

Simulating Control Strategies for Johne's Disease on NZ Dairy Farms: effects on the prevalence and economic impact of disease

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Introduction

Johne's disease (JD), caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP) is a chronic wasting syndrome in ruminants that is endemic in many countries. It is thought to occur on about 70% of New Zealand dairy farms and to cause economic loss due to premature culling and reduced milk production.

Widespread speculation about the possible role of MAP in Crohn's disease in humans has led to concern within the dairy industry, particularly since some studies have shown that the organism can survive pasteurization. A national control strategy would promote and protect New Zealand dairy export sales and match efforts by other major dairy producers such as the US, Australia and some EU countries.

The insidious nature of JD and poor performance of diagnostic tests suit computer simulation methods for investigation of potential control strategies. JD was first modelled by Walker in 1988. A modified version of Walker's model was used by Collins et al (1991) while a considerably more complex model, JohneSSim, was published by Groenendaal in 2001. JohneSSim is a stochastic, dynamic simulation model initially developed to evaluate control strategies for JD in The Netherlands (Groenendaal 2002; Weber 2004) and later the United States (Groenendaal 2003). The aim of this study was to adapt JohneSSim to model JD in the New Zealand dairy system and simulate possible control strategies.

Material and Methods

1. The JohneSSim model

JohneSSim simulated JD at the cow level at six month intervals over 20 a year period. Results were average values for a population of herds representing New Zealand dairy farms. This population was comprised of sub-populations representing different management proficiencies. Model input was derived from recent case/control and longitudinal studies conducted by the EpiCentre, Massey University, data provided by Livestock Improvement Corporation, expert opinion and international data. Probability distributions were used to describe variation in key parameters such as replacement, infection with JD, pathogenesis, mortality, and testing for the disease. True prevalence (henceforth prevalence), costs and benefits were simulated for the control strategies.

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Herd characteristics

The average New Zealand dairy herd was described as seasonal calving with 280 cows, an annual increase in herd size of 3% and replacement rate of 23%. Milk production was 311kgMS per cow per year. Voluntary culling was based on a retention pay-off value (RPO) (Groenendaal 2004), representing future expected profits for an individual cow. Heifers calved at two years of age with calf mortality rate of 8% and for older cows 5%.

Characteristics of Johne's disease

JD was assumed to be present on 70% of New Zealand dairy farms at a within farm seroprevalence of 2–4%, equating to a true prevalence of approximately 15%. JD cows progressed through six possible infection states (Table 1) and transmission could occur by six possible routes (Table 2). The sensitivity of testing methods for JD varied depending on the infection state of the individual.

Table 1. Infection states simulated by JohneSSim

Infection state	Description
1	Susceptible calves
2	Resistant animals (not infected and > 1 year old)
3	Latent infection but not shedding
4	Low infectiousness, excreting for 2 months post calving
5	Highly infectious, infected and shedding
6	Clinical, infected and constantly shedding

Table 2. Transmission routes simulated by JohneSSim

Transmission route	Description
1	Fetal infection
2	Infection during birth
3	Consumption of infectious colostrum
4	Consumption of infectious milk
5	Infection from environmental contamination
6	Infection due to introduction (purchase) of an infected animal

Milk production was reduced by 5% and 20% for cows in infection state 5 and 6. There was a 20% probability that pooled milk became infective after milk/colostrum from a constantly shedding cow was added. Ninety five percent of calves fed from an infective pool became infected.

The purchase of bulls was not considered a major risk factor for the introduction of JD. Bulls were assumed to be kept for a short mating period (October-February), separate from young stock, and then sold. Bulls are mostly between 2-3 years of age and selected on good condition.

Economics

Input parameters describing economic values were derived from industry statistics and where no other data source was available from expert opinion.

The economic benefit of a control strategy was defined as the reduction in the losses caused by JD at the farm level relative to the no-control situation.

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The Net Present Value (NPV) is a standard economic measure for valuing investments with an extended time component. It represents the economic attractiveness of each strategy, defined as the benefits minus the costs, with future financial values discounted to their present-day value. Thus it is the value of the strategy to the farmer at the time it commences.

Net Present Value = total discounted profits – total discounted costs

The Risk Profile

The simulated population of dairy farms was divided into four sub-populations with different risk profiles based on 'good' and 'bad' calf management with respect to JD. 'Good management' was defined as separation of the calf and dam less than 12 hours after birth and sending young stock off farm for grazing, while 'bad management' was defined as having longer than 12 hours of contact between calf and dam, and not using off-farm grazing. The proportion of farms in each of the four possible combinations of these two practices was estimated by the expert group.

2. Control Strategies

Control strategies were derived from suggestions by the expert group and from strategies used by other countries (Table 3).

Table 3. Control strategies for New Zealand dairy farms simulated by JohneSSim

	Strategy	Test-and-cull	Calf management	Other
1	Annual test-and-cull, ELISA (AnELISA)	ELISA (cows > 3 yrs) confirmed by faecal culture	None	None
2	Annual test-and-cull, faecal culture (AnFC)	Faecal culture (cows > 2 yrs)	None	None
3	Improved Farm Management (Mgt)	None	Improved mgt. ¹	None
4	Improved Farm Management and annual test and cull, faecal culture (MgtAnFC)	Faecal culture (cows < 2 yrs)	Improved mgt.	None
5	Vaccination (Vac)	None	None	Vac ²
6	Improved Farm Management and vaccination (MgtVac)	None	Improved mgt.	Vac
7	Remove offspring of clinical cows (OfSCIC)	None	None	Remove calves of clinical cows
8	Test-and-cull (bi-annual pooled faecal culture (BiAnFC)	Bi-annual pooled faecal culture	None	None
9	Genetic Resistance (GenRes)	Genetic resistance		
10	Bi-annual test-and-cull (pooled faecal culture), Improved Farm Management and off farm grazing (BiAnFCMO)	Bi-annual pooled faecal culture	Improved mgt and hygiene	Off farm grazing

¹ mgt = management

² vac = vaccination

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Key Assumptions

We have assumed that vaccination increases the average period between infection and onset of heavy shedding from 5 to 7 years.

Improved Farm Management comprised improved calf hygiene during birth and in the first few days of life, provision of non-infectious pooled milk/colostrum and reducing the likelihood of faecal/oral contact by using off farm grazing for young stock.

Genetic resistance was assumed to gradually reduce the probability that a calf would be infected, such that it's probability of infection at year 20 was 50% less than at year one. In addition, resistant but infected cows were assumed to be most likely to begin shedding at 7.5 years old, while non-resistant cows were most likely to begin shedding at 5.5 years old.

3. Sensitivity Analysis

Input parameters for this model were associated with varying and in some cases substantial amounts of uncertainty. Sensitivity analysis was conducted on ten disease spread parameters (Table 4) to illustrate their relative importance.

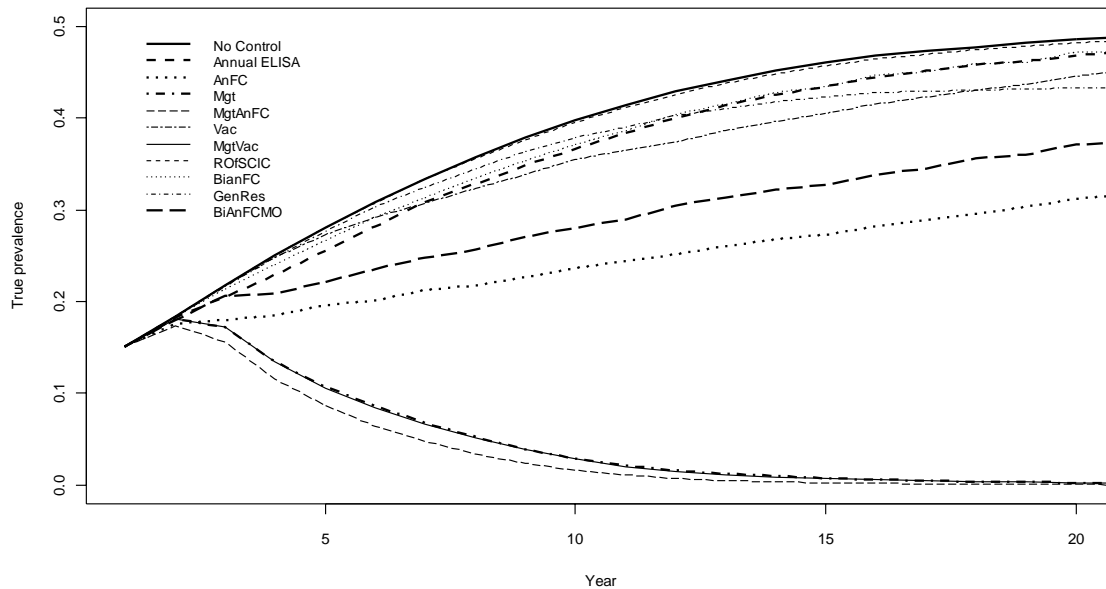
Table 4. Target parameters and variations applied for sensitivity analysis of JohneSSim

Parameter	Label	Variation from default
Infectiousness of pooled feed	NoCollInf	Assumed that pooled milk/colostrum is never infectious
Infection rate around birth	LowPPI	Assumed probability of infection around birth is 90% lower than default
Faecal/oral contact rate	LoFORat	Assumed faecal/oral contact rate is 90% lower for on-farm grazing
Culling rate	HiCulRat	Culling rate is 28% rather than 23%
Culling rate	LowCulRat	Culling rate is 18% rather than 23%
Duration of disease	ErlyShdg	Infected cows shed MAP for 2 yrs rather than 1 before clinical illness
Replacement practice	OpnHrds	Assume 70% rather than 100% of herds did not purchase female stock
Milk production of JD cows	JDMPSim	Assume production by infected cows was less reduced than default
Foetal infection rate	HiFetInf	Foetal infection rate is approximately twice the default value
Improved farm management	PPMgtPor	Improving peri-natal management reduced infection rate by 50% instead of 90%

Results

1. Epidemiology

Figure 1. Prevalence of Johne's disease on the average infected dairy farm without control and under control strategies



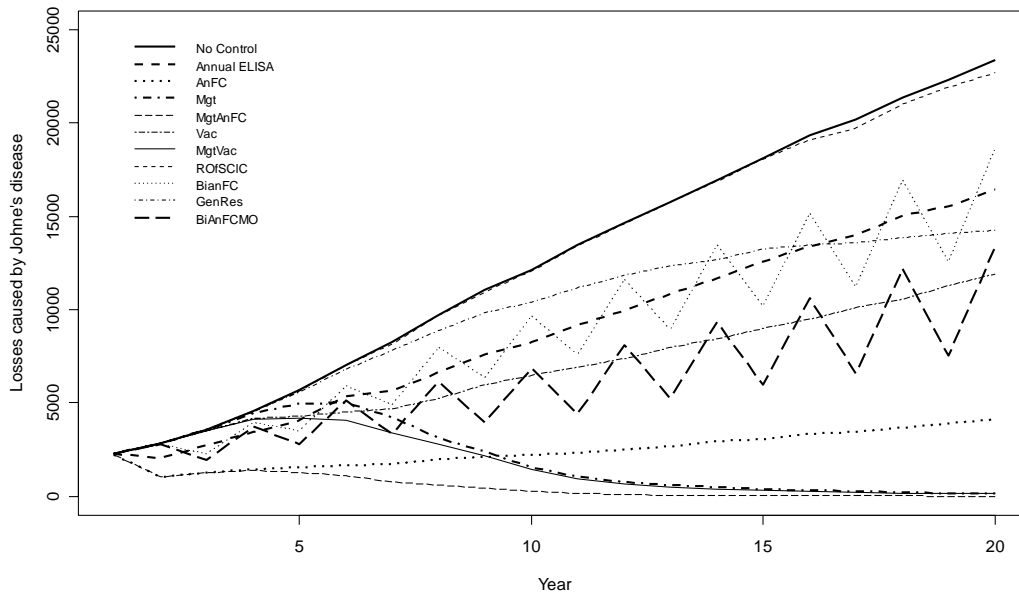
The prevalence of JD on the average infected farm without control increases from 15% to 48% over 20 years (Figure 1). Most strategies failed to reverse the trend of increasing prevalence though did slow the rate at which it increased. The exceptions were strategies using Improved Farm Management (Mgt, MgtAnFc, MgtVac) which reduced prevalence to less than 1% after 11 years.

2. Economic impact of the disease

In the absence of control, annual losses due to JD for the average infected farm increased gradually from \$2298 to \$23,395/yr after 20 years (Figure 2).

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Figure 2. Annual losses caused by Johne's disease on the average infected dairy farm without control and under control strategies



Greatest benefits were obtained when using the three strategies incorporating Improved Farm Management (Mgt, MgtAnFc, MgtVac). This reduction was achieved after 11 years if Improved Farm Management was combined with annual test-and-cull using faecal culture, or after 18 years if used alone or in combination with vaccination. Annual test-and-cull using faecal culture substantially reduced, but did not reverse, the increase in losses over time. Under all other strategies, losses increased steadily over time. Bi-annual test-and-cull methods cause oscillation in the losses due to JD.

Annual costs of control strategies steadily increased for strategies that failed to reduce the prevalence from its initial value. Highest costs were associated with the test-and-cull strategy using faecal culture (\$29,500 at year 20) but were also high using an ELISA test (\$12,900 at year 20). In contrast vaccination was low cost at \$2,200 after 20 years.

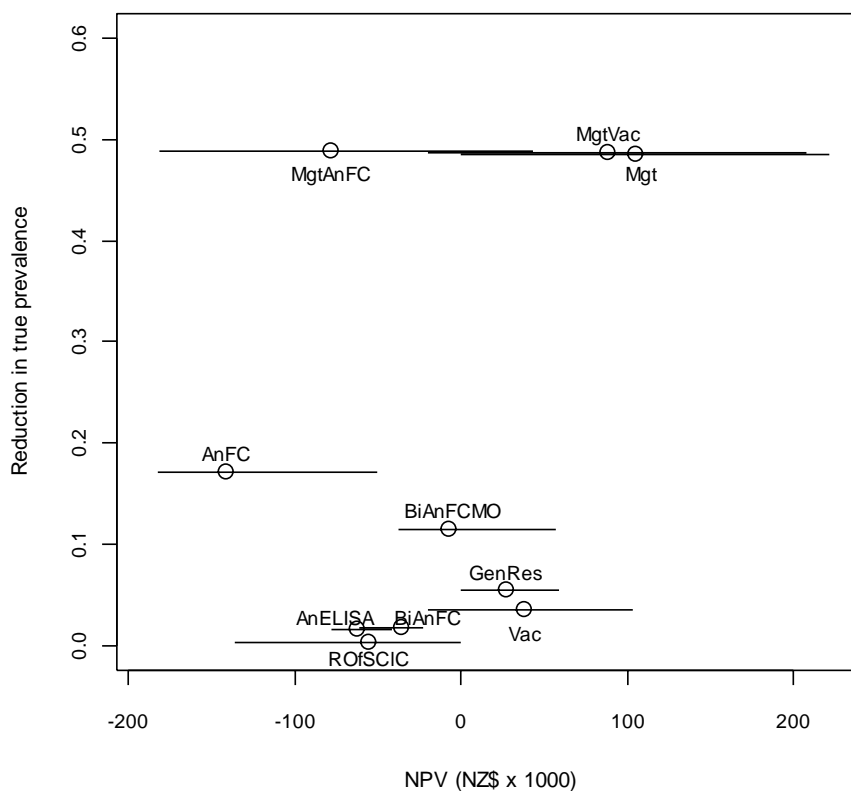
A positive Net Present Value (NPV) (Table 5) represents an economically attractive option to the average infected dairy farm. Where no cost was estimated for a strategy the NPV is equivalent to the benefits of that strategy. Where no cost was estimated the NPV represents the maximum cost at which a strategy remains economically attractive.

Costs of the Improved Farm Management and Genetic Resistance strategies were not estimated. The cost associated with no control was zero, while other zero values in Table 5 were explained by both the cost and benefit of a strategy being zero.

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Table 6. Net present value (\$NZ) of simulated control strategies for Johne's disease to the average New Zealand dairy farm and range containing the central 80% of dairy farms

Control strategy	Net Present Value		
	10%	Average	90%
No control	0	0	0
Annual test-and-cull (ELISA)	-78136	-61798	-41086
Annual test-and-cull (faecal culture)	-182132	-141000	-50447
Improved Farm Management	0	105275	221662
Improved Farm Management and annual test-and-cull (faecal culture)	-181743	-78184	42807
Vaccination	-19964	38563	103494
Improved Farm Management and vaccination	-19956	88500	207938
Remove offspring of clinical cows	-136405	-54971	0
Test-and-culling with bi-annual faecal culture	-60943	-35946	-22735
Genetic Resistance	0	27641	58361
Bi-annual test-and-cull (pooled faecal culture), Improved Farm Management and off farm grazing	-37779	-7482	56709

Figure 3. Comparison of reduction in prevalence of Johne's disease and Net Present Value after 20 years for ten simulated control strategies

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Strategies were ranked by reduction in prevalence and NPV (Figure 3) after 20 years. Strategies toward the top right of the figure being both economically attractive and effective at reducing the prevalence of JD while strategies toward the bottom left were both expensive and ineffective at reducing disease prevalence.

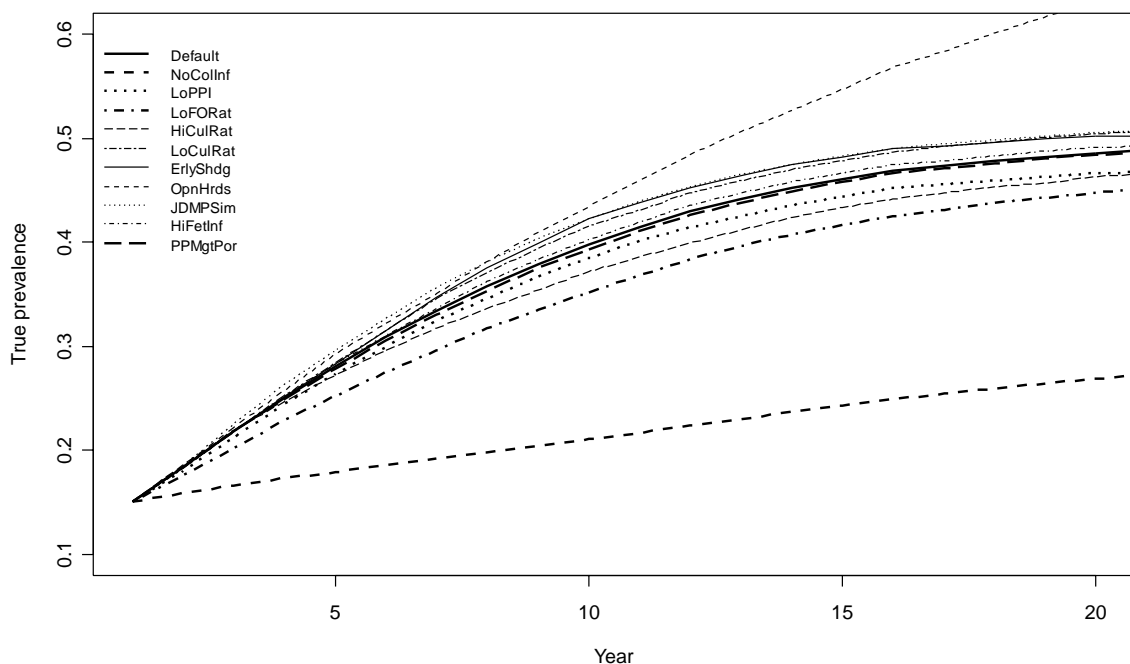
Improved Farm Management was clearly the superior method for disease control. Combining it with other strategies returned very little further benefit in the case of vaccination, and in the case of test-and-culling using faecal culture, increased the cost such that the strategy was no longer economically attractive. Removing the offspring of clinical cows caused no appreciable change in disease prevalence.

The interval containing the NPV for the central 80% of farms was wide for strategies that caused a large reduction in losses. Under such strategies, the difference between farms maximising the benefit and those getting no benefit was large. In contrast, strategies causing a small reduction in losses had a small difference between farms maximising the benefit of the strategy and those getting no benefit, thus the range of these strategies was narrow.

3. Sensitivity Analysis

Many of the input variables were based on uncertain data. A limited amount of New Zealand data was available, data from other countries was collected from dairying systems that differ from those used in New Zealand and opinion would occasionally vary within the expert group. Sensitivity analysis was performed on ten variables for which input data was considered uncertain and compared to the default situation (No Control) to evaluate model behaviour and stability (Figure 4).

Figure 4. Sensitivity analysis for prevalence of Johne's disease on the average infected dairy farm with no control strategy



For eight of the ten variables changing the input value produced results very similar to the default settings. Assuming that pooled colostrum was never infectious (NoCollnf) resulted in a much slower increase in prevalence. In the default situation a highly infectious cow contributing to the pool had a 0.2 probability of making that pool infectious to calves. After 20 years the prevalence was estimated at 27% compared with the default situation of 50%. Assuming that 70% of herds infrequently buy small numbers of animals (OpnHrds) caused prevalence to increase more quickly in the second half of the simulation period to 65% after 20 years compared to 50% in the default situation where all herds were closed.

Discussion

The JohneSSim model was adapted to simulate JD within New Zealand's unique pasture based dairy production system. It was then used to simulate the reduction in prevalence and cost effectiveness of ten possible control strategies. The current understanding of the epidemiology of JD is incomplete and varying degrees of uncertainty were inherent in epidemiological input parameters. Thus, focus should be on the general trends described by the model rather than specific values. However the model was stable and produced sensible output.

Prior to selecting a method for controlling JD on a national level, the aim of this control must be clearly defined as one of two options. The first is a reduction in the effects of disease, the second is eradication. Eradication represents a lofty goal and a very long process, in reality, equivalent to reducing the disease to very low levels. It requires that the increase in prevalence over time observed with No Control be reversed. Alternatively, a reduction in the effects of disease relative to the No Control situation was achieved to varying levels by all strategies.

JohneSSim generates a population of farms to represent New Zealand dairy farms and variation within this population to represent variation in farm level prevalence and management practices. Control strategies were more beneficial on heavily infected, poorly managed farms and non-existent on well managed farms free of JD. Accumulation of individual farm effects formed a distribution from which the average effect and range could be observed.

In the absence of control the prevalence of JD on the average infected farm increased from 15% to 48% and the losses from \$2,300 to \$23,400 over 20 years. This trend conflicts with anecdotal evidence that JD is less prevalent in New Zealand today than 20 years ago. However data to support or refute such anecdotes is scant.

Improved Farm Management was the most effective strategy by a large margin and the only one to reverse the trend of increasing prevalence, such that it declined to <1% after 11 years. Subsequently, the costs associated with the disease also decline to negligible levels. The costs of implementing this strategy were not estimated due to the high degree of uncertainty. However using the Net Present Value this strategy will be economically attractive provided it costs the average infected farm less than \$105,000 over 20 years. Combining Improved Farm Management with an annual test-and-cull strategy using faecal culture caused losses to decline more quickly, but hugely inflated the cost such that the combination was not economically attractive. In the New Zealand dairy production system the exceptionally high workload during the calving period represents a challenge to implementing the additional measures required to meet the Improved Farm Management criteria.

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Annual test-and-cull using faecal culture provided the best disease control of non-management strategies. However, this strategy was the most costly and even when accounting for its financial benefits, still cost the average infected farm \$141,000 over 20 years. On farms with low levels of disease, where whole herd testing would cause a minor reduction in losses and prevalence, the Net Present Value was estimated at \$-182,000. In addition, the logistic challenges associated with laboratory capabilities suitable for handling a national scale testing program must not be underestimated. Substituting an ELISA test for faecal culture reduced the level of disease control and while providing a lower cost, remained economically unattractive. Diagnostic tests are important tools in disease control, for example screening herds for disease (Muskens, Barkema et al. 2000; Quist, Nettles et al. 2002; Pence, Baldwin et al. 2003), but for a sustained control strategy more cost effective options should be sought.

We assumed the effect of vaccination to extend the period prior to shedding thus increasing the lifespan and milk production of infected cows and reducing premature culling. This strategy was economically attractive due to a very low cost of implementation and provided substantial reduction of JD associated losses. However, it provided only minor reduction in prevalence. Combining this strategy with a low cost strategy that effectively reduces disease prevalence, such as Improved Farm Management provides optimum control. Existing vaccines appear to have a protective effect (Kormendy 1992; Wentink 1994), though the specific mechanism for this protection is not identified. An improved vaccine would be valuable, however the time and investment involved in development is likely to be substantial. Any vaccine used in New Zealand must be compatible with current test methods for tuberculosis in cattle.

The Genetic Resistance strategy provided a unique approach to the control of JD. It was relatively slow to affect the prevalence of disease, but after 20 years had achieved a zero rate of increase, a feat matched only by Improved Farm Management. The costs of implementing this strategy were not estimated due to much uncertainty. If the costs were less than the Net Present Value to the average infected farm (\$27,641), this strategy would be economically attractive. We assumed that the first cohort of resistant calves were born in year one of the simulation period and did not include a period or costs for identifying and developing resistant genes to the point where they were included in a calf's genetic makeup. The time and costs associated with this process would be substantial, almost certainly larger than the Net Present Value, and given the current debate over the link between JD and Crohn's disease in humans, a faster acting control strategy would be more appropriate.

Removing the offspring of clinical cows appears to be a direct and low cost method of reducing the on-farm prevalence of disease. However this strategy had no appreciable effect on the prevalence of disease and was not economically attractive due to the costs of replacing culled young stock, most of which would have normal milk production.

A thorough sensitivity analysis assessed ten parameters and showed the model behaved sensibly within the normal range of operation. Unfortunately no data was available with which to validate the model output. Of the ten parameters varied, infectivity of pooled milk/colostrum caused the greatest change in model predictions while the frequency of reintroduction (through purchase) of disease on to a farm had the second largest effect. More detailed data describing purchase patterns would enable default input to be confirmed as representative of the true situation.

Assuming that pooled milk/colostrum was not infectious to calves, through dilution of infective milk to non-infective levels by pooling, substantially reduced the rate at which prevalence

increased. This reduced rate was considered a more accurate representation of the true situation than the default rate by some members of the expert group. However, other adjustments or combinations of adjustments could be made to generate an identical curve.

More detailed information on the infectivity of pooled milk/colostrum would be valuable but such a study would face some challenges. Most importantly, the minimum infective dose for a calf and the route of infection is not known with certainty, while the concentration of MAP in infected milk is generally at the lower limit of existing detection methods (Sweeney, Whitlock et al. 1992; Streeter 1995). Sweeney et al (1992) reported 2-8 CFU/50mL milk sample by cows shedding large amounts of MAP. If a calf consumes four litres of milk per day, this equates to 160-640 CFU consumed daily. However it is possible that faecal contamination of the udder is the cause of infection, rather than MAP within the milk. Currently no broadly accepted techniques are available to accurately enumerate MAP levels in milk (Grant and Rowe 2001).

In conclusion, the JohneSSim model has provided insight into JD on New Zealand dairy farms. Results should be interpreted as trends rather than definitive values due to uncertainty in many input parameters. Never the less, the model clearly indicates the benefits of improving farm management for reducing the prevalence of JD and the benefits of vaccination for reducing losses due to JD. A control strategy based on Improved Farm Management and combined with a suitable vaccine, if possible, is recommended on the basis of model results. An initial whole herd test and cull for farms beginning a control program may also be worthwhile. Test-and-cull and cull approaches were neither economically or epidemiologically attractive. Sensitivity analysis showed the infectiousness of pooled milk/colostrum and the frequency of reintroduction of infection to have a strong influence on prevalence of disease and additional information to accurately describe these parameters would be valuable.

References

- Collins, M. and I. Morgan (1991). "Epidemiological model of paratuberculosis in dairy cattle." *Preventive Veterinary Medicine* 11: 131-146.
- Grant, I. and M. Rowe (2001). "Methods for detection and enumeration of viable mycobacterium paratuberculosis from milk and milk products." *Bulletin of the International Dairy Federation* 362: 41-52.
- Groenendaal, H., Galligan, DT (2003). "Economic consequences of control programs for paratuberculosis in midsize dairy farms in the United States." *Journal of the American Veterinary Medical Association* 223(12): 1757-1763.
- Groenendaal, H., Galligan, DT, Mulder, H (2004). "An economic spreadsheet model to determine optimal breeding replacement decisions for dairy cattle." *Journal of Dairy Science*.
- Groenendaal, H., Nielen, M and Hesselink, JW (2001). Development of the Dutch Johne's disease control programme supported by a simulation model. SVEPM, Netherlands.
- Groenendaal, H., Nielen, M and Hesselink, JW (2002). "Johne's disease control: a simulation approach." *Preventive Veterinary Medicine* 54: 225-245.
- Kormendy, B. (1992). "Paratuberculosis vaccine in a large dairy herd." *Acta Veterinaria Hungarica* 40: 171-184.
- Muskens, J., H. Barkema, et al. (2000). "Prevalence and regional distribution of paratuberculosis in dairy herds in the Netherlands." *Veterinary Microbiology* 77: 253-261.

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- Pence, M., C. Baldwin, et al. (2003). "The seroprevalence of Johne's disease in Georgia beef and dairy cull cattle." *Journal of Veterinary Diagnostic Investigation* 15(5).
- Quist, C. F., V. F. Nettles, et al. (2002). "Paratuberculosis in Key deer (*Odocoileus virginianus clavium*)."
Journal of Wildlife Diseases 38(4).
- Streeter, R., Hoffsis, GF, Bech-Nielsen, S, Shulaw, WP, Rings, DM (1995). "Isolation of *Mycobacterium paratuberculosis* from the colostrum and milk of subclinically infected cows." *American Journal of Veterinary Research* 56(10): 1322-1324.
- Sweeney, R., R. Whitlock, et al. (1992). "*Mycobacterium paratuberculosis* cultured from milk and supramammary lymph nodes of infected asymptomatic cows." *Journal of Clinical Microbiology* 30(1): 166-171.
- Weber, M., Groenendaal, H, van Roermend, HJ and Nielen, M (2004). "Simulation of alternatives for the Dutch Johne's disease certification-and-monitoring program." *Preventive Veterinary Medicine* 62: 1-17.
- Wentink, G., Bongers, JH, Zeeuwen, JH (1994). "Incidence of paratuberculosis after vaccination against *M. paratuberculosis* in two infected dairy herds." *Zentralbl Veterinarmed [B]* 41: 517-522.