maximizing profit is changed to 2.30 and 2.32%, where the RPV is 1.80 and 1.90%, respectively. In this case, the amounts of RPMet required to increase the percentage of Met in MP from each RPV to the 2.30 and 2.32% are 18.0 and 14.9 g/d, respectively. In each case, the additional daily profit per cow is estimated to be $0.26 and $0.19. These additional profit estimates are $0.03 and $0.02 higher than the additional profit estimates for maximizing milk protein production. Similarly, if we change the milk protein price of $0.0046 per gram in 2006 to $0.0057 per gram in 2004[6], the optimal level of Met in MP for maximizing profit is changed to 2.33 and 2.36%, respectively. The amounts of RPMet required to increase the percentage of Met in MP from each RPV to the 2.33 and 2.36%

[5] $0.0037 per gram was the lowest average producer price for milk protein over the last seven years.

[6] $0.0057 per gram was the highest average producer price for milk protein over the last seven years.

are 19.1 and 16.4 g/d, respectively. In each case, the additional daily profit per cow is estimated to be $0.54 and $0.42. These additional profit estimates are $0.02 higher than the additional profit estimates for maximizing milk protein production.

Although additional profit per cow is always higher for maximizing profit than the additional profit per cow for maximizing milk production, the computed optimal levels of Met in MP for both maximizing protein production and maximizing profit are similar given the prices used for Met in MP and milk protein. Other prices will change the optimal profit input quantity which may differ more significantly from the input quantity to maximize milk protein output. Therefore, in targeting the percentage of Met in MP and the amounts of RPMet application, farmers should focus on maximizing profit and not maximizing milk protein production.

Conclusion

This study examines the profitability of rumen-protected methionine (RPMet) supplement on milk protein production. The impact of Met in metabolizable protein (MP) on milk protein production is first estimated from empirical data using a quadratic Box-Cox functional form. Then the additional daily profit per cow by adding various amounts of RPMet supplement to the diet of lactating cows is analyzed and reported using relevant input and output prices. The

optimal amount of RPMet to maximize daily profit per cow is compared to the RPMet required to maximize milk protein production. These optimal quantities are very similar given current prices for RPMet and milk protein, but additional profit estimates for maximizing daily profit per cow are $0.02 higher than the additional profit estimates for maximizing milk protein production given National Research Council reference production values of 1.80 and 1.90%.

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CHAPTER 2

COMPARTMENT MODEL FOR CONTROLLING INFECTIOUS LIVESTOCK DISEASE: COST EFFECTIVE CONTROL STRATEGIES FOR JOHNE'S DISEASE IN DAIRY HERDS

Abstract

An animal compartment framework is used to develop a conceptual model which incorporates the complexity inherent in disease-specific epidemiology in livestock. This conceptual model is empirically implemented with a discrete optimal control model to evaluate the economic and epidemiological consequences of various control strategies for Mycobacterium avium subspecies paratuberculosis (MAP), the pathogen causing Johne's disease (JD), in dairy herds. The empirical results indicate that control of MAP will significantly improve profitability for dairy producers with a JD-affected herd. The empirical application will aid in developing a comprehensive and effective JD control program and the result will help dairy producers understand the economic benefits of controlling MAP by either hygiene management or testing and slaughtering test-positive animals.

Introduction

Infectious diseases in livestock play a critical role in determining profitability of individual farms and maintaining the sustainability of livestock industries. Some of these diseases are also linked to human diseases (Bender and Shulman, 2004, Groenendaal and Zagmutt, 2008, LeBlanc et al., 2006). This potential threat of infectious animal diseases to human health, coupled with their high cost to the livestock industry, has increased public interest in developing successful and

cost-effective control programs that reduce the social and economic impact associated with livestock epidemics and to develop effective biosecurity programs.

Controlling infectious diseases in livestock is not straightforward, since the majority of these diseases have neither a fail-safe method of prevention nor a cure. In such cases, the success of infectious disease control in livestock becomes dependent on the producers' willingness to initiate a control program and the effectiveness of these controls in reducing transmission of the disease. Consequently, successful control programs need to be determined based on joint consideration of the economic gain for livestock producers and the effects of control strategies on the infection dynamics of the disease. This implies that control strategies in such programs should be cost-effective in order to provide an economic incentive to livestock producers to adopt.

Prior literature on infectious livestock disease controls, however, has largely focused on either the reduction of farm-level economic losses while disregarding the infection dynamics of the disease (Chi et al., 2002b, Gramig et al., 2010, Mclnerney, 1996) or else on the eradication of the disease while the economic costs and benefits of disease control are either ignored or computed only for the predetermined control strategies satisfying the eradication conditions (Diekmann et al., 1990, Haydon et al., 1997, Matthews et al., 2006). Recently, the dynamic optimization approach with a simple susceptible-infected (SI) mathematical model has been increasingly applied to infectious wildlife disease control because it allows simultaneous evaluation of the economic and epidemiological tradeoffs associated with disease control (Fenichel and Horan, 2007, Fenichel et al., 2010, Horan and Wolf, 2005, Horan et al., 2008). However, none of these studies applied this approach to infectious disease control in livestock given the consideration of disease control characteristics in livestock.

Wildlife disease control can be characterized as nonselective control since identifying infected wildlife prior to harvest is almost impossible and control options are basically limited to nonselective harvesting. In such a case, the epidemiological aspects of infectious diseases can be captured in a simple model, as the infection status is minimally important in nonselective disease control. In contrast, the health status of livestock can be largely controlled and monitored by producers. As a consequence, control strategies can be selectively applied to animals in different groups according to their production and health status. Therefore, a comprehensive disease-specific epidemiological model is often required in livestock disease control.

The objectives of this study are twofold: first, to develop a conceptual framework for evaluating the economics of an infectious disease control which can incorporate the complexity inherent in disease-specific epidemiology in livestock, and second, to evaluate the economic and epidemiological consequences of various control strategies for *Mycobacterium avium* subspecies *paratuberculosis* (MAP), the pathogen causing Johne's disease (JD), which is a particularly serious infectious disease of dairy cattle due to its high prevalence and economic impact on the dairy industry (Tiwari et al., 2009, USDA NAHMS 2008, Wilson et al., 2010).

Approximately 32% (Tiwari et al., 2009) and 68% (USDA NAHMS 2008) of dairy herds had at least one MAP-infected cow in Canada and the U.S., respectively. Given this high MAP prevalence, JD can have a devastating impact on the dairy industry; the annual cost per JD-infected cow has been estimated to be as high as CD$2472 (Chi et al., 2002a) in Canada and US$1094 (Ott et al., 1999) in the U.S.. This high economic cost of JD prompted the creation of a national voluntary control program in Canada (2005) and the U.S. (2002), but relatively few producers have participated given the lack of solid information and evidence that these programs will economically benefit producers.

A limited number of simulation and field studies have attempted to estimate the economic benefits of controlling MAP infections and JD (Dorshorst et al., 2006, Groenendaal et al., 2002, Ott et al., 1999, Pillars et al., 2009). However, these studies did not take into account either the differences in the characteristics of various methods within a control strategy or their effects on the level of knowledge available to the producers in their decision making process. Moreover, given the nature of simulation and field studies, the results of most of these studies were limited to a predetermined set of control strategies.

Our empirical control model for the causal pathogen of JD, MAP, incorporates both the disease-specific epidemiology in dairy cattle and the effect of the various possible controls on the epidemiological process, incorporating the dairy producers' decision making process. The model allows the level of controls, such as optimal culling (harvesting) levels, to be endogenously determined, rather than predetermined as a scalar. The empirical results will help dairy producers understand the economic benefits of controlling MAP, resulting in reduction of the prevalence and economic costs of JD, by providing answers to producers' main questions, namely whether MAP control will improve their profitability and which control measures generate the most economic benefits with consideration of the economic impact of JD.

Materials and methods

Economic model for infectious animal disease control

Animals within a herd or region can be grouped into different compartment $i \in \boldsymbol{I}=\{1,\ldots,\mathrm{I}\}$ according to their characteristics such as production- and infection-status. Let $x(t)=\{x_1(t),...,x_{\mathrm{I}}(t)\}$ be the set of $x_i(t)$, $i \in \boldsymbol{I}=\{1,\ldots,\mathrm{I}\}$, representing the number of animals in compartment i at time t. $y=\{y_1,...,y_{\mathrm{N}}\}$ is the set of control strategies y_n, $n \in \boldsymbol{N}=\{1,\ldots,\mathrm{N}\}$. $u=\{u_1,...,u_{\mathrm{M}}\}$ is the set of control

options u_m, $m \in \boldsymbol{M}=\{1,\ldots,\mathrm{M}=\sum_{k=1}^{N}\binom{N}{k}\}$, that is a combination of control strategies such as improved hygiene management together with culling infected animals. Also, $w_{i,j}(x(t),u_m)$ is the transition rate[7] from compartment i to j and can be interpreted as the net growth rate when $i=j$. Finally, V_i is the set of adjacent compartments of compartment i, which implies that animals in compartments in set V_i are moved into or out of compartment i in the next time period t+1 due to aging, production stage change, or disease progress. Then, the state dynamics of animals in compartment i can be represented by

$$\begin{aligned}\dot{x} &\equiv x_i(t+1)-x_i(t)\\ &= w_{i,i}(x(t),u_m)x_i(t)+\sum_{k\in V_i} w_{k,i}(x(t),u_m)x_k(t)-\sum_{j\in V_i} w_{i,j}(x(t),u_m)x_i(t)\end{aligned} \tag{2.1}$$

The first term in the right hand side (RHS) of Equation (2.1) represents the changes in the number of animals in compartment i due to net growth. The second term in the RHS of Equation (2.1) represents the number of animals moved into compartment i from adjacent compartments $k \in V_i$. The third term in the RHS of Equation (2.1) represents the number of animals moved to adjacent compartments $j \in V_i$ from compartment i. Compartments k and j can be identical to or different from each other depending upon the epidemiological process of a disease. When compartment i represents offspring from parent animals in compartment s, Equation (2.1) can be augmented with the term $\sum_{s\in Z_i} b_{s,i}(x(t),u_m)x_s(t)$ where $b_{s,i}(x(t),u_m)$ is the birth rate of parent animals in compartment s that produce offspring in compartment i and Z_i is the set of compartments for parent animals.

[7] This is the general form of the transition rate between compartments since the rate is generally affected by control strategies in a control option and can be also affected by the number of animals in different compartments when this rate is frequency- or density-dependent.

Given a discount factor $\rho \in (0,1)$[8], net benefit function N, terminal function F, and control option u_m, a livestock producer or a social planner's economic objective is

$$\underset{\{x_i(t)\}_{i=1}^{I}}{Max} \sum_{t=1}^{T-1} \rho^t N(x(t), u_m) + \rho^T F(x(T)) \tag{2.2}$$

subject to a total of I equations of motion having the form of Equation (2.1), initial number of animal stock $x(1)=\{x_1(1),...,x_I(1)\}$, and other possible feasibility conditions such as capacity constraints that define and limit the domain of $x(t)$. Since this is a finite-dimensional optimization model, a solution exists provided that objective function and equations of motion are continuous and that $x(t)$ is a compact set.

In disease control, the majority of control strategies are generally treated as parameters (determined outside of the optimization process), as in Equation (2.2), since such strategies (e.g. a certain level of hygiene management) are assumed to be determined at the initial period of control and consistently performed by producers. However, some control strategies can be variables (determined in the optimization process). For example, culling rates of cows associated with the control strategy involving diagnostic testing and slaughter of test-positive cows can vary depending on the number of cows in a herd and the capacity constraints of farm. In this case, the control strategy will also be a choice variable and affect the number of animals in associated compartments, such as compartments for cows and future newborn animals.

When set V_i in Equation (2.1) is identical to set I, the above optimization model becomes the prototype bioeconomic model used in prior economic studies on wildlife disease control and analytic or qualitative solutions are generally obtained by using either dynamic programming- or maximal principle-techniques (Fenichel and Horan, 2007, Fenichel et al., 2010, Horan and Wolf,

[8] ρ can be represented by 1/(1+r) where r is a discount rate.

2005, Horan et al., 2008). Otherwise, $V_i \neq I$ implies that animals in compartments belonging to V_i are linked to other compartments not belonging to V_i via different time lags due to the complex epidemiological progress of a disease, such as multi-stage infection. This complexity often precludes obtaining analytic or qualitative solutions and the optimization model may only be solved by numerical computation, which is the case in the present study, which has 14 different animal compartments.

Epidemiology of Johne's disease and control strategies

JD is a chronic, infectious, untreatable disease of ruminants, caused by the pathogen MAP. Animal infection states of MAP in a dairy herd are classified as: susceptible, resistant, transient, latent, low-shedding, and high-shedding (Lu et al., 2010, Mitchell et al., 2008). Animals in the susceptible and resistant states are non-infected (free of MAP infection). Animals in the transient state are infected animals that shed MAP transiently at a low level and are not generally tested with currently available MAP diagnostic tests due to their young age. Animals in the latent state are infected animals that shed no MAP. Animals in the low-shedding state shed low levels of MAP, $\leq$ 30 cfu/g, while animals in the high-shedding state shed high levels of MAP, >30 cfu/g (Whitlock et al., 2000).

Animals are typically susceptible to infection up to the age of 12 months and then become resistant (Collins and Morgan, 1991). Susceptible animals can be infected following contact with MAP in fecal shedding from infected animals (Whitlock et al., 2005), in colostrum and milk of infected adults (Sweeney et al., 1992a), and in contaminated environments (USDA NAHMS 1997). Newly infected animals enter the transient state, which often develops within a few days of infection and continues up to 6 months (Rankin, 1961). Some newborn animals from

infected dams directly enter this state at the time of birth via in-utero infection (Sweeney et al., 1992b). Given the duration of susceptible and transient states, animals in this state are typically younger than 18 months old. The latent state generally occurs following the transient state and continues for a long duration, but animals older than 24 months in this state begin to enter the low-shedding state and then the high-shedding state as the disease progresses.

Symptoms of JD are most commonly seen in adults and include reduced milk production, body weight losses, and increased mortality (USDA NAHMS 1997, Groenendaal et al., 2002, Nielsen and Toft, 2008, NRC, 2003, Smith et al., 2009). The transient and latent states are considered to be the incubation stage of JD since they are generally non-detectable with no symptoms. The low-shedding state can be considered to be the subclinical stage of JD as its symptoms begin to appear, that is, milk production and body weight begins to decrease. The high-shedding state can be considered to be the clinical stage of JD as considerable reduction in milk production and body weight is often present in animals in the high-shedding state. Animals in the high shedding state may develop diarrhea and have a higher mortality rate.

Typical MAP and JD control strategies include hygiene management and test-and-cull. Hygiene management reduces infection transmission rate in animals in the susceptible state by decreasing exposure to MAP. Test-and-cull is the diagnostic testing and slaughter of test-positive animals. A fecal culture (FC) test and an enzyme-linked immunosorbent assay (ELISA) test are the two main tests for detecting MAP infection (USDA NAHMS 2008), generally applied to adult cows. Test-and-cull reduces both MAP infection prevalence and JD-affected animals by removing infectious animals, but the efficacy of test-and-cull significantly varies depending on the test frequency and the characteristics of MAP diagnostics such as the test sensitivity, test specificity, and identification ability.

Test specificity is the probability of classifying uninfected animals as test-negative. Since currently available MAP tests generally fail to detect infected animals shedding no MAP, animals in the test-negative classification are assumed to be a combination of animals free of MAP infection and infected animals shedding no MAP, which includes infected animals in the latent state of MAP infection. Therefore, a test with specificity less than 1 would generate false positive test results for not only animals free of MAP infection, but also infected animals shedding no MAP. On the other hand, test sensitivity is the probability of classifying infected, shedding animals as test-positive. In contrast to the test-negative classification, animals in the test-positive classification are assumed to be infected animals shedding MAP, which include animals in the low- and high-shedding states of MAP infection. Therefore, a test with sensitivity less than 1 would generate false negative test results for low- and high-shedding animals (Lu et al., 2008, Smith et al., 2009, Whitlock et al., 2000). Identification ability is the test's ability to detect specific MAP infection states of animals in the test-positive classification. A test, such as FC, that has identification ability allows producers to apply different culling rates for animals in low- and high-shedding states. With tests that do not have identification ability (such as an ELISA test), producers can only apply a single culling rate for test positive animals since they cannot separately identify whether these animals are low- or high-shedding.

Empirical model

In this study, animals are grouped into 14 discrete and disjoint compartments (Table 2.1), $\boldsymbol{I}=\{1,\ldots,14\}$, that are constructed based on the epidemiology of MAP infection described in the previous section. Each compartment $i \in \boldsymbol{I}$ represents animals in different infection states and ages

with 6-month time steps. Infection states are related to the level of infectiousness[9], productivity[10], and mortality[11]. Age is related to susceptibility to infection, duration of infection states, and production stage.

Table 2.1. Definition of animal compartments

Compartment	Description
1	Compartment for calves 0-6 months in the susceptible state
2	Compartment for calves 0-6 months in the transient state
3	Compartment for calves 6-12 months in the susceptible state
4	Compartment for calves 6-12 months in the transient state
5	Compartment for calves 6-12 months in the latent state
6	Compartment for heifers 12-18 months in the resistant state
7	Compartment for heifers 12-18 months in the transient state
8	Compartment for heifers 12-18 months in the latent state
9	Compartment for heifers 18-24 months in the resistant state
10	Compartment for heifers 18-24 months in the latent state
11	Compartment for cows in the resistant state
12	Compartment for cows in the latent state
13	Compartment for cows in the low-shedding state
14	Compartment for cows in the high-shedding state

Note: The terms calves, heifers, and cows are defined as animals younger than 12 months, between 12 and 24 months, and older than 24 months that produce offspring and milk, respectively.

[9] Infected animals shedding higher levels of MAP for longer periods infect more susceptible animals either directly or indirectly through contaminating their environments. Thus, horizontal infectiousness of infected animals follows this order: high-shedding, low-shedding, transient.

[10] Milk production and body weight begins to decrease in animals in the low-shedding state and they decrease considerably in animals in the high-shedding state.

[11] Only animals in the high-shedding state have a high mortality rate due to JD.

The equations of motion for animals in compartments 1 and 2 take the form of Equation (2.1) with the additional term $\sum_{s \in Z_i} b_{s,i}(x(t),u_m)x_s(t)$ where $b_{s,i}(x(t),u_m)$ is the birth rate of newborn animals in compartment i from parent animals in compartment s and Z_1={11, 12, 13, 14} and Z_2={12, 13, 14} are the set of compartments for parent animals that produce offspring in compartments 1 and 2, respectively, while the equations of motion for animals in other compartments take the form of Equation (2.1) without the additional term. All rates associated with the equations of motion for animals in each compartment are presented in Tables 2.2-2.3.

Table 2.2. Birth rate for female calves and net growth rate of animals (6 month basis)

Rate	Description	Value
$b_{11,1}$	Birth rate for susceptible female calves from resistant cows	0.215
$b_{12,1}$	Birth rate for susceptible female calves from latent cows	0.183
$b_{12,2}$	Birth rate for transient female calves from latent cows	
$b_{13,1}$	Birth rate for susceptible female calves from low shedders	0.183
$b_{13,2}$	Birth rate for transient female calves from low shedders	
$b_{14,1}$	Birth rate for susceptible female calves from high shedders	0.178
$b_{14,2}$	Birth rate for transient female calves from high shedders	
$w_{i,i}$	Natural death rate of calves (animals in compartments i=1,2,3,4,5)	0.046
	Natural death rate of heifers (animals in compartments i=6,7,8,9,10)	0.0
$w_{11,11}$	Removal rate of resistant cows	Varies
$w_{12,12}$	Removal rate of transient cows	Varies
$w_{13,13}$	Removal rate of low-shedding cows	Varies
$w_{14,14}$	Removal rate of high-shedding cows	Varies

Sources: Birth rates are obtained from USDA NAHMS (2007) and Lu et al (2010). Natural death rates are obtained from USDA NAHMS (2007).

Note: In our age-structured compartment model, natural growth of herd size is allowed only through birth of newborn calves. Hence, the net growth rate of calves and heifers becomes the natural death rate of these animals and that of cows becomes the removal rate, which is the sum of natural death rate, general culling rate due to low production or diseases other than Johne's disease, and additional culling rate due to test-and-cull. General and additional culling rates associated with removal rate of cows are obtained by solving the control model empirically.

Table 2.3. Transition rate between adjacent compartments (6 month basis)

Rate	Description	Value
$w_{1,3}$	Susceptible calves 0-6 months → Susceptible calves 6-12 months	Varies
$w_{1,4}$	Susceptible calves 0-6 months → Transient calves 6-12 months	Varies
$w_{2,5}$	Transient calves 0-6 months → Latent calves 6-12 months	
$w_{3,6}$	Susceptible calves 6-12 months → Resistant heifers 12-18 months	Varies
$w_{3,7}$	Susceptible calves 6-12 months → Transient heifers12-18 months	Varies
$w_{4,8}$	Transient 6-12 months → Latent 12-18 months	
$w_{5,8}$	Latent 6-12 months → Latent 12-18 months	
$w_{6,9}$	Resistant heifers 12-18 months → Resistant heifers 18-24 months	
$w_{7,10}$	Transient heifers 12-18 months → Latent heifers 18-24 months	
$w_{8,10}$	Latent heifers 12-18 months → Latent heifers 18-24 months	
$w_{9,11}$	Resistant heifers 18-24 months → Resistant cows	
$w_{10,12}$	Latent heifers 18-24 months → Latent cows	
$w_{12,13}$	Latent cows → Low-shedding cows	
$w_{13,14}$	Low-shedding cows → High-shedding cows	

Sources: All rates are obtained from USDA NAHMS (2007) and previous studies on *Mycobacterium avium* subspecies *paratuberculosis* and Johne's disease in dairy herds. Detailed information on these rates is explained in the empirical model section.

Note: Movement of animals from one compartment to another is due to aging, infection, or infection progress. Transition rates due to aging are $w_{1,3}$, $w_{3,6}$, $w_{5,8}$, $w_{6,9}$, $w_{8,10}$, $w_{9,11}$, and $w_{10,12}$. Transition rates due to infection are $w_{1,4}$ and $w_{3,7}$. Transition rates due to infection progress are $w_{2,5}$, $w_{4,8}$, $w_{12,13}$, and $w_{13,14}$.

The relationship between compartments is illustrated in Figure 2.1, where x_i represents the number of animals in compartment $i \in \boldsymbol{I}$ (Table 2.1), $b_{s,i}$ is the birth rate of parent animals in compartment s that produce offspring in compartment i (Table 2.2), $w_{i,j}$ is the transition rate from compartment i to adjacent compartment j (Table 2.3). This flow diagram of animal compartments is constructed based on our previous mathematical model for MAP infection in dairy herds (Lu et al., 2010, Mitchell et al., 2008). Detailed information on the animal movement between compartments is described in these

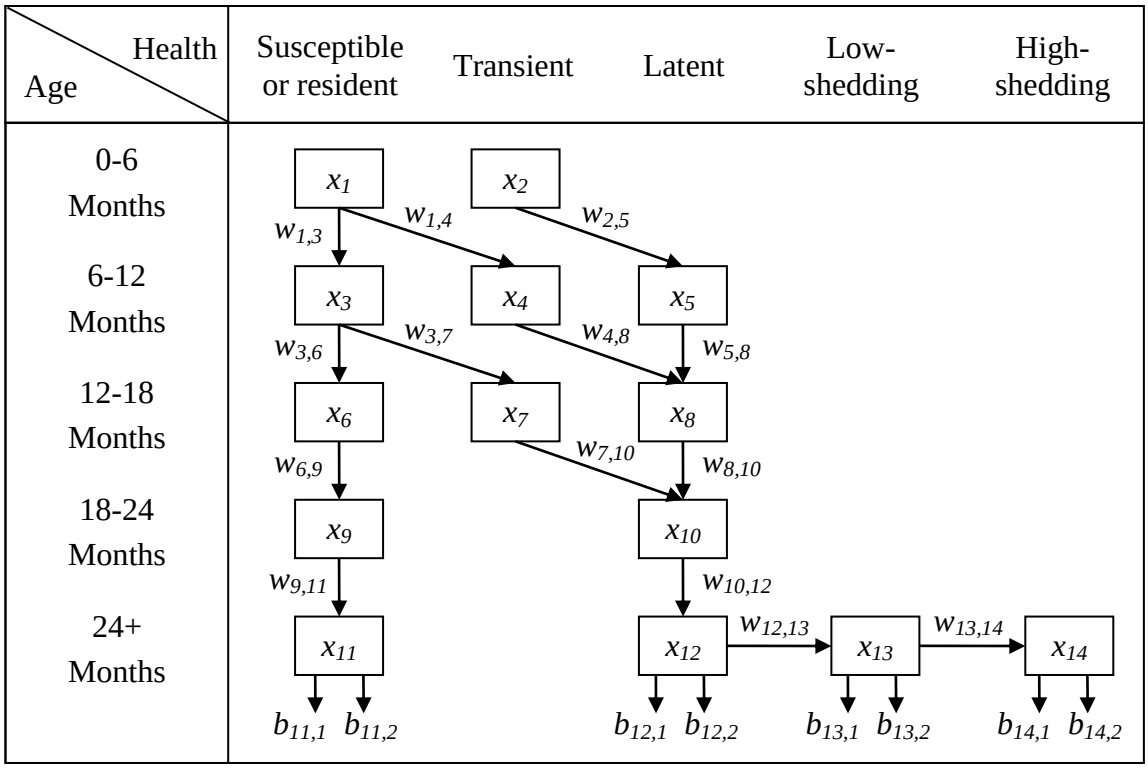

Figure 2.1. The flow diagram of animal compartments and infection with MAP

In this study, vertical infections from parent animals to their offspring are captured in the birth rates for transient calves. These vertical infections are set at γ_{12}=0.15, γ_{13}=0.15, and γ_{14}=0.17 representing portion infected at birth given infected dams in compartments 12 (latent cows), 13 (low-shedding cows), and 14 (high-shedding cows) as in a prior modeling study (Lu et al., 2010). Given these proportional parameters, the birth rates for transient female calves from infected dams ($b_{12,2}$, $b_{13,2}$, and $b_{14,2}$ in Table 2.2) are obtained from $b_{12,2}=b_{11,1}\gamma_{12}$, $b_{13,2}=b_{11,1}\gamma_{13}$, and $b_{14,2}=b_{11,1}\gamma_{14}$, while the birth rates for susceptible female calves from those dams ($b_{12,1}$, $b_{13,1}$, and $b_{14,1}$ in Table 2.2) are obtained from $b_{12,1}=b_{11,1}(1-\gamma_{12})$, $b_{14,1}=b_{11,1}(1-\gamma_{13})$, and $b_{14,1}=b_{11,1}(1-\gamma_{14})$, where $b_{11,1}$=0.215 represents the average birth rate for female calves on a 6-month basis (USDA NAHMS 2007).

Horizontal MAP infection is generally determined by the number of infected animals that shed MAP in transient (x_2, x_4, and x_7), low-shedding (x_{13}), or high-shedding states (x_{14}), since manure containing MAP is the main source of infection for susceptible animals either directly or indirectly through contaminated environments. In a prior modeling study (Lu et al., 2008), this horizontal infection is captured in the force of infection $\lambda(t)$:

$$\lambda(t) = [\beta_{Tr}\{x_2(t) + x_4(t) + x_7(t)\} + \beta_{13}x_{13}(t) + \beta_{14}x_{14}(t)] / N(t) \quad (2.3)$$

where $N(t)$ is the total number of animals on a farm at time t and β_{Tr}=1, β_{13}=2, and β_{14}=10 are transmission rates between susceptible animals and infected animals in transient (compartments 2,4, and 7), low-shedding (compartment 13), and high-shedding states (compartment 14), respectively.

The JD control strategies considered in this study include two different levels of hygiene management and four different test-and-cull methods, summarized in Table 2.4. These control

strategies reduce the horizontal infection transmission rate in animals in the susceptible state by decreasing the exposure of susceptible animals to infected manure. Either improved or advanced hygiene management reduces the force of infection $\lambda(t)$ in Equation (2.3). Given the force of infection, together with the impact of hygiene management, the transmission rates of animals from the susceptible state to the transient state ($w_{1,4}(t)$ and $w_{3,7}(t)$ in Table 2.3) can be represented by $w_{1,3}(t)=w_{1,4}(t)=(1-\tau)\lambda(t)$, where τ represents the effect of hygiene management on reduction of the force of infection with the assumption of τ=0.85 for improved hygiene and τ=0.95 for advanced hygiene. These estimates of τ are based on prior studies (Dorshorst et al., 2006, Groenendaal et al., 2002). Susceptible animals remaining after infection with $\lambda(t)$ and natural death move to other susceptible or resistant compartments due to aging. These movements are captured in transition rates $w_{1,3}(t)$ and $w_{3,6}(t)$ in Table 2.3, which are obtained from $w_{1,3}(t)=1-[(1-\tau)\lambda(t)+w_{1,1}]$ and $w_{3,6}(t)= 1-[(1-\tau)\lambda(t)+w_{3,3}]$, where both $w_{1,1}$ and $w_{3,3}$ are –0.046, which is the natural death rates of calves (USDA NAHMS 2007).

Table 2.4. Control strategies for Johne's disease

Control strategy	Description
Improved hygiene	Improved hygiene includes harvesting colostrum from cows with cleaned and sanitized udders and preventing contact of calves with adult cow manure
Advanced hygiene	Advanced hygiene includes feeding calves with only milk replacer or pasteurized milk, preventing contamination of calf feedstuffs, water, or bedding by effluent from the adult herd as well as hygiene practices included in improved hygiene
Test-and-cull using annual FC test	Testing cows once a year (half at midyear and the other half at the end of year) using fecal culture test and culling test-positive cows
Test-and-cull using annual ELISA test	Testing cows once a year using enzyme-linked immunosorbent assay test and culling test-positive cows
Test-and-cull using biannual FC test	Testing cows twice a year (once at midyear and once at the end of year) using fecal culture test and culling test-positive cows
Test-and-cull using biannual ELISA test	Testing cows twice a year using enzyme-linked immunosorbent assay test and culling test-positive cows

Note: Both improved hygiene and advanced hygiene include additional hygiene practices defined previously, as well as all hygiene practices assumed to be currently implemented by typical dairy farms. In particular, advanced hygiene is designed to provide a hygiene environment identical to off-farm calf rearing. The difference between improved hygiene and advanced hygiene is that while both are assumed to decrease infection transmission between susceptible and infectious animals, the latter is additionally assumed to decrease infection transmission between susceptible animals and surrounding environments contaminated mainly by manure containing *Mycobacterium avium* subspecies *paratuberculosis*.

Four different test-and-cull methods in Table 2.4 affect the removal rate of cows depending on test frequency and the characteristics of the test including specificity, identification ability, and sensitivity for low- and high-shedding cows[12]. In this study, cows are assumed to exit the herd in three different ways: a natural death, a general culling due to low production or diseases other than JD, or an additional culling due to test-and-cull for cows with a positive MAP test result. Given this assumption, the removal rate of cows ($w_{11,11}(t)$, $w_{12,12}(t)$, $w_{13,13}(t)$, $w_{14,14}(t)$ in Table 2.3) can be represented by:

$$w_{11,11}(t) = -[\mu_c + \{1-\phi(1-\varepsilon)\}\delta_c(t) + \phi(1-\varepsilon)\{\eta_L\delta_L(t) + \eta_H\delta_H(t)\}] \quad (2.4)$$

$$w_{12,12}(t) = -[\mu_c + \{1-\phi(1-\varepsilon)\}\delta_c(t) + \phi(1-\varepsilon)\{\eta_L\delta_L(t) + \eta_H\delta_H(t)\}] \quad (2.5)$$

$$w_{13,13}(t) = -[\mu_c + (1-\phi\theta_L)\delta_c(t) + \phi\theta_L\delta_L(t)] \quad (2.6)$$

$$w_{14,14}(t) = -[\mu_c + \alpha + (1-\phi\theta_H)\delta_c(t) + \phi\theta_H\delta_H(t)] \quad (2.7)$$

where μ_c=0.126 represents the natural death rate (USDA NAHMS 2007). δ_c represents the general culling due to low production or diseases other than JD. δ_L represents the additional culling due to test-and-cull for the low-shedding cows with a positive MAP test result. δ_H represents the additional culling due to test-and-cull for the high-shedding cows with a positive MAP test result. The parameter ϕ represents test frequency, indicating either annually[13] (ϕ=0.5) or biannually[14] (ϕ=1). ε represents specificity of a MAP test with ε=0.95 for an ELISA test and ε=1 for a FC test. θ_L and θ_H represent test sensitivity for low- and high-shedding cows, respectively, with θ_L=0.3 and θ_H=0.75 for an ELISA test and θ_L=0.5 and θ_H=0.9 for a FC test (Collins et al., 2006, Nielsen and Toft, 2008, Whitlock et al., 2000). η_L and η_H represent the

[12] Test specificity, identification ability, and test sensitivity are defined in the previous section.
[13] An annual test is one in which all animals are tested once a year, half at midyear and the other half year-end.
[14] A biannual test is one in which all animals are tested twice a year, once at midyear and once year-end.

proportion of cows with a positive test result that are erroneously identified as low- or high-shedding cows due to imperfect identification ability of a diagnostic test[15]. A FC test has identification ability, but an ELISA test does not. In this study, the proportions η_L and η_H are assumed to be determined by the ratio of the test sensitivity for low- and high-shedding cows as $\eta_L=\theta_L/(\theta_L+\theta_H)$ and $\eta_H=\theta_H/(\theta_L+\theta_H)$, where $\eta_L+\eta_H=1$.

In Equations (2.4)–(2.7), the proportion of resistant and latent cows with a positive test result is represented by $\phi(1-\varepsilon)$ and these positive test results are false positive due to imperfect test specificity ($\varepsilon<1$)[16]. On the other hand, the proportion of low- and high-shedding cows with a positive test result is represented by $\phi\theta_L$ and $\phi\theta_H$, respectively, and these positive test results are true positive given the perfect test specificity associated with FC of low- and high-shedding cows. All cows in each compartment $i=\{11,12,13,14\}$ exit the herd at fixed rate μ_c due to natural death. All cows in the high-shedding state also exit the herd at an additional rate $\alpha=0.25$ due to the clinical symptoms of JD (Whitlock et al., 2000). All cows with a positive test result can exit the herd by additional culling rates $\eta_L\delta_L+\eta_H\delta_H$ for resistant and latent cows, δ_L for low-shedding cows, and δ_H for high-shedding cows, where $\delta_L=\delta_H$ for a test does not have identification ability[17]. Thus, $\phi(1-\varepsilon)\{\eta_L\delta_L+\eta_H\delta_H\}$, $\phi\theta_L\delta_L$, and $\phi\theta_H\delta_H$ in Equation (2.4)–(2.7) can be interpreted as the proportion of cows in each compartment that are removed from the herd because of test-

[15] η_L and η_H equal zero for a FC test since this test has identification ability, while they are non-zero for an ELISA test since this test does not have perfect identification ability.

[16] There will be no cows with a false-positive test result for a FC test since it is assumed to have perfect test specificity ($\varepsilon=1$), while some false-positive test results are observed for an ELISA test due to its imperfect test specificity ($\varepsilon<1$).

[17] A test, such as FC, that has identification ability allows producers to apply different culling rates for cows in low- and high-shedding states. Otherwise, producers can only apply a single culling rate for test positive cows since they cannot separately identify whether these cows are low- or high-shedding. This is the case for an ELISA test.

positive status. Remaining cows, which are untested or have a negative test result, can exit the herd by a general culling rate δ_c due to low production or diseases other than JD.

In general, a dairy farm has an upper limit on the number of cows due to limited cow housing and management capacity and also a minimum number of cows necessary to generate cash flow for living and fixed expenses. These constraint factors can be imposed in the model by the following capacity constraint:

$$N_{\text{mincow}} \leq N_{\text{cow}}(t) \leq N_{\text{maxow}} \tag{2.8}$$

where $N_{\text{cow}}(t)$ denotes the total number of cows at time t, N_{mincow} denotes the minimum number of cows, and N_{maxcow} denotes the maximum number of cows on a farm.

Given the epidemiological[18] and capacity constraints, the producer's objective is to maximize the expected net present value (NPV) from the sales of milk and cull cows for slaughter by deciding upon a combination of the control strategies in Table 2.5. Hygiene-associated control strategies are discrete and treated as parameters (determined outside of the optimization process) in the model since these are assumed to be determined at the initial period of control and we assume that producers do not alter their initial choices of hygiene management unless the disease is eliminated. On the other hand, culling-associated control strategies are continuous variables (determined in the optimization process) in the model and determine the number of cows in each compartment. In addition, this study assumed that the farm would no longer implement any control strategies when the disease was eliminated.

[18] Epidemiological constraints are the equations of motion for age-structured compartments describing the epidemiological process of Johne's disease.

Table 2.5. Control strategy combinations

Notation	Definition
u_1	Improved hygiene
u_2	Advanced hygiene
u_3	Test-and-cull using annual FC test
u_4	Test-and-cull using annual ELISA test
u_5	Test-and-cull using biannual FC test
u_6	Test-and-cull using biannual ELISA test
u_7	Improved hygiene with test-and-cull using annual FC test
u_8	Improved hygiene with test-and-cull using annual ELISA test
u_9	Improved hygiene with test-and-cull using biannual FC test
u_{10}	Improved hygiene with test-and-cull using biannual ELISA test
u_{11}	Advanced hygiene with test-and-cull using annual FC test
u_{12}	Advanced hygiene with test-and-cull using annual ELISA test
u_{13}	Advanced hygiene with test-and-cull using biannual FC test
u_{14}	Advanced hygiene with test-and-cull using biannual ELISA test

The expected NPV of a producer's net cash flow from the sales of milk and cull cows for slaughter is specified as:

$$\begin{aligned}&\sum_{t=1}^{T-1}\frac{1}{(1+r)^t}[P_{\text{milk}}Q_{\text{milk}}Z(t)+P_{\text{milk}}Q_{\text{milk}}(1-\varphi_L)L(t)+P_{\text{milk}}Q_{\text{milk}}(1-\varphi_H)H(t)\\&+P_{\text{cull}}Q_{\text{cull}}Z(t)\delta_c(t)+P_{\text{cull}}Q_{\text{cull}}(1-\zeta_L)L(t)\delta_L(t)+P_{\text{cull}}Q_{\text{cull}}(1-\zeta_H)H(t)\delta_H(t)\\&-C_{\text{calf}}N_{\text{calf}}(t)-C_{\text{heifer}}N_{\text{heifer}}(t)-(C_{\text{cow}}+C_{\text{mgt}}+\phi C_{\text{test}})N_{\text{cow}}(t)]\\&+\frac{1}{(1+r)^T}[P_{\text{cull}}Q_{\text{cull}}N_{\text{cow}}(T)+P_{\text{sale}}\{N_{\text{calf}}(T)+N_{\text{heifer}}(T)\}]\end{aligned} \tag{2.9}$$

This Equation (2.9) includes the expected revenue from milk sales, the expected revenues from cull cows sold for slaughter, and the operating cost of raising animals and the cost associated with a combination of control strategies in Table 2.5. The entire herd is liquidated at the

beginning of the terminal year. For the sake of model brevity, all remaining cows in the terminal years are sold at the price of healthy cows. This is a reasonable approach given that, with controls, effectively no cows show symptoms of JD[19] in the final year of the 50-year simulation period. Young stock is all sold at the price of one year old animals, the average age of young stock. The variables and parameters in Equation (2.9) are presented in Table 2.6.

[19] Reduction in milk production and body weight.

Table 2.6. Definition of variables and parameters used in the net present value equation

Rate	Description	Value[a]	Reference
C_{calf}	Base operating cost of raising a calf	395.00	Karszes et al 2008
C_{cow}	Base operating cost of raising a cow	1231.46	USDA NASS 2003-2007
C_{heifer}	Base operating cost of raising a heifer	395.00	Karszes et al 2008
C_{mgt}	Extra cost associated with advanced hygiene	26.25	Dorshorst et al 2006
	Extra cost associated with improved hygiene	15	Dorshorst et al 2006
C_{test}	Cost of ELISA test per sample	5.00	Collins et al 2006
	Cost of FC test per sample	19.00	Collins et al 2006
H	Suspected numbers of cows in clinical stage	Varies	Calculated
L	Suspected numbers of cows in subclinical stage	Varies	Calculated
N_{calf}	Number of calves	Varies	Calculated
N_{cow}	Number of cows	Varies	Calculated
N_{heifer}	Number of heifers	Varies	Calculated
P_{cull}	Cull-cow price per pound	0.4788	USDA NASS 2003-2007
P_{milk}	Milk price per pound	0.1539	USDA NASS 2003-2007
P_{sale}	Sale price of a one year old animal	867[c]	Karszes et al 2008
Q_{cull}	Pounds (weight) of cull cow	1500	USDA NASS 2003-2007
Q_{milk}	Pounds of milk production per cow	9719.5	USDA NASS 2003-2007
r	Discount rate	0.02	Assumed
T	Total follow up time of a dairy farm	100	Assumed
Z	Suspected numbers of cows in non-clinical stage	Varies	Calculated
$_c$	General culling rate for cows	Varies	Calculated
$_H$	Extra culling rate for low-shedders	Varies	Calculated
$_L$	Extra culling rate for high-shedders	Varies	Calculated
	Test frequency	0.5 or 1	Assumed[b]
$_H$	Production adjustment factor for high-shedders	0.1	Groenendaal et al 2002[d]
$_L$	Production adjustment factor for low-shedders	0.05	Groenendaal et al 2002[d]
$_H$	Cull-weight adjustment factor for high-shedders	0.1	Assumed
$_L$	Cull-weight adjustment factor for low-shedders	0.05	Assumed

a. Values are 6-month basis.

b. ϕ=0.5 represents annual testing and ϕ=1 represents biannual testing.

c. Sale price of a one year old animal is assumed to be identical to total cost of raising replacement heifer up to one year.

d. Production reduction due to Johne's disease has been reported 5% to 20%.

The differences in the characteristics of various testing options affect the level of knowledge available to the producers in their decision making process. In Equation (2.9), *Z* is suspected numbers of cows in the non-clinical stage (resistant and latent state), while L and *H* are suspected numbers of cows in the subclinical stage (low-shedding state) and the clinical stage (high-shedding state), respectively. Producers expect *Z* to have normal milk production and body weight, while they expect *L* and *H* to have lower milk production and body weight due to the disease. These production reductions due to JD are captured in the parameters φ_L, φ_H, ζ_L, and ζ_H in Equation (2.9) and presented in Table 2.6.

Given imperfect specificity or sensitivity of currently available diagnostic tests, *L* and *H* represent producers' expectation on the number of low- and high-shedding cows in their herd and they are determined based on the number of cows with a positive-test result as shown in Equations (2.10) and (2.11).

$$L(t) = \begin{cases} \phi\theta_L x_{13}(t) \text{ for a FC test} \\ \phi\theta_L x_{13}(t) + \phi\theta_H x_{14}(t) + \phi(1-\varepsilon)\{x_{11}(t) + x_{12}(t)\}]\eta_L \text{ for an ELISA test} \end{cases} \tag{2.10}$$

$$H(t) = \begin{cases} \phi\theta_H x_{14}(t) \text{ for a FC test} \\ \phi\theta_L x_{13}(t) + \phi\theta_H x_{14}(t) + \phi(1-\varepsilon)\{x_{11}(t) + x_{12}(t)\}]\eta_H \text{ for an ELISA test} \end{cases} \tag{2.11}$$

Since a FC test has perfect identification ability and test specificity, cows with a positive-test result[20] are either low-shedding **(**$\phi\theta_L x_{13}$) or high-shedding ($\phi\theta_H x_{14}$) in Equations (2.10) and (2.11). On the other hand, cows with a positive-test result[21] based on an ELISA test, which has imperfect test specificity, are either resistant ($\phi(1-\varepsilon)x_{11}$)**,** latent ($\phi(1-\varepsilon)x_{12}$), low-shedding

[20] The proportion of low- and high-shedding cows with a positive test result is represented by $\phi\theta_L$ and $\phi\theta_H$ in Equations (6) and (7), respectively.

[21] The proportion of low- and high-shedding cows with a positive test result is represented by $\phi\theta_L$ and $\phi\theta_H$ in Equations (6) and (7), respectively. Similarly, a proportion of resistant and latent cows will have a positive test result given test specificity and this is expressed as $\phi(1-\varepsilon)$ in Equations (4) and (5)**.**

($\phi\theta_L x_{13}$), or high-shedding ($\phi\theta_H x_{14}$) in Equations (2.10) and (2.11). In addition, since an ELISA test doesn't have identification ability, a portion (η_L) of these cows is considered in low-shedding and the remaining portion (η_H) of these cows is considered in high-shedding[22]. The number of suspected cows (Z) in the non-clinical stage is the total number of cows (N_{cow}) minus the numbers of suspected low- and high-shedding cows (L and H, respectively).

$$Z(t) = N_{\text{cow}}(t) - L(t) - H(t) \tag{2.12}$$

Since a mean true prevalence level of 10% MAP infection within a dairy herd is commonly assumed (Dorshorst et al., 2006, Van Schaik et al., 2003, Wells et al., 2002), three initial MAP infection levels (0%, 10%, and 20%)[23] were considered for the baseline farm, in order to take into account the majority of dairy farm situations. The model described in this section was coded using the general algebraic modeling system (GAMS) software and empirically solved for a farm with these possible MAP infection levels.

Results and discussion

For a farm free of MAP (0% MAP infection level), the NPV is $374,305 for the 50-year simulation period. The NPV is estimated to be considerably lower at $161,938 and $98,830 when the initial infection rate is 10% and 20%, respectively, in the absence of controls. This illustrates the potentially high cost of JD on dairy farms without control. The number of infected cows for a farm without MAP control in place increases continuously as reported in previous

[22] η_L and η_H represent the proportion of cows with a positive test result that are erroneously identified as low- or high-shedding cows due to imperfect identification ability of a diagnostic test, $\eta_L+\eta_H=1$. These are previously discussed with Equations (4) and (5).

[23] An initial infection distribution for animal groups was simulated for a farm with an initial herd of 99 non-infected cows and 1 latently infected cow, and no control implemented. The initial conditions for the state variables for a farm with three different MAP infection levels were drawn from time-points in this simulation that matched the desired infection level. Each infection level represents a percentage of MAP infected cows per all cows in a herd.

studies (Groenendaal and Galligan, 2003, Groenendaal et al., 2002). These low NPV values would not be sustainable and implies that a farm would need to engage in some type of remedial action before JD becomes pervasive in the herd. Indeed, removing the lower cow number constraint eventually results in the sale of all cows, which would be expected with an epidemic infection rate.

With MAP present, the results show that culling all test-positive animals over time is optimal for maximizing the NPV of a farm's net cash flow. The optimal rate of base line culling[24] varies depending up on the number of healthy and MAP-infected cows, but the steady-state rate is 0.192 (19.2% replacement rate) when there are no MAP-infected cows. This steady-state rate is close to the average cow removal rate of 23.6%, reported by USDA NAHMS (2007). A herd size of 100 cows, the upper cow constraint, is the steady-state herd size when there are no MAP-infected cows or at the conclusion of a successful control program. The NPV and expected elimination[25] period of MAP and of test-positive animals for various control scenarios are summarized in Table 2.7.

[24] The general culling rate δ_c in Equations (2.4)-(2.7).
[25] MAP is considered to be eliminated when its prevalence rate is less than 1%, while test-positive cows are considered to be eliminated when the total number is less than 0.5.

Table 2.7. Farm NPV and expected elimination period of the disease and of test-positive animals for a farm with a MAP-infected herd

Control option		Infection level	NPV	Elimination of MAP[a]	Elimination of test-positive cows[a]
Test-and-cull	Hygiene				
Annual FC test	None	10%	$331,502	31 years	16 years
		20%	$319,304	40 years	24.5 years
Annual FC test	Improved hygiene	10%	$345,603	6 years	4 years
		20%	$336,873	7.5 years	5.5 years
Annual FC test	Advanced hygiene	10%	$337,611	5.5 years	4 years
		20%	$329,091	6.5 years	5 years
Biannual FC test	None	10%	$332,975	12 years	9 years
		20%	$320,201	15.5 years	12.5 years
Biannual FC test	Improved hygiene	10%	$341,857	5 years	4 years
		20%	$333,404	6 years	5.5 years
Biannual FC test	Advanced hygiene	10%	$336,569	4.5 years	4 years
		20%	$326,262	5.5 years	5 years
Annual ELISA test	None	10%	$327,942	Never	Never
		20%	$313,313	Never	Never
Annual ELISA test	Improved hygiene	10%	$337,963	9 years	Never
		20%	$328,501	11 years	Never
Annual ELISA test	Advanced hygiene	10%	$329,376	7.5 years	Never
		20%	$321,258	8.5 years	Never
Biannual ELISA test	None	10%	$307,066	Never	Never
		20%	$298,546	Never	Never
Biannual ELISA test	Improved hygiene	10%	$334,697	7.5 years	Never
		20%	$322,893	9.5 years	Never
Biannual ELISA test	Advanced hygiene	10%	$327,352	6.5 years	Never
		20%	$314,935	8 years	Never
None	Improved	10%	$336,182	11 years	-
		20%	$319,040	14 years	-
None	Advanced	10%	$327,559	8.5 years	-
		20%	$310,351	10.5 years	-

a. MAP is considered to be eliminated when its prevalence rate is less than 1%. Test-positive

cows are considered to be eliminated when total number of infected cows is less than 0.5.
Note: For a farm free of MAP (0% MAP infection level), the NPV is $374,305, while the NPV at 10% and 20% with no controls are 57% lower at $161,938 and 74% lower at $98,830 when the initial infection rate is 10% and 20%, respectively, in the absence of controls.

The most cost-effective control option is improved hygiene management and test-and-cull using an annual FC test. This control option generates an NPV of $345,603 and $336,873, which are significantly higher compared to a farm without control given the initial infection rate of 10% and 20%, respectively. Implementing this option eliminates the MAP from the herd within 8 years for both MAP prevalence levels. Figure 2.2 shows the annual net cash flow associated with this control option together with no control for comparison. Although MAP control generates additional cost until the infection is eliminated, the overall benefit of control is much higher than no control with both 10% and 20% prevalence. This Figure also illustrates one reason farmers may not start a control strategy; the control costs are much higher initially than the lost income from JD. Reluctance to engage in MAP control is especially strong when farms would clearly experience the definite control cost but with actual losses from JD being nebulous. Therefore, it is important to inform producers that although initiating a control program results in a higher net cash flow compared to no control, they will experience a negative net cash flow at the beginning of initiating a control program. The control program will result in a higher NPV than no control and provide an economic rationale to producers for initiating a control program.

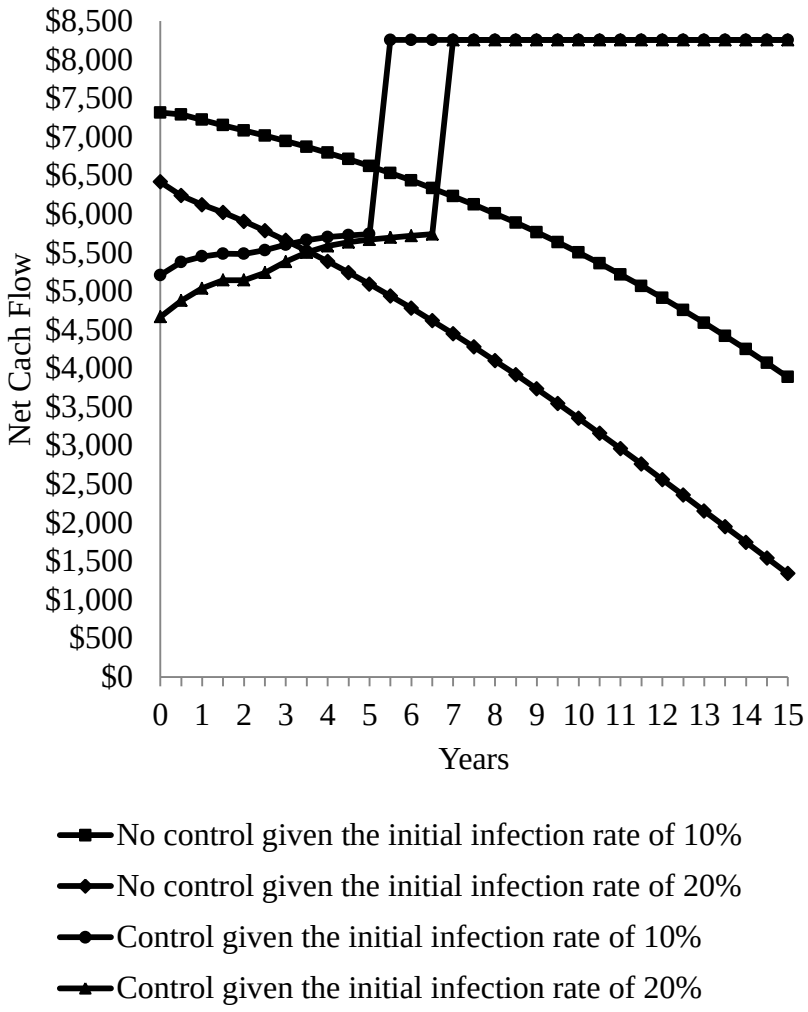

Figure 2.2. Annual net cash flows over first 15 years with no controls and with controls of improve hygiene and culling using an annual fecal test

Note: The sudden increases in net cash flow are caused by discontinuation of controls.

For producers whose goal is to control MAP by implementing only a single control strategy, improved hygiene management generates the overall highest NPV among all single control strategies available for a farm with JD present. Test-and-cull using a FC test is an effective control strategy since it eliminates MAP, but this control strategy requires a considerably longer elimination period compared to that for a farm implementing improved

hygiene management. On the other hand, test-and-cull using an ELISA test is an ineffective control strategy. This control strategy decreases the MAP infection prevalence, but fails to eliminate MAP over the extended planning duration of a dairy farm.

Due to imperfect test sensitivity or specificity, it is difficult to identify whether MAP has been eliminated or not when using a MAP test only, especially an ELISA test. However, elimination of MAP can be ascertained in the model by observing the computed net cash flow[26]. When the net cash flow associated with a control option reaches a steady state net cash flow in our model, which equals $8,255 minus the cost of implementing the control option, it implies that MAP has been eliminated. This is because a net cash flow of $8,255 is identical to the net cash flow for a farm free of MAP. Thus, a net cash flow of $8,255 minus the cost of implementing the control option implies that there are no losses caused by JD.

In reality, producers may halt a control program if there are no test-positive animals in their herd, but the disease would resurface due to undetected infected animals remaining or reintroduced into the herd. Table 2.7 shows the lag between the period of MAP elimination and the last period of detecting test-positive animals. Given the lag between those periods, it is important for producers to keep screening their herd using a MAP test after eliminating the last test-positive animals in order to eliminate the disease entirely. However, the ELISA test may not be efficient for this monitoring due to the imperfect test specificity, which generates false-positive test results in the herd free of MAP. Moreover, with the low test sensitivity of the ELISA test, infected animals may escape detection and infect many other animals before they are identified. Therefore, the FC test, which has near-perfect test specificity and high test sensitivity, is recommended even though the FC test is more expensive with slower results than the ELISA

[26] Note that the NPV in this study is the sum of discounted net cash flows.

test. In short, a combination of improved hygiene management and test-and-cull using either an annual or biannual FC test is highly recommended since these are the most and second most cost-effective control options considered in this study.

The empirical results show the number of animals infected with MAP and animals in the subclinical and clinical stages of JD increases during the planning duration of 50 years in the absence of a control program as in previous studies (Groenendaal and Galligan, 2003, Groenendaal et al., 2002). However, in practice, it could be possible to observe that even in the absence of an active control program, elimination of JD, though not necessarily of the causal pathogen MAP, has been successful in some infected herds. There could be several reasons for this discrepancy between field experience and our empirical results. The most probable explanation is that it is unlikely that a farm with a serious production problem would not engage in some form of implicit control. Therefore, low producing and sick cows are culled regardless of the causation and it could, in effect, eliminate JD, though animals infected with the causal pathogen MAP may still remain in the herd.

In sharp contrast, although our empirical results imply that the causal pathogen MAP can be eliminated from the herd entirely, which is consistent with previous studies (Groenendaal and Galligan, 2003, Groenendaal et al., 2002), in practice complete elimination is generally difficult to accomplish. For example, in Canada or the U.S., we could not find an evidence to prove that a control program successfully eliminates MAP and JD. There are two possible explanations for this. One is that most producers who have a JD problem have initiated a control program only recently, as Canada and the U.S. only created a national voluntary control program in 2005 and 2002, respectively. Given that the elimination of MAP and JD requires a long-term plan, as shown in Table 2.7, more time might be required to document the success of

MAP and JD control strategies. Another is that elimination of MAP and JD in our empirical results could be due to the fact that the potential risk of stochastic re-introduction of MAP (e.g., via purchased animals or humans with contaminated clothing) which, given the lack of information on this risk assessment, is ignored in this study.

Conclusion

This study presented a conceptual framework for developing an infectious disease control model in livestock which is applied as a discrete optimal control model to evaluate the long-term feasibility and profitability of various control methods for the causal pathogen MAP which causes Johne's disease in dairy herds. Results show that elimination of the disease requires a long-term plan with implementation of at least one of the control strategies. Any MAP control method yields a higher NPV of the farm's net cash flow compared to no control. Implementing either additional calf-hygiene management or test-and-cull using a FC test can control the disease, but these are most effective when combined with each other in reducing the infection rate in MAP-infected herds.

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CHAPTER 3

ECONOMIC ANALYSIS OF *MYCOBACTERIUM AVIUM* SUBSPECIES *PARATUBERCULOSIS* VACCINES IN DAIRY HERDS

Abstract

Johne's disease, or paratuberculosis, is a chronic infectious enteric disease of ruminants, caused by infection with *Mycobacterium avium* ssp. *paratuberculosis* (MAP). Given the absence of a fail-safe method of prevention or a cure, Johne's disease can inflict significant economic loss on the U.S. dairy industry, with an estimated annual cost of over $200 million. Currently available MAP control strategies include management measures to improve hygiene, culling MAP serologic- or fecal-positive adult cows, and vaccination. Although the two first control strategies have been reported to be effective in reducing the incidence of MAP infection, the changes in herd management needed to conduct these control strategies require significant effort on the part of the dairy producer. On the other hand, vaccination is relatively simple to apply and requires minor changes in herd management. Despite these advantages, only 5% of U.S. dairy operations use vaccination to control MAP. This low percentage of adaption of this technology is due to limited information on its cost-effectiveness and efficacy and some important inherent drawbacks associated with current MAP vaccines.

This study investigates the epidemiological impacts and economic values of MAP vaccines in various stages of development. We create scenarios for the potential epidemiological impacts of MAP vaccines, and then estimate economically justifiable values at which vaccines become economically beneficial to dairy producers such that a net present value (NPV) of a farm's net cash flow can be higher than the NPV of a farm employing no control or alternative

non-vaccine controls. Any vaccination with either low or high efficacy considered in this study yields a higher NPV compared to no control. Moreover, high-efficacy vaccines generate an even higher NPV compared to a farm that employs alternative controls, making vaccination economically attractive. Two high-efficacy vaccines are particularly effective in MAP control and NPV maximization. One is a high-efficacy vaccine that reduces susceptibility to MAP infection. The other is a high-efficacy vaccine that has multiple efficacies on the dynamics of MAP infection and disease progress. Only one high-efficacy vaccine, in which the vaccine is targeted at reducing MAP shedding and the number of clinical cases, is not economically beneficial to dairy producers compared to an alternative non-vaccine control, when their herds are highly infected with MAP.

Introduction

Johne's disease (JD), or paratuberculosis, is a chronic enteric disease of ruminants, caused by infection with *Mycobacterium avium* ssp. *paratuberculosis* (MAP). JD is one of the most serious infectious diseases in dairy cattle given that it produces considerable economic losses and that, at present, there is no cure or fail-safe prevention. MAP infection routes in dairy cattle include intrauterine infection, postpartum infection via fecal-oral contact and the uptake of MAP-contaminated colostrum and milk (Sweeney, 1996, USDA, 1997, Benedictus et al., 2008). MAP infection normally occurs very early in the life of dairy cattle, but clinical symptoms of JD are most commonly seen in adults and include reduced milk production, decreased fertility, decreased body-weight, and increased mortality (USDA, 1997, Kudahl and Nielsen, 2009, Smith et al., 2009, Aly et al., 2010). Although not all MAP-infected animals develop clinical JD, the

production inefficiencies alone can cause significant economic loss for dairy producers (Ott et al., 1999, Groenendaal et al., 2002, Pillars et al., 2009, Raizman et al., 2009).

In the U.S., the annual cost to the dairy industry was estimated to be more than $200 million in 1997 when herd-level MAP prevalence was approximately 22% (USDA, 1997). This cost has likely risen as the percent of the U.S. dairy herds infected with MAP has increased to at least 68% (USDA, 2008). Moreover, a potential link between MAP and Crohn's disease (Feller et al., 2007, Waddell et al., 2008, Hermon-Taylor, 2009) could further increase the cost of MAP to the dairy industry by either prompting strict regulations on dairy production or altering consumption of dairy products (Groenendaal and Zagmutt, 2008). These animal and human health concerns, together with the economic losses associated with MAP, have increased public interest in minimizing the spread of MAP infection and ultimately in eradicating MAP altogether.

In the absence of effective treatment, calf hygiene management[27] and test-and-cull[28] control strategies are usually recommended and practiced for controlling MAP. Both control strategies are economically beneficial for dairy producers compared to no control and are reported to be effective in reducing the incidence of MAP infection (Dorshorst et al., 2006, Collins et al., 2010, Lu et al., 2010, Sorge et al., 2010, Cho et al., 2011). However, these two control strategies require significant added effort on the part of the dairy producer in order to achieve effective MAP control. Moreover, test-and-cull often allows a large portion of MAP-infected animals, particularly infected animals shedding low amounts of MAP, to remain in the herd and act as a source of further MAP infection due to the low sensitivity of currently available

[27] Calf hygiene management aims to prevent postpartum infection of calves, the most susceptible animals, by providing MAP-free colostrum and milk and avoiding MAP-contamination of the calving area.
[28] Test-and-cull aims to remove MAP shedding animals, the main source of MAP infection and economic loss, by testing adults and slaughtering those found to be test-positive.

MAP tests (Collins et al., 2006). The limitations associated with these two-control strategies often result in limited adoption or success of the control and elimination of MAP in dairy herds.

Besides the above control strategies, MAP vaccinations are currently available and reported to be cost-effective and provide partial protection by decreasing fecal shedding of MAP and reducing the clinical symptoms of JD (Van Schaik et al., 1996, Kalis et al., 2001, Muskens et al., 2002, Groenendaal and Galligan, 2003, Rosseels et al., 2006). However, vaccination is the least used strategy for controlling MAP because 1) the reported efficacy of the vaccines is varied and inconclusive (Harris and Barletta, 2001, Köhler et al., 2001, Muskens et al., 2002); 2) there has been only one study investigating the cost-effectiveness of vaccination based on field trial data rather than assumptions (Van Schaik et al., 1996); and 3) there are some inherent drawbacks associated with current MAP vaccines (Harris and Barletta, 2001, Köhler et al., 2001, Muskens et al., 2002).

Killed MAP vaccines, which are most commonly used worldwide, have been found to cause cross-reactivity with bovine tuberculosis (TB) diagnostics, which may potentially result in false-positive TB test results for MAP-vaccinated animals. Such false-positive TB tests may have a large impact on TB control and therefore MAP vaccination is limited to farms that are under close monitoring of regulatory agencies. This, together with limited information on their efficacy on MAP control, results in vaccination being used by only 5% of dairy operations in the U.S. as a control method for MAP (USDA, 2008). Alternatives such as live vaccines, though generally more effective, have the potential risk of spreading viable MAP and therefore have not been approved in the U.S.

Despite such limitations, vaccination has distinct advantages over calf hygiene management and test-and-cull. In particular, its ease of application and minimal need for changes

in herd management might make it an attractive MAP control strategy. In addition, several types of improved MAP vaccines, including subunit-based, DNA-based, and recombinant, are in various stages of research, development and evaluation worldwide to overcome the limitations associated with currently available vaccines and to enhance efficacy in MAP control (Koets et al., 2006, Rosseels and Huygen, 2008, Keeble and Walker, 2009). Although reports of the cost-effectiveness and efficacy of MAP vaccines are not yet fully informed or conclusive, these new developments, together with the aforementioned advantages make vaccination of increasing interest to the dairy industry. Moreover, in the U.S., potential additional costs caused by cross-reactivity between certain MAP vaccines and the TB test have been mitigated under a new federal order which has removed restrictions on herd movement and TB testing obligations even in states where TB has been found (USDA, 2010). Consequently, investigating the economics and epidemiological consequences of various MAP vaccines can help the dairy industry to make informed choices for MAP control.

The objective of this study is to evaluate the economic value of various MAP vaccines in dairy herds based on their impacts on MAP control. Because information on the efficacy and availability of vaccines is limited, we first create scenarios for the potential effects of various vaccines on epidemiological progress of MAP infection, and then identify economically justifiable values for them to be economically beneficial to dairy producers. To do this, we developed a discrete dynamic model that incorporates both economics and different epidemiological effects of vaccines on MAP transmission in a dairy herd. This model is coded using a mathematical programming and optimization software and empirically solved for a farm with alternative initial MAP infection levels to take into account a wide array of dairy farm situations.

Materials and methods

A discrete dynamic model is constructed to evaluate the economic value of various MAP vaccines based on their epidemiological consequences in MAP control. Because MAP infection takes several years to develop into JD, control measures require years to show tangible effectiveness. Therefore, evaluating the economic value of vaccination is best accomplished by using a dynamic model which incorporates: 1) the dynamics of MAP transmission within a herd and 2) the net present value (NPV) of a farm's cash flow over a long-term planning duration. The following section presents a MAP transmission model within a dairy herd that incorporates the epidemiological impact of various MAP vaccines. Scenarios representing various MAP vaccine impacts are then discussed. Lastly, an NPV formula is presented for dairy operations, taking into account the economic benefits and costs associated with vaccination.

MAP transmission model

Animal compartment model is developed from a previous multi-group model that described MAP transmission in a dairy herd (Lu et al., 2008, Mitchell et al., 2008, Lu et al., 2010, Cho et al., 2011). This animal compartment model is described in Figure 3.1, where the definitions of symbols are presented in Table 3.1. In Figure 3.1, animals within a herd are grouped into discrete and disjoint compartments according to their 1) infection state, 2) age with 6-month time steps, and 3) vaccination state. Animal infection states of MAP in a dairy herd are classified as: susceptible, resistant, transient, latent, low-shedding, and high-shedding. Animals in susceptible and resistant states are non-infected (free of MAP infection), whereas animals in transient, latent, low-shedding, and high-shedding states are infected with MAP. Animals in the

transient state do not show signs of JD and shed MAP transiently at a low level shortly after initial MAP infection (Whitlock et al., 2000). Animals in the latent state also do not show signs of JD, and shed no MAP. Animals in the low-shedding state are in a subclinical stage of JD and shed low levels of MAP $\leq$ 30 cfu/g (Whitlock et al., 2000), whereas animals in the high-shedding state are potentially showing clinical signs of JD and shed high levels of MAP >30 cfu/g (Whitlock et al., 2000).

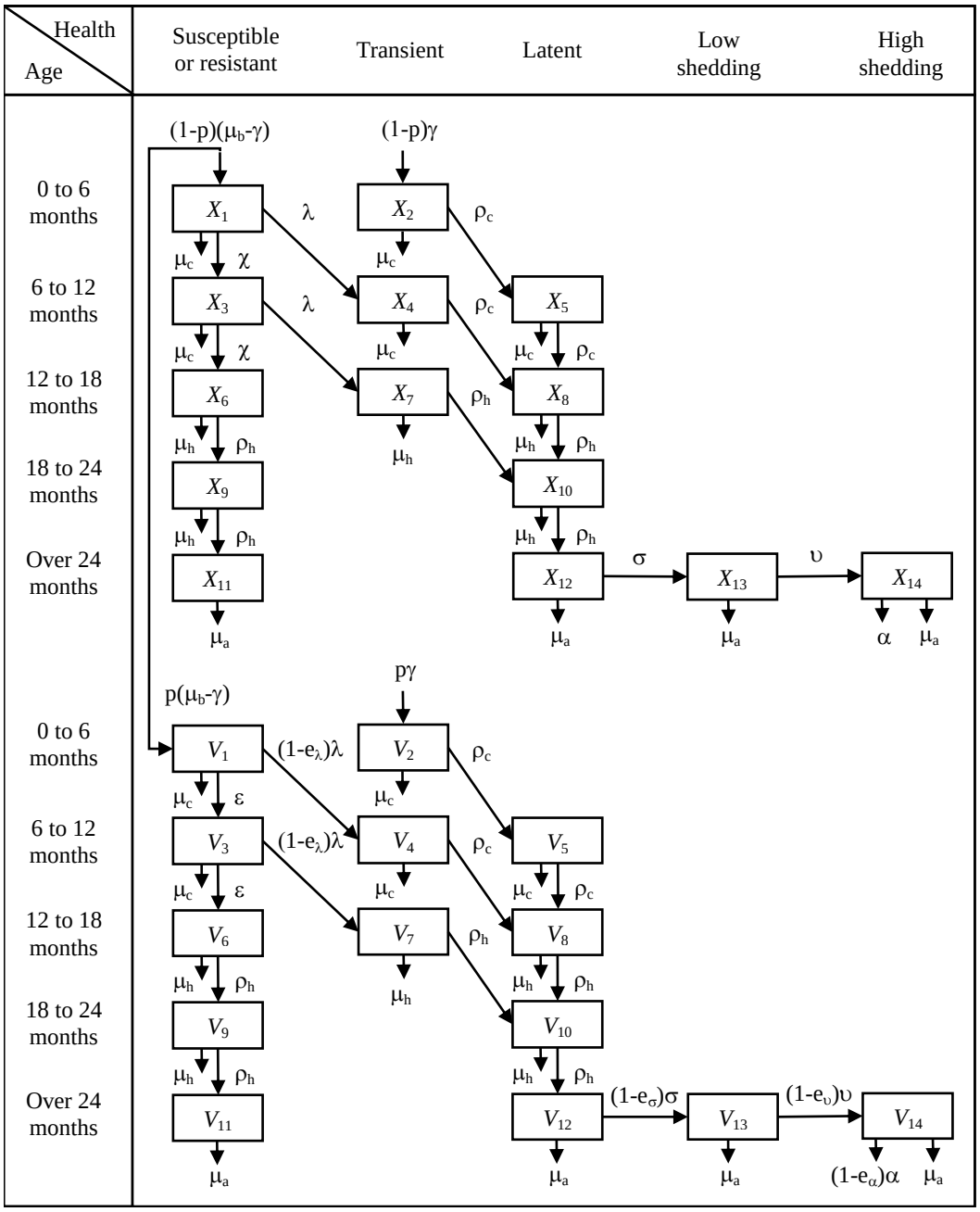

Figure 3.1. Animal compartment model, with the top segment representing no vaccination and the bottom segment representing vaccination across animal groups

Table 3.1. Definition of symbols in the animal compartment model describing animal movements and Mycobacterium avium ssp. paratuberculosis transmission within a herd

Symbol	Definition	Value[1]	Reference
α	Exit rate of high-shedding cows due to the clinical signs	0.25	Whitlock et al., 2000
	Exit rate of unvaccinated susceptible calves due to aging	Varies[a]	Calculated
	Exit rate of vaccinated susceptible calves due to aging	Varies[b]	Calculated
	Vertical MAP transmission rate	Varies	Calculated
	Horizontal MAP transmission rate	Varies	Calculated
μ_a	Exit rate of cows due to death, productivity, other diseases	Varies	Calculated
μ_b	Birth rate for female calves	0.215	USDA, 2007
μ_c	Exit rate of calves due to death	0.046	USDA, 2007
μ_h	Exit rate of heifers due to death	0.009	USDA, 2007
ρ_c	Exit rate of calves due to aging and disease progress	0.954[c]	Calculated
ρ_h	Exit rate of heifers due to aging and disease progress	0.991[d]	Calculated
σ	Exit rate of latent cows due to disease progress	0.5	Mitchell et al., 2008
υ	Exit rate of low-shedding cows due to disease progress	0.165	Van Schaik et al., 2003a
e_α	Vaccine efficacy in reducing the number of clinical cases	0-1	Defined
e_β	Vaccine efficacy in reducing MAP shedding level	0-1	Defined
e_λ	Vaccine efficacy in reducing susceptibility	0-1	Defined
e_σ	Vaccine efficacy in prolonging the latent period	0-1	Defined
e_υ	Vaccine efficacy in slowing progression from low to high shedding	0-1	Defined
p	Proportion of susceptible calves vaccinated	0-1	Defined

[1] Values are 6-month basis.

[a] $\chi=1-\mu_c-\lambda$ represents animal movements for unvaccinated susceptible calves due to aging.

[b] $\varepsilon=1-\mu_c-(1-e_\lambda)\lambda$ represents animal movements for unvaccinated susceptible calves due to aging.

[c] $\rho_c=1-\mu_c=0.954$ represents animal movements for infected calves due to either aging or infection progress: all calves 6 to 12 month old in the latent state become heifers 12 to 18 month old in the latent state for the next time period due to aging. Thus, the rate ρ_c representing this movement is $1-\mu_c$ where μ_c is the death rate of calves. On the other hand, all calves 6 to 12 month old in the transient state become heifers 12 to 18 month old in the latent state for the next time period due to infection progress. Therefore, this movement can also be represented by $\rho_c = 1-\mu_c$.

[d] $\rho_h=1-\mu_h=0.991$ represents animal movements for infected heifers due to either aging or infection progress, with the same reason as ρ_c representing animal movements for infected calves due to either aging or infection progress.

Animal age is closely related to susceptibility to infection and duration of infection states. In a dairy herd, animals are typically susceptible to infection up to the age of 12 months (Collins and Morgan, 1991, Sweeney, 1996, Whitlock and Buergelt, 1996) and then become resistant afterwards. Though some animals born to infected dams may be directly infected with MAP via intrauterine infection (Sweeney et al., 1992b), most likely susceptible animals are infected following contact with MAP from infected animals (Sweeney et al., 1992a, Whitlock et al., 2005a) and in contaminated environments (USDA, 1997). These newly infected animals enter the transient state, which often develops within a few days of infection and continues up to 6 months (Rankin, 1961). Given the duration of susceptible and transient states, animals in this state are typically younger than 18 months old. The latent state generally occurs following the transient state and continues for a long duration, but animals older than 24 months in this state

may begin to enter the low-shedding state and then the high-shedding state as the disease progresses.

Although there is some variation in the duration of infection states, 14 different infection and age classifications $i \in \boldsymbol{I} = \{1,...,14\}$ are defined to describe the above relationship between MAP infection progress and animal age: calves 0 to 6 month old in susceptible (i = 1) or transient state (i = 2), calves 6 to 12 month old in susceptible (i = 3), transient (i = 4), or latent (i = 5) state; heifers 12 to 18 month old in resistant (i = 6), transient (i = 7), or latent (i = 8) state, heifers 18 to 24 month old in resistant (i = 9) or latent (i = 10) state, and adult cows older than 24 months in resistant (i = 11), latent (i = 12), low-shedding (i = 13), or high-shedding (i = 14) state.

In order to examine the impact of MAP vaccines, animals are further classified into their vaccination state, unvaccinated or vaccinated, the number of which are represented respectively as X_i and V_i in Figure 3.1 for 14 different infection and age classifications $i \in \boldsymbol{I} = \{1,...,14\}$. In this model, some newborn calves enter the herd as non-infected, susceptible, calves (X_1 and V_1), whereas the others (X_2 and V_2) directly enter the transient state at the time of birth via intrauterine infection, which is represented by the rate γ, as shown in Figure 3.1. All calves, heifers, and adult cows are assumed to exit the herd at rates μ_c, μ_h, and μ_a in Figure 3.1, respectively. In addition, all high-shedding cows exit the herd at an additional rate α due to clinical symptoms of JD. All remaining animals in each compartment for the current time period are assumed to move to an adjacent compartment for the next time period due to aging (χ, ε, ρ_c, ρ_h), infection with MAP (λ), or infection progress (ρ_c, ρ_h, σ, υ)[29]. An arrow in Figure

[29] In the model, the rates ρ_c and ρ_h represent an animal movement for infected calves and heifers, respectively, due to either aging or infection progress. For example, all calves 6 to 12 month old in the latent state become heifers 12 to 18 month old in the latent state for the next time period due to aging. Thus, the rate ρ_c representing this movement is 1-μ_c where μ_c is the death rate of calves. On the other hand, all calves 6 to 12 month old in the transient state

3.1 indicates this movement. The equations of motion that represent the animal compartment model of Figure 3.1 are shown in Appendix.

Because revaccination or boosting has been reported to be ineffective to enhance an animal's ability to resist MAP infection (Harris and Barletta, 2001), only single vaccination of newborn calves is modeled in this study. In Figure 3.1, a proportion of newborn calves are vaccinated with parameter p ($0 \le p \le 1$) where p = 0 indicates that no calves are vaccinated, whereas p = 1 indicates that all calves are vaccinated. Once newborn calves are vaccinated, they move along the vaccinated animal compartments at the bottom of Figure 3.1, whereas unvaccinated newborn calves move along the unvaccinated animal compartments at the top of Figure 3.1. For the sake of model brevity, all new born calves are assumed to be vaccinated (p = 1) when producers implement vaccination as a control strategy for MAP.

The MAP infection routes of both intrauterine infection (vertical transmission) and postpartum infection (horizontal transmission) are considered in Figure 3.1. Vertical MAP transmission due to infected dams determines the number of transient calves 0 to 6 month old (X_2 and V_2) and is formulated in the vertical transmission rate γ in Figure 3.1:

$$\gamma(t) = \mu_b[\gamma_{12}\{X_{12}(t)+V_{12}(t)\}+\gamma_{13}\{X_{13}(t)+V_{13}(t)\}+\gamma_{14}\{X_{14}(t)+V_{14}(t)\}] \qquad (3.13)$$

where μ_b is the birth rate of female calves, and γ_{12}, γ_{13}, and γ_{14} (Table 3.2) are the proportion of calves infected in-utero by latent (X_{12}, V_{12}), low-shedding (X_{13}, V_{13}), or high-shedding (X_{14}, V_{14}) dams at time *t*, respectively. These parameters (γ_{12}, γ_{13}, and γ_{14}) may vary for unvaccinated and vaccinated infected dams. However, given the lack of information on these potential differences,

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become heifers 12 to 18 month old in the latent state for the next time period due to infection progress. Therefore, this movement can also be represented by $\rho_c = 1-\mu_c$.

the intrauterine transmission parameters are assumed to be identical for both unvaccinated and vaccinated infected dams.

Table 3.2. Definition of parameters in vertical and horizontal infection transmission rate formulas

Symbol	Definition	Value[1]	Reference
β_{Tr}	Transmission rate between transient animals and susceptible calves	0.5	Lu et al., 2008
β_{13}	Transmission rate between low-shedders and susceptible calves	1.0	Lu et al., 2008
β_{14}	Transmission rate between high-shedders and susceptible calves	5.0	Lu et al., 2008
γ_{12}	Portion of newborn calves infected at birth by latently infected dams	0.15	Sweeney et al., 1992b
γ_{13}	Portion of newborn calves infected at birth by low-shedding dams	0.15	Whitlock et al., 2005a
γ_{14}	Portion of newborn calves infected at birth by high-shedding dams	0.17	Whitlock et al., 2005b

[1] Values are 6-month basis.

Susceptible calves (X_1, X_3, V_1, V_3) may be infected by horizontal MAP transmission via fecal-oral contact, and the uptake of MAP-contaminated colostrum and milk: infection by transiently shedding calves (X_2, X_4, X_7, V_2, V_4, V_7) at the same housing site (calf-calf transmission) or by adult shedding cows (X_{13}, X_{14}, V_{13}, V_{14}) through direct fecal-oral transmission and indirect transmission via contaminated colostrum and milk (cow-calf transmission). To keep the modeling process manageable, three transmission rates β_{Tr}, β_{13}, and β_{14} (Table 3.2) are used to represent the multiple transmission routes: calf-calf transmission (β_{Tr}) and cow-calf transmission

by low (β_{13}) and high (β_{14}) shedding cows. The force of infection for unvaccinated susceptible calves (X_1, X_3) is formulated as λ in Figure 3.1:

$$\begin{aligned}\lambda(t) = \beta_{Tr}\{X_2(t) + X_4(t) + X_7(t)\} + \beta_{13}X_{13}(t) + \beta_{14}X_{14}(t) \\ +(1-e_\beta)[\beta_{Tr}\{V_2(t) + V_4(t) + V_7(t)\} + \beta_{13}V_{13}(t) + \beta_{14}V_{14}(t)]\end{aligned} \tag{3.2}$$

where potential vaccine efficacy in reducing fecal shedding level is represented by parameter e_β ($0 \le e_\beta \le 1$): $e_\beta = 0$ indicates that no vaccination is implemented or a vaccine has no decreasing effect on MAP shedding, whereas $e_\beta = 1$ indicates that a vaccine completely prevents MAP shedding. On the other hand, the force of infection for vaccinated susceptible calves (V_1, V_3) is modeled as $(1-e_\lambda)\lambda$ in Figure 3.1 to represent potential vaccine efficacy in reducing susceptibility e_λ ($0 \le e_\lambda \le 1$): $e_\lambda = 0$ indicates that a vaccine has no reducing effect on susceptibility to infection, whereas $e_\lambda = 1$ indicates that a vaccine completely prevents postpartum MAP infection.

In addition to reducing MAP shedding levels and susceptibility to infection, three other vaccine efficacies are considered for either current or next generation vaccines. These efficacies include prolonging the latent period of infected animals by delaying fecal shedding, slowing the progression of infectious animals from low- to high-shedding, or decreasing the number of clinical JD cases (Harris and Barletta, 2001, Rosseels et al., 2006, Rosseels and Huygen, 2008, Romano and Huygen, 2009). These potential efficacies are represented by the parameters e_σ, e_υ, and e_α in Figure 3.1, respectively.

Scenarios of MAP vaccine efficacy

Five possible efficacies are assumed for MAP vaccines (Figure 3.1): reduction of susceptibility (e_λ), reduction of MAP shedding level (e_β), slower progression from latency to low shedding (e_σ), slower progression from low to high shedding (e_υ), and a slower progression to clinical JD status (e_α). These efficacies range from 0, not effective at all, to 1, fully effective. Because information on MAP vaccine efficacies is limited, specific values for the parameters listed above are not fixed; instead, each efficacy is assigned a representative value of either 0.3 (relatively low efficacy) or 0.9 (relatively high efficacy). The economic values of vaccines with these two representative values can be used as reference values for those vaccines having different levels of efficacy.

The eight scenarios in Table 3.3, which comprise various combinations of vaccine efficacies, are developed for representing the potential impact of different types of vaccines on the epidemiological process of MAP. These scenarios allow us to compare different epidemiological impacts of current and possibly next generation vaccines on MAP control. Scenarios 1 and 2 represent vaccines with low- and high-efficacy levels, respectively, which specifically target reduction of susceptibility (perhaps the most desirable feature of MAP vaccines). Scenarios 3 and 4 represent vaccines with low- and high-efficacy values, respectively, for the vaccine effects reported in previous studies (Van Schaik et al., 1996, Kalis et al., 2001, Muskens et al., 2002, Groenendaal and Galligan, 2003, Rosseels et al., 2006), including decrease of fecal MAP shedding and reduction of clinical JD symptoms. Scenarios 5 to 8 represent vaccines having other multiple efficacies that could be produced by some of the currently available or next generation vaccines.

Table 3.3. Scenarios of Mycobacterium avium ssp. paratuberculosis vaccine efficacy

Scenario	Description	Value
1	Vaccine decreases susceptibility of susceptible calves	e =0.3
2		e =0.9
3	Vaccine reduces shedding level and the number of clinical Johne's disease (JD) cases	e =e =0.3
4		e =e =0.9
5	Vaccine delays the onset of low shedding and slows the progression from low to high shedding	e =e =0.3
6		e =e =0.9
7	Vaccine reduces MAP shedding level, delays the onset of low shedding and progression from low to high shedding, and decreases the number of clinical JD cases	e =e =e = e =0.3
8		e =e =e = e =0.9

Net present value

Given a set of epidemiological[30] constraints, the producer objective is to maximize the expected NPV from the sales of milk and cull cows for slaughter by deciding upon a choice of vaccination in Table 3.3. Although not all infected animals show clinical JD symptoms, this study assumes that animals in the low-shedding state show decreased milk production and body weight. As these animals progress to the high-shedding state, they are assumed to show considerable reduction in milk production and body weight, and have a higher mortality rate. The expected NPV of a producer's net cash flow from the sales of milk and cull cows for slaughter is specified as:

[30] Epidemiological constraints are the equations of motion in Appendix 1 describing the epidemiological process of Johne's disease described in Figure 3.1.

$$
\begin{aligned}
NPV = \sum_{t=1}^{T-1} \frac{1}{(1+r)^t} [& \{P_{\text{milk}} Q_{\text{milk}} + P_{\text{cull}} Q_{\text{cull}} \mu_a(t)\} \{X_{11}(t) + X_{12}(t) + V_{11}(t) + V_{12}(t)\} \\
& + P_{\text{milk}} Q_{\text{milk}} (1-\varphi_L) \{X_{13}(t) + V_{13}(t)\} + P_{\text{milk}} Q_{\text{milk}} (1-\varphi_H) \{X_{14}(t) + V_{14}(t)\} \\
& + P_{\text{cull}} Q_{\text{cull}} (1-\zeta_L) \{X_{13}(t) + V_{13}(t)\} \mu_a(t) + P_{\text{cull}} Q_{\text{cull}} (1-\zeta_H) \{X_{14}(t) + V_{14}(t)\} \mu_a(t) \\
& - C_{\text{calf}} N_{\text{calf}}(t) - C_{\text{heifer}} N_{\text{heifer}}(t) - C_{\text{cow}} N_{\text{cow}}(t) - M_{\text{vaccine}}(t) \mu_b N_{\text{cow}}(t)] \\
& + \frac{1}{(1+r)^T} [P_{\text{cull}} Q_{\text{cull}} N_{\text{cow}}(T) + P_{\text{sale}} \{N_{\text{calf}}(T) + N_{\text{heifer}}(T)\}]
\end{aligned}
\tag{3.3}
$$

In Equation (3.3), resistant (X_{11} and V_{11}) and latent (X_{12} and V_{12}) cows are expected to have normal milk production (Q_{milk}) and body weight (Q_{cull}), Low-shedding cows (X_{13} and V_{13}) and high-shedding cows (X_{14} and V_{14}), due to the disease, are expected to have lower milk production, $(1-\varphi_L)Q_{\text{milk}}$ and $(1-\varphi_H)Q_{\text{milk}}$ respectively, and lower body weight, $(1-\zeta_L)Q_{\text{cull}}$ and $(1-\zeta_H)Q_{\text{cull}}$ respectively, where the parameters φ_L, φ_H, ζ_L, and ζ_H represent milk production and body weight reductions due to JD (Table 3.4). In addition to milk and weight losses, high-shedding cows can exit the herd due to clinical JD symptoms, but these cows are assumed to be freely disposal instead of selling in market.

Table 3.4. Definition of variables and parameters used in the net present value equation

Rate	Description	Value[1]	Reference
C_{calf}	Base operating cost of raising a calf	\$395.00[a]	Karszes et al., 2008
C_{cow}	Base operating cost of raising a cow	\$1231.46	USDA, 2003-2007
C_{heifer}	Base operating cost of raising a heifer	\$395.00[a]	Karszes et al., 2008
$M_{vaccine}$	Maximum vaccination cost per dose	Varies	Calculated
N_{calf}	Number of calves	Varies	Calculated
N_{cow}	Number of cows	100	Calculated
N_{heifer}	Number of heifers	Varies	Calculated
P_{cull}	Cull-cow price per kg	\$1.0556	USDA, 2003-2007
P_{milk}	Milk price per kg	\$0.3393	USDA, 2003-2007
P_{sale}	Sale price of a one year old animal	\$867[b]	Karszes et al., 2008
Q_{cull}	Average cull cow weight	680.4 kg	USDA, 2003-2007
Q_{milk}	Average milk production per cow	4408.7 kg	USDA, 2003-2007
r	Discount rate	0.02	Assumed
T	Total follow up time of a dairy farm	100	Assumed
$_{H}$	Production adjustment factor for high-shedders	0.1[c]	Groenendaal et al., 2002
$_{L}$	Production adjustment factor for low-shedders	0.05[c]	Groenendaal et al., 2002
$_{H}$	Cull-weight adjustment factor for high-shedders	0.1	Assumed
$_{L}$	Cull-weight adjustment factor for low-shedders	0.05	Assumed

[1] Values are 6-month basis.

a. For the sake of simplicity, all heifer-raising operating costs for two years, \$1580 per heifer, are evenly assigned to the calf- and heifer-rearing activities.

[b] Sale price of a one year old animal is assumed to be identical to total cost of raising replacement heifer up to one year.

[c] Production reduction due to Johne's disease has been reported 5% to 20%.

The entire herd is assumed to be liquidated at the beginning of the terminal year ($T = 50$). For the sake of model brevity, all remaining cows in the terminal years are sold at the price of healthy cows. This is a reasonable assumption given that, with effective controls, no cows will show clinical symptoms of JD at the end of the 50 year period. Young stock is all sold at the price of one year old animals, the average age of young stock. The variables and parameters in Equation (3.3) are presented in Figure 3.1 (animal compartments) and Tables 3.1 (μ_a, μ_b, μ_c, and μ_h) and 3.4 (all other parameters).

Because information on retail price of the vaccines is unavailable, Equation (3.3) includes a variable (M_{vaccine}) representing the maximum vaccination cost per dose (MVC) for new-born calves. This MVC is determined endogenously in the optimization process by equating the NPV under vaccination to the NPV under an alternative control strategy: 1) the no-control alternative or 2) the best non-vaccine alternative. This allows us to obtain the uppermost cost level of vaccination, or MVC, that the farmer would be willing to pay for vaccination in order for them to be indifferent between applying vaccination and either alternative control strategy, as illustrated in Figure 3.2. In other words, a vaccination that cost less than the MVC generates a higher NPV to the farm than the NPV obtained using the no-control alternative or the best non-vaccine alternative. A positive MVC implies that there is a positive gross return that can be shared by a dairy producer (profit and implementation cost if any) and a vaccine company (profit and production cost). Conversely, a negative MVC implies that the vaccination is economically unattractive to a dairy producer because it generates a lower NPV than the no-control or the best non-vaccine alternative cases.

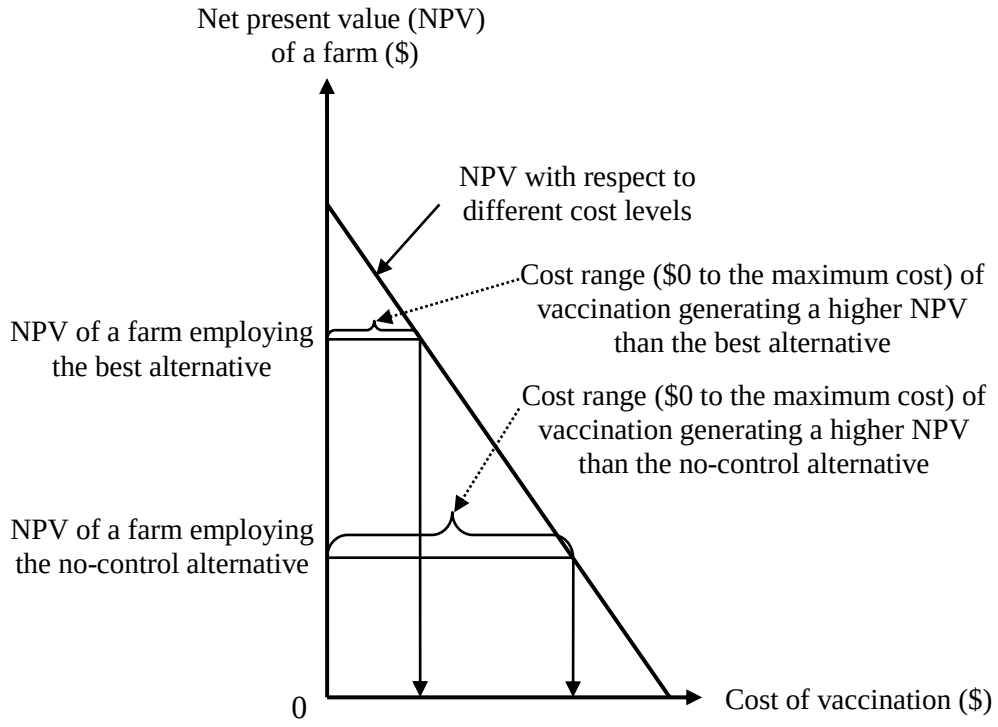

Figure 3.2. Maximum cost level of a vaccination at which farmers are indifferent between applying vaccination and either the no-control alternative or the best control alternative (Improved hygiene with test-and-cull using annual fecal culture test)

The NPV with the best non-vaccine alternative were obtained from our earlier study (Cho et al., 2011). This previous study utilized unvaccinated animal compartments at the top of Figure 3.1, to examine the cost-effectiveness of various MAP control options over the 50-year simulation period which included 1) improved hygiene, 2) advanced hygiene, 3) test-and-cull using annual fecal culture test, 4) test-and-cull using annual enzyme-linked immunosorbent assay (ELISA) test, 5) test-and-cull using biannual fecal culture test, 6) test-and-cull using biannual ELISA test, 7) improved hygiene with test-and-cull using annual fecal culture test, 8) improved

hygiene with test-and-cull using annual ELISA test, 9) improved hygiene with test-and-cull using biannual fecal culture test, 10) improved hygiene with test-and-cull using biannual ELISA test, 11) advanced hygiene with test-and-cull using annual fecal culture test, 12) advanced hygiene with test-and-cull using annual ELISA test, 13) advanced hygiene with test-and-cull using biannual fecal culture test, and 14) advanced hygiene with test-and-cull using biannual ELISA test.

This earlier study (Cho et al., 2011) utilized the same parameter values for the animal compartment model (Figure 3.1) and NPV equation (Equation 3.3) described in this study with the exception that the present study assumes a fixed herd size of 100 cows, whereas the previous study allowed herd size variation of 80 cows (minimum herd requirement) to 100 cows (maximum farm capacity), which allowed heavy culling of animals for test-and-cull strategy. The results of the previous study showed that the most cost-effective control option for MAP control was improved hygiene management and test-and-cull using an annual fecal culture test. Therefore, we used this control option as the best alternative to vaccination, which is the main focus of this study.

Because a mean true prevalence level of 10% MAP infection within a dairy herd is commonly assumed (Wells et al., 2002, Van Schaik et al., 2003b, Dorshorst et al., 2006), two initial MAP infection levels (10%, and 20%) are considered for the baseline farm, to account for the majority of dairy farm situations. Each infection level represents a percentage of MAP infected adult cows (sum of latent, low-shedding, and high-shedding cows) per all adult cows in a herd, and these initial MAP infection levels are obtained from a simulation of unvaccinated animal compartments at the top of Figure 3.1: an initial infection distribution among unvaccinated animal groups is simulated for a farm with an initial herd of 99 non-infected cows

and 1 latently infected cow, with no control implemented. The initial conditions for the state variables for a farm with two different MAP infection levels are drawn from time-points in this simulation that matched the desired infection level. These initial conditions are also identical to that used in Cho et al. (2011).

The model described in this section is coded using the General Algebraic Modeling System (version 22.5, GAMS Development Corporation, Washington, DC) and empirically solved for a farm with two possible MAP infection levels for a long-term, 50-year simulation period. The result of this optimization would allow identification of both epidemiological consequences of the eight vaccination options and the MVC value which makes a certain vaccination option economically more attractive in the long term, rather than either no control or the best alternative.

Results and discussion

In the absence of MAP control, simulation of unvaccinated animal compartments (the top of Figure 3.1) shows that MAP prevalence increases continuously (Figure 3.3), as reported in previous studies (Groenendaal et al., 2002, Groenendaal and Galligan, 2003). With any type of low-efficacy vaccines, elimination[31] of MAP is not observed in the 50-year simulation period given initial infection levels of 10% or 20% (Table 3.5). Only a low-efficacy vaccine with multiple effects on the dynamics of MAP infection and progress (Scenario 7)[32] will control MAP at a fairly constant rate after 5 years of vaccination (Figure 3.4). All other low-efficacy vaccines result in an increase in MAP prevalence (Figure 3.4), especially those targeted at reducing MAP-

[31] MAP is considered to be eliminated when its prevalence rate is less than 1%.
[32] This low-efficacy vaccine is targeted at reducing MAP shedding level, delaying the onset of shedding and progression from low to high shedding, and decreasing the number of clinical JD cases.

shedding level and the number of clinical JD cases (Scenario 3), and delaying the onset of MAP shedding and slowing the progression from low to high shedding states (Scenario 5). These vaccination scenarios result in a rapid increase of MAP prevalence because they only have partial and limited effects on reducing sources of MAP infection, which results in a slower elimination process than the MAP infection process within a herd.

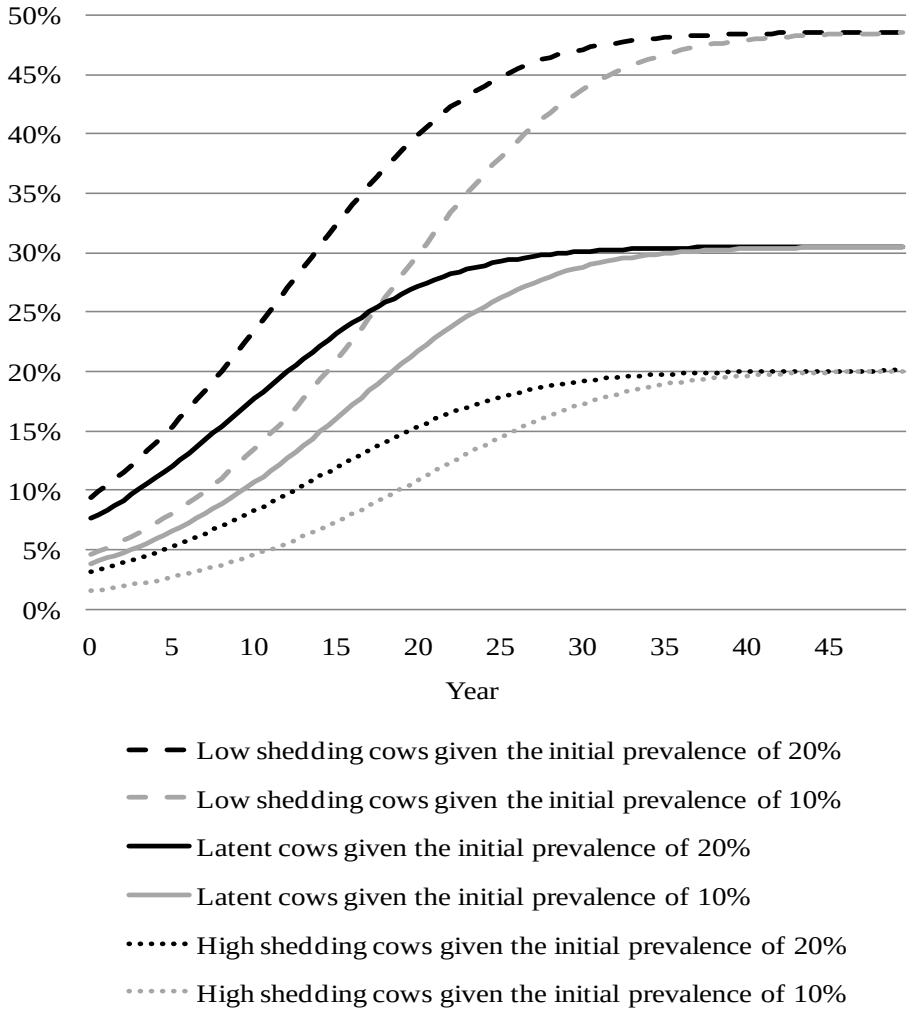

Figure 3.3. Dynamics of Mycobacterium avium ssp. paratuberculosis (MAP) infection without control: the portions of latent, low-shedding, high-shedding adult cows in the herd with a total of 100 cows and the initial MAP prevalence of 10% and 20%

Table 3.5. Expected elimination period of Mycobacterium avium ssp. paratuberculosis (MAP) for a herd with vaccination and the initial infection level of 10% and 20%

Scenario	Expected elimination[1] period of MAP	
	Initial MAP infection level of 10%	Initial MAP infection level of 20%
1	Never	Never
2	10.5 years	13 years
3	Never	Never
4	22.5 years	26 years
5	Never	Never
6	29 years	34 years
7	Never	Never
8	17.5 years	20 years

[1] MAP is considered to be eliminated when its prevalence rate is less than 1%, which implies that total number of MAP-infected cows is less than one given a fixed herd size of 100 cows.

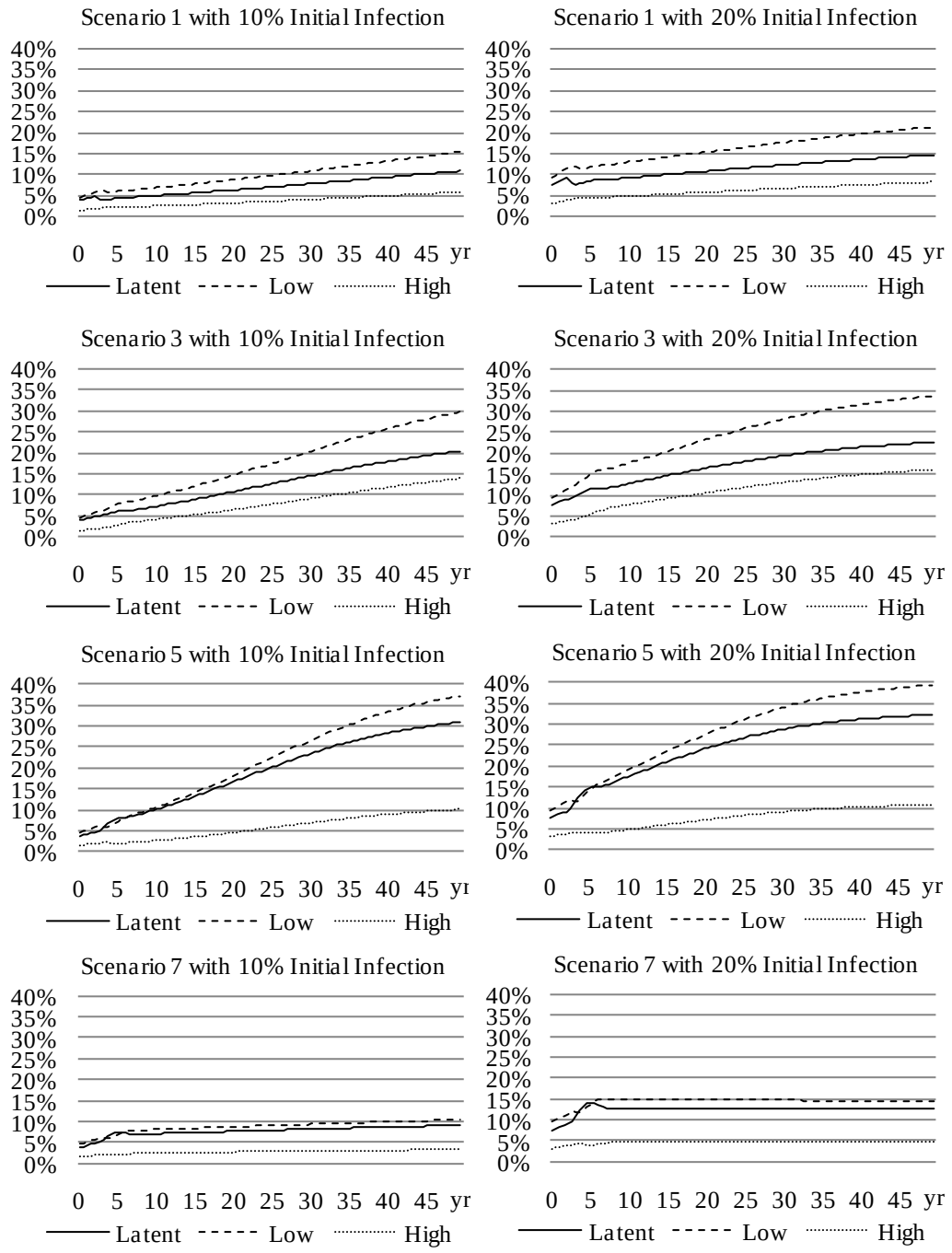

Figure 3.4. Impact of low efficacy vaccines on the dynamics of Mycobacterium avium ssp. paratuberculosis (MAP) infection: the portion of latent, low-shedding, high-shedding cows in a herd of 100 and the initial MAP prevalence of 10% and 20%

In sharp contrast, all high-efficacy vaccines successfully eliminate MAP within 29 years and 34 years for a herd with initial infection levels of 10% and 20%, respectively (Table 3.5), though none of these high-efficacy vaccines eliminates MAP quicker than the best alternative of improved hygiene management and test-and-cull using an annual fecal culture test, which eliminated MAP from the herd within 8 years for both MAP prevalence levels (Cho et al., 2011). Impact of these high-efficacy vaccines on the dynamics of MAP infection (Figure 3.5) suggests that the most effective vaccine scenario for eliminating MAP is a high-efficacy vaccine that reduces susceptibility of susceptible calves (Scenario 2), which results in eliminating MAP within 10.5 years (initial prevalence of 10%) and 13 years (initial prevalence of 20%), as shown in Table 3.5 and Figure 3.5. This finding implies that the prevention effect is the most useful possible effect of vaccines in MAP control.

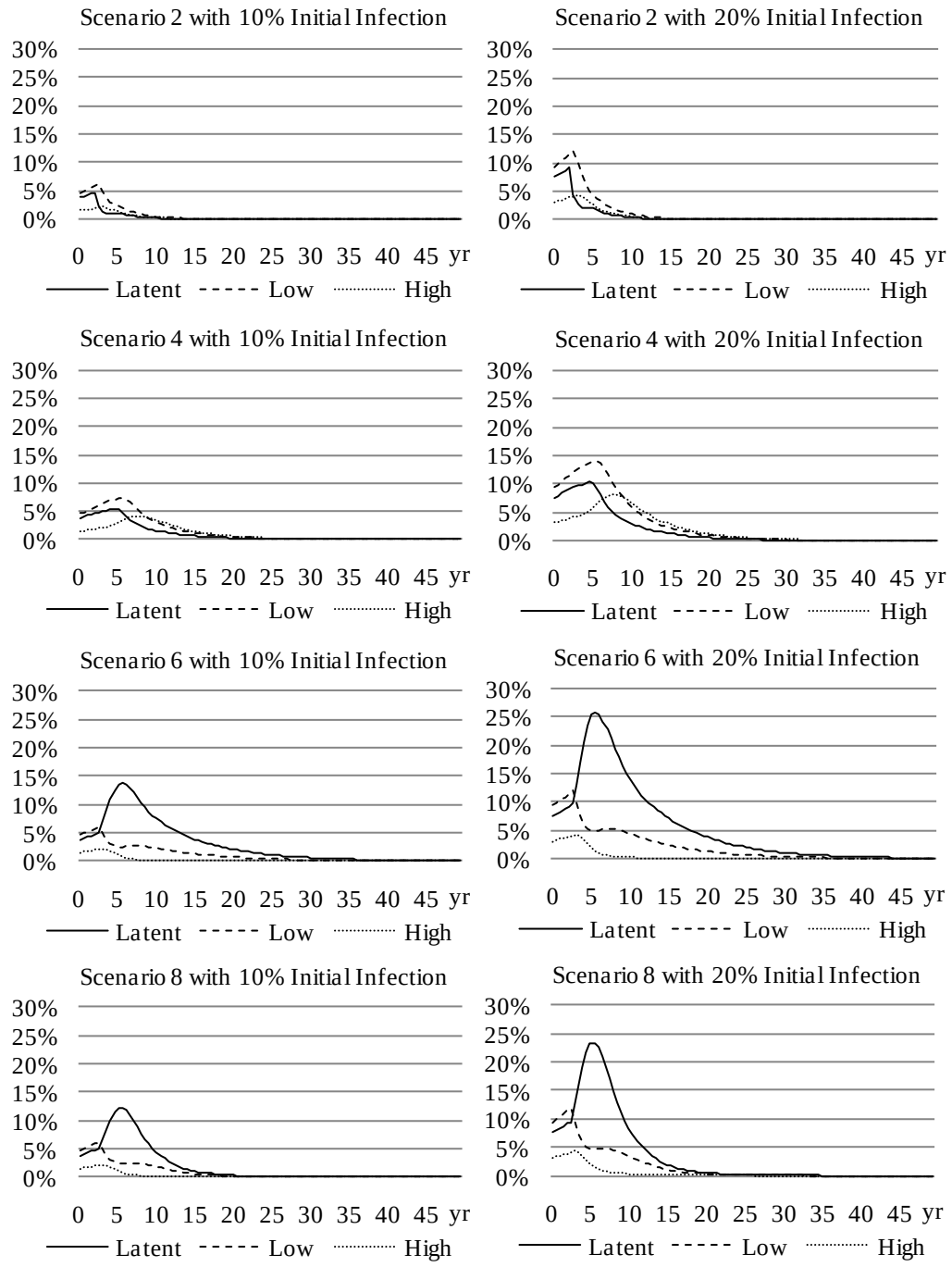

Figure 3.5. Impact of high efficacy vaccines on the dynamics of Mycobacterium avium ssp. paratuberculosis (MAP) infection: the portions of latent, low-shedding, high-shedding cows in a herd of 100 cows and the initial MAP prevalence of 10% and 20%

The second most effective vaccine scenario for eliminating MAP is a high efficacy vaccine with multiple effects on the dynamics of MAP infection and progress (Scenario 8)[33], eliminating MAP within 17.5 years (initial prevalence of 10%) and 20 years (initial prevalence of 20%), as shown in Table 3.5 and Figure 3.5. Given the multiple efficacies associated with this vaccine, a large portion of infected cows are non-clinically infected (latent cows), which does not cause economic loss. In addition, the aforementioned low-efficacy (Scenario 7 in Figure 3.4) with the same epidemiological impact with this high-efficacy vaccine in Scenario 8, is the only low-efficacy vaccine that controls MAP at a fairly constant rate. Therefore, dairy producers might want to control MAP using this low-efficacy vaccine (Scenario 7 in Figure 3.4) among all available vaccines when only low-efficacy vaccines are available, whereas they might want to control MAP using a high-efficacy vaccine (Scenario 2 in Figure 3.4) that reduces the susceptibility of eligible calves if high-efficacy vaccines become available.

Two other high efficacy vaccines also eliminate MAP. One vaccine is targeted at reducing both the shedding level and the number of clinical JD cases (Scenario 4) within 22.5 years (initial prevalence of 10%) and 26 years (initial prevalence of 20%), as shown in Table 3.5 and Figure 3.5. The other is targeted at delaying the onset of shedding and slowing the progression from low to high shedding (Scenario 6) within 29 years (initial prevalence of 10%) and 34 years (initial prevalence of 20%), also shown in Table 3.5 and Figure 3.5. Although the vaccine in Scenario 6 takes longer to eliminate MAP than that in Scenario 4, the portion of latent cows among all infected cows in Scenario 6 is much larger. The fact that latent cows do not cause economic loss, coupled with the epidemiological consequences of the second most

[33] This high-efficacy vaccine is targeted at reducing MAP shedding level, delaying the onset of shedding and progression from low to high shedding, and decreasing the number of clinical JD cases.

effective vaccine in Scenario 8, implies that prolongation of latency and slowed progression from low to high shedding may be the more economically beneficial effects of vaccination rather than reductions of MAP shedding level and reductions in the number of clinical JD cases. However, given the short MAP elimination period associated with Scenario 6, the relative economic benefit of the vaccines in Scenarios 4 and 6 is not as clear when considering epidemiological consequences alone. The epidemiological impacts of low- and high-efficacy vaccinations in Figures 3.4 and 3.5 suggest that the level of efficacy of vaccines are a more important feature of vaccination, than either MAP infection level within a herd, or the effects of a vaccine on the dynamics of MAP infection. In conclusion, any high-efficacy vaccine shows considerably better effects on MAP control compared to any low-efficacy vaccines.

In this study, the NPV of a MAP-free farm (0% initial infection level) is estimated to be $374,270 for the 50-year simulation period with a fixed herd size of 100 cows. On the other hand, the NPV of a MAP-infected farm is estimated to be considerably lower at $155,710 (10% initial infection level) and $88,819 (20% initial infection level) in the absence of MAP control. These low NPV values are not sustainable and imply that a farm would eventually need to engage in some type of remedial action as the number of subclinical (low-shedding) and clinical (high-shedding) cows increase over time, and before JD becomes pervasive in the herd. According to Cho et al. (2011), the best control alternative generated an NPV of $345,603 and $336,873[34], which are significantly higher compared to the above NPV of a farm without control, given the initial infection level of 10% and 20%, respectively. With MAP vaccinations, the upper-most cost level of vaccination, MVC, for the eight MAP vaccination scenarios, are standardized as the

[34] These NPVs were obtained when the herd size of 80 to 100 cows was allowed in order to allow heavy culling of test-positive animals under a test-and-cull strategy.

average present value per dose are presented in Figures 3.6 and 3.7. These results suggest that any MAP vaccination would yield a higher NPV than that using the no-control alternative (Figure 3.6), and most of the high-efficacy vaccines have potential to generate a higher NPV than using the best alternative (Figure 3.7).

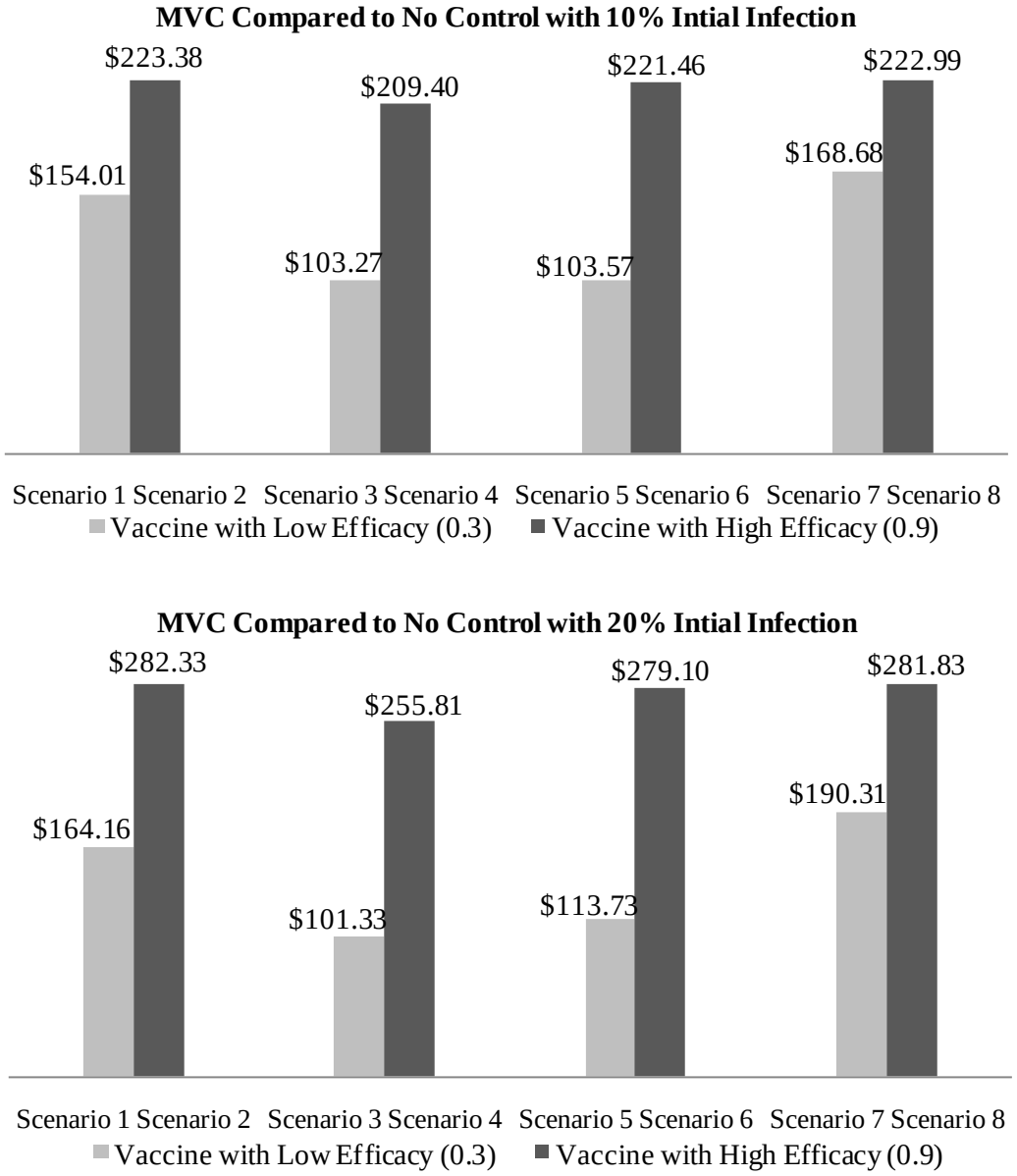

Figure 3.6. Maximum vaccination cost per dose (MVC) for Mycobacterium avium ssp. paratuberculosis (MAP) vaccine, which makes that vaccination option economically more attractive than no control when the initial MAP infection level is 10% or 20%

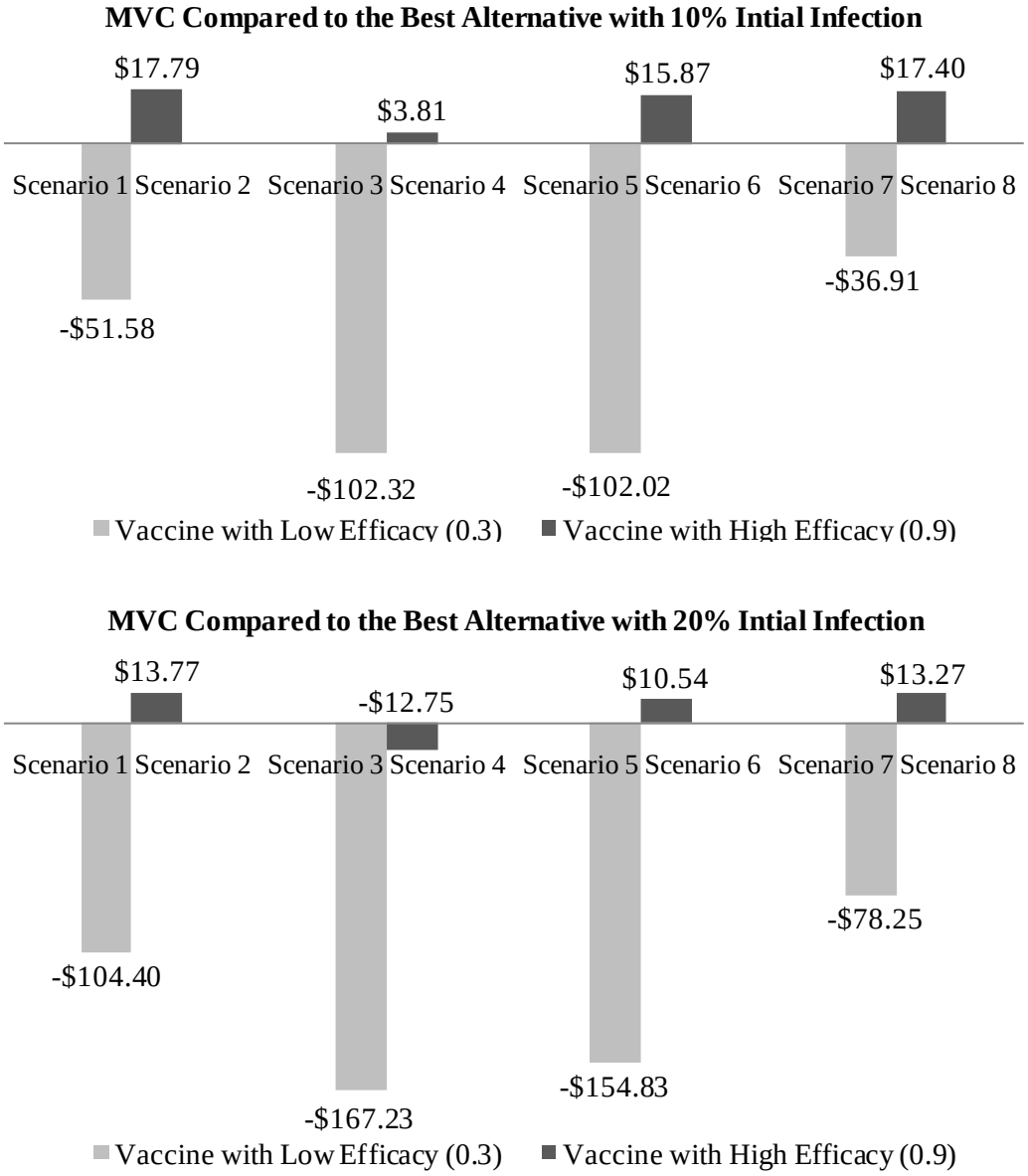

Figure 3.7. Maximum vaccination cost per dose (MVC) for Mycobacterium avium ssp. paratuberculosis (MAP) vaccine, which makes that vaccination option economically more attractive than the best alternative (improved hygiene management and test-and-cull using an annual fecal culture test) when the initial MAP infection level is 10% or 20%

Each MVC in Figures 3.6 and 3.7 is the maximum amount dairy producers should be willing to pay for implementing each vaccination instead of the no-control alternative or the best alternative control not involving vaccination. The high MVC in Figure 3.6 implies that any vaccination option has a high potential to be greatly beneficial to dairy producers, compared to no control. In particular, two high-efficacy vaccines should be particularly attractive to dairy producers: 1) a vaccine that reduces susceptibility to MAP infection (Scenario 2), and 2) a vaccine that has multiple efficacies (Scenario 8)[35]. These two scenarios in Figure 3.6 have MVC of $223.38 (initial prevalence of 10%) and $282.33 (initial prevalence of 20%), and $222.99 (initial prevalence of 10%) and $281.83 (initial prevalence of 20%), respectively. These MVC imply that JD inflicts an annual cost of $96.03 (=$222.99×43÷100) to $121.18 (=$282.33×43÷100) per cow in the herd[36]. These two high-efficacy vaccines also have the highest MVC of $17.79 (initial prevalence of 10%) and $13.77 (initial prevalence of 20%), and $17.40 (initial prevalence of 10%) and $13.27 (initial prevalence of 20%) when compared to the best alternative, respectively (Figure 3.7). Considering that these two high-efficacy vaccinations are the most effective (Scenario 2) and the second most effective (Scenario 8) vaccination options in controlling MAP, as discussed in the previous section, a high-efficacy vaccine that reduces susceptibility (Scenario 2) might be the best vaccination option overall, followed by a high-efficacy vaccine with multiple efficacies on the dynamics of MAP infection and progress (Scenario 8)[37].

[35] This vaccine targeted at reducing MAP shedding level, delaying the onset of shedding and progression from low to high shedding, and decreasing the number of clinical JD cases.
[36] 43 are the number of vaccinated calves per year and 100 are the number of cows in the herd.
[37] Vaccine targeted at reducing MAP shedding level, delaying the onset of shedding and progression from low to high shedding, and decreasing the number of clinical JD cases.

In the bottom of Figure 3.7, only one high-efficacy vaccine described in Scenario 4 has a negative MPV of -$12.75, which implies that this vaccination always generates a lower NPV than that using the best alternative, given the initial infection level of 20%. This implies that the vaccine in Scenario 4, in which the vaccine is targeted at reducing MAP shedding level and the number of clinical JD cases, may not be economically beneficial to dairy producers when their herds are highly infected with MAP. This result also implies that many of the currently available MAP vaccines may not be economically attractive compared to the best alternative of improved hygiene management and test-and-cull using an annual fecal culture test, when the herd is highly infected with MAP. This is because the vaccine in Scenario 4 is designed to represent the commonly reported effects of currently available MAP vaccines, which reduces MAP shedding level and the number of clinical JD cases. In addition, the negative MVC associated with the low-efficacy vaccine scenarios (Figure 3.7) suggest that none of the low-efficacy vaccine scenarios can generate a higher NPV compared to the best alternative, given the same infection levels, and therefore, they may not be an economically more attractive control method than the best alternative. Nevertheless, low-efficacy vaccines have high potential to generate a higher NPV compared to the no-control strategy, given that their MVC values are significantly positive for all scenarios, as shown in Figure 3.6.

The MVC values discussed above, however, are maximum values based upon breakeven estimates, and do not reflect profit sharing with vaccine developers nor take risk considerations into account. Therefore, even though a vaccination has a positive MVC, it may or may not be an economically better MAP control method compared to either alternative, since market prices for these hypothetical vaccines are not know at this time. For example, the maximum MVC for the high-efficacy vaccine in Scenario 2 is reported in Figure 3.7 as $17.79, given the initial infection

level of 10%. However, this MVC is not the potential economic benefit of the vaccination for a dairy producer relative to the best alternative. In fact, this number represents the potential maximum gross return from the vaccination, which would be shared by a dairy producer (profit and vaccination cost if any) and a vaccine company (profit and production cost). Therefore, whether or not this vaccination would generate a higher economic benefit, in terms of NPV, for a dairy producer, than the best alternative is inconclusive given the lack of information on the actual cost of the vaccine to the dairy producer. Nevertheless, this vaccination could generate a higher NPV of $362,034 and $349,592, compared to using the best alternative ($345,603 and $336,873) given an initial infection level of 10% and 20%, respectively, when the cost of the vaccination to the dairy producer is zero.

Although the MVC of the various vaccination scenarios are presented in Figures 3.6 and 3.7, it is useful to convert these into maximum feasible NPV[38] of vaccination (Table 3.6). Given a constant herd size of 100 cows and a birth rate of female calves of 0.215 per 6-months, the maximum feasible annual economic benefit[39] associated with vaccination compared to either no control or the best alternative can be calculated by multiplying a MVC value for a MAP vaccine times 43 (=100×0.215×2), which is the number of vaccinated calves per year. Adding the NPV of either no control or the best alternative to this annual economic benefit associated with vaccination represents the maximum feasible NPV of vaccination. The high-efficacy vaccination which decreases susceptibility of susceptible calves has the highest MVC value, (Scenario 2), and could generate an NPV of $362,034 and $349,592, which are significantly higher compared

[38] Maximum feasible NPV is the NPV with the vaccination compared to either no control or the best alternative when the cost of the vaccination is zero.
[39] Maximum feasible annual economic benefit is the annual economic benefit with the vaccination compared to either no control or the best alternative when the cost of the vaccination is zero. Positive value represents benefit, whereas negative value represents loss.

to a farm without control with an NPV of $155,710 and $88,819 given the initial infection level of 10% and 20%, respectively. These NPVs are also higher compared to a farm employing the best alternative (NPV of $345,603 and $336,873)[40].

Table 3.6. Maximum feasible net present value (NPV) of vaccination given the initial Mycobacterium avium ssp. paratuberculosis (MAP) infection level of 10% and 20%

Scenario	Maximum feasible NPV[1] of vaccination	
	Initial MAP infection level of 10%	Initial MAP infection level of 20%
1	$297,961	$240,445
2	$362,034	$349,592
3	$251,095	$182,412
4	$349,122	$325,097
5	$251,372	$193,865
6	$360,261	$346,609
7	$311,511	$264,598
8	$361,674	$349,130

[1] Maximum feasible NPV is the NPV with the vaccination compared to either no control or the best alternative when the cost of the vaccination is zero.

Conclusion

This study evaluates both the epidemiological consequences and economic value of various MAP vaccines in dairy herds, using a discrete dynamic model which incorporates dynamics of

[40] These NPVs were obtained when heavy culling of test-positive animals was allowed in the herds of 80 to 100 cows from our previous study for maximizing NPVs.

MAP transmission within a herd and maximized NPV of the farm's cash flow over a planning duration. Eight vaccination scenarios, which comprise various combinations of vaccine efficacies, are developed for representing the potential impact on the epidemiological process of MAP of different types of vaccines,. These scenarios allow us to compare different epidemiological impacts of current and possibly next generation vaccines on MAP control.

Results show that elimination of MAP requires a long-term plan with implementation of at least one of the high-efficacy vaccines. Any vaccination with either low or high efficacy yields a higher NPV compared to no control when the cost of these vaccinations is less than their MVC. Any high-efficacy vaccines, with the exception of the vaccine targeted at reducing MAP shedding level and the number of clinical JD cases (Scenario 4), generates an even higher NPV compared to a farm with the best alternative when the cost of these vaccinations is less than their MVC. Given the epidemiological consequences and economical benefits of various vaccination options, a high-efficacy vaccine that reduces susceptibility (Scenario 2) might be the best vaccination option, and a high-efficacy vaccine that has multiple efficacies on the dynamics of MAP infection and progress (Scenario 8)[41] might be the second best vaccination option for dairy producers in MAP control.

[41] Vaccine targeted at reducing MAP shedding level, delaying the onset of shedding and progression from low to high shedding, and decreasing the number of clinical JD cases.

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APPENDIX

The dynamics of MAP transmission within a herd described in the animal compartment model of Figure 3.1 are represented by the following equations of motion:

$$X_1(t+1) = (1-p)\{\mu_b - \gamma(t)\}[\sum_{i=11}^{14}\{X_i(t)+V_i(t)\}]+[1-\{\lambda(t)+\mu_c+\chi(t)\}]X_1(t) \quad [A1]$$

$$X_2(t+1) = (1-p)\gamma(t)+[1-(\mu_c+\rho_c)]X_2(t) \quad [A2]$$

$$X_3(t+1) = \chi(t)X_1(t)+[1-\{\lambda(t)+\mu_c+\chi(t)\}]X_3(t) \quad [A3]$$

$$X_4(t+1) = \lambda(t)X_1(t)+[1-(\mu_c+\rho_c)]X_4(t) \quad [A4]$$

$$X_5(t+1) = \rho_c X_2(t)+[1-(\mu_c+\rho_c)]X_5(t) \quad [A5]$$

$$X_6(t+1) = \chi(t)X_3(t)+[1-(\mu_h+\rho_h)]X_6(t) \quad [A6]$$

$$X_7(t+1) = \lambda(t)X_3(t)+[1-(\mu_h+\rho_h)]X_7(t) \quad [A7]$$

$$X_8(t+1) = \rho_c[X_4(t)+X_5(t)]+[1-(\mu_h+\rho_h)]X_8(t) \quad [A8]$$

$$X_9(t+1) = \rho_h X_6(t)+[1-(\mu_h+\rho_h)]X_9(t) \quad [A9]$$

$$X_{10}(t+1) = \rho_h[X_7(t)+X_8(t)]+[1-(\mu_h+\rho_h)]X_{10}(t) \quad [A10]$$

$$X_{11}(t+1) = \rho_h X_9(t)+[1-\mu_a(t)]X_{11}(t) \quad [A11]$$

$$X_{12}(t+1) = \rho_h X_{10}(t)+[1-\{\mu_a(t)+\sigma\}]X_{12}(t) \quad [A12]$$

$$X_{13}(t+1) = \sigma X_{12}(t)+[1-(\mu_a(t)+\upsilon)]X_{13}(t) \quad [A13]$$

$$X_{14}(t+1) = \upsilon X_{13}(t)+[1-(\mu_a(t)+\alpha)]X_{14}(t) \quad [A14]$$

$$V_1(t+1) = p\{\mu_b - \gamma(t)\}[\sum_{i=11}^{14}\{X_i(t)+V_i(t)\}]+[1-\{(1-e_\lambda)\lambda(t)+\mu_c+\varepsilon(t)\}]V_1(t) \quad [A15]$$

$$V_2(t+1) = p\gamma(t)+[1-(\mu_c+\rho_c)]V_2(t) \quad [A16]$$

$$V_3(t+1) = \varepsilon(t)V_1(t)+[1-\{(1-e_\lambda)\lambda(t)+\mu_c+\varepsilon(t)\}]V_3(t) \quad [A17]$$

$$V_4(t+1) = (1-e_\lambda)\lambda(t)V_1(t) + [1-(\mu_c+\rho_c)]V_4(t) \quad [A18]$$

$$V_5(t+1) = \rho_c V_2(t) + [1-(\mu_c+\rho_c)]V_5(t) \quad [A19]$$

$$V_6(t+1) = \varepsilon(t)V_3(t) + [1-(\mu_h+\rho_h)]V_6(t) \quad [A20]$$

$$V_7(t+1) = (1-e_\lambda)\lambda(t)V_3(t) + [1-(\mu_h+\rho_h)]V_7(t) \quad [A21]$$

$$V_8(t+1) = \rho_c[V_4(t)+V_5(t)] + [1-(\mu_h+\rho_h)]V_8(t) \quad [A22]$$

$$V_9(t+1) = \rho_h V_6(t) + [1-(\mu_h+\rho_h)]V_9(t) \quad [A23]$$

$$V_{10}(t+1) = \rho_h[V_7(t)+V_8(t)] + [1-(\mu_h+\rho_h)]V_{10}(t) \quad [A24]$$

$$V_{11}(t+1) = \rho_h V_9(t) + [1-\mu_a(t)]V_{11}(t) \quad [A25]$$

$$V_{12}(t+1) = \rho_h V_{10}(t) + [1-\{\mu_a(t)+(1-e_\sigma)\sigma\}]V_{12}(t) \quad [A26]$$

$$V_{13}(t+1) = (1-e_\sigma)\sigma V_{12}(t) + [1-\{\mu_a(t)+(1-e_\upsilon)\upsilon\}]V_{13}(t) \quad [A27]$$

$$V_{14}(t+1) = (1-e_\upsilon)\upsilon V_{13}(t) + [1-\{\mu_a(t)+(1-e_\alpha)\alpha\}]V_{14}(t) \quad [A28]$$

where the definitions of parameters and transition rates are presented in Tables 3.1 to 3.2 and the vertical (γ) and horizontal (λ) MAP transmission rates are described in Equations (3.1) and (3.2), respectively.

CHAPTER 4

DISSERTATION CONCLUSION

Worldwide, infectious diseases in livestock play a critical role in the profitability of an individual farm, the survival of the livestock industry itself, and international trade and trade policies. Besides their direct economic effect on a nation's economy, some infectious animal diseases are linked to diseases in humans, increasing the critical need to identify cost-effective control programs. Although economic models are available to examine the economics of animal diseases and their control strategies, they exhibit limitations in their ability to incorporate the complexity inherent in disease-specific epidemiology in livestock. Therefore, the main objective of this dissertation was to create and empirically apply a control model to examine the economics of infectious disease control in livestock, using *Mycobacterium avium* ssp. *paratuberculosis* (MAP) and Johne's disease (JD) control in dairy herds as its paradigm.

The conceptual model in Chapter 2 represents an animal compartment model which allows animal herd dynamics within a herd or region to be accounted for by placement into different compartments according to their characteristics such as production- and infection-status. The application of this general model to JD in dairy herds illustrates its usefulness as a complex animal disease control model in that it presents not only the economic benefit of control strategies, but also the consequences of control strategies on specific disease dynamics within a herd. Therefore, the model is a useful tool for evaluating the economic impact of livestock disease and its control, and for developing a cost-effective disease control program on farms. The empirical results of applying the conceptual model to JD control in a dairy herd in Chapter 2 illustrates that control of JD will significantly improve profitability for dairy producers with

MAP infected herds. The empirical results also show that elimination of the disease requires a long-term plan with implementation of at least one of the control strategies. The most effective control option in reducing the infection rate in a MAP infected and therefore JD-affected herd being a combination of different types of control strategies.

Chapter 3 examined the economics of potential control strategies on livestock disease control. Although there are many different ways to evaluate the potential economic value of a prospective disease control strategy, it is extremely difficult to incorporate all necessary evaluation tools into a single model structure. This dissertation presented a method for examining the epidemiological impact and economic value of hypothetical Johne's disease vaccines in dairy herds using net present value together with economic value analysis. This was accomplished by creating various scenarios for the potential epidemiological impact of currently existing and to be developed vaccines. Utilizing the empirical model presented in Chapter 2, economically justifiable values at which such vaccines could become economically beneficial to dairy producers were estimated. The empirical results in Chapter 3 show that any vaccination with either low or high efficacy yields a higher net present value compared to no control, while elimination of MAP, the causal pathogen of Johne's disease, requires a long-term plan with implementation of at least one of the high-efficacy vaccines. Moreover, most of the high-efficacy vaccines generated an even higher net present value compared to alternative controls currently used on farms, making future vaccinations economically attractive.

The models and results presented in Chapters 2 and 3 of this dissertation provide meaningful tools for examining the economics of infectious disease and its actual and potential control strategies in livestock. It must be acknowledged, however, that the potential risk of stochastic re-introduction of the disease (e.g., via purchased animals or humans with

contaminated clothing) was ignored in this dissertation. In addition, the animal disease control model presented did not provide the optimality conditions of either a conceptual or empirical model. This was due to the complexity of both the general animal compartment model and MAP infection dynamics within a herd. Therefore, an extension of this dissertation would be to develop a stochastic dynamic model for livestock disease control to illustrate the optimality conditions for the more realistic stochastic dynamic model.