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An Agent-Based Model Evaluation of Economic Control Strategies for Paratuberculosis in a Dairy Herd

Leslie J. Verteramo Chiu*, ljv9@cornell.edu

Loren W. Tauer†, lwt1@cornell.edu

Mohammad A. Al-Mamun*, ma875@cornell.edu

Karun Kaniyamattam*, kk898@cornell.edu

Rebecca L. Smith‡, rlsdvm@illinois.edu

Yrjo T. Grohn* ytg1@cornell.edu

***Section of Epidemiology, College of Veterinary Medicine**
Cornell University, Ithaca, NY
† Charles H. Dyson School of Applied Economics and Management
Cornell University, Ithaca, NY
‡Department of Pathobiology, College of Veterinary Medicine
University of Illinois, Urbana, IL

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ABSTRACT

This paper uses an agent-based simulation model to estimate the costs associated with *Mycobacterium avium* subsp. *paratuberculosis* (MAP), or Johne's disease, in a milking herd, and the net benefits of implementing various control strategies. The net present value (NPV) of a 1,000 cow milking herd is calculated, parametrized to a representative New York State herd. We estimate the NPV of a baseline scenario with no infection, with an expected endemic infection distribution, and with various controls. Control strategies include testing using ELISA and fecal culture tests and culling of cows shedding high amounts of MAP, and culling based on observable milk production decreases**.** Results show that culling subclinically infected cows based on tests results does not increase the herd's NPV and in most cases decreases NPV due to test costs, as well as false positives and negatives with their associated costs (e.g., culling healthy cows and keeping infected cows). A better strategy is to cull consistently low producing cows when MAP is thought to be present in the herd. Our model estimates that the annual MAP associated cost to farmers in the U.S. is $212 million.

Key words: agent-based model, paratuberculosis infection simulation, paratuberculosis economic cost, infection control strategy.

INTRODUCTION

Johne's Disease is a chronic enteric disease in ruminants caused by the bacteria *Mycobacterium avium* subsp. *paratuberculosis* (MAP). Only adult animals show clinical symptoms of MAP infection, although infection can start in utero. Infected cows show progressive weight loss, periods of diarrhea, decrease milk production, lower reproductive rates, and are culled earlier, thereby affecting a dairy farm's profitability (Collins, 2003; Kennedy and Benedictus, 2001; Smith et al., 2009; Smith et al., 2010). The majority of dairy operations in the U.S. are believed to be infected with MAP (Lombard et al., 2013). It is estimated that MAP-associated costs to the milking industry in the U.S. are between \$200 to \$250 million per year (Ott et al., 1999), assuming a MAP prevalence of 22%. There has been speculation that MAP may be a contributing factor to Crohn's disease in humans (Shulaw and Larey-Naugle, 2003; Naser et al.,2004), although the linkage is only for association and not causation.

MAP susceptibility is believed to be highest at birth and during the first days of an animal's life. In utero infection of MAP can occur even if the dam doesn't show clinical signs of the disease. Calves can become infected through bacterial shedding of infected dams in colostrum and feces. It has been suggested that animals must be infected when they are calves in order to show clinical signs of MAP, since animals develop resistance to MAP infection as they get older (Collins and Morgan, 1992; Mortier et al., 2013; Windsor and Whittington, 2010). The first six months of age may be the period of greatest MAP infection susceptibility. Animals infected as adults may show less pronounced symptoms and fewer bacilli than those infected when young, and sometimes may recover from MAP (Helgerson et al., 2006; Larsen et al., 1975; Taylor, 1953; Windsor and Whittington, 2010). Infected calves become infected heifers and adult cows; although subclinical at first, adult cows may show progression of MAP to clinical levels. The degree of MAP infection in adult cows may be categorized by the number of bacteria colony forming units per gram (CFU/g) of fecal sample, with classifications of: latent (0 CFU/g), low shedders (<300 CFU/g), and high shedders (≥300 CFU/g).

A major problem with MAP control is the difficulty in detecting subclinical animals that can be culled before they spread the disease. Two commonly used tests for MAP detection are Enzyme-Linked Immunosorbent Assay (ELISA) and Fecal Culture (FC) tests. ELISA tests can produce results in a day; a FC test results can take up to 90 days for a negative result, although it is possible to identify high shedding cows in 45 days. While the FC test is assumed to have a specificity (true negative probability) of 1, eliminating the probability of false positives, ELISA tests have imperfect specificity and therefore produce false positives. Both tests have low sensitivities (true positive probability) for detecting low shedding animals.

Some control strategies used to minimize the spread of MAP within a herd include: test and cull, improved hygiene (in facilities and animals), separate calves from dams at birth, use clean milk to feed calves, and vaccination. Test and cull is a strategy widely studied, however, there is the associated risk of culling false positives and keeping false negatives in the herd (Cho et al., 2013; Groenendaal et al., 2002; Smith, Al-Mamun, and Gröhn, 2017). Improved hygiene, including cattle management, reduces transmission rates. The benefits of improved hygiene depend on the magnitude of that reduction and the benefit is not consistent. Some studies conclude that it is no better than test and cull (Smith et al., 2017), while others conclude that it is the most cost effective control for MAP (Groenendaal and Galligan, 2003). The benefits of vaccination have been difficult to estimate empirically because farms performing vaccination typically also improve their hygiene and management practices; thus, the effect of vaccines alone is difficult to quantify. Even with hypothetical high efficacy vaccines, the results would be similar to improved hygiene or test and cull strategies (Cho et al., 2012). Some studies conclude that even with a hypothetical high efficacy vaccine, MAP may still be endemic in a herd due to vertical transmission (Lu et al., 2013).

The benefits of various strategies to control MAP in a milking herd have been previously estimated. Cho et al. (2012, 2013), using a control model with a 20% MAP prevalence, estimated the cost of MAP per cow per year at $28, and the NPV benefit, over 20 years, of using a hypothetical high efficacy vaccine in a 100 cow herd to be $349,130. Groenendaal et al. (2002) estimated the associated costs of MAP in a 100 cow herd in PA to be $31/cow per year. In a later paper, Groenendaal et al. (2015), estimated the net economic benefits of vaccination against MAP at $8/cow per year. Lu et al. (2013) estimated that with a hypothetical high efficacy vaccine, MAP prevalence in a herd decreases by 55% by year 10. Smith et al., (2017) found that ELISA testing and culling maximizes NPV relative to other tests or improved hygiene with a 20% prevalence, but when MAP prevalence was only 10%, FC and PCR tests were prefered. In a similar study, Collins, and Morgan (1991) concluded that when MAP prevalence is less than 5% in the herd, test and cull is not cost-effective.

High shedding animals produce significantly less milk, about 10 to 30% less, than low shedding or subclinical animals (Smith et al., 2016). Based on this difference in production, it may be possible for the farm manager to implement a culling decision based on decreased milk production or weight loss, such that high shedding animals are culled when either milk or weight reduction is observed. However, this requires the farmer to develop the ability to detect milk and weight loss outside of a normal range, which may occur well after high shedders continuously shed bacteria.

Most of these previous studies used compartment models where movement of animals is modeled as a group rather than by individual animal. In compartment models, the herd is divided into homogeneous groups, or compartments, based on criteria like age and infection status. The transition of animals between compartments is determined by differential or difference equations or by stochastic processes. Unlike agent-based models, compartment models cannot account for decisions made at the individual animal level. This is the advantage gained by using an agent-based model, as actual decisions on the farm occur with individual animals. It provides full information of the agent, allowing more control on the data generated by each individual and the possibility of specific controls based on each individual animal characteristics at any point in time. Previous agent-based models focused on MAP transmission dynamics (Al-Mamun and Grohn, 2017; Al-Mamun et al., 2016; Robins et al., 2015). Similarly, this paper uses an agent-based model to capture the transmission dynamics, however, our focus is on estimating the economic costs of MAP in a herd and the benefits of some MAP control strategies.

Consequently, this paper analyzes the cost associated to MAP infection using an agent-based simulation model. The description of the population and infection processes are presented in the next section, then the control scenarios analyzed are described, followed by results and conclusion.

METHODOLOGY

The simulation model is depicted in Figure 1, following Smith et al. (2017) and Mitchell et al. (2008). Population and infection dynamics parameters are described in Table 2. The model is simulated daily for 20 years. The results are estimated at the end of the simulation period. The herd is initialized with 1,000 cows under a representative endemic infection distribution, and a no infection case.

Population Dynamics

The herd and each animal (agent) is divided into three age groups: calves, heifers, and cows. Calves are classified as animals from 0 to 60 days of age; heifers from 61 to 719 days of age; and cows from 720 days old and above. When calves are born they spend one day in the cow group, in the presence of their dam. At the end of day 1 they are moved to the calf group. At 61 days of age, they are transferred to the heifer group. All heifers are transferred to the cow group once they reach 720 days of age, regardless of their pregnancy status.

There are two main processes in the population dynamics: pregnancy and culling. Pregnancy rates (conception rate x heat detection rate) were used for simplicity; the pregnancy rate of heifers is set to 18%, while that of cows is 14%. Their values are shown in Table 8 in the Appendix and were used to determine the success of insemination events. Once a heifer reaches 440 days of age it is inseminated. If the insemination is successful, the heifer will calve at 720 days of age (280-day pregnancy), otherwise the heifer will be re-inseminated every 21 days. Once a cow gives birth, it will be put on a voluntary waiting period of 60 days before being inseminated for the next parity, after which it will be inseminated every 21 days until insemination is successful. All cows and heifers are culled if they do not become pregnant by the 8th insemination attempt. The cow will enter the milk production process the day after it gives birth, and will continue milking until 60 days before the next calving. The 60 days prior to calving are the dry period of the cow.

Every day each animal is subject to the natural culling process. The probability of culling depends on the age group of the animal and its parity. Natural culling occurs for two main reasons: involuntary culling that is outside of the farmer's control (accidents, sudden deaths) and voluntary culling based on the farmer's decision. The natural culling rates are shown in Table 8 in the Appendix; calves are randomly culled with a daily probability of 3.04×10^{-4} and heifers are randomly culled with a daily probability of 1.92×10^{-5}. Culling rates for cows were adjusted as to increase with parity. Culling rates were based on Mitchell et al., (2008) and modified in order to reach stability in the simulation. Voluntary culling is based on loss of milk production, diseases other than MAP, failure of insemination, and exceeding farm cow capacity. Additional voluntary culling beyond the baseline voluntary culling rate is modeled under the controls of test and cull for MAP, or low milk production from MAP.

Voluntary culling due to overpopulation occurs if the number of animals surpasses the limit of an animal classification group or a value established by the farmer. This culling decision is based on the expected value of the cow or age. The milking herd limit is set at 1,000 cows; the number of cows surpasses the limit when heifers are transferred to the cow compartment when they reach 720 days of age. When this occurs, all cows are ranked according to their expected milk production, and those with the lowest values are culled until the limit is reached again. As part of the management program to keep a stable number of replacement heifers, we also included a limit in the number of calves at any time, which is set to 67. The excess calves are culled based on age (youngest calves are culled first) and their sale value contributes to the farm's revenue.

For simplicity, without affecting the final results, animals are assumed to be culled and removed from the herd at the end of the simulation day. Animals complete any other processes (for instance, milk production or calving) before being culled in the same day.

Infection Dynamics

A flow chart of the model with the parameters of the population and infection dynamics is shown in Figure 1, with parameter descriptions in Table 3. The three age groups in Figure 1 (calves, heifers, and cows) are indicated by the subscripts 1, 2, and 3, respectively. Each group is further divided into two infection status levels for calves and heifers, and four infection status levels for cows. Calves and heifers can be susceptible (free of infection) or latent (sub-clinically infected). Cows have two additional infection status: low shedding and high shedding. Low shedding cows are defined as those cows which have MAP concentration of < 300 CFU/g of fecal culture tube. High shedding cows are defined as having > 300 CFU (van Roermund et al., 2007; van Schaik et al., 2005; Whitlock et al., 2000). Unlike low and high shedders, latent cows do not shed MAP or their levels are undetectable. Susceptible, latent, low and high shedders are denoted S, L, I_L, and I_H, respectively.

Parameters, as well as variables and formulas estimated in the agent model are listed in Table 2. MAP infection and progression rates, as well as natural culling rates, were taken from previous studies (Mitchell et al., 2008; Smith et al., 2017); however, in most cases these were adjusted to reflect the daily agent-based simulation context.

The sequence of infection probability events is such that calves have a probability of being infected in utero, γ_v, of 15% if the dam is latent or low shedder and 17% if the dam is a high shedder. The referenced values for γ_v were obtained from (Sweeney et al., 1992) and (Whitlock et al., 2005a, 2005b). Once the calf is born, it may be infected from the environment with probability λ_e, which captures the infection from the shared colostrum, and feces contact onto the calf. This infection rate depends on the proportion of low and high shedders in the cow compartment and accounts for the spread of contaminated feces and colostrum. Calves spend one day exposed to environmental transmission in this compartment. Once this day is over, all calves are transferred to the calf group, where they will remain until 60 days of age before being transferred to the heifer group at 61 days of age. The parameter λ_1 is the probability of horizontal infection of calves when they are in the calf compartment. λ_1 was based on Smith et al. (2015). The values of σ_L and σ_H, 0.0018 and 0.000904 respectively, as well as λ_e were based on Mitchell et al. (2008), referencing van Schaik et al. (2003), and modified in order to reach the stable endemic infection population.

Infected calves become infected heifers, which in turn become latent cows. Animals were assumed to acquire MAP immunity as they age. Susceptible heifers and cows do not become infected at any time. Infected cows progress to a higher level of infection. The daily progression rate from latent to low shedders is σ_L, and from low shedders to high shedders is σ_H. High shedders, being the highest infection level, do not progress to another level.

The effect of MAP on milk production is considerable for high shedding cows, although low shedding cows also produce less milk on average than healthy cows (see Figure 2). We follow a milk production function described in Smith et al. (2016). The milk production of susceptible, latent, and low shedders is very similar and was not considered a criteria for determining infection status. The production loss of high shedders compared to susceptible cows with the same characteristics can reach 10% at early stages of lactation, more than 20% after 180 days into lactation, and up to 30% about 280 days of lactation. When high shedders are in the herd and the number of cows exceeds its limit, they are assumed to be culled first as long as they are more than 90 days in milk due to this low production.

Costs, Revenues, and MAP Controls

The costs associated with raising the animals in each age group, as well as the revenues from milk sale and culling, were computed daily. The cost and revenue parameters are shown in Table 3. The cost parameters of raising a replacement heifer were obtained from Karszes (2014), and are used to model the daily costs from newborn to heifer. Feed costs, in $/ kg of dry matter intake, were obtained from the USDA's Economic Research Service (ERS, 2015) as the average cost paid by farms larger than 200 cows in 2015. The milk price is the 2015 average and is obtained from the USDA's National Agricultural Statistics Service (NASS, 2017). Both milk and feed costs are in dollars per kg of milk. That is, the feed price represents the cost of a standardized feed ration required to produce a kg of milk. The difference between the price of milk and the feed cost is called the milk margin. In the model this margin is $0.244 per kg of milk. For simplicity, throughout the simulation, we assumed that the milk price stays constant.

The estimation of body weight for cows follows the estimations described in Nutrient Requirements of Dairy Cattle (National Research Council, 2001). There are three components in calculating total body weight: age, lactation, and pregnancy. These functions were estimated by Korver, van Arendonk, and Koops (1985).

Herd Scenarios and Control Strategies

The NPV of the herd under the endemic infection distribution, and under no infection (baseline) are first estimated. Then, the NPV of the endemic infected herd under different control strategies are estimated. These control strategies are described in Table 4.

Control strategy ELISA-FC performs an ELISA test first, and then follows up with an FC test for all ELISA positive cows the following day. The results of the FC test are obtained 90 days after the sample collection. Positive FC tested cows are either culled immediately, or in a separate scenario when the cow enters the dry period. Both culling times are analyzed for each scenario listed in Table 4. Culling during the dry period allows the cow to generate more cash flow, which would be desirable to most farmers. The ELISA test is performed once a year. The different ELISA-FC scenarios differ among each other on the starting parity of the cows tested.

All test strategies include the additional scenario of having the FC test results in 45 days, to capture the benefit of improvements in FC testing.

In control strategy Cull Low Producers in Table 4, we assume the farmer understands that MAP may be a possibility (possibly due to an ELISA milk bulk tank test) and thus scrutinizes any consistent decrease in milk production by cow. Under scenario Cull Low Producers 90, if a cow's milk production drops below the expected production of a healthy cow's milk production for 90 days, it will be culled on the 91th day. We also analyzed the scenarios where the high shedder cows are identified and culled when they are 30 and 60 days in milk. Under these scenarios, culling happens even if the herd size is below the herd size limit of 1,000 cows. In our model, all replacement heifers are raised within the farm and culled cows are not replaced by heifers from outside the farm. We did analyze scenarios (results not shown) that includes replacement heifers bought from outside at a 10% margin over the cost of producing heifers, and found that the NPV was lower compared to having all heifers raised in the farm.

Each scenario, including the endemic infection without controls, and a healthy herd, was simulated 100 times to arrive at measures of standard deviations. Under the Smith et al. (2016) milk production assumption, latent infected cows produce slightly more milk than non-infected cows. We test the sensitivity of this assumption by running some scenarios modifying the milk production function as to keep latent cows' milk production the same as that of susceptible cows, instead of modeling the increase in milk production of latent cows. The results of these scenarios are not qualitatively different than under the Smith et al. (2016) production function.

Model Simulation

We began the simulation with the initialization of a 1,000 cow herd. The initial herd population was distributed in the following way: 45% of the cows were assigned in parity 1, 30% in parity 2, and 25% in parity 3. The initial cows had their age (in days), pregnancy status, pregnant days, and days in milk randomly distributed according to parity. We allowed the simulation to run for 3,000 days in order to reach a stable population distribution of uninfected animals.

The next step was to incorporate MAP infection based on an average endemic infection distribution of 62% uninfected cows, 22% latent, 13% low shedders, and 4% high shedders. Previous studies have estimated the MAP shedding prevalence (low plus high shedders) between 7 to 27%, with a mean of 14%, however, MAP prevalence was higher in larger dairy herds (Raizman et al., 2011). The description of the infection distributions is given in Table 1. Susceptible and latent animals were randomly assigned to parities 1 through 5; low and high MAP shedding animals were assigned from parities 3 through 5. The disease was introduced at day 3001 of the simulation. The infected herd ran for 15,000 more days in order to reach a stable endemic infection distribution. To assure that we started the analysis with comparable endemic distributions, we ran the warm up period with the same random number generation seed. In this way, all simulations began from the same initial condition (described in Table 1). After the warm-up period, each iteration followed a random path.

Once the population reached the stable endemic distribution, we incorporated various MAP control strategies and ran the analysis for another 20 years and estimated the NPV of each intervention, including no intervention and no infection.

The agent model was built in Matlab$^{©}$, rather than commercially available agent-based simulation software, because it provides greater flexibility in modelling the relationship among agents and in the design of control strategies for MAP. Our analysis consisted of calculating the

NPV of a 1,000 cow herd under an endemic MAP infection using different control strategies, including no control. Before estimating the NPV, we randomly initialized the herd and ran the simulation until the herd population distribution (number of cows, heifers, and calves) and endemic infection distribution (number of healthy and infected animals) achieved stability. Once the herd became stable, we ran a 20 year simulation to measure the NPV of the control strategies.

RESULTS AND DISCUSSION

The expected NPVs and standard deviations of each scenario, with the associated cost of carrying out each scenario, are listed in Table 5. Control costs are embedded into the NPV. Under no infection, the NPV of a 1000 cow herd is estimated to be $8,252,587 over a 20 year analysis period. A herd in an endemic MAP infection state has a lower estimated NPV of $7,781,119, a lower difference of $471,468 with respect to the no infection case. Our result is about 23% lower per cow than the result reported by Cho et al. (2013), where they found that the NPV difference between a healthy and endemic 100 cow herd over a 20 year analysis period was $61,310; however, their initial MAP prevalence was slightly higher at 20%, the discount rate was two percent, and the milk price was higher.

Under all ELISA-FC test and cull scenarios, the estimated NPV is lower than that of the endemic infected herd with no implicit control strategy implemented. This suggests that an endemically infected herd should not engage in any ELISA-FC test and cull strategy. However, the costs of performing an ELISA-FC test and cull strategy does decrease, and the NPV increase, when testing begins in later parities. Testing and culling parity 2 and above results in a greater NPV than testing and culling parity 1 and above, for instance. Testing and culling parity 1 and 2 cows not only leads to unnecessary tests, because few of these cows have progressed to become low or high shedders, but testing in early parities also increases the likelihood of culling healthy cows due to false positive test results. Similarly, beginning testing and culling at even higher parities results in higher NPV and lower test expenses. Thus, if a farm is considering a test and cull strategy, it should test cows beginning in higher parities (parity 4 or higher).

In order to analyze the benefits of improved FC test turnaround time, we estimated the NPV of the test and cull strategy for parities 3 and 4 when the time to obtain the FC results is reduced from 90 days to 45 days. For this 45 day test scenario, the NPV for testing cows in parity 3 and above is $7,488,714, which is $20,488 more than the scenario with a 90 day FC test turnaround. However, comparing for a test and cull strategy beginning at parity 4, the NPV of the 45 day FC result waiting period gives a lower NPV than the 90 day FC result waiting period. This decrease in NPV occurs when FC test positive cows are culled immediately after the FC test results. If a cow is lactating when tested positive and culled, there is no cash flow from the rest of her lactation. In order to understand the effect of culling cows immediately when FC tests are positive, we ran the same scenarios depicted in Table 5 but with culling occurring when cows are in their dry period, or not lactating. That is, if a cow is tested positive, or decided to be culled, in the middle of her lactation, it will be allowed to complete her lactation and will be culled as soon as it enters its dry period. Culling cows when they are not lactating produce higher NPV for all scenarios. For instance, test and culling parity 3 and above (with a 90 and 45 day test result waiting period) when cows are not lactating results in NPV of $7,566,324 and $7,509,491, respectively, or $98,098 and $20,777 more than the NPV when culling occurs immediately after positive test results. The results of culling cows when they are not lactation are presented in Table 6.

The control scenarios of culling low producing cows, as an indicator of high MAP infection, even when the number of cows in the herd may below the herd limit of 1,000 cows, is a better alternative than testing and culling. In the Cull Low Producers scenarios, farmers know that their herd is MAP infected and pay more attention to a persistent decrease in milk production compared to a healthy cow. This would signal to the farmer that the cow may be MAP infected, and thus, immediate culling is warranted. We assume that no extra costs are associated with the Cull Low Producers strategy, since it only relies on measurement or observation and experience. The degree to which farmers can effectively detect a MAP infected cow through observation of decreased milk production would depend on the experience and accurate production measurement capacity on the farm. In these scenarios, we assume that the farmer can detect high shedders if they are 90, 60, and 30 days in milk, reflecting differences in monitoring milk yield. The NPV of each of the three scenarios (90, 60, and 30 days in milk) are 7,697,882; 7,638,895; and 7,648,741, respectively. All three Cull Low Producers scenarios have similar NPV, but culling the low producing cow (high shedder) after 90 days in milk results in the higher NPV than culling them earlier because it allows them to produce milk for more days.

The NPV of the scenarios when culling occurs during the dry period of the cow are higher than when culling immediately after the cow tests FC positive or identified as a low producer. The largest NPV difference between the two culling times is for the testing and culling scenario for parity 3 and above ($98,098). For both culling times, the highest NPV scenario is to cull low producers 90 days in milk. The strategy of testing and culling using ELISA and FC tests produces a lower NPV, and in some cases not statistically different, than the endemic infection case with no controls implemented. This suggests that a better strategy than to test and cull is to do nothing; however, a better strategy than to do nothing is to cull low producing cows if MAP is suspected.

Our milk production function models the production of latent cows higher than that of susceptible cows (Smith et al.,2016). The reason for this empirical observed incremental increase in milk production for latent cows is not well understood, but may cause these cows to remain in the herd if the value of this incremental milk is greater than the externality cost of infecting calves. To determine the impact of the assumption of latent cows producing more milk than susceptible cows, we estimate the NPV of some scenarios assuming that the milk production of latent and susceptible cows are equal. Results are shown in Table 7; keeping milk production the same for latent and susceptible cows has an impact on expected NPV. Under the endemic infection state, the NPV of the herd is $192,112 lower without the milk production boost of latent cows. For the ELISA-FC test scenario for Parity 3 and above, the NPV with milk production boost of latent cows is $215,406 larger than without the production boost assumption; and for the Cull Low Producers 90 scenario, the NPV is $124,362 more for the milk production boost of latent cows. However, these differences are not statistically different.

None of the control strategies modeled is sufficient to eradicate MAP from the herd. Figure 3 shows the MAP infection distribution at the end of 20 years of simulation for the endemic state and the various control scenarios. In the endemic infection state without control strategies, the average number of high shedders in a 1000 cow herd is 38. That number under the ELISA-FC test and cull strategy from parity 1 to 4 are: 10, 11, 15, and 24, respectively. These numbers for the Cull Low Producers at 90, 60, and 30 days in milk are: 7, 3, and 1; with standard deviations of 3, 2, and 1, respectively. Even though culling low producers greatly reduces the number of high shedders in the herd, the spread of the infection still occurs and MAP is not eliminated. Strategies like those modeled mostly control the number of high shedders in the herd, which are the cows that cause the most MAP transmission.

Total MAP associated costs to the U.S. dairy sector can be estimated from our results. Assuming that the average dairy herd in the U.S. has the modeled endemic MAP infection rate of 17% (low and high shedders) and feed cost and milk prices are the same as those assumed in this study, the difference between the NPV of a representative herd without MAP and one with the endemic infection is $471,468 (with a standard deviation of 84,779) equivalent to $23.57 per cow per year. With the estimated number of dairy cows in the U.S. to be 9 million, the total yearly MAP associated costs in the U.S. is estimated to be $212 million (with a 95% confidence interval between $136 and $288 million). A previous estimate of MAP cost in the U.S. was between $200 to $250 million per year (Ott et al., 1999).

CONCLUSION

This paper estimated the Net Present Value (NPV) of a 1000 cow herd endemically infected with MAP and implementing various MAP control strategies. We also estimated the NPV of a healthy herd. We applied two general control strategies: Test and cull, modeled as following up all ELISA positive test cow with an FC test, and culling FC positive cows, implemented for various cow parities; and culling high MAP shedding cows identified by daily milk production consistently lower than that of a corresponding non-high shedding cow. Our results show that the ELISA-FC test strategy where all cows are first tested using the ELISA test and if positive followed up with a FC test, generates a lower NPV than no controls in a MAP infected herd. This implies that the test and cull strategy employing the ELISA test as a pre-filter for the FC test would not be recommended given the parameters of our model. In contrast, a strategy of culling low producing cows, which may be suspected of MAP infection, provides a higher NPV than the no control case (although the difference is statistically not significant). Our results are consistent with empirical and anecdotal evidence found on New York State farms. Many farmers with infected herds appear to not engage in costly MAP control strategies, instead they carry out business as usual. The result is economic control of MAP in their herds although not MAP elimination. We find that the cost per cow per year in an endemically infected herd, to be $23.57. Consequently, the yearly MAP cost for the U.S. is estimated to be $212 million at a milk production margin of $0.13/Kg milk.

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TABLES AND FIGURES

Table 1. Percent Distribution of Cow Population by Infection Scenario

Scenario	**Susceptible**	**Latent**	**Low Shedding**	**High Shedding**
No Infection	100	0	0	0
Endemic Infection	62	22	13	4

Values as percentage of total cows in the herd.

Table 2. Infection and Herd Parameters

Parameter	**Description**	**Formula/Value**
$S_{1,2,3}$	Number of Susceptible animals	N/A
$L_{1,2,3}$	Number of Latent animals	
$I_{L,H}$	Number of Low (L) and High (H) shedding cows	N/A
C_1	Voluntary Culled Calves (if number above limit)	N/A
C_3	Voluntary Culled Cows (if number above limit/ if positive MAP test or low production due to MAP)	N/A
N_3	Number of cows not culled	$(S_3+L_3+I_L+I_H)(1-\mu_3)-C_3$
N_{3L}	Number of calves that are vertically infected	$N_3\mu_b\gamma_v$
N_{3S}	Number of calves that are not vertically infected	$N_3\mu_b(1-\gamma_v)$
γ_v	Vertical Infection Rate (in utero)	0.15 (from L_3, I_L); 0.17 (from I_H)
λ_e	Infection Rate from the Environment (Calf)	$\beta_e(\beta_L I_L+ \beta_H I_H)/ (S_3+L_3+I_L+I_H)$
λ_1	Horizontal Infection Rate (Calf-Calf)	$\beta_c(\beta_L L_1)/ (S_1+L_1)$
λ_L	MAP Progression Rate (L_3-I_L)	0.000725
λ_H	MAP Progression Rate (I_L-I_H)	0.00041
μ_b	Birth rate (female calves)	0.5
μ_1	Natural Culling Rate for Calves	See Appendix Table 7

μ_2	Natural Culling Rate for Heifers	See Appendix Table 7
μ_3	Natural Culling Rate for Cows	See Appendix Table 7

Daily values. Subscripts 1, 2, 3 refer to calves, heifers, and cows, respectively. Abbreviations: N/A, not applicable.

Table 3. Cost, Revenue, and Control Parameter Description

Description	**Formula/ Value**	**Source**
Test specificity, ELISA	0.97	Sweeney et al. (2014); Vitale et al. (2014)
Test specificity, FC	1	Sweeney et al. (2014); Vitale et al. (2014)
Test sensitivity for low shedders, ELISA	0.24	Clark et al. (2008); Sweeney et al. (2006)
Test sensitivity for low shedders, FC	0.50	Whitlock et al. (2000)
Test sensitivity for high shedders, ELISA	0.78	Clark et al. (2008); Sweeney et al. (2006)
Test sensitivity for high shedders, FC	0.90	Collins et al. (2006)
Cost per ELISA test	\$6	Cornell University AHDC (2017); Smith et al. (2017)
Cost per FC test	\$36	Cornell University AHDC (2017); Smith et al. (2017)
Days to get results after ELISA test	0	Smith et al. (2017)
Days to get results after FC test	90, 45	Smith et al. (2017),
Number of days a cow's milk production is observed to decrease below normal before it is culled	90, 60, 30	Assumed
Maximum number of cows allowed	1,000	Assumed

Maximum number of calves allowed	67	Estimated from Model
Insemination cost, per event	20	Kaniyamattam et al. (2016);
Pregnancy Diagnosis, per event	8	Kaniyamattam et al. (2016);
Milk Price, $/Kg	0.375	USDA:NASS (2015)
Dry Matter Intake Cost, $/Kg	0.244	USDA:ERS (2015)
Fixed Costs per Cow, $/day	2.5	Karszes (2014)
Discount Rate, yearly	0.05	Assumed
Fixed Cost of a Newborn Calf	$150	Karszes (2014)
Male Calf Sale Price	$150	Karszes (2014)
Female Calf Sale Price	$250	Karszes (2014)
Culled Cow Price	$600	USDA (2017)
Culled Price of a High Shedder	$540	Smith et al. (2017)

Table 4. MAP Control Strategies

Control Strategy	**Description**
ELISA-FC Parity 1 (90d)	Test and cull all parity 1 cows once a year using ELISA and FC test. Test FC if ELISA positive. Cull at 90dafter positive FC test.
ELISA-FC Par 2 (90d, 45d)	Test and cull all parity 2 cows once a year using ELISA and FC test. Test FC if ELISA positive. Cull at 90d or 45d after positive FC test.
ELISA-FC Par 3 (90d, 45d)	Test and cull all parity 3 cows once a year using ELISA and FC test. Test FC if ELISA positive. Cull at 90d or 45d after positive FC test.
ELISA-FC Par 4 (90d, 45d)	Test and cull all parity 4 cows once a year using ELISA and FC test. Test FC if ELISA positive. Cull at 90d or 45d days after positive FC test.
Cull Low Producers (90d)	Observe and cull cows when production is consistently lower from that of a healthy cow for 90d. Cull immediately after 90d.
Cull Low Producers (60d)	Observe and cull cows when production is consistently lower from that of a healthy cow for 60d. Cull immediately after 60d.
Cull Low Producers (30d)	Observe and cull cows when production is consistently lower from that of a healthy cow for 30d. Cull immediately after 30d.

Abbreviations: d, days

Table 5. Net Present Value (NPV) by Control Scenario and Endemic Infection State, Assuming Immediate Culling of Test-Positive Animals

Scenarios	**NPV (Std. Dev.)**	**Scenario Expenses (Included in NPV)**
No infection	8,252,587 (68,722)	N/A
Endemic Infection	7,781,119 (152,852)	N/A
ELISA-FC Test Cull Par 1 (90d)	7,300,552 (195,512)	107,871 (1,607)
ELISA-FC Test Cull Par 2 (90d)	7,391,252 (194,912)	75,387 (1,302)
ELISA-FC Test Cull Par 3 (90d)	7,468,226 (132,796)	51,368 (1,294)
ELISA-FC Test Cull Par 4 (90d)	7,617,436 (171,644)	33,608 (885)
ELISA-FC Test Cull Par 3 (45 d)	7,488,714 (190,298)	51,332 (1,181)
ELISA-FC Test Cull Par 4 (45 d)	7,587,830 (168,353)	33,722 (961)
Cull Low Producers (90d)	7,697,882 (150,936)	N/A
Cull Low Producers (60d)	7,638,895	N/A

	(185,468)	
Cull Low Producers (30d)	7,648,741	N/A
	(194,810)	

Values in USD. Standard deviation in parenthesis. Abbreviations: d, days; N/A, not applicable.

Table 6. Net Present Value (NPV) by Control Scenario, Assuming Culling of Test-Positive Animals when Cows are not Lactating

Scenario	NPV (Std. Dev.)	Scenario Expenses (Included in NPV)
ELISA-FC Test Cull Par 2 (90d)	7,471,526 (170,902)	76,267 (1,133)
ELISA-FC Test Cull Par 3 (90d)	7,566,324 (141,312)	51,825 (985)
ELISA-FC Test Cull Par 4 (90d)	7,632,638 (167,980)	33,859 (845)
ELISA-FC Test Cull Par 3 (45d)	7,509,491 (208,314)	51,480 (1,171)
ELISA-FC Test Cull Par 4 (45d)	7,643,472 (170,384)	33,661 (914)
Cull Low Producers (90d)	7,752,641 (145,483)	N/A
Cull Low Producers (60d)	7,686,070 (181,327)	N/A
Cull Low Producers (30d)	7,654,543 (214,592)	N/A

Values in USD. Standard deviation in parenthesis. Abbreviations: d, days; N/A, not applicable.

Table 7. Net Present Value (NPV) for Selected Scenarios and Endemic Infection State with Equivalent Milk Production in Latent and Susceptible Cows, Assuming Culling Occurs when Cows are not Lactating

Scenario	NPV (Std. Dev.)	Scenario Expenses (Included in NPV)
Endemic Infection	7,612,544 (150,764)	N/A
ELISA-FC Test Cull Parity 3 (90d)	7,405,275 (179,601)	51,778 (926)
ELISA-FC Test Cull Parity 3 (45d)	7,345,340 (207,727)	51,568 (1,020)
Cull Low Producers (90d)	7,548,959 (163,071)	N/A

Values in USD. Standard deviation in parenthesis. Abbreviations: d, days; N/A, not applicable.

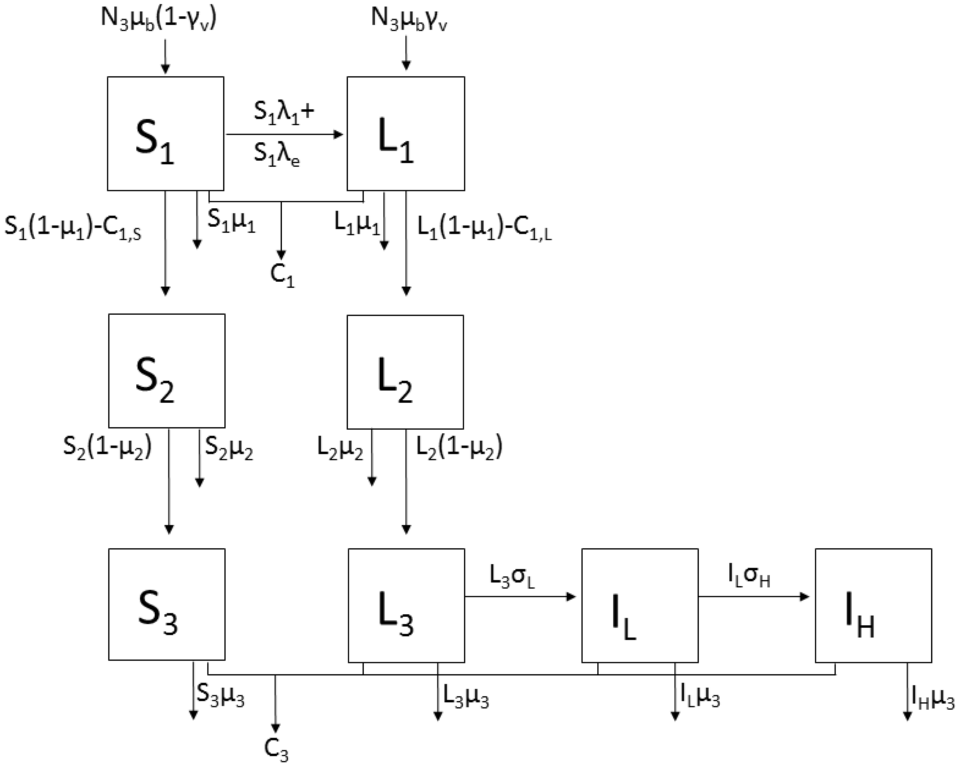

Figure 1. Animal dynamics across *Mycobacterium avium subsp. paratuberculosis* (MAP) infection status. There are eight mutually exclusive animal compartments based on age and infection status: susceptible calves (S1), latent calves (L1), susceptible heifers (S_2), latent heifers (L_2), susceptible cows (S_3), latent cows (L_3), low MAP shedding cows (I_L), and high MAP shedding cows (I_H). Parameters are described in Table 2

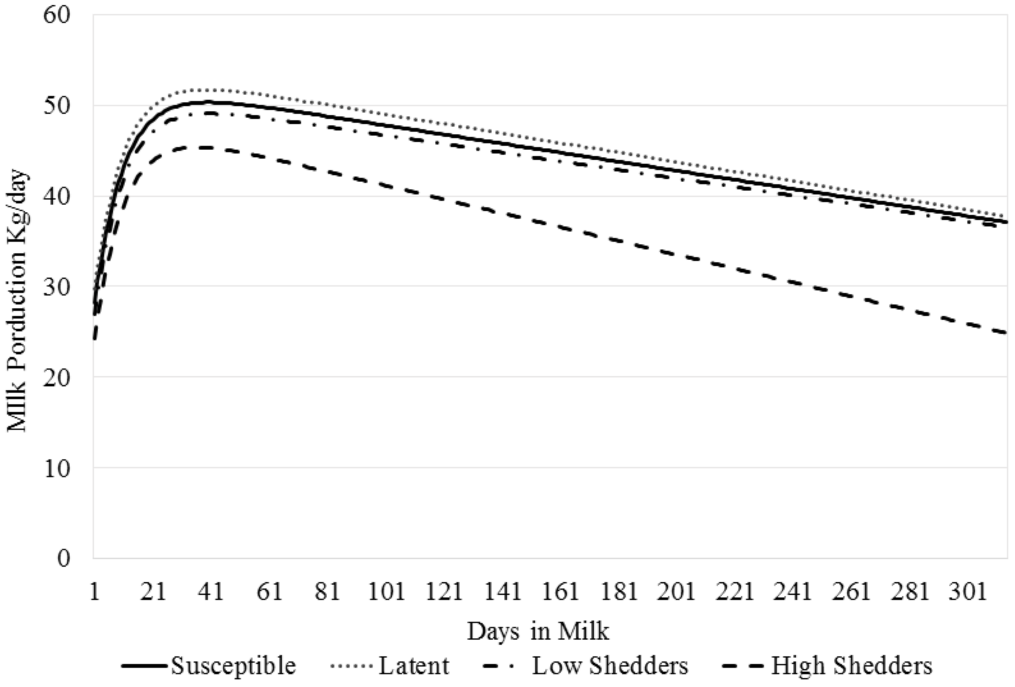

Figure 2. Milk production by MAP infection status for third parity cows. Cows are assumed to become infected at calving

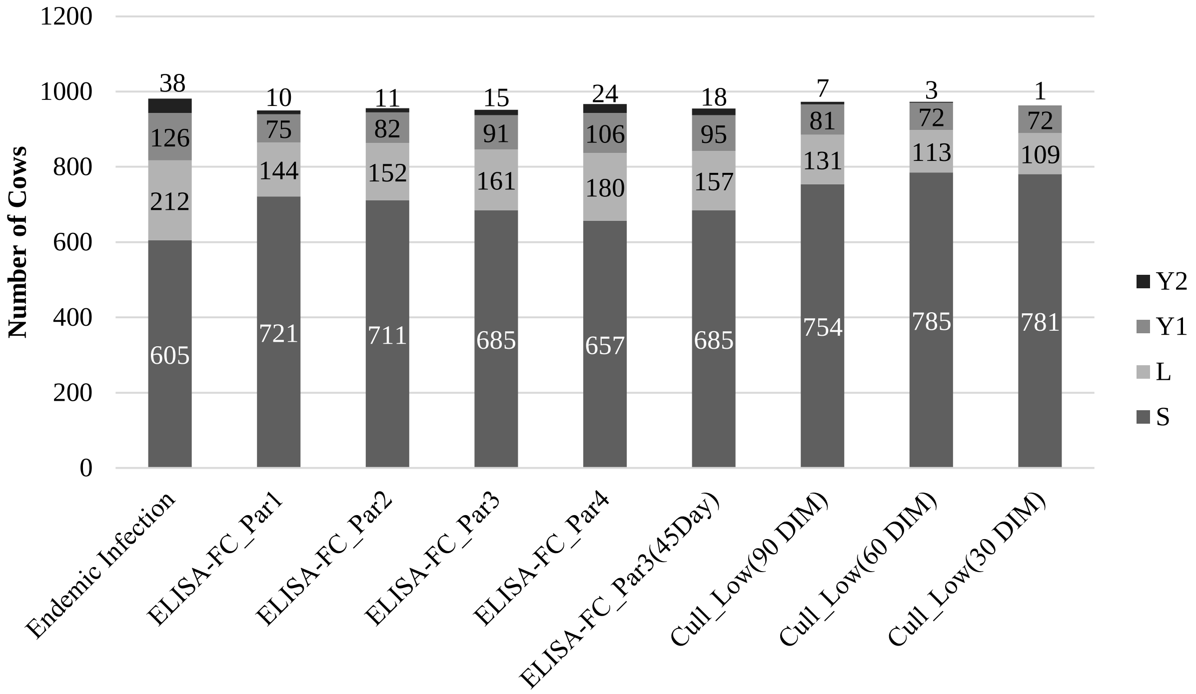

Figure 3. Distribution of Cows by Infection Status at the End of Analysis (20 years) by Control Scenario. S: susceptibles, L: latents, Y1: low shedders, Y2: high shedders

APPENDIX

Table 1. Pregnancy and Natural Culling Rates. Values based from Mitchell et al. (2008) and modified in order to reach a stable population distribution

Age Group	**Pregnancy Rate (per attempt)**	**Natural Culling Rate (daily)**
Calves	N/A	0.000304
Heifers	18%	0.0000192
Cows (parity)		
1	14%	0.0001096
2	14%	0.000132
3	14%	0.0001918
4	14%	0.0002192
5	14%	0.0002466
6	14%	0.0002739
7	14%	0.0003014
8	14%	0.0003836
≥ 9	14%	0.000411