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Economic consequences of paratuberculosis control in dairy cattle: A stochastic modeling study

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ABSTRACT

The cost of paratuberculosis to dairy herds, through decreased milk production, early culling, and poor reproductive performance, has been well-studied. The benefit of control programs, however, has been debated. A recent stochastic compartmental model for paratuberculosis transmission in US dairy herds was modified to predict herd net present value (NPV) over 25 years in herds of 100 and 1000 dairy cattle with endemic paratuberculosis at initial prevalence of 10% and 20%. Control programs were designed by combining 5 tests (none, fecal culture, ELISA, PCR, or calf testing), 3 test-related culling strategies (all test-positive, high-positive, or repeated positive), 2 test frequencies (annual and biannual), 3 hygiene levels (standard, moderate, or improved), and 2 cessation decisions (testing ceased after 5 negative whole-herd tests or testing continued). Stochastic dominance was determined for each herd scenario; no control program was fully dominant for maximizing herd NPV in any scenario. Use of the ELISA test was generally preferred in all scenarios, but no paratuberculosis control was highly preferred for the small herd with 10% initial prevalence and was frequently preferred in other herd scenarios. Based on their effect on paratuberculosis alone, hygiene improvements were not found to be as cost-effective as test-and-cull strategies in most circumstances. Global sensitivity analysis found that economic parameters, such as the price of milk, had more influence on NPV than control program-related parameters. We conclude that paratuberculosis control can be cost effective, and multiple control programs can be applied for equivalent economic results.

1. Introduction

Paratuberculosis, or Johne's Disease, is a disease of ruminants caused by intestinal infection with *Mycobacterium avium* subsp. *paratuberculosis* (MAP). Animals are chronically infected, usually at a young age, and are generally believed to undergo an extended latent period (Marcé et al., 2010). Infection is known to result in lower milk production (Aly et al., 2010; Gonda et al., 2007; Kudahl et al., 2004; Lombard et al., 2005; Nielsen et al., 2009; Raizman et al., 2007; Sorge et al., 2011), decreased reproductive performance (Kennedy et al., 2016; Marcé et al., 2009; Raizman et al., 2007; Smith et al., 2010; Vanleeuwen et al., 2010), and early culling (Lombard et al., 2005; Tiwari et al., 2005). Control of MAP in dairy herds has been difficult, partly due to the poor diagnostic sensitivity of many tests, the resistance of MAP in the environment, difficulties associated with use of available vaccines, and the long course of the disease (Garcia and Shalloo, 2015). Some analyses of the economic impacts of MAP control have found them to be cost-effective (Pillars et al., 2009; Radia et al., 2013), while others have found that MAP control is cost-effective only if testing is subsidized (Groenendaal and Wolf, 2008) or if MAP decreases milk production during latency (Wolf et al., 2014).

Simulation models attempting to identify the most cost-effective controls have produced equivocal results, indicating cost-effectiveness for quarterly serum enzyme-linked immunosorbent assay (ELISA) testing (Robins et al., 2015), quarterly milk ELISA testing (Kudahl et al., 2007), risk-based testing accompanied by infection control (Kudahl et al., 2008), vaccination or infection control (Groenendaal and Galligan, 2003), testing in series with ELISA and qPCR (Aly et al., 2012), and annual fecal culture accompanied by infection control (Cho et al., 2013). The lack of consensus is in part due to different model assumptions.

In particular, previous model-based economic analyses of MAP control programs were based on the assumption that all animals progressed to clinical disease over time (Aly et al., 2012; Cho et al., 2013; Groenendaal and Galligan, 2003; Kudahl et al., 2008, 2007;

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Robins et al., 2015).The findings of these analyses, therefore, were biased by the assumption that test-positive animals would eventually suffer from clinical disease, greatly decreased milk production, and decreased slaughter value. In addition, previous economic analyses (with one exception, (Robins et al., 2015)) have not considered adult infection, which molecular analysis has revealed to be a possibility (Pradhan et al., 2011) and which has been found to change simulation model outcomes (Smith et al., 2015). As hygiene programs are aimed at decreasing infectious pressure for calves, they are likely to be less effective than previously believed in the presence of adult infections.

Recent research indicates that while some animals (progressors) will progress to clinical disease, signified by wasting and diarrhea with large amounts of MAP shed in the feces, most animals (non-progressors) will remain in a latent or subclinical phase, intermittently shedding small amounts of MAP in their feces (Mitchell et al., 2015a, 2015b). The impact of paratuberculosis on milk production in dairy cattle differs significantly between these two groups of animals, with progressors demonstrating a continuous decrease in milk production (Smith et al., 2016). Non-progressors, by contrast, will experience a brief and limited decrease in milk production (Smith et al., 2016), from which their production levels will recover over time. This implies that the economic efficacy of test-and-cull programs will depend on their ability to distinguish between progressors and non-progressors. It has been found that repeated positive ELISA tests can identify progressive milk production decreases, which raises another option for MAP control, culling of cows after repeated ELISA positive results; this option was explored previously without the progression/non-progression dichotomy and found to be cost-effective if combined with improved hygiene (Kudahl et al., 2008). However, the cost-efficacy of this program and others has not previously been determined without the assumption that all animals will eventually progress to high-shedding, and this assumption could change the benefit estimated for control programs.

The goal of this research is to examine the economic consequences of paratuberculosis in US dairy herds by considering the new understanding of MAP infection dynamics, using a model that includes adult infection and non-progressing infections. The model considers age stratified MAP infection dynamics along with the economic efficacy of a variety of control programs. This will allow the estimation of the value of culling test-positive animals that may not progress to clinical disease by comparing control programs with varying ability to detect disease progression.

2. Methods

The infection and testing model (Fig. 1) have been previously described (Smith et al., 2015). This is a continuous-time model, and was simulated over 25 years using values representative of US dairy herds. Results were calculated after 5 and 25 years.

2.1. Births and vertical infection

Briefly, cows are grouped by age (calf, heifer, and adult) and by infection status. Female calves are born at rate

$$\mu_b = \frac{\mu_{b,base} * (S_3 + E_H + E_L + L_H + L_L) + \mu_{b,H} H}{S_3 + E_H + E_L + L_H + L_L + H} \quad (1)$$

where $\mu_{b,base}$ is the base birth rate in the herd and $\mu_{b,H}$ is the birth rate observed in high-shedding animals; male calves are not modeled. Animal categories consist of susceptible adults (S_3), latent adults (E_j), low-shedding adults (L_j), and high-shedding adults (H). Categories are further separated by path j, with a subscript H indicating a progressing (high-path) animal and a subscript L indicating a non-progressing (low-path) animal. Calves may be born susceptible S_1, but a proportion γ were born transiently shedding T_1. The proportion of calves born infected (probability of vertical transmission) was calculated as

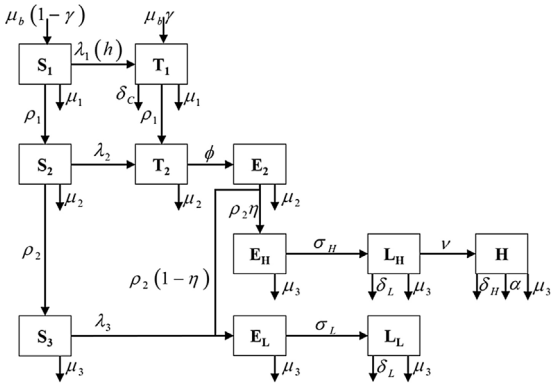

Fig. 1. Schematic of model for Mycobacterium avium subsp. paratuberculosis in cattle herds. Animals exist in one of 11 states: susceptible calves (S_1), transiently shedding calves (T_1), susceptible heifers (S_2), transiently shedding heifers (T_2), latent heifers (E_2), susceptible adults (S_3), latent progressing adults (E_H), low-shedding progressing adults (L_H), high-shedding adults (H), latent non-progressing adults (E_L), and low-shedding non-progressing adults (L_L). All parameters are defined in Table 1.

$$\gamma = \gamma_E (E_L + E_H) + \gamma_L (L_L + L_H) + \gamma_H H \quad (2)$$

where γ_i is the probability that a cow in infection category i gives birth to a vertically infected calf. We assume that γ_L and γ_H are equal, as there is insufficient evidence to parameterize different values at this time.

2.2. Horizontal infection

Susceptible calves (S_1) may be infected at rate λ_1 by direct contact with infected calves (T_1) or by indirect contact with shedding heifers or adults,

$$\lambda_1(h) = \left(1 - e_\beta(h)\right) \beta (T_1 + T_2 + L_L + L_H + H) \quad (3)$$

where β is the transmission coefficient of all contacts (direct and indirect) and $e_\beta(h)$ is the proportional decrease in transmission due to improved hygiene. It is assumed that improved hygiene is focused on transmission to calves, as that is recommended by most control programs, and so does not impact transmission to heifers or adults. Susceptible heifers (S_2) may be infected at rate λ_2 by direct or indirect contact with transiently shedding heifers (T_2),

$$\lambda_2 = \beta_a T_2 \quad (4)$$

where β_a is the transmission coefficient for adults and heifers. Transiently shedding heifers became latent heifers (E_2) at rate φ. Susceptible adults (S_3) may be infected at rate λ_3 by direct or indirect contact with shedding adults,

$$\lambda_3 = \beta_a (L_L + L_H + H). \quad (5)$$

We assumed no effective contact between heifers and cows and that heifers and cows have no exposure to calf feces sufficient for transmission.

Transmission parameters were calculated empirically, assuming that calves were twice as susceptible as adults ($\beta_a = \beta/2$). Briefly, 100 iterations of a disease-free herd were modeled for 200 years following introduction of a single latently infected adult. All iterations in which MAP persisted in the herd after 200 years were used to calculate an average endemic shedding prevalence, $(L_L + L_H + H)/(S_3 + E_L + E_H + L_L + L_H + H)$. The transmission parameters were adjusted to produce the desired average shedding prevalence (10% for well-managed herds and 20% for poorly-managed herds). The endemic herd populations produced