ECONOMIC CONSEQUENCES ASSOCIATED WITH JOHNE'S DISEASE IN COW-CALF OPERATIONS

A Dissertation

by

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ABSTRACT

Johne's disease (JD) in cattle is a disease of economic importance caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP). Studies were conducted to estimate the losses due to lower weaning weight of beef calves from MAP test-positive dams, to compare the perceptions of producers and veterinarians on the burden and economic aspects of MAP infection in cow-calf herds, and to evaluate whether testing and culling MAP test-positive cows is economically beneficial.

Calves from cows with strong-positive ELISA results were 21.5 kg lighter at weaning compared to calves from ELISA-negative cows. Calves from heavy MAP shedding cows were 58.5 kg lighter, and calves from moderate shedders were 40.8 kg lighter compared to the calves from fecal-culture negative cows. Based on average feeder calf value during 2007 to 2012, these losses corresponded to US $57 per calf for ELISA strong-positive dams, US $157 per calf for heavy fecal shedder dams, and US $109 per calf for a moderate fecal shedder dam.

Seedstock producers and the producers enrolled in control programs were more likely to have MAP uninfected herds. The average prevalence reported by producers was 0.8%. Compared to the small herds (<50 head), the average test-positive percentages and estimated prevalences were reported to be higher in medium (50-149) and highest in large (≥150) herds. Veterinarians reported an overall animal level prevalence in their client herds of 5%. Seedstock herds had a lower prevalence and these producers were more likely to enroll in a JD control program.

Income lost due to the presence of JD in an infected cattle herd was perceived to be higher by veterinarians. Compared to the veterinarians, seedstock producers were more likely to perceive genetic losses due to culling MAP positive cows. Average annual loss due to JD in a 100 cow herd with a 7% MAP prevalence was $1,644 and $1,747 based on information provided by producers and veterinarians, respectively.

Herd level production decreased with increasing prevalence. Compared to test and cull after ELISA or ELISA followed by fecal culture, using fecal culture alone

provided the fastest reduction in herd prevalence. Fecal culture was also the least costly alternative based on long-term cumulative costs of an annual test and cull program. Results from the current study suggest that although testing provides faster progress, limiting within herd transmission by sale of all weaned calves and purchasing only low-risk replacements can also reduce prevalence.

Results suggest that MAP infection in cows causes significant losses for the calves that are produced. While the knowledge about JD varied between producers and veterinarians, seedstock producers were more enthusiastic about MAP control programs and had lower MAP prevalence in their herds. Overall losses due to MAP infection in the herd might be substantial. It is very costly to control or eliminate MAP once the infection is established in a herd.

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1. INTRODUCTION

Johne's disease (JD) or paratuberculosis was first described in a German dairy cow (Johne and Frothingham, 1895). *Mycobacterium avium* subspecies *paratuberculosis* (MAP) is the etiologic agent of bovine JD, which is characterized by a chronic granulomatous ileocolitis, a long pre-clinical phase terminating in diarrhea, debilitation (Chiodini et al., 1984; Harris and Barletta, 2001), cachexia, and death (Manning and Collins, 2001). In infected cattle, JD is progressive with the first stage characterized by silent, subclinical, non-detectable infection, and the second stage with subclinical infection with detectable antibodies. The third appears as clinical disease showing normal or occasionally increased appetite and increased thirst, and the fourth stage is advanced clinical disease (Chiodini et al., 1984; Rossiter and Burhans, 1996; Whitlock and Buergelt, 1996; Radostits, 2000; Fecteau and Whitlock, 2010).

Infected animals shed MAP into the environment increasing the risk of infection to susceptible calves through ingestion (Kovich et al., 2006; Pickup et al., 2006; Fecteau and Whitlock, 2010). Infection typically occurs due to exposure in early calfhood prior to weaning (Streeter et al., 1995; Benedictus et al., 2008; Windsor and Whittington, 2010). The organism is maintained in herd through either retention of infected replacements or purchase of infected additions (Sweeney, 1996). Because of the chronic nature of the disease, transmission can occur prior to the development of clinical signs (Whitlock and Buergelt, 1996). Identification of infected animals for herd-level control is hindered because tests have low sensitivity in subclinical animals (Collins et al., 2006; Kudahl et al., 2007b; Kudahl et al., 2008) and identification based on clinical signs is not effective as the disease has a long latent period (Whitlock and Buergelt, 1996). Control by vaccination is restricted in some countries including the US (Stabel, 1998; Kalis et al., 2001; Juste, 2012) because vaccinated cattle can have false-positive test results hindering the testing programs for MAP (Stabel, 1998; Harris and Barletta, 2001) and bovine tuberculosis (Patton, 2011).

Bovine JD is present in many regions of the world (Chiodini et al., 1984; Barkema et al., 2010). The overall burden is lower in beef herds compared to dairy herds (NAHMS, 1999; Dargatz et al., 2001; Wells et al., 2008; Good et al., 2009). It is mainly a disease of cattle in the US although MAP has been isolated from 19 different ruminants and wildlife hosts (Stevenson et al., 2009). It is less commonly reported in farmed deer (van Kooten et al., 2006), sheep, goats, and South American camelids (Stehman, 1996). It has also been reported in primates, rabbits, stoats, foxes, giraffe, feral cats, and birds (Manning and Collins, 2001; Corn et al., 2005; Stevenson et al., 2009). Interspecies transmission has occurred among goats, alpaca, and farmed deer (Kennedy and Allworth, 2000).

1.1 Johne's disease distribution

It is possible that JD is present in almost all countries of the world because transboundary cattle export is common (Barkema et al., 2010). Underreporting is possible because of the long subclinical phase of JD and poor diagnostics (Chiodini et al., 1984; Harris and Barletta, 2001) even though it is a notifiable disease in numerous countries (Kennedy and Allworth, 2000; Manning and Collins, 2001). Underreporting is also a problem in countries that lack dedicated surveillance and reporting systems where the magnitude of disease might very high. Bovine JD is also a problem in the developed world including the USA (Whitlock, 2010), Canada (Waldner et al., 2002; Meadus et al., 2008; Tiwari et al., 2009), France (Dufour et al., 2004), South Korea (Park et al., 2006), Spain (Dieguez et al., 2007), Ireland (Good et al., 2009), Denmark (Kudahl et al., 2008), and Australia (Manning and Collins, 2001). Sweden has an eradication program and a very low probability of infected herds (Frossling et al., 2012). Only one MAP-infected herd associated with imported animals was confirmed in 2005 (Sternberg Lewerin et al., 2007). A systematic review of multiple studies in Europe estimated that 50% of herds and 20% of cattle were infected (Nielsen and Toft, 2009).

The first report on bovine JD was published in 1895 by Johne and Frothingham (Johne and Frothingham, 1895). Prior to the discovery of MAP, a case with signs

consistent with JD was reported in an emaciated six year old cow with chronic extremely thin blackish diarrhea that contained large numbers of air-bubbles and this condition was described as “shooting” disease. The cow was unthrifty and emaciated but retained a good appetite. Gross lesions on necropsy included “corrugated” intestine with thick mucus. The colon and cecum were principally affected and described as having “dirty color with blackish streaks”(Cartwright, 1829). A subsequent report established the characteristics of clinical JD as a progressive wasting accompanied by a persistent untreatable diarrhea, emaciation, and culminating in recumbency and death. Muscle wasting was described as being particularly severe in the hind quarter. There were also thickened enteric mucosa with a wrinkled appearance, enlarged lymph nodes, and an enlarged, inflamed, and edematous ileocecal valve (Dunkin, 1936).

Dunkin (1936) reported that it was found in the UK, France, Germany, Holland, Italy, New Zealand, India, and South Africa. Probably the first report of JD in North America was by Pearson (1908), reported as a chronic bacterial dysentery of cattle characterized by diarrhea, normal appetite, and loss of weight eventually terminating in death due to extreme emaciation and exhaustion. Bang (1906) reported similar clinical signs and also that the feeding of enteric mucosa from affected animals could transmit the disease. Several studies were conducted in the 1930s to better understand the incubation period, methods of transmission and economic aspects (Whitlock, 2010). A large national survey was conducted by the National Animal Disease Center, Ames, IA. The prevalence in samples from 76 slaughterhouses from 32 states and Puerto Rico was 2% during 1983-84 (Merkal et al., 1987). Subsequent to the widespread evidence of JD within the US, many states started JD management, control and quarantine programs (Chiodini et al., 1984).

1.2 Johne’s disease burden in US cattle

The overall prevalence of MAP infection is lower in beef herds compared to dairy herds. The NAHMS Dairy’96 study estimated that 3.4% of dairy cows were infected (NAHMS, 1999) compared to 0.4% beef cows being seropositive in Beef’97

study (NAHMS, 1999; Dargatz et al., 2001). Beef herds in a JD control program in Minnesota had lower (0 - 4.5%) overall seroprevalence compared to dairy herds (3.4 to 9.9%) during 2001 through 2006 (Wells et al., 2008). Seroprevalence in samples from 1,954 dairy cattle was 8% compared to 5% in beef herds of Missouri (Thorne and Hardin, 1997). Cull dairy cows from sale barns in Georgia had a seroprevalence of 10% compared to 4% in cull beef cows (Pence et al., 2003). Another study from 76 slaughterhouses in 32 US states and Puerto Rico submitting ileocecal lymph nodes from 7,540 cows estimated a prevalence of 2.9% in dairy culls compared to 0.8% in beef culls (Merkal et al., 1987). A survey of cattle herds with MAP shedders estimated a true animal-level prevalence of 8% in beef compared to 21% in dairy herds in Ireland (Good et al., 2009).

There have been several published reports evaluating JD in US beef cattle utilizing a variety of testing and reporting methods. ELISA-based seroprevalence of JD in beef cattle was 5% in Missouri (Thorne and Hardin, 1997) and 9% in beef cattle in Alabama (Hill et al., 2003). Three percent of purebred beef cattle in Texas were seropositive and 7.3% of seropositive cattle were MAP culture positive (Roussel et al., 2005). Culture of ileocecal lymph nodes from slaughterhouses across the US estimated 0.8% prevalence in beef cows (Merkal et al., 1987), although this method is less sensitive compared to the culture of ileum itself (McKenna et al., 2005). Therefore, the reported prevalence might be an underestimate. Reported seroprevalences suggest a true prevalence of up to 28% based on adjustment for the sensitivity and specificity of currently available tests (Collins et al., 2006).

A study of US beef herds estimated that 8% of herds had at least one seropositive animal (NAHMS, 1999; Dargatz et al., 2001). Approximately 44% of purebred beef herds in Texas had at least one seropositive animal and 18% of seropositive herds had at least one animal that was MAP culture positive (Roussel et al., 2005). Sixty-three percent of beef herds were positive in Alabama (Hill et al., 2003), and 40% of beef herds were positive in Missouri (Thorne and Hardin, 1997). Herd

prevalence is also reported to be associated with herd size in the US where 40% of herds of more than 300 head were found to be infected (Manning and Collins, 2001).

1.3 MAP transmission

Major methods of MAP transmission in cattle as classified by Sweeney (1996) are: (i) prenatal transmission – including transplacental or *in utero* transmission, and (ii) postnatal transmission – including fecal shedding and transmission to young calves by oral ingestion through the udder, manger, feeding utensils, and sometimes from contaminated milk. Experimental studies to evaluate the routes of transmission were conducted as early as 1916. An experiment demonstrated that pathological lesions following oral and intravenous administration of MAP were possible, but not from subcutaneous administration (M'Fadyean and Sheather, 1916). MAP transmission has been studied extensively in dairy cattle because of a higher prevalence and greater economic impact (Manning and Collins, 2010).

1.3.1 Prenatal transmission

Transplacental or *in utero* transmission is a particular concern in cows at advanced stages of infection, when bacteria are disseminated to organs including the uterus (Seitz et al., 1989; Sweeney, 1996). A meta-analysis and review indicated that fetal infections are possible *in utero* from clinically or sub-clinically infected cows (Whittington and Windsor, 2009) and farmed deer (van Kooten et al., 2006). Presence of MAP has been confirmed in the uterine horns of clinical JD cows (Rohde and Shulaw, 1990) as well as subclinically infected embryo donor cows (Bielanski et al., 2006).

Semen is a possible source of infection and MAP has been detected in the semen of an infected bull for over a year (Khol et al., 2010). MAP has also been isolated from the testes, epididymis, and seminal vesicles of naturally infected bulls (Ayele et al., 2004). Freezing semen does not reduce the viability of MAP (Richards and Thoen, 1977). A study with tissue samples obtained from clinical cattle demonstrated MAP mainly in seminal vesicles, but less frequently in prostate and bulbourethral glands. Isolated

organisms were subjected to similar procedures for commercial semen processing. Cultural growth occurred on medium inoculated with MAP in semen extender, but no growth was observed in samples when the semen extender contained antibiotics (Larsen and Kopecky, 1970).

Nine percent (5/58) of fetuses were infected from MAP-shedding but subclinical pregnant cows. Infection status was determined by fetal tissue culture and positive results were identified only from heavy shedding cows (Sweeney et al., 1992b). A meta-analysis of *in utero* infection estimated that 9% of fetuses from subclinical cows and 39% from clinical JD cows were infected with MAP (Whittington and Windsor, 2009). Both studies (Sweeney et al., 1992b; Whittington and Windsor, 2009) estimated significantly higher risks for fetuses from high shedders and clinical animals. Twenty-six percent of fetuses from cows that had positive ileocecal lymph nodes were also MAP tissue culture positive (Seitz et al., 1989). There is a published case report concerning MAP transmission via an embryo transferred to an ELISA and fecal culture negative cow. The cow became ELISA positive and necropsy lesions including irregular jejunal corrugation, thickened mucosa, and enlarged mesenteric lymph nodes were suggestive of JD. Acid-fact stained bacilli were isolated in radiometric culture. The offspring was necropsied at 24 months of age after being raised under strict hygiene. Post-mortem lesions included enlarged mesenteric lymph nodes, thickened enteric mucosa along with microscopic evidence of giant cells, activated macrophages in Peyer's patches, and stained bacilli suggestive of MAP (Manning et al., 2003). However, embryo transfer is considered an unlikely source of transmission when embryos are washed as recommended by the International Embryo Transfer Society (Bielanski et al., 2006). A study of 14 cows did not identify MAP culture positive embryos after harvesting from moderate shedder cows having necropsy lesions suggestive of MAP infection (Kruip et al., 2003).

Compared to calves born to seronegative dams, calves born to MAP seropositive dams were seven times more likely to be seropositive (Aly and Thurmond, 2005) presumably due to an infection acquired either congenitally or shortly after birth.

Offspring of cows with higher response to serum ELISA were more likely to also develop a higher response to ELISA (Osterstock et al., 2008).

1.3.2 Postnatal transmission

1.3.2.1 Cow-to-calf transmission

The majority of scientific literature suggests that the fecal-oral route via MAP contaminated feces, colostrum, or milk is the primary mode of transmission (Clarke, 1997). Cow-to-calf transmission within the calving area is one of the major sources of MAP infection (Benedictus et al., 2008). Transmission prior to weaning also occurs in beef herds feeding on large, round bales of hay especially on snow-covered fields. The accumulation of cattle and their manure in a concentrated area facilitates the contamination of teats and udder with manure (Fecteau and Whitlock, 2010). As beef calves are not normally weaned until 5-6 months of age, this is one of the important routes of MAP transmission

There is age-related resistance to infection (Sweeney, 1996; Windsor and Whittington, 2010). Necropsy of 1-month-old, 9-month-old and 5-11-year-old animals experimentally exposed to MAP identified the most severe lesions in the 1-month-old calves (Larsen et al., 1975). Fifty-seven percent (13/23) of calves born in an infected herd had evidence of JD after 26 months. However, only 17% (1/6) of older calves introduced to the herd developed clinical signs of JD and no cattle (0/6) greater than a year of age when introduced into the herd developed signs over the 26 month observation period (Hagan, 1938). A higher susceptibility has been attributed to the first few hours after birth when the gut is open to macromolecules and has a less developed mucosal barrier (Sweeney, 1996). Momotani et al. (1988) also hypothesize that passively transferred maternal antibodies facilitate MAP entrance into the intestinal mucosa of young calves from infected dams.

Exposure to higher quantities of MAP also facilitates the establishment of infection. A review suggested 50-1000 CFU as an infective dose for dairy calves (Chiodini, 1996) implying that only a few milligrams of contaminated feces would be

sufficient to induce infection after ingestion by a young calf. A dose of 1.5 million CFU given orally at 21 days and again at 22 days of age induced infection in dairy calves and MAP was detected in the jejunum and ileum 21 days after inoculation (Sweeney et al., 2006). Higher amounts of MAP are present in colostrum compared to milk and the chance of contamination is more likely in high shedding cows (Streeter et al., 1995). MAP contamination of colostrum (Nielsen et al., 2008), milk (Nielsen et al., 2008), and water or feed for neonates facilitates transmission (Kudahl et al., 2008). Feeding practices including the transferring of manger sweepings from cows to younger animals is a significant risk factor for spreading MAP (Rossiter and Burhans, 1996).

Contaminated manure in the environment poses a risk of infection to neonatal calves via oral ingestion (Chiodini, 1996; Windsor and Whittington, 2010). In an experiment of horizontal cow-to-calf transmission, all calves started shedding and four out of five calves continued shedding even after the in-contact shedding cows were removed (van Roermund et al., 2007). A meta-analysis did not find a difference in risk by removing calves 12h versus 24h after birth (Windsor and Whittington, 2010). However, this study also concluded that exposure to MAP at birth increases the risk of progressing to clinical JD.

While feces are the primary source of MAP, colostrum and milk of cows with advanced disseminated disease are also contaminated (Slana et al., 2008). Intensity of fecal shedding is proportional to the concentration of organisms in the colostrum (Streeter et al., 1995). Older infected cows in an advanced disease state are more likely to have offspring that also progress to JD (Benedictus et al., 2008).

1.3.2.2 Calf-to-calf transmission

Calf-to-calf transmission has been reported in an experiment conducted with 20 animals housed individually for three years. Two out of five susceptible calves were infected upon being housed with fecal culture positive calves (van Roermund et al., 2007). Transmission might still be possible in larger groups of calves housed for a prolonged period of time. One of the susceptible calves was infected after introduction

of an infected calf indicating that there is a possibility of transmission within calves housed together; however, the probability of transmission is low (Santema et al., 2012). Ten percent (25/264) of calves from test-negative dams that were not exposed to contaminated calving pens became infected (Benedictus et al., 2008). Although the specific route of transmission was not documented, intensive housing and mixing of calves from different production units without known disease free status appear to increase the exposure and, consequently, increase probability of transmission.

1.3.2.3 Risk factors for transmission

Three aspects affecting the risk of MAP transmission are: (i) the age at time of exposure; (ii) dose or frequency of MAP exposure (affected by stocking density); and (iii) prevalence of MAP within the herd (Rossiter and Burhans, 1996). One of the most important methods of transmission between herds is the addition of subclinically infected animals (Merkal, 1984; Sweeney, 1996; Fecteau and Whitlock, 2010). A previously uninfected herd typically becomes infected through the purchase of infected carrier animals, which act as a source of infection when they shed the organism (Fecteau and Whitlock, 2010). Purchase of replacement cattle from herds participating in a control program reduces the MAP risk compared to home-reared cattle (Kovich et al., 2006). This is based on the assumption that the cattle reared in the participating herd are less likely to be infected with MAP based on repeated serum and fecal tests. This also assumes that the purchasing herd has not tested for JD.

In Canadian dairy herds, ELISA-seropositivity was significantly associated with "open heifers purchased during the last 12 months" and “group housing for pre-weaned calves” in a multivariable model adjusted for the effects of lactation number, herd size, and province (Tiwari et al., 2009). In Australian beef herds, 67% of index cases were introduced animals; often having a direct or indirect association with dairy or dairy cross-breed cattle (Larsen et al., 2012). Comingling of dairy and beef breeds is an important risk factor for introducing JD (Tiwari et al., 2009; Larsen et al., 2012) along with having multiple cows per maternity pen (Tiwari et al., 2009). Water sources, using

dairy-type nurse cows, previous reports of clinical JD, and *Bos indicus* breeds are risk factors for seropositivity in purebred beef herds (Roussel et al., 2005). The same report suggested increased risk associated with the mixing of cattle, using dairy cattle as embryo transfer recipients, increased cattle density at calving, and collective grazing.

Management related activities appear to affect transmission in both beef and dairy herds. There is a theoretical possibility of transmission due to shared farm equipment, boots and clothing of farmers, and other breaches in biosecurity (Fecteau and Whitlock, 2010). Wildlife might be responsible for transmission between herds or premises. Different ruminant and non-ruminant wild animals and birds have been implicated in the transmission of MAP to domestic stock (Manning and Collins, 2001; Corn et al., 2005; van Kooten et al., 2006; Stevenson et al., 2009).

An environment contaminated with MAP increases the risk of infection to susceptible animals (Kovich et al., 2006; Pickup et al., 2006; Benedictus et al., 2008). An environment contaminated with feces in conjunctionwith young animals that suck, lick, and browse is a continuous source of exposure through ingestion of MAP contaminated feces (Chiodini, 1996). Oral exposure with feces has produced similar results (Sweeney et al., 1992a; Sweeney et al., 2006).

The soil and water in cattle aggregating areas may promote infection in animals and possibly humans through consumption of contaminated water (Pickup et al., 2005; Pickup et al., 2006). Survival of MAP in contaminated water under normal atmospheric conditions was reported as early as 1944 (Lovell et al., 1944). Water could be a significant reservoir as MAP survive for up to 48 weeks in water or sediment in shade and 12 weeks in soil or manure (Whittington et al., 2005). Survival was up to 55 weeks in a dry and fully shaded environment, and 24 weeks on grass germinated through infected fecal material (Whittington et al., 2004). Freezing of MAP contaminated feces for three and 15 weeks did not reduce viability (Richards and Thoen, 1977) suggesting that MAP could survive even in very cold climates.

MAP is resistant to heat and chemicals including chlorine and can replicate in protozoa (Mura et al., 2006; Whan et al., 2006). This might explain the ability to survive

in the environment. Runoff from grazing areas used by MAP infected sheep has contaminated downstream rivers in the UK (Pickup et al., 2005; Pickup et al., 2006). Insects and earthworms (Fischer et al., 2003) as well as wildlife are less important hosts (Corn et al., 2005).

1.4 Laboratory diagnosis of JD

The diagnosis of subclinical JD in cattle is difficult because infected animals go through several subclinical stages that can have long durations (Whitlock and Buergelt, 1996). Gross lesions on necropsy and histopathological examination of the ileum and associated mesenteric lymph nodes can be used for early diagnosis. Other than necropsy, there are three general approaches to diagnose MAP infection: (i) detection of a cell-mediated response; (ii) detection of the organism (or part of it); and (iii) detection of a humoral (antibody) response (Manning and Collins, 2001; Barkema et al., 2010). Staining of fecal samples and tissue impression slides, fecal and tissue culture, and direct fecal PCR have been used to detect MAP organisms. Humoral immune responses can be measured using Agar Gel Immunodiffusion (AGID), complement fixation (CF), and ELISA. Cellular immunity can be assessed using delayed-type hypersensitivity responses by skin testing, and gamma interferon release (Manning and Collins, 2001). Because fecal culture itself has imperfect sensitivity, estimated sensitivity of other tests using fecal culture as the gold standard are likely biased (Jubb et al., 2004; McKenna et al., 2005).

1.4.1 Serologic tests

Antibody ELISAs are rapid, easily standardized, and relatively inexpensive methods suitable for whole herd screening (Kudahl et al., 2007b). Serum ELISAs are the most common serological tests for the diagnosis of MAP infection in cattle and other farm animals, but the sensitivity varies by species and is poor in wildlife (Pruvot et al., 2013). Currently available commercial ELISAs detect antibody to MAP. Humoral

immune response against MAP at an early stage of MAP infection can also be detected using appropriate antigens such as MAP stress-associated proteins (Kawaji et al., 2012).

Sensitivity of ELISA has been reported to be between 26% and 59% (Sockett et al., 1992b; Sweeney et al., 1995; Kalis et al., 2002; van Schaik et al., 2007a). An expert consensus reported the sensitivity of available ELISAs for serum or milk as 25 to 35% with a specificity between 98 and 100% (Collins et al., 2006). Different ELISA cutoffs will have different sensitivity and specificity and interpretation at a higher cutoff could be cost-effective when a higher specificity is desired (Kalis et al., 2002). Subclinical and light shedding cattle are usually seronegative, while high shedders are likely to be seropositive (Sweeney et al., 1995). The sensitivities of current ELISAs improve with increasing parity or lactation, stage of the disease (Kudahl et al., 2007b) and in older animals (Nielsen and Toft, 2006). Sensitivity of ELISA also increases with subsequent testing of a cohort of cattle. ELISA positivity is more common in animals over four years of age (Kalis et al., 2002) and also increases with the level of fecal shedding (Sweeney et al., 1995; Nielsen and Toft, 2006). Therefore, ELISAs are less useful for detecting cattle with low, moderate or intermittent MAP shedding.

ELISA sensitivity was significantly higher for clinical cases of JD (87%) compared to subclinical, light-shedding cattle (15%) (Sweeney, 1996). Sensitivities of three types of ELISAs using tissue culture as the reference standard were 9%, 7%, and 17% compared to 17%, 14%, and 28% using fecal culture as the gold standard (McKenna et al., 2005). ELISA sensitivity based on tissue culture was 12% for cows less than four years of age and between 20 and 30% in older cattle (Jubb et al., 2004). This increase in sensitivity might be related to fecal shedding as the probability of detection of MAP shedding increased with the age of cattle (Kalis et al., 2002). These sensitivity estimates for ELISAs are considerably lower than previous estimates measured against fecal culture as the gold standard. Fecal culture can have low sensitivity, and there is often a long time period prior to detectable fecal excretion in infected animals (Jubb et al., 2004).

1.4.2 Fecal culture

Fecal culture for MAP is considered the gold standard, but the sensitivity is less than perfect. Therefore it is not a good gold standard for negative results (Jubb et al., 2004; McKenna et al., 2005). Fecal culture requires a long incubation period that can be three months for bovine samples (Chiodini et al., 1984) and up to six months for small ruminants (Collins et al., 1993). Difference in the length of incubation is related to the MAP strain rather than host factors. One specific strain of MAP (type I/III) from cattle took over three months to grow on solid media (de Juan et al., 2006). Different MAP strains may also have different growth requirements. Herrold's egg yolk (HEY) medium is the most commonly used solid media (de Juan et al., 2006), but Löwenstein-Jensen with mycobactin is necessary for isolation of type I/III strains of MAP.

The HEY medium was developed in 1931 but subsequently modified to promote growth of MAP (Whipple et al., 1991). Fecal culture of dairy cow samples using HEY had a sensitivity of 54% in one population (van Schaik et al., 2007a) and 38% in another (Whitlock et al., 2000). Another study estimated a sensitivity of 41% (Sockett et al., 1992a). An expert consensus reports the sensitivity of fecal culture for MAP as 55 to 65% with a specificity between 99.8 and 100% (Collins et al., 2006) although, specificity of fecal culture is typically considered to be 100% (Chiodini et al., 1984; Merkal, 1984; Sockett et al., 1992b; Whitlock et al., 2000; van Schaik et al., 2007a; Benedictus et al., 2008).

Fecal culture is considered to be expensive relative to serological methods. Pooling feces is an approach to reduce cost, but the sensitivity depends upon shedding intensity (van Schaik et al., 2007b). In the developmental phase of cultural examination, this method was sensitive to detect 100 organisms per gram while techniques able to detect one organism per gram of feces have been available since 1980s (Merkal, 1984). Individual results will require more time once a positive pool has been identified. The sensitivity of diagnostic tests for JD, based on detection of MAP in fecal samples, is adversely affected by the long subclinical phase with or without MAP shedding (Sockett et al., 1992a). Targeted sampling of older animals is a viable option because the

sensitivity of fecal culture improves linearly from two to five years of age (Nielsen and Toft, 2006). Sensitivity of fecal culture might also be increased by prolonging the incubation period to eight weeks for slower growing strains (de Juan et al., 2006).

Manual Mycobacteria Growth Indicator Tube (MGIT) is a medium consisting of liquid broth. After supplementation, it can grow a range of mycobacterial species (Siddiqi and Rüsch-Gerdes, 2006). The first report of liquid culture system used in M. paratuberculosis detection was the BACTEC 460 based on a modified 12B (radiometric) culture medium. The results indicated a better sensitivity (92%) compared to conventional method (60) (Collins et al., 1990b). After several decades of use of liquid culture for MAP, non-radiometric liquid culture protocol was developed using fluorescent compound activated by culture isolates. Results indicated that MGIT-liquid culture is a robust diagnostic culture system with a potential to perform better than traditional HEY media (Fyock et al., 2006). Non radiometric BACTEC MGIT 960 system was also recommended to be used with solid media to improve sensitivity (Cruciani et al., 2004). Performance of MGIT and radiometric BACTEC 460 culture systems for MAP isolation from milk were similar (Grant et al., 2003) although radiometric BACTEC is recommended for ovine fecal samples (Gumber and Whittington, 2007).

Radiometric culture systems provide faster results with an increased sensitivity compared to conventional solid media. Growth is detected by the release of $^{14}CO_2$ during metabolism of a ^{14}C-labeled substrate. Radiometric measurements were strongly correlated to spectrophotometric ($r = 0.962$) and plate count ($r = 0.992$) methods for measuring growth of MAP (Lambrecht et al., 1988). Sensitivity of radiometric culture methods and conventional fecal culture in HEY was 54% and 45%, respectively (Sockett et al., 1992a). Radiometric methods have greater analytical sensitivity because the specimens are filter-concentrated (Collins et al., 1990a) and can be positive in samples with as few as three viable bacteria (Lambrecht et al., 1988). Another study with samples from sheep also found that the BACTEC 12B medium had a better sensitivity in sheep feces compared to conventional solid media (Whittington et al., 1999). Another study

also recommended BACTEC 12B for culture and identification of MAP from contaminated soil and pasture samples (Whittington et al., 1998).

The differences in sensitivity estimates from studies could be due to the difficulty in isolating specific strains, limited number of viable bacteria in some samples, time between collection and culture, sample handling techniques, and possible loss of MAP viability during the decontamination process.

1.4.3 Culture of tissue

Even though fecal culture is considered the gold standard, culture of ileum and ileocecal lymph nodes is more sensitive because it can detect a wider spectrum of infected animals representing all stages of disease. In a study of slaughter cows, 16% were MAP positive by the culture of ileum and associated lymph nodes while only 4% were fecal culture-positive (McKenna et al., 2005). Tissue culture might have the highest sensitivity for detection of MAP, but biopsy of individual animals is difficult. Further, it is expensive relative to other available alternatives. Tissue culture has been used in slaughter beef and dairy culls in the US (Merkal et al., 1987).

1.4.4 Polymerase chain reaction

Polymerase chain reaction amplifies target DNA of MAP in the sample. This method can also provide genetic profiles for molecular epidemiological studies from different hosts and different geographical locations. Many of the MAP PCRs target the 5' end of the DNA insertion sequence IS900 (Sockett et al., 1992a; Collins et al., 1993; Whittington et al., 1998; Jaravata et al., 2007; Okura et al., 2011). However, presence of IS900-like sequences have been identified in other mycobacteria suggesting that isolation on solid media is necessary to confirm phenotypic characteristics (Cousins et al., 1999). IS900 PCR can be used for identification of MAP from soil and pasture samples (Whittington et al., 1998) although false positives due to *Mycobacterium scrofulaceum* or a similar organism have been reported (Cousins et al., 1999).

1.4.5 Intradermal test

In early stages of MAP infection, the microorganism elicits a cell-mediated response by the host that can be described as strong delayed-type IV hypersensitivity reactions (Stabel, 2000). The delayed type hypersensitivity reaction is the typical response to an intradermal injection of a small quantity of antigen with the positive result characterized by monocytic infiltration into the injection site within 24 to 72 hours. This reaction involves memory T cells with involvement of both the CD4+ and CD8+ fractions (Black, 1999). The currently available Johnin Test employs a purified protein derivative (PPD) of *M. avium*, (e.g. Johnin OT 133-8707) (Steadham et al., 2002). This test is able to detect MAP infections before animals become infectious (Kalis et al., 2003). This test is easy to conduct and inexpensive, but has limited reliability in some populations because there is a possibility of cross reactions leading to a very low specificity (Manning and Collins, 2001). Specificity of intradermal test has been reported to be 94% using a skin thickness increase of 4mm or more as the cut-off value (Kalis et al., 2003).

1.4.6 Interferon gamma assay

Gamma interferon is a cytokine produced by sensitized lymphocytes as part of the cellular immune response to MAP infections. This test measures the amount of interferon gamma released by peripheral blood monocytes in response to stimulation with MAP antigens (Manning and Collins, 2001). The test is carried out with whole blood samples (Wood et al., 1990) and useful even in subclinically affected animals (Stabel, 1996; Stabel and Whitlock, 2001). The sensitivities of the gamma interferon assays were 72%, 93%, and 100% in detecting subclinical non-shedders, subclinical shedders, and clinical cows, respectively (Billman-Jacobe et al., 2008). Specificity of gamma interferon test has been reported to be 94% using a new algorithm, but ranged from 66 to 67% using two algorithms provided by the manufacturer (Kalis et al., 2003).

1.4.7 Complement fixation test

The complement fixation test (CFT) is often required prior to international shipments. This test is based on detection of complement-fixing antibodies to MAP. The sensitivity and specificity of the CF assay are considered to be lower than ELISA (Sockett et al., 1992b; Collins, 1996). The CFT has a sensitivity of 38.4 and specificity of 99.0 (Sockett et al., 1992b), but ranged from 62-100% in different herds (Kalis et al., 2002).

1.5 Testing strategies

A consensus of experts (Collins et al., 2006) recommend three basic testing options for commercial cow-calf and seed-stock beef herds as: (i) testing whole herd by fecal culture for MAP; (ii) testing whole herd with ELISA and confirm positives with fecal culture; and (iii) target testing of "high-risk" (thin and older) animals by fecal culture.

A test with higher sensitivity is desired at the beginning of a control program when many diseased animals are expected to be identified and culled. However, available tests for JD have low sensitivity and this is a major issue for control programs (Collins et al., 2006; Kudahl et al., 2007b; Kudahl et al., 2008). Lower sensitivity leads to higher number of false negatives allowing them to stay in the herd and infect more herdmates. Lower sensitivity of ELISA compared to fecal culture complicates test based JD control. Because of the lower sensitivity to detect even the MAP shedding cows, serological tests alone are not recommended especially for the herds with higher prevalence (Sockett et al., 1992a).

Cost is an important factor to consider when designing testing strategies. A practical control strategy for a higher prevalence herd may be to reduce the prevalence after several testing-cycles and improved hygiene (Collins et al., 2006; Benedictus et al., 2008). Sampling cows at third or higher lactation improves the test sensitivity while reducing the cost of sampling and testing a group (Nielsen and Toft, 2006; Tavornpanich et al., 2006). As a high risk group, ELISA titer is expected to be higher in cows over four years of age (Kalis et al., 2002) in addition to fecal shedding being greater in older

animals (Sweeney et al., 1995; Nielsen and Toft, 2006). Older cows are more likely to be infectious (shedding) rather than simply infected and these animals are more important to identify in the herd. The main focus of control should be the removal of infectious animals to reduce the spread of MAP within the herd.

Simulation studies suggest that with an estimated prevalence of 0.1% in Swedish herds, the probability of freedom at the end of three years was 0.63 under ongoing surveillance system (Frossling et al., 2012). Despite an existing surveillance system, this study recommended that new surveillance activities or an intensification of current activities are required. After implementing semi-annual fecal culture of all adult (≥2 year) animals in a Pennsylvania dairy farm the apparent prevalence was reduced from 60% to less than 20% during the first five years. However, the prevalence did not decline to zero even after 20 years of a continuous effort (Benedictus et al., 2008). Sensitivity of fecal culture and ELISA appears to decrease with repeated herd testing (Whitlock et al., 2000) because heavy shedders with good ELISA responses will be culled first from the herds. Prevalence in offspring from test-negative dams was 10% and significantly higher (27%) in infected dams when a control program was implemented in a mid-sized dairy herd (Benedictus et al., 2008).

Higher testing costs should also be weighed against the cost of failing to detect an infected animal or misclassifying and culling a non-infected animal. The most cost-effective sampling method does not necessarily have the best sensitivity. Based on the priority of a production unit, a farm manager may be willing to accept the higher risk of culling false-positive cows and prefer a lower specificity but higher sensitivity of the test or vice versa. Such decisions should vary based on all applicable costs, but direct testing costs are typically the most important factor affecting test selection. In the initial stages of control programs, cost effectiveness can be increased by targeted sampling to improve the positive predictive value of the testing scheme. Alternatively, pooling ten fecal samples has been suggested for herd monitoring (van Schaik et al., 2007b), which reduces the cost several fold, but the sensitivity may be lower than individual culture.

There are limited field reports concerning MAP eradication and is likely not feasible unless a herd has low (< 5%) test prevalence and has an effective herd hygiene management program (Collins et al., 2006). This is a limitation associated with the sensitivity and specificity of currently available tests (Wang et al., 2006; Benedictus et al., 2008). Under ideal conditions, selected tests should have maximal sensitivity and the whole herd must be tested with positive reactors culled for several cycles of testing (Collins et al., 2006). A simulation model estimated that a test with more than 70% sensitivity is necessary to reduce the prevalence of JD to less than 1% within ten years (Collins and Morgan, 1992).

1.6 Johne's disease control programs in the US

Control programs are in effect within the USA and other countries including Australia, Scotland, and Japan. Some countries including Australia have a mandatory control program (Larsen et al., 2012) and Sweden is near countrywide eradication (Sternberg Lewerin et al., 2007). Control programs should be designed based on the disease prevalence, economic losses due to the disease and whether the objective is control or eradication. Decision-making for the control of animal diseases should be a dynamic and flexible process allowing the priorities to change over time (Ge et al., 2007). Two major components of JD control programs are: (i) preventive management and hygiene improvement to reduce exposure to manure, and (ii) cull or managing test-positive animals to avoid further infections and contamination of premises (Rossiter and Burhans, 1996).

The United States Department of Agriculture (USDA) initiated regulatory control of JD in 1952 with a notice issued in Puerto Rico and in all continental states except Maine, New Hampshire, Rhode Island, Utah, and Wyoming (Carter, 2011). Although JD was recognized and described in the US in 1908, JD management at the state level started only in the 1980s (Whitlock, 2010). Initial control efforts in the US were small, voluntary, and of limited scope (Chiodini et al., 1984). A national JD task force of state and federal government, researchers, and other stakeholders of the Johne's

Committee of the United States Animal Health Association (USAHA) developed the first national JD certification program for cattle (Whipple, 1993). Another strategic plan was developed in 2001, and a recommendation to develop a new strategic plan for JD was made by the USAHA-JD Committee meeting in 2007 (USAHA, 2007b). The need for a new five year plan was proposed to the USDA-Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS), and the VS accepted the strategic plan approved by USAHA in 2008 (USAHA, 2008).

The US Voluntary Bovine Johne's Disease Control Program (VBJDCP) was developed in cooperation with the National JD Working Group and the JD committee of the USAHA, state veterinarians and industry representatives. It was approved by the USDA Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS). The VBJDCP was administered at the individual state level and supported by industry and the US federal government(VBJDCP, 2002). The USDA-APHIS-VS provided financial support for implementation of the control program and to assist producers with the cost of risk assessments, management changes, and diagnostic testing (Collins et al., 2006). The general approach of the VBJDCP was that cattle herds were to be identified and classified based on MAP test status. Herds were certified at different positive and negative categories. Subsequent annual tests with entirely negative results were evidence of a higher probability that the herd was free of JD. Tests were required to be conducted at laboratories that had passed the check tests developed by the National Veterinary Services Laboratories (USDA, 2002, 2005, 2010).

The VBJDCP consisted of three elements: education, management, and herd classification (Carter, 2011). An important component of education was veterinarian certification and an Internet-based training program was maintained at the University of Wisconsin. The management component was implemented by veterinarians trained and certified to perform JD risk assessments and develop management plans. JD certified veterinarians must be USDA accredited and have received additional training on JD epidemiology, sample collection, testing, test interpretation, state and federal program requirements, on-farm risk assessments, and herd management plan development. A JD

risk assessment is a structured investigation of management practices affecting MAP transmission performed by appropriately trained veterinarians and approved by state JD coordinators. The risk assessment is performed by assigning ordinal scores based on an on-farm evaluation of risk factors, environment, and owner responses related to management practices with respect to biosecurity. A completed risk assessment with assigned risk scores is used to develop the herd management plan designed to reduce MAP transmission. The herd management plan and laboratory testing were voluntary components of the program. If the producer elects to test, then it is classified as a positive or negative herd, with an increasing probability of JD-free status if the herd is negative in subsequent annual tests. Probability of a herd being free of MAP infection is assigned classification levels and herds at Levels 3 and 4 have 98 and 99% probability of being free from MAP infection, respectively herds (USDA, 2002; VBJDCP, 2002). Further classifications ranging from Level 1 to 6 were created in 2010 (USDA, 2010).

The National Johne's Disease Demonstration Herd Project (NJDDHP) was implemented in 66 dairy and 22 beef herds from 17 states (Fossler, 2007). This project monitored enrolled herds for a change in the prevalence of MAP infection due to management practices implemented to minimize transmission. The NJDDHP began in 2003 and ended in 2010. The project was started in 2003, but final herd enrollment numbers were not reached until 2005. The program focused on educating producers, improving herd management, and testing herds (VBJDCP, 2002). This program also received federal funding until 2009 and the data collection for all herds ended in September 2010 (USAHA, 2010).

In certain territories of Australia, infected herds are quarantined and eradication is undertaken whenever an infection is suspected or confirmed (Kennedy and Allworth, 2000). Eradication is almost complete in Sweden, but there were confirmed cases in imported beef cattle in 2005 (Sternberg Lewerin et al., 2007). Control of JD requires very effective herd biosecurity management protocols and possibly the use of diagnostic tests to remove existing infected stock. In the US, as a biosecurity measure, the Code of Federal Regulations effective May 2000 restricted the interstate movement of JD

positive animals to prevent the dissemination of disease (USDA, 2000). National Animal Health Monitoring System (NAHMS) periodically conducts field studies to monitor the disease situation and producers' perceptions to inform policy decisions and formulate control strategies (NAHMS, 1994, 1999, 2010).

1.7 Herd level Johne's disease control strategies

Bovine JD control programs have two key strategies for preventing spread between herds and preventing spread within the herd. Eradication is possible by a strong commitment to these strategies over a long period of time (Sykes, 2000). A certification of test-negative or low-risk herds was recognized as an important step forward in efforts to control JD in US beef herds (Sockett, 1996) and provide better marketing opportunities (Benjamin et al., 2009).

Culling only cows shedding large quantities of MAP could be effective in preventing MAP transmission in combination with good management (Lu et al., 2008). However, a limitation of this study was arbitrary assignment of the effect of good and poor management. Another simulation model reported that improved management can cause a marked decrease in herd prevalence and total costs by reducing transmission routes during the early stages of JD (Bennett et al., 2010).

Total herd depopulation, barn cleaning and disinfection along with the removal of fecal material has been recommended for small herds (Chiodini et al., 1984). Immunization against MAP infection was first studied many years ago (Sigurdsson and Tryggvadottir, 1949, 1950). Vaccination is restricted in the US, but used effectively in Latin America and Europe (Stabel, 1998; Kalis et al., 2001; Juste, 2012). Vaccination is beneficial from an economic perspective, but improvement in calf management is important for a faster reduction in disease prevalence (van Schaik et al., 1996; Groenendaal et al., 2002). The only approved JD vaccine in the US is a killed MAP product in mineral oil adjuvant and use is limited to heavily infected areas where husbandry and management changes alone were not effective for control (Whitlock, 2010).

Vaccination has preventive and therapeutic effects although the infection itself might not be prevented (Juste et al., 2009; Juste, 2012). Vaccination has been criticized for this insufficient protection and the possibility of false-positive test results complicating control programs (Stabel, 1998; Harris and Barletta, 2001; Santema et al., 2012). Vaccination against JD is cost-effective but the export of vaccinated animals is prohibited (van Schaik et al., 1996; Juste et al., 2009).

1.8 Economic issues

1.8.1 Financial impact

The losses attributed to JD in US cattle were reported to be "tremendous" in the absence of control measures (Meyer, 1913). However, estimation of the economic impact of JD in the US is complicated by lack of data and the difficulty in defining disease-associated losses. Despite these limitations, losses are believed to be substantial with an estimated annual loss of up to $1.5 billion ($1.95 when adjusted for 2013) (Harris and Barletta, 2001).

The collection of field-level economic data is expensive and time consuming due to the long latent period of JD. There is also a slow clinical progression and lower sensitivity of available tests for subclinical cases. A study of JD associated economic losses in dairy cattle reported a decrease in milk production of 20% compared to the lactation two years prior to developing clinical JD (Benedictus et al., 1987).

A net present value approach estimated $6 million ($9.32 million in 2013) loss and a market value approach estimated $5.7 million ($8.9 million in 2013) loss in the Kentucky cattle industry (Meyer and Hall, 1994). However, such results are dependent upon assumptions regarding cattle cost, production levels and age of disease onset. Fecal culture positive cows produced 1,355 kg lower milk, and were three times more likely to be culled (Raizman et al., 2009). Lowered milk production and replacement due to JD causes a loss of $100 ($138 in 2013) and it doubles to $200 ($277 in 2013) annually per cow when 10% or more cows are clinically affected (Ott et al., 1999). In Michigan dairy herds, there was a 73.5 lb decrease in mean weight of cull cows for each 10% increase in test prevalence leading to a loss of $1,150 ($1,590 in 2013) for a typical (136 cow) herd.

Further, test-positive cows had 3% higher mortality proportions compared to test-negative cows, leading to an average annual loss between $1,607 ($2,221 in 2013) and $4,400 ($60,818 in 2013) in average (136 cow) herds on the basis of lost slaughter value and cost of replacement heifers (Johnson-Ifearulundu et al., 1999). A typical 61-cow Canadian dairy herd with 8 MAP seropositive cows had a mean loss of Canadian $49 (US$51 in 2013) per cow per year due to decreased milk production, additional culling, mortality, and reproductive losses accounting for 9%, 46%, 16%, and 29% of the losses, respectively (Tiwari et al., 2008).

Extrapolation of results from dairy herds suggests that the economic impact in the beef sector could be substantial. Losses in beef cattle can also be classified as direct (losses from infected animals' productivity) and indirect (culling and replacement changing the herd demographics) (Dorshorst et al., 2006; Kudahl et al., 2007a; Tiwari et al., 2008). JD in beef cattle production may cause premature culling of affected animals, decreased milk production ultimately reducing the weaning weights of calves, reduced body weight of culled animals and loss of potential markets (Ott et al., 1999). Regression estimates of cow and calf traits on ELISA scores in a multibreed beef herd indicated that higher ELISA scores were associated with longer open periods, lower ability to maintain weight, and lower weight of calves born and weaned (Elzo et al., 2009), all of which may contribute to direct economic losses.

Indirect losses due to MAP in beef herds include reduced sales, loss of valuable genetic material due to premature culling, loss of export markets, lowered consumer confidence and the cost of litigation (Roussel, 2011). Due to regulatory and ethical implications, it is an ethical responsibility of producers to avoid selling infected stock (Rossiter and Burhans, 1996). Absence of a definitive diagnosis does not protect producers in such a scenario (NAHMS, 1999). Owners of infected herds, veterinary practitioners, and regulatory personnel should be aware of the potential liability of selling MAP infected livestock. Liability may extend beyond the value of the infected animal and include all consequential damages to the buyer. An apparently healthy

animal from an infected herd will not protect the seller from this liability (Chiodini et al., 1984).

Mortality losses exceed those associated with culling alone because the salvage value of the animal is also lost. Other possible losses that are not easily estimable include loss of breeding value of purebred cattle, poor feed conversion, increased susceptibility to other diseases, infertility, and costs of control programs (Jones, 1988). However, there are also some reports from dairy cows indicating that the mean days open (number of days from calving to conception) were similar between MAP fecal culture positive and negative cows (Raizman et al., 2009), and even a higher pregnancy rate in MAP-infected cows has been reported (Gonda et al., 2007). These counterintuitive findings may have been due to confounding factors including cow-age and production potential.

Beef cow-calf operations in the US are not always profitable (TAMU, 2009). This reflects, in part, the contribution of beef producers that choose to raise cattle for reasons other than as the primary source of income. Return over total costs for cow-calf producers in Kansas were negative for ten of the years between 1972 and 1989 (Krause, 1992) and for 26 of the 30 years between 1979 and 2008 (Pope et al., 2011). Producers might be hesitant to adopt new practices due to lack of specific knowledge. Reasons for beef producers not adopting best management practices include unfamiliarity, non-applicability, cost, and need for more time to adopt. Unfamiliarity and non-applicability were the most common reasons associated with non-adoption of management practices (Gillespie et al., 2007).

1.8.2 Tools for economic analysis

Animal health economics provides a framework of concepts and tools to optimize animal health management. Practical application of these tools includes the quantification of financial impacts, optimization of decisions and cost-benefit analysis for the control of disease in herds. Partial budgeting, cost-benefit analysis, decision analysis, and systems simulation are the four most common techniques for veterinary

decision making at the animal, herd, and national levels (Dijkhuizen et al., 1995). Such tools have been used since the late 1940s in agriculture, which were mostly influenced by 'operational research' or 'management science' as guidance to decision makers in industries (McCown, 2002).

The benefits of disease control can be evaluated using partial budgeting that estimates financial consequences under the scenario of a control intervention (Dijkhuizen et al., 1995). Decision support systems are computer-based approaches that employ existing data and knowledge to help a decision maker develop an economically prudent decision or series of decisions (Power and Sharda, 2009). Decision tree models are a type of decision support system that can be useful for the estimation of the overall economic return from a control program. Decision-making for the control of livestock diseases should be dynamic and flexible to avoid unnecessary cost that would otherwise incur due to trial and error to identify the most economic decision (Ge et al., 2007).

There are a limited number of studies evaluating economic aspects of JD control strategies in beef cow-calf herds. A deterministic cost-benefit model was created to simulate the control of MAP in UK cow-calf herds under various control measures over ten years (Bennett et al., 2010). Inputs were based on the opinions of stakeholders rather than collected field data. Most parameters were obtained from previous models for dairy herds (Groenendaal et al., 2002) with some adjustment based on the results from another model (Kudahl et al., 2007a). Calving percent, age at first calving, calving interval, calf growth rate, and weaning weights were assigned based on expert opinion of the authors. Such model inputs are often the key components influencing the results of decision support tools (McCown, 2002). The Bennett et al. (2010) model accounted for the effect of JD and control measures in terms of changing herd prevalence and the shedding states of animals within the herd. The model also estimated the financial costs of the disease and control measures. The improvement of herd hygiene reduced newborn calf infections, but test and cull programs were not effective at reducing prevalence or disease cost after ten years. Slow progress towards eradication with test and cull programs has been described by previous reports from dairy herds (Collins and Morgan,

1992; Collins et al., 2006; Benedictus et al., 2008), mostly attributable to lower sensitivity of available tests (Collins and Morgan, 1992; Jubb et al., 2004; Collins et al., 2006; Wang et al., 2006; Kudahl et al., 2007b; Benedictus et al., 2008; Kudahl et al., 2008). Another limitation of the Bennett et al. (2010) study is the lack of data from beef herds to test and validate the model.

Webb Ware et al. (2012) developed a spreadsheet simulation model for beef herds in Australia and results suggested that eradication is only profitable in the longer term when discounts on the sale of stock from infected herds are high. Control rather than eradication may be the preferred option for many commercial beef herds. Factors that affect the decision include the discounts applied to sold animals, the duration of trading restrictions, and the adopted strategy. Control was important in seedstock herds because of the restrictions imposed on the sale of cattle through current policy and regulations in Australia (Kennedy and Allworth, 2000; Webb Ware et al., 2012). One of the major strengths of the Webb Ware et al. (2012) model was the use of data collected from beef producer surveys, and economic data obtained by farm monitoring. Estimates of annual cash flow enabled comparisons between commercial and seedstock herds.

Decision support models for the control of JD in dairy herds based on specific management alternatives have been developed (Collins and Morgan, 1991; Collins and Morgan, 1992; Dorshorst et al., 2006). Collins and Morgan (1991) developed a simulation model for JD control in dairy cattle evaluating alternative courses of action with regard to testing and culling in an infected herd. This model estimated parameters from the literature and used the Reed-Frost technique to predict the rate of new infections. Reed-Frost techniques might be efficient when the effective contact time and probability of contact can be derived from field studies. Testing and culling was profitable when there was greater than 6% prevalence and a decrease in milk production of greater than 6% assuming test sensitivity of 50%, test specificity of 98%, and testing costs of $4 per cow. This model was further refined by developing another spreadsheet model for dairy herds incorporating iterative sampling techniques to account for uncertainty (Collins and Morgan, 1992). Both models assumed annual culling of the test-

positive animals. The refined model used age-specific culling rates and was validated using published data.

A more comprehensive decision analysis model with several farm related costs and benefits was developed for dairy herds by Dorshorst et al. (2006). This model included decision paths for herd management, testing and post-test actions. The Reed-Frost technique was used to estimate the rate of new infections within a 100 cow herd tested annually. Costs associated with lowered output and costs associated with new JD infections were calculated for herds at different intensity of control efforts. Improving herd hygiene management practices was beneficial and using less expensive tests was better than more sensitive tests. The model suggested that it was profitable to retain test-positive cows that were in an early stage of infection.

1.8.3 Economic benefit of control

The benefit perceived by producers, potential implications associated with knowing herd status, and available marketing opportunities will determine whether a producer will implement a control program (Rossiter and Burhans, 1996). The financial evaluation of losses and benefits due to JD is difficult because of the chronic nature of the disease. In a survey of beef cattle producers in Texas and Nebraska, more than half admitted that they did not have enough knowledge to estimate the financial risks and benefits (Hall et al., 2003). Sixty-four percent of beef producers with herds having a low-risk of JD (Level 4 of the US VBJDCP) perceived some form of benefit due to participation in the JD control program (Benjamin et al., 2009). Thirty-eight percent of US dairy producers perceived a financial benefit, but only 13% of producers perceived an increase in revenue (Groenendaal and Wolf, 2008). Another study of low-risk dairy herds enrolled in the VBJDCP (Level 3 and 4) perceived that it is an economically beneficial strategy mainly due to improved health (43% respondents), and better market opportunities for surplus animals (29%) (Kovich et al., 2006).

Classification at test-negative status Level 4 in the VBJDCP led to increased marketing opportunities for more than one-third (13/35) of producers (Benjamin et al.,

2009). A similar report of low-risk dairy herds (at Levels 3 and 4 of VBJDCP) estimated that 90% (19/21) of producers perceived a financial benefit, and 95% (20/21) reported that the benefit was higher than investment (Kovich et al., 2006). Classification as low-risk will be beneficial when market discrimination favors higher prices for cows from low-risk herds (Sockett, 1996; Barlow and McKenzie, 2000; Kennedy and Allworth, 2000).

There is a difference in the perceptions of veterinarians and producers concerning JD and voluntary control programs (Benjamin et al., 2010). Many beef producers reported financial losses due to JD and those enrolled in the NJDDHP perceived an increase in revenue and financial benefit (Benjamin et al., 2010). However, the recognition of losses is complicated by the fact that only 59% of producers and 50% of veterinarians attribute substantial losses in beef cattle production to JD (Benjamin et al., 2010). Two percent of US beef producers strongly agreed and 10% of them agreed that JD was a significant problem for the beef industry (NAHMS, 1994). Producers reported that brucellosis, tuberculosis and trichomoniasis were more significant infectious disease problems. A subsequent NAHMS study in 1997 estimated that 92% of beef producers were either unaware of JD or recognized the name but knew very little about the disease (NAHMS, 1999). This might be due to a lower prevalence of disease in beef compared to dairy herds (NAHMS, 1999; Wells et al., 2008). Few beef herds tested for JD (0.2%) and this is likely a reflection of the producers' lack of knowledge (NAHMS, 1998). Another NAHMS study during 2007–08 estimated that only 11% of producers strongly agreed and another 27% agreed that JD is a significant problem in the US beef industry (NAHMS, 2010).

Only 13% of VBJDCP enrolled beef producers reported that they observed a lower JD incidence on their operations that they attributed to changes made based on the program (Benjamin et al., 2009). There was steady increase in program participation by Minnesota cattle producers in the NJDDHP and over 30% of dairy producers and 2% of beef producers in the state were participating by the end of 2006 (Wells et al., 2008). There was significant within-herd seroprevalence reduction for beef herds that

participated in the Management Program (set of prescribed herd hygiene recommendations) for at least three years. However, enrollment in management and herd classification programs was low among beef producers compared to dairy herds.

A lower appreciation of the economic impacts of JD in beef herds presumably reduces the motivation of producers to adopt a control program. Producers enrolled in the NJDDHP were generally positive about their experience with the control program. With the knowledge about the losses due to JD, 95% of dairy producers enrolled in NJDDHP were happy to participate and 74% of producers indicated that general herd health improved with adoption of the control program. However, producers that enrolled in the NJDDHP would be more likely to perceive benefits compared to producers in general since they enrolled voluntarily with the possible expectation of accruing benefits.

2. EFFECT OF POSITIVE TEST RESULTS FOR *MYCOBACTERIUM AVIUM* SUBSPECIES *PARATUBERCULOSIS* ON WEANING WEIGHTS IN BEEF COW-CALF HERDS

2.1 Introduction

Johne's disease (JD) is caused by infection with *Mycobacterium avium* subspecies *paratuberculosis* (MAP) in cattle and has a long pre-clinical phase that progresses into diarrhea, debilitation, (Chiodini et al., 1984; Harris and Barletta, 2001) cachexia and death (Manning and Collins, 2001). In a specific beef herd, the presence of MAP-specific antibody as determined by ELISA was associated with longer open period, reduced ability to maintain weight, and lower weight of offspring (Elzo et al., 2009). In addition, mortalities and sale of underweight MAP-infected cows represent a loss of capital for beef producers and may have negative impacts on producer reputation and marketability of breeding stock (Roussel, 2011). All of these factors contribute to direct or indirect economic losses.

The burden of JD in the beef industry has been studied in different parts of the US but with considerable variation in methodology. A study of US cow-calf herds from 23 states estimated that 8% of cow-calf herds were infected (NAHMS, 1999; Dargatz et al., 2001) with an overall ELISA-based cow-level seroprevalence of 0.4% (Dargatz et al., 2001). However, serum ELISA based prevalence up to 9% has been reported for different US beef herds (Thorne and Hardin, 1997; Hill et al., 2003; Pence et al., 2003; Roussel et al., 2005).

While general recommendations for JD control are available, the effectiveness of JD control measures is largely unknown. The USDA National Johne's Disease Demonstration Herd Project (NJDDHP) was initiated to evaluate the effectiveness of JD control methods to reduce disease in herds. The NJDDHP began in 2003 and ended in 2010. Some states had demonstration projects prior to 2003, and their data were incorporated into the NJDDHP database in some cases, with the earliest data dating back to 1999. With an objective to evaluate long-term effectiveness and feasibility of

management for JD control on dairy and beef cattle operations, the NJDDHP progress in JD control by evaluating herd management practices and test results over time (USAHA, 2007a).

Information on JD associated losses is important because producer consensus regarding the need for disease control drives the success of any coordinated control or eradication program. The Beef 2007-08 study by the National Animal Health Monitoring System study estimated that only 37% of cow-calf producers from 24 states believed that JD is a significant problem in US beef industry (NAHMS, 2010). Despite ongoing educational and scientific efforts to aid in producers' understanding of JD and its potential impacts, a 2009 report indicated that only 25% of beef producers perceived a significant benefit of participation in control or eradication programs (Benjamin et al., 2009).

A potential factor impacting producers' perceptions regarding the benefits of participation in control and eradication programs is the lack of estimates of the direct economic impacts of JD in beef cattle operations. The objective of this study was to estimate the association between calf weaning weight and MAP test status of the dam as determined by serum ELISA or bacterial culture of feces. Associated monetary losses relative to calves born to seronegative or culture negative cattle were estimated for cow-calf herds enrolled in the NJDDHP.

2.2 Materials and methods

2.2.1 Study design

This study was a retrospective analysis of data collected for the NJDDHP, a USDA funded project to evaluate the long-term effectiveness and feasibility of management-related disease control for JD on dairy and beef cattle operations.

2.2.2 Procedures

Data from 22 beef herds enrolled in the NJDDHP for the period from 1999 to 2009 were obtained. Participating herds were tested for JD on an annual basis. A flexible

testing strategy was employed with a goal for at least 80% of adult cattle in the herd to be tested annually by a combination of ELISA and bacterial culture of feces (BCF). Some herds used both whole herd ELISA and BCF. Random testing of a statistical subset of cattle was permissible for very large herds or in states in which resources were limited. At a minimum, all cattle (or a statistical subset) must have been tested using ELISA with all ELISA-positive cattle confirmed using BCF. Testing was required to be performed at accredited laboratories that had passed the National Veterinary Services Laboratories' JD proficiency test (USDA, 2002, 2005, 2010). Different ELISA (Table 1) and BCF (Table 2) tests were employed and varied by location.

Table 1: Classification of serum-ELISA results for samples obtained from beef cows in participating herds

ELISA type	ELISA result S/P ratio cutoff			
	Strong-positive	Positive	Suspect	Negative
ELISA 1[a*]	>0.99	0.25-0.99	0.10-0.24	<0.10
ELISA 2[b†]	>3.49	1.00-3.49	0.50-0.99	<0.50

[*] Used for the samples from FL herds
† Used for the samples from ND herd
[a] HerdChek M. pt. Antibody Test Kit, IDEXX Laboratories Inc., Westbrook, ME.
[b] Parachek®, CSL/ Biocor Animal Health, Omaha, NE.

Table 2: Classification fecal culture results for samples obtained from beef cows in participating herds

Culture method	Shedding level			
	Heavy	Moderate	Low	Very low
BCF 1[a*]	>50 cfu / tube	6-50 cfu / tube	1-5 cfu / tube	N/A
BCF 2[b†]	<21 days to positive	22-28 days to positive	29-35 days to positive	36-42 days to positive

[*] Used for the samples from FL herds
† Used for the samples from ND herd
[c] Herrold's Egg Yolk Medium, Becton Dickinson & Co, Sparks, MD.
[d] ESP® Culture System II, Trek Diagnostic Systems Inc., Cleveland, OH.

2.2.3 Statistical analysis

Weaning weights were adjusted to a standard of 205 days (AWW) by dividing the observed weaning weight by age of calf at weaning and multiplying by 205. Multilevel mixed effects models were used to estimate associations including random effects to account for repeated tests within individual cows and cows nested within herds. Models were fit using the *lme4* package (Bates and Maechler, 2011) for statistical freeware R (The R Project http://sourceforge.net) and results were interpreted at the 5% level of significance. The association between test result (positive or negative) and AWW was evaluated independently for serum ELISA and BCF. Expert opinion suggests that these tests at evaluated cutoffs have sensitivities of 0.30 and 0.60 and specificities of 0.99 and one for ELISA and BCF respectively (Collins et al., 2006). The AWW served as the outcome of interest and test results for the dam in the year of birth for the corresponding calf were modeled as a fixed effect. Separate models were developed evaluating serum ELISA results as a dichotomy (i.e., positive or negative) and as a categorical variable based on interpretation guidelines (i.e., negative, suspect, positive, or strong-positive). Similarly, BCF was modeled as a dichotomy (i.e., negative or positive) and categorical variable (i.e., negative, very low shedder, low shedder, moderate shedder, or heavy shedder).

Simple models were developed including random effects, but without additional covariates other than the ELISA or BCF status. Potential confounding of the association between test outcomes and AWW due to herd and cow-level covariates was evaluated on the basis of change in regression coefficients by more than 20% after inclusion of the covariate in the model. Age of cow, parity of cow, source of cow (i.e., purchased or home-raised), years since the inception of a control program, herd-size, breed, and testing laboratory were evaluated individually for potential confounding. Covariates that were not confounders were retained in the final models on the basis of reduction in the Bayesian Information Criterion (BIC) (Dohoo et al., 2003). The decrease in AWW was expressed in US Dollars based on 5-year (2007 to 2011) average feeder calf values from the National Agricultural Statistics Service (USDA, 2012).

A simple benefit-cost ratio was constructed to evaluate the effect of JD prevalence on the economic benefit of screening. Benefits were estimated as the possible recovery of the amount lost due to lowered weaning weight in calves from test-positive dams. Cost of testing were considered to be $9.60 and $18.00 for ELISA and BCF, respectively (TVMDL, 2013). Cost of labor was ignored because it was assumed that sample collection could be performed during annual pregnancy examinations or similar routine procedure. True prevalence was varied between 0 and 100% and apparent prevalence was estimated for serum ELISA and BCF based on reported sensitivities and specificities (Collins et al., 2006). Percentage of nationwide beef herds across different levels of true prevalence were plotted assuming 20% of the herds being infected and the distribution of within herd prevalence elicited by beta distribution of reported prevalences (Hill et al., 2003; Roussel et al., 2005).

2.3 Results

A total of 50,099 test occasions during 1999 to 2009 from 16,925 beef cattle were available from the 22 herds within the NJDDHP database. Total observations included 29,455 ELISA and 20,614 BCF results. Recording of weaning weight data was optional for participating herds and was only available for four herds. Within these four herds, one did not record both the weight and age at weaning. Within the three herds with both weaning weight and age, the average (minimum, median, maximum) percentage of test-positive cows in a given year was 4.0% (0%, 1.5%, 19%) for ELISA, and 0.6% (0%, 0%, 3.5%) for BCF (Figure 1).

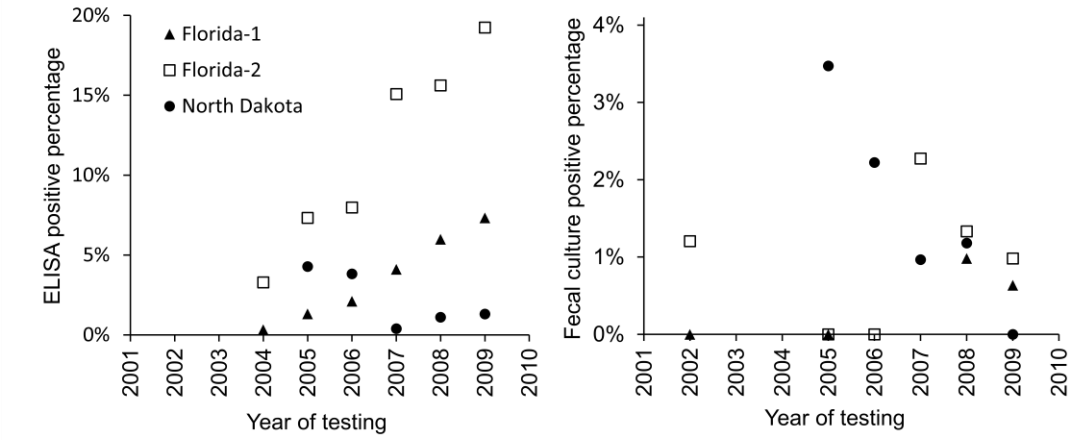

Figure 1: Test-positive percentage of cows from beef herds tested with fecal culture and serum ELISA for *Mycobacterium avium* subspecies *paratuberculosis*

The 4,842 cows with calf weaning age and weight data had 3,482 serum ELISA and 2,103 BCF test results available for analysis. Of the 5.5% (192/3482) ELISA positive results, 1.1% (39/3482) were strong-positive and 4.4% (153/3482) were positive. Of the 0.8% (17/2103) fecal culture positive results, one fecal culture positive observation had missing data for shedding intensity. Of the remaining 2,102 observations, 0.2% (5/2102) were heavy shedders, 0.1% (3/2102) moderate shedders, 0.2% (4/2102) low shedders, and 0.2% (4/2102) very low shedders.

Data were available from a herd in Florida with 1,166 cow-AWW-test observations for ELISA and 454 for BCF. Of the cows with breed information, 71% (1000/1404) of the observations were from Angus, 1% (13/1404) Angus cross, and 28% (389/1404) from Brahman dams. Another herd in Florida had 1,179 cow-AWW-test observations for ELISA and 543 for BCF which were comprised of 21% (229/1066) Angus, 55% (585/1066) Angus crossbreds, and 24% (252/1066) Brahman or Brahman crosses. The herd from North Dakota had 1,137 cow-AWW-test observations for ELISA and 1,106 for BCF which were comprised of 61% (1377/2243) Angus, 32% (711/2243) Angus cross and the remainder other crosses. Both Florida herds were tested from 2002 to 2009. The herd from North Dakota was tested from 2005 to 2009.

Table 3: Difference in 205-day adjusted weaning weight of calves from cows with positive ELISA and fecal culture results in participating beef cow-calf operations

Model[*]	Test type	Decrease in 205-day adjusted weaning weight of calf[†]			
		Kg	95% CI, kg	P-value	US$ Value[‡]
Simple model	Fecal culture positive	27.33	12.35 to 42.31	<0.001	73.16
	ELISA positive	5.79	1.18 to 10.41	0.014	15.50
Adjusted model[§]	Fecal culture positive	33.26	18.79 to 47.73	<0.001	89.01
	ELISA positive	5.53	1.05 to 10.02	0.016	14.81

[*] All models included random effects for repeated tests within each cow and for cows nested within herds
[†] Loss relative to test-negative classification
[‡] Based on 5 year (2007 to 2011) average feeder calf value from http://www.nass.usda.gov
[§] Adjusted for cow-age, lactation number and years since the inception of a control program

The final models included test status and fixed effects for age of dam at testing, parity of dam, and number of years since inception of the control program. Calves from seropositive dams were associated with a 5.5 kg (12.2 lb, $P < 0.001$) decrease in AWW relative to calves from seronegative dams (Table 3). This represents an average loss of US $15 per head among offspring of seropositive dams. Results from models with categorical ELISA outcomes demonstrated decreases in AWW of 21.5 kg (47.4 lb, $P < 0.001$), 2.9 kg (6.3 lb, $P = 0.261$), and 2.8 kg (6.1 lb, $P = 0.139$) in offspring of strong-positive, positive, and suspect dams, respectively, relative to calves from seronegative dams (Table 4). Losses in offspring of cows classified as strong-positive based on serum ELISA are equivalent to US $57 when sold at weaning based on average feeder calf values. This would support losses of approximately US $135 for an affected herd of 100 cows at a seroprevalence of 9% (Hill et al., 2003), which corresponds to 28% true prevalence (Collins et al., 2006).

Calves born to dams with positive BCF for MAP were associated with a decrease in average AWW of 33.3 kg (73.3 lb, $P < 0.001$) corresponding to a loss of US $89 per affected calf (Table 3). When BCF outcomes were classified based on level of shedding, the heavy, moderate, low, and very low shedders produced calves with average AWW 58.5 kg (129.0 lb, $P < 0.001$), 40.8 kg (90.0 lb, $P = 0.016$), 17.8 kg (39.3 lb, $P = 0.284$),

and 12.8 kg (28.1 lb, P = 0.395) lighter than non-shedders, respectively (Table 5). Associated economic losses were US $156, US $109, US $48 and US $34 among calves from heavy, moderate, low and very low shedders, respectively.

Table 4: Reduced weaning weights in calves from cows with different levels of ELISA test results in participating beef cow-calf operations

Model[*]	ELISA results	Decrease in 205-day adjusted weaning weight of calf[†]			
		Kg	95% CI, kg	P-value	US$ Value[‡]
Simple model	Strong-positive	22.45	12.75 to 32.15	<0.001	60.10
	Positive	2.83	-2.32 to 7.99	0.282	7.58
	Suspect	3.35	-0.40 to 7.09	0.080	8.96
Adjusted model[§]	Strong-positive	21.48	11.66 to 31.30	<0.001	57.49
	Positive	2.85	-2.13 to 7.99	0.261	7.64
	Suspect	2.78	-0.90 to 7.84	0.139	7.43

[*] All models included random effects for repeated tests within each cow and for cows nested within herds
[†] Loss relative to test-negative classification
[‡] Based on five year (2007 to 2011) average feeder calf value from http://www.nass.usda.gov
[§] Adjusted for cow-age, lactation number and years since the inception of a control program

Table 5: Reduced weaning weights in calves from cows with different levels of fecal test results in participating beef cow-calf operations

Model*	Fecal culture results	Decrease in 205-day adjusted weaning weight of calf[†]			
		Kg	95% CI, kg	P-value	US$ Value[‡]
Simple model	Heavy	57.25	29.49 to 85.00	<0.001	153.22
	Moderate	34.99	-0.38 to 70.36	<0.053	93.65
	Low	9.83	-20.49 to 40.16	0.525	26.32
	Very low	11.04	-20.37 to 42.46	0.491	29.56
Adjusted model[§]	Heavy	58.51	32.50 to 84.53	<0.001	156.60
	Moderate	40.81	7.64 to 73.99	0.016	109.23
	Low	17.81	-14.76 to 50.37	0.284	47.66
	Very low	12.75	-16.63 to 42.13	0.395	34.12

[*] All models included random effects for repeated tests within each cow and for cows nested within herds
[†] Loss relative to test-negative classification
[‡] Based on five year (2007 to 2011) average feeder calf value from http://www.nass.usda.gov
[§] Adjusted for cow-age, lactation number and years since the inception of a control program

An economic benefit of BCF testing was observed at a true prevalence of 31% or greater (Figure 2) and this corresponds to a BCF apparent prevalence of at least 20%. ELISA testing was not economically feasible at any prevalence level.

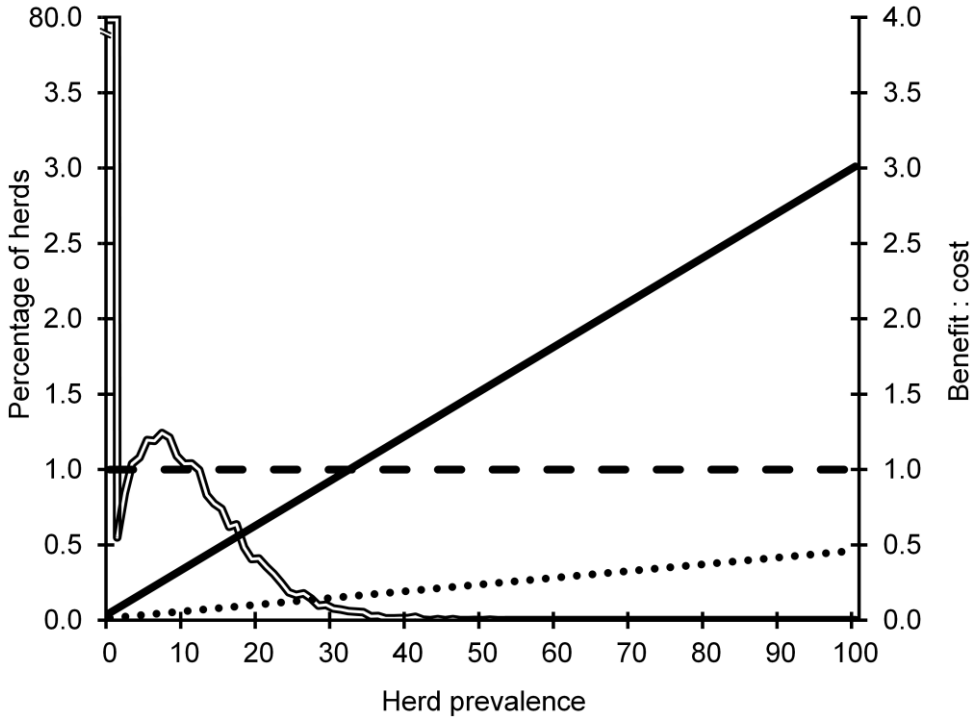

Figure 2: The effect of true prevalence on the benefit-cost ratio of screening a beef herd for *Mycobacterium avium* subspecies *paratuberculosis.* Plot of the estimated frequency distribution of US beef cow-calf herds by true prevalence of MAP-infected cattle within the herd (solid open line) with the results of the benefit-cost ratios for screening individual beef cows for MAP by serum ELISA (dotted line) or BCF (solid black line) calculated in the present study overlaid on that plot.

2.4 Discussion

Lower AWW is a primary economic concern for many commercial beef cow-calf producers because the weight of calves sold at weaning is often the most important component of herd income. Lower weaning weights can be a consequence of production inefficiencies in the dam including lower milk yield (Johnson-Ifearulundu et al., 1999;

Johnson-Ifearulundu et al., 2000; Manning and Collins, 2001; Gonda et al., 2007; Benedictus et al., 2008; Raizman et al., 2009) and thus reduced plane of nutrition in the calf (Roussel, 2011). Direct impacts on AWW are unlikely in infected calves given the prolonged latency of MAP infection (Chiodini et al., 1984; Harris and Barletta, 2001). Substantial compensatory post-weaning weight gain would be necessary for offspring of test-positive cows to achieve similar performance as calves from other herd mates. However, severe or chronic retardation in growth in early life is associated with lighter weight at all ages (Greenwood, 2006) indicating that the time required to achieve a desired endpoint may be extended for these animals.

Results from this study demonstrate a significant reduction in AWW in the offspring of cows positive for MAP via BCF or serum ELISA, particularly those classified as having either high levels of serum antibody or shedding high levels of MAP in their feces. A previous study reported a reduction in AWW of 2.3 kg (95% CI: 0.5 to 4.1 kg) in calves from suspects (ELISA score 1) and of 6.9 kg (95% CI: 1.6 to 12.2) in calves from strong-positive (ELISA score 3) cows (Elzo et al., 2009). The differences between the work presented here and the prior study may be attributed to their use of ELISA score as a linear covariate whereby scores of 1, 2 or 3 would be associated with reductions in AWW of 2.3 kg, 4.6 kg, and 6.9 kg, respectively. The current analysis modeled ELISA scores as discrete categories and the difference in AWW observed here did not approximate a linear relationship.

The decreases in AWW were higher with increasing ELISA scores and levels of MAP shedding in the feces. Similar estimates of reduced AWW between fecal culture positive and strong ELISA positive cows is likely due to an increasing probability that both conditions represent truly infected cows in more advanced stages of disease (lower probability of false-positive results). Classification of tested cows in two categories (i.e., positive and negative) appears to be less discriminating relative to impacts on AWW, especially for ELISA, presumably due to greater propensity for false positive outcomes. However, a fecal culture positive animal, irrespective of the shedding intensity, is a persistent threat of new infections in the herd.

Our results demonstrate measurable losses in the weaning weight of calves estimated for different cow-test outcomes. Although reduced weaning weight of calves may be the primary economic concern for cow-calf producers, premature culling of affected cows and lowered weight of culled animals contribute to the cumulative economic effect at the herd level. There are also losses associated with longer open period, reduced weight of offspring (Elzo et al., 2009), increased mortalities and loss of revenue, negative impacts on the reputation of seedstock producers (Roussel, 2011) Other potential economic consequences not readily estimable include loss of valuable genetics, potential litigation (Roussel, 2011), as well as contamination of land, market discrimination and legal liabilities (Kennedy and Allworth, 2000).

Failure to offset the costs of ELISA testing in a herd at any prevalence is due to the small difference in weaning weight between calves from ELISA positive and negative dams. Therefore, this simple estimate should only be used as a basic guideline until more comprehensive estimates are available.

A limitation of this study is that the weaning weight could not be adjusted for birth weight, which was available for very few observations in the database. Estimation of adjusted weaning weight accounts for birth weight among healthy animals. However, infected dams might have lower weight calves and therefore adjustment for birth weight might remove some of the effect associated with dam's infection status. Conclusions based on these results thus represent overall loss in weaning weight rather than effects on pre-weaning weight gain. Comparison of differences in weaning weights of calves from cows with and without clinical signs indicative of JD was not possible in the current study because weaning weight was available for only a single calf with a dam exhibiting clinical signs consistent with JD. Weaning weight data from 19 of 22 enrolled herds could not be used for analysis because weaning weight, dates, calving season and sex were not recorded.

There is potential selection bias associated with sourcing data for analysis from the NJDDHP as these three herds may not reflect the entire U.S. beef cattle industry in general. In order to participate in the NJDDHP, herds needed to be MAP-positive as

determined by an organism detection test. Producers who opted to record accurate weaning weight data for the herds used in this analysis may be more concerned about JD. The conclusions that test-positive cows produce a lighter calf is likely to be true across non-enrolled beef cow-calf herds, but the magnitude may be different based on animal and herd-level factors not evaluated in this study. These limitations may affect the external relevance of reported results. The overall test-positive percentage in herds included in this study is similar to that reported from beef herds across the US (Thorne and Hardin, 1997; NAHMS, 1999; Hill et al., 2003; Roussel et al., 2005). Different diagnostic laboratories were used but all were accredited to meet certain pre-determined standards (USDA, 2010) to ensure reproducible results.

Efforts to control JD are hindered by the limitations due to a lack of proven preventive practices and difficulties in diagnosis including lack of a gold standard (Wang et al., 2006), low sensitivities of available tests (Kudahl et al., 2007b; Kudahl et al., 2008), and potential for impaired test specificity attributed to exposure to *Mycobacteria* spp. other than MAP (Osterstock et al., 2007; Roussel et al., 2007). As demonstrated in this study, the greatest decreases in AWW were observed among offspring of heavy shedders and cows with high serum antibody titers to MAP. This has important implications for commercial cow-calf producers that desire a method to minimize economic losses associated with JD as opposed to disease eradication. Testing programs designed to reduce economic losses may choose to emphasize detection of cattle with the greatest likelihood of MAP infection based on higher ELISA titer or heavy fecal shedders. In the absence of regulatory components or market assurance and incentives for low-risk herds, dissemination of information about potential economic losses including those reported here will be important to help producers appreciate the impact of JD in infected herds. This may motivate greater interest in developing and sustaining testing and control programs.

3. PERCEPTIONS OF VETERINARIANS AND PRODUCERS CONCERNING JOHNE'S DISEASE PREVALENCE AND CONTROL IN US BEEF COW-CALF OPERATIONS

3.1 Introduction

Mycobacterium avium subspecies *paratuberculosis* (MAP) is the etiologic agent of bovine paratuberculosis commonly known as Johne's disease (JD). In cattle, JD is characterized by a chronic granulomatous ileocolitis, a long pre-clinical phase terminating in diarrhea, debilitation (Chiodini et al., 1984; Harris and Barletta, 2001), cachexia and death (Manning and Collins, 2001). Reported estimates of the prevalence of MAP infected beef cattle and herds in the United States vary widely, ranging from 0.4% to 9% of animals and 8% to 63% of herds based on detection of MAP-specific antibodies in serum (Thorne and Hardin, 1997; NAHMS, 1999; Dargatz et al., 2001; Hill et al., 2003; Roussel et al., 2005).

The Beef' '97 and Beef 2007-08 studies by the National Animal Health Monitoring System (NAHMS) estimated that 92% and 69%, respectively, of beef producers were unaware of JD or only recognized the name without having direct knowledge about the disease (NAHMS, 1999). The United States Voluntary Bovine JD Control Program (VBJDCP) was implemented to provide minimum national standards for the control of JD and to educate veterinarians and producers regarding management, prevention and control of JD (VBJDCP, 2002). A survey in Texas during 2006 suggested that only 20% of beef producers were familiar with the VBJDCP and 16% considered participation (Benjamin et al., 2010). Sixty-four percent of veterinarians in Texas had educated beef producers on management strategies for the control or elimination of JD. However, only 36% of these veterinarians had received specific training regarding JD epidemiology and 29% were JD-certified (Benjamin et al., 2010).

The objective of this study was to compare the perceptions of producers and veterinarians on the burden of MAP infection in cow-calf herds and measures to control new infections using responses from mailed questionnaire surveys. A secondary

objective was to compare the differences in perceptions among different types of cow-calf producers and veterinarians to identify the differences in knowledge about JD in field condition.

3.2 Materials and methods

The study protocol was approved by the Institutional Review Board at Texas A&M University (protocol number 2010-06666).

3.2.1 Questionnaire development

Questionnaires were developed to investigate the perceptions of veterinarians and producers regarding the burden of JD and potential control measures. Questions concerning biosecurity and pathogen reduction were based on the recommendations from "How to Do Risk Assessments and Management Plans for Johne's Disease" (VBJDCP, 2002).

The beef producer questionnaire contained 31 questions with applicable sub-questions in three major sections. The first section considered general herd information. The second section included questions about disease burden, perceived losses and differences between the productivity of MAP infected and non-infected cattle, possible costs associated with implementing control programs, facility upgrades deemed necessary for testing, and herd health management. The final section included questions related to activities for the control of MAP transmission.

The majority of questions for the veterinarian questionnaire were designed to be comparable to those in the producer questionnaire. There were three major sections with 35 main questions with some sub-questions, and two open ended questions for explanations related to preceding questions. The first section considered general demographic information including type and size of the veterinary practice. The second part was related to estimating disease burden in practice clientele herds, perceived losses, and differences between the productivity of MAP infected and non-infected cattle. The final section included questions related to control of MAP transmission in

client herds. The veterinarian questionnaire was pre-tested by administration to bovine practitioners in the listserv of a professional organization via the internet and revised based on the responses and comments.

Both questionnaires utilized a combination of free numerical or text responses, 5-category Likert scales, dichotomies (yes/no), and multiple choice questions. Both questionnaires were designed to be completed within 30 minutes. All questionnaires were printed in booklet form with a page containing survey information, rights of the respondents, and ethical approval. The survey packet also included a signed cover letter that described the purpose of the questionnaire. Guidelines for completing the questionnaire were explained in the cover letter and information sheet.

3.2.2 Survey administration

Surveys were mailed during November and December, 2010 to all beef producers that had risk assessments performed and herd management plans developed for JD. Participants were contacted by the Designated Johne's Coordinates (DJCs) of nine states in the USA (FL, GA, IA, MO, ND, SC, SD, WI, WV). Sample size calculation was not performed since all eligible participants were selected for the survey. A personal cover letter from the State DJCs was included with the questionnaire booklet. Introductory letters prior to the questionnaire, incentives and reminders were not sent to producers because information concerning questionnaire recipients was not disclosed to investigators.

Veterinarians with active membership in a nationwide professional organization who listed "bovine" as one of their practice types as of July 2011 served as the sampling frame. Sample size calculation was not performed because it was decided to contact all listed veterinarians satisfying the inclusion criteria from the same nine states used for the producer survey. Surveys were uniquely coded to protect confidentiality. Veterinarians were contacted with an introductory letter 12 days prior to the mailing of questionnaires. Reminder post-cards were mailed eight days after the questionnaire. A business reply

envelope and a $2 bill were included in each questionnaire packet as an incentive to improve response proportions (Bhattarai and Fosgate, 2010).

3.2.3 Analysis

Responses from the completed questionnaires were recorded on a secure server using SelectSurvey (ClassApps.com, 2006, SelectSurvey.NET 1.5.1). Unsolicited personal information revealed by some producers in free text comments were not recorded in the database. Data were analyzed using Stata® (StataCorp. 2011. Stata® Statistical Software: Release 11.2. College Station, TX: StataCorp LP) and OpenEpi (Dean et al., 2011). Continuous outcomes were reported with mean, minimum, median, and maximum values. Wilcoxon rank-sum tests were used to compare variables not normally distributed based on the Shapiro–Wilk test. Two-sided statistical tests were performed and results were interpreted at the 5% level of significance.

Responses regarding whether the herd was ever tested for JD or currently enrolled in any JD control program were compared between respondents with and without specific herd types. Burden of MAP infection in producer herds and veterinarian client herds were summarized and compared among types of herds. Likert scale responses concerning the frequency of selected disease control activities performed by producers and perceived by veterinarians were dichotomized. The “always” and “mostly” categories were collapsed into a single “yes” category and the categories “seldom” and “never” were collapsed into “no.” The category “sometimes” was handled as missing data. Frequencies of these activities performed with intent of controlling JD were evaluated using odds ratios with corresponding 95% confidence intervals and mid-point exact P values. Three herd size categories were created with each group having an approximately equal number of observations: small (<50 head), medium (50-149 head) and large (≥150 head) herds.

3.3 Results

3.3.1 Description of producers

Questionnaires were mailed to 989 cow-calf producers. Twenty-four questionnaires were undeliverable due to incorrect addresses. The response proportion was 17% with 160 questionnaires returned. The average (minimum, median, maximum) herd size was 155 head (3, 70, 2500). Thirty-five percent (54/155) of herds had less than 49 adult cows, 35% (55/155) of herds had 50 to 149 cows and 30% (46/155) of herds had 150 or more cows. Average (minimum, median, maximum) number of years in the cow-calf business was 32 (6, 32, 83) years. Angus was the predominant breed reported by 52% (81/156) of respondents. A total of 58% of producers had commercial cow-calf herds and 56% had seedstock (Table 6).

Table 6: Description of the herds of producers (n=160) and client herds of veterinarians (n=325) who responded to Johne's disease questionnaire survey

Variables	Producers	Veterinarians
Number (%) of herd types		
Commercial cow calf - registered	37 (23.1)	224 (70.2)
Commercial cow-calf not registered	64 (40.0)	275 (86.2)
Seedstock registered	86 (53.8)	189 (59.3)
Seedstock not registered	10 (6.3)	107 (33.5)
Feedlot	0	184(57.8)
Backgrounder, stocker and dairy herds	0	64 (20.1)
Herd attributes		
Average herd size (min, median, max)	155 (3,70,2500)	105 (0,50,3000)
Percentage of infected herds	21.9	26.3
Average prevalence (min, median, max)	0.8 (0,0,10)	4.8 (0,2,60)

Ninety-five percent (149/157) of producers had tested their herds for JD at least once and 74% (117/158) of producers were currently enrolled in either VBJDCP or had some JD control program designed by their veterinarian. A total of 89% (100/113) of enrolled producers also indicated that they were in the VBJDCP. The average

(minimum, median, maximum) number of years since the inception of a control program was seven (1, 6, 30) years. Thirty-eight percent (56/149) of respondents maintained a closed herd. Seedstock producers were four times more likely (P< 0.01) to be currently enrolled in a JD control program compared to non-seedstock producers. Enrollment was ten times less likely (P< 0.01) in producers with commercial cow-calf herds, and three times less likely (P=0.03) for producers with JD clinical cows (Table 7).

Table 7: Involvement of US beef cow-calf producers in Johne's disease testing, enrollment in a control program and maintenance of a closed herd during 2010-2011

Variable				Odds ratio	95% CI	P[a]
Tested herd for MAP		Yes	No			
Commercial cow-calf	Yes	85	7	0.19	0.02 to 1.58	0.099
	No	64	1			
Seedstock	Yes	86	3	2.28	0.52 to 9.87	0.292
	No	63	5			
Closed herds	Yes	52	4	0.59	0.14 to 2.49	0.499
	No	87	4			
With clinical cow	Yes	23	4	0.25	0.05 to 1.20	0.101
	No	69	3			
Enrolled in a control program		Yes	No			
Commercial cow-calf	Yes	56	37	0.10	0.03 to 0.30	<0.001
	No	61	4			
Seedstock	Yes	76	13	3.99	1.87 to 8.53	<0.001
	No	41	28			
Closed herds	Yes	42	14	1.12	0.52 to 2.39	0.780
	No	67	25			
With clinical cow	Yes	14	13	0.35	0.14 to 0.89	0.031
	No	55	18			
Maintained a closed herd		Yes	No			
Commercial cow-calf	Yes	37	50	1.68	0.84 to 3.33	0.145
	No	19	43			
Seedstock	Yes	31	54	0.90	0.46 to 1.75	0.749
	No	25	39			
With clinical cow	Yes	8	15	0.98	0.36 to 2.64	0.975
	No	24	44			

[a] Mid-point exact P values

3.3.2 Description of veterinarians

Surveys were sent to 1080 veterinarians. Thirty-one questionnaires were undeliverable due to incorrect addresses. A total of 382 questionnaires were returned but 57 of them lacked useful information. The most common reasons for not completing the questionnaire were that the respondents were not currently involved in beef practice (n=24), there were no cattle (dairy or beef) clients in the practice (n=23) and the respondents were retired (n=20). Twenty-eight of these veterinarians also returned the $2 incentive along with the reason for not completing the survey. The overall response percentage based on questionnaires that were useful for analysis was 31%.

Forty-one percent (132/325) of veterinarians reported that they currently are or were JD certified and 38% (121/317) had performed a JD risk assessment. One or more risk assessments for JD were performed by 62% (78/126) of JD certified veterinarians and by 22% (42/190) of veterinarians that had never been certified. Eighty-eight percent (279/318) of veterinarians currently served cow-calf herds and 7% (22/318) of respondents had cow-calf clients in the past. Average (minimum, median, maximum) number of herds served by respondents as the primary veterinarian was 58 (0, 30, 1000). Average size of herds currently served by veterinarians was 105 (0, 50, 3000).

A total of 65% (200/306) of veterinarians reported Angus as the predominant breed in client herds and another 19% (59/306) listed Angus as the second most common breed. Unregistered cow-calf operations (86%; 275/319) were the most frequent type of herds served by veterinarians followed by registered commercial cow-calf (70%), registered seedstock (59%), and unregistered seedstock operations (34%). Feedlot operations were clients of 57% (184/319) of veterinarians and 20% (64/319) of veterinarians also had backgrounder, stocker or dairy clients.

3.3.3 Burden of MAP infection

Twenty-two percent (34/155) of producers reported having infected animals in their herds. Average (minimum, median, maximum) prevalence reported by producers was 0.8% (0, 0, 10). Basis of estimation for the percentage of infected animals by

producers was personal experience (n=51), veterinarian's opinion (n=51), and an extrapolation from local and regional data (n=4). Of the producers who wrote a free-text response, 87% (110/127) also mentioned a formal testing process as the basis for estimation. In tested herds, the average reported apparent prevalence was 2% (0, 0, 100). A total of 27% (27/100) of producers had at least one animal with clinical signs suggestive of JD during the previous year. The average frequency of clinical animals calculated using the number of reported clinical animals divided by herd size was less than 0.01% (0, 0, 0.2).

Table 8: Burden of *Mycobacterium avium* subspecies *paratuberculosis* infection in cow-calf operations reported by US beef cow-calf producers

Herd type	Responses		Median (IQR) of	Range of all	P[a]
	Total	Non-zeros	Non zero responses (%)	responses (%)	
Prevalence					
Seedstock	86	17	2 (1 to 4)	0 to 10	0.381
Non-seedstock	69	17	3 (1.5 to 5)	0 to 10	
Closed herds	55	9	1 (0.5 to 4)	0 to 8	0.184
Open herds	90	22	2.8 (1.5 to 5)	0 to 10	
Enrolled herds	114	23	2(1 to 4)	0 to 8	0.287
Not-enrolled herds	41	11	4 (1 to 10)	0 to 10	
Clinical animals					
Seedstock	53	10	0.010 (0.006 to 0.017)	0 to 0.04	0.045
Non-seedstock	44	16	0.013 (0.005 to 0.030)	0 to 0.2	
Closed herds	32	8	0.007 (0.006 to 0.08)	0 to 0.031	0.883
Open herds	59	15	0.014 (0.005 to 0.033)	0 to 0.2	
Enrolled herds	67	13	0.011 (0.006 to 0.016)	0 to 0.111	0.011
Not-enrolled herds	30	13	0.015 (0.006 to 0.029)	0 to 0.2	
Test-positive animals					
Seedstock	80	13	1.5 (1 to 3)	0 to 100	0.005
Non-seedstock	55	21	2 (1 to 5)	0 to 100	
Closed herds	49	10	1.1 (1 to 5.5)	0 to 100	0.300
Open herds	78	22	2 (0.8 to 5)	0 to 100	
Enrolled herds	105	18	1.75 (1 to 4)	0 to 100	<0.001
Not-enrolled herds	30	16	1.8 (0.9 to 5.25)	0 to 100	

[a] Wilcoxon rank-sum test based on all responses

The odds of testing the herd for MAP and enrolling in a control program were lower for commercial cow-calf herds compared to producers without commercial cow-calf herds (Table 7). Compared to non-seedstock herds, seedstock herds had a higher percentage of test-positive animals (P <0.01, Table 8), but a lower percentage of clinical cows (P<0.05). Compared to herds not enrolled in a control program, enrolled herds had a lower percentage of test-positive cows (P<0.01) and a lower percentage of clinical animals (P=0.01). Average test-positive percentage, and prevalence estimated by producers were higher in medium (50-149 head) and highest in large (≥150 head) herds. Compared to small herds (<50 head), the odds of having a clinical animal were four times higher (P=0.045) in medium and seven times higher (P<0.01) in large herds.

Table 9: Burden of *Mycobacterium avium* subspecies *paratuberculosis* infection in cow-calf operations reported by the US cow-calf veterinarians

Respondent type	Responses		Median (IQR) of non-zero responses(%)	Range of all responses (%)	P[a]
	Total	Non-zeros			
Cattle infected with MAP in practice clientele					
JD certified	109	105	2 (1–5)	0–60	0.483
Not certified	162	154	2 (1–5)	0–30	
Performed risk assessment	111	109	2 (1–5)	0–50	0.723
Did not perform risk assessment	154	144	3 (1–5)	0–60	
Client herds with animal(s) infected with MAP					
JD certified	110	106	20 (5–50)	0–100	0.006
Not certified	166	156	10 (3–34)	0–100	
Performed risk assessment	112	110	15 (5–50)	0–100	0.010
Did not perform risk assessment	158	146	10(2–50)	0–100	
Infected cattle within MAP infected client herd					
JD certified	107	107	5 (3–10)	1–80	0.454
Not certified	154	154	5 (2–10)	0.01–40	
Performed risk assessment	111	111	5 (2–10)	0.05–80	0.268
Did not perform risk assessment	143	143	5(3–10)	0.01–70	

[a] Wilcoxon rank-sum test based on all responses

Table 10: Frequency of activities performed by cow-calf producers with clinical cattle and perceived by veterinarians to be performed by producers with the sole or a partial intent of controlling Johne's disease

Activities to control Johne's disease (JD):	Respondent	Yes	No	Odds ratio	95% CI	P[a]
Remove calves from dams suspected of being infected with MAP prior to nursing	Producers	3	23	1.33	0.37 to 4.80	0.642
	Veterinarians	21	214			
Cull cows showing signs consistent with a diagnosis of JD prior to testing	Producers	15	7	0.48	0.18 to 1.26	0.154
	Veterinarians	165	37			
Cull cows with signs consistent with a diagnosis of JD after laboratory testing	Producers	19	7	0.19	0.07 to 0.52	0.003
	Veterinarians	240	17			
Cull calves from dams suspected or confirmed to be infected with MAP based on testing or clinical signs	Producers	15	9	1.44	0.60 to 3.46	0.419
	Veterinarians	105	91			
Early weaning of calves from dams with positive results from JD-tests	Producers	7	13	1.82	0.68 to 4.83	0.245
	Veterinarians	45	152			
Cull cows without clinical signs consistent with a diagnosis of JD, but positive serology (ELISA)	Producers	14	8	1.96	0.79 to 4.88	0.153
	Veterinarians	92	103			
Test purchased additions for JD	Producers	6	14	5.19	1.77 to 15.24	0.007
	Veterinarians	17	206			

[a] Mid-point exact P values

Average animal level prevalence (minimum, median, maximum) reported by veterinarians for their client herds was 5% (0, 2, 60). Average percentage of herds with at least one infected animal in client herds was 26% (0, 10, 100). Average reported percentage of infected cows within infected herds was 9% (0.01, 5, 80) (Table 9). Percentage of client herds with at least one infected cow were reported to be higher by

JD certified veterinarians (P<0.01) and veterinarians who had performed a risk assessment (P=0.01). The methods used by veterinarians to derive these estimates were the number of animals with clinical signs of JD (62%, 237/382), ELISA results (44%, 169/382), fecal culture results (27%, 103/382), and an extrapolation from regional or national data (13%, 51/382).

3.3.4 Management and testing

Although 95% of producers had tested their herds at least once, only 30% of producers with clinical animal(s) in their herd tested purchased additions, 35% weaned calves early from test-positive dams, and 12% removed calves from JD suspect dams. Compared to veterinarians' perceptions, producers were less likely to cull cows with signs consistent with JD (P<0.01), but more likely to test purchased additions for JD (P<0.01, Table 10). Veterinarians also reported that only 8% of their clients tested purchased additions for JD.

Miscellaneous free-text comments from producers indicated that some purchased only pre-tested cattle from trusted or test-negative herds. One producer not only tested every purchased addition but also segregated those animals for six months. Producers were not specifically asked about the disposition of cows with clinical signs consistent with JD, but three producers noted that they culled such cows. A producer also reported that they would remove or destroy all suspect cows. Regarding the disposition of calves, one producer wrote that calves from infected dams are not retained as replacements and are marketed as feeder cattle. Another producer raised replacement heifers separately until three years of age. One producer noted that breeders should be encouraged, if not required, to only sell bulls and replacement females that are from test-negative dams. Another producer had a strong belief that MAP transmission is due to the reuse of palpation gloves during pregnancy diagnosis. One producer also mentioned that their management and facilities were designed to control JD by elevating feed bunks and reducing stocking density within winter feeding areas.

Questions regarding recommendationded test(s) by veterinarians (n=277) for the initiation of a testing program in beef cow-calf herds allowed multiple responses. The responses were bacterial culture of feces (3%), polymerase chain reaction (PCR, 14%), enzyme linked immunosorbent assay (ELISA, 35%) and a combination of these tests (47%). The recommended interval between testing was 12 months by 79% (198/252) of respondent veterinarians. Eleven percent (28/252) of veterinarians recommended testing every six months while one respondent recommended testing more frequently than six months. Three percent (8/252) of veterinarians recommended 18 months, 7% (18/252) recommended testing interval of more than 18 months, and 3% (7/252) of respondents did not believe periodic testing was necessary. A total of 46% (124/270) of respondents preferred combination of ELISAs with PCR or fecal culture for herds starting a testing program. Thirty-four percent (42/136) of these respondents preferred a combination of tests based on the assumption that it would improve sensitivity, specificity or "accuracy." Thirty-six percent (97/270) of veterinarians preferred ELISA because it is rapid (49%, 48/97), inexpensive (46%, 45/97), and easy (38%, 37/97) for whole herd screening.

3.4 Discussion

Seedstock producers were more likely to enroll in a JD control program. This can be related to an overall awareness of seedstock producers concerning the importance of improved herd health for better economic outcomes. The average value of animals in a seedstock herd is typically higher than those in commercial cow-calf operations. Seedstock producers were also more likely to purchase additions compared to non-seedstock producers which increases risk of introduction of infected animals.

The producer estimated average cow-level prevalence was 0.8%. Similarly, a nationwide study estimated that 0.4% of US beef cattle were seropositive (NAHMS, 1999; Dargatz et al., 2001). Other studies have reported a seroprevalence of 3% (Roussel et al., 2005), 5% (Thorne and Hardin, 1997), and 9% (Hill et al., 2003) and this suggests that the true prevalence may be 7% to 28% after adjustment for the sensitivity and

specificity of available serum ELISAs (Collins et al., 2006). Producers with infected herds (22%) and the average percentage of infected herds estimated by veterinarians (26%) were lower than previous field studies. Forty percent of beef herds in Missouri (Thorne and Hardin, 1997), 44% of herds in Texas (Roussel et al., 2005), and 63% of herds in Alabama (Hill et al., 2003) have been reported as seropositive for JD. The perception that there is a higher percentage of infected herds by veterinarians with JD certification or risk assessment experience might be due to a better understanding of disease burden. Another possible explanation towards this perception is that producers suspecting that their herd is infected might seek the services of a JD certified veterinarian. Some differences in perceptions are expected because published reports were based on seroprevalence, while respondents answered based on test results, regional or national data, and experience. Furthermore, veterinarians estimated the prevalence based on a typical client herd rather than the testing of a specific herd. The majority of producers had tested their herd, or a part of the herd in the past, but their responses were not necessarily an accurate representation of this test-based prevalence.

Commercial cow-calf producers were less likely to enroll in a control program compared to producers without commercial cow-calf herds. Commercial cow-calf producers tended to maintain a closed herd, which may enable producers to eliminate contamination from additions. A lower comparative prevalence in closed herds also suggests reduced probability of introduction of infected stock. In a previous study, only 25% of the producers perceived significant financial and non-financial benefits associated with participation in the VBJDCP (Benjamin et al., 2009) and those results were from producers with an extremely low probability of having MAP infected cows in the herd (classification Level 4). Although 84% (46/55) of closed herds were already reported to be infected, maintaining a closed herd is an effective method to prevent further introduction of infected cows. Mixing replacement heifers from different production units without known low-risk status might also increase exposure and chance of transmission from subclinically infected animals (Sweeney, 1996; Kovich et al., 2006). Excluding dairy cattle and ensuring more effective farm biosecurity will reduce

the risk of introducing MAP infection into beef herds (Larsen et al., 2012). Strict biosecurity by not allowing infected cattle to enter the farm is the only necessary control measure for uninfected herds (Roussel, 2011).

Compared to small herds (<50 head), test-based prevalence and producers' estimates of the herd prevalence were higher in medium sized herds (50-149 head) and highest in large (≥150 head) herds. The odds of having a cow with clinical signs of JD were higher in larger herds, possibly due to an increased probability of detecting rare events in larger herds. Larger herds might also be more likely to have a higher MAP infection prevalence because of an expected higher rate of animal movements and increased density of animals in areas where cattle congregate for feed, water, and shade (Sweeney, 1996). Only 63% (100/160) of producers answered the question concerning having a cow with clinical signs during the previous year. The true percentage of herds with clinical animals during the previous year might have been lower than estimated because producers who left the answer blank (handled as missing data) might have had no clinical animals. Most herds with clinical JD reported having only a single case in the previous year.

The number of producers employing herd testing was higher among those enrolled in a control program. Ninety-five percent of herds were tested for MAP at least once although only 74% of producer respondents were currently enrolled in a control program. Disinclination from regular testing may be attributed to the low sensitivity of available tests (Wang et al., 2006; Benedictus et al., 2008). One respondent producer commented that until a test is developed that is more than 50% accurate it would be "stupid and irresponsible" to perform the management practices proposed in the questionnaire. While it is true that test sensitivities are low, perhaps this illustrates that producers do not have an adequate understanding of test interpretation and the importance of herd hygiene.

Responses from veterinarians regarding testing were mostly in favor of ELISA for herds starting a control program. Fecal culture is considered more sensitive and specific than ELISA (Collins et al., 2006; van Schaik et al., 2007b) although it is costly

and there is a long delay in the availability of results due to the slow growth of MAP in culture (Kudahl et al., 2007b). The majority of respondent veterinarians recommended a 12-month interval similar to the VBJDCP (USDA, 2002, 2005, 2010). Specific client and herd needs may warrant a different test type and interval. One producer implemented 6-monthly intervals when testing was subsidized by the program.

Testing purchased additions was a preferred practice for only 30% of producers and 8% of veterinarians. One of the most important routes of transmission between herds is the addition of subclinically infected animals (Sweeney, 1996). In Canadian dairy herds, ELISA-seropositivity was significantly associated with "open heifers purchased during the last 12 months" (Tiwari et al., 2009). While producers in general appeared less concerned about infected replacements, one respondent tested and quarantined additions for six months before mixing into the herd. One of the reasons for not testing additions was that some producers only purchased animals from herds with known JD-low-risk status. In Canada, veterinarians perceived that less than half of beef producers would prefer purchasing replacements from herds where a risk assessment had been performed (Sorge et al., 2010).

The immediate removal of calves from an infected dam was only practiced by 12% of producers and perceived to be performed by 9% of veterinarians. Cow-to-calf transmission occurs most commonly within the calving area and this would be expected to reduce the risk of transmission (Benedictus et al., 2008; Windsor and Whittington, 2010). Producers within the VBJDP are educated concerning possible routes of cow-to-calf transmission during enrollment into the program (USDA, 2010). More than half of the responses from both producers and veterinarians favored culling calves based on a positive test or suspect clinical signs in the dam. One producer indicated that such calves can still be fattened and sent to slaughter, which would be economically more rewarding than immediate removal.

A major limitation of this study is the exclusive enrollment of producers who had on-farm risk assessments performed and herd management plans developed. Only 17% of the producers and 31% of veterinarians responded to the questionnaires and this

indicates a possibility of non-response bias. Information regarding non-responders was not available and the impact of this potential bias could not be assessed. Comparability was attempted by recruiting producers and veterinarians from the same nine states, but respondent veterinarians might not have served the producers included in this study. Only producers with clinical cows during the previous year were included in the analysis of disease control activities because such activities would not be applicable to JD-free herds. However, only 27 herds had clinical animals leading to a lower precision of estimated measures of association.

The percentage of producers currently enrolled in a control program among the responders of this study (75%) is quite high because the DJCs in each state contacted the producers who had had risk assessments performed in their herds. Therefore, these producers presumably have more knowledge concerning JD than US beef producers in general. The power to detect statistical significance for some associations was low due to limited numbers. A few of the associations might be counterintuitive. Seedstock producers were more likely to have uninfected herds even though they were more likely to introduce new animals onto their premises (maintain an open rather than closed herd). A possible explanation is that the infected seedstock producers did not adopt a formal control program because they feared lack of confidentiality. Closed commercial cow-calf herds were more likely to have infected and clinical cows despite the protection from JD introduction via MAP infected purchased animals. There is the possibility that the herd was closed as a control measure after the producer discovered that the herd was infected.

4. PERCEPTIONS OF VETERINARIANS AND PRODUCERS CONCERNING ECONOMIC LOSSES ASSOCIATED WITH JOHNE'S DISEASE IN US BEEF COW-CALF OPERATIONS

4.1 Introduction

Johne's disease (JD), or paratuberculosis, caused by infection with *Mycobacterium avium* subspecies *paratuberculosis* (MAP) is a disease of worldwide economic importance (Johnson-Ifearulundu et al., 1999; Harris and Barletta, 2001). Infection with MAP causes reduced production in dairy herds (Ott et al., 1999; Harris and Barletta, 2001; Tiwari et al., 2008; Raizman et al., 2009). Mortalities and sale of underweight infected cows represent a loss of revenue for beef producers and may have negative impacts on the reputation of seedstock producers (Roussel, 2011). There are negative impacts related to regulatory and ethical issues (Rossiter and Burhans, 1996) as well as legal liabilities for the sale of an infected cow, contamination of land, and breeding animals from infected herds (Kennedy and Allworth, 2000).

The National Animal Health Monitoring System (NAHMS) periodically evaluates producer attitudes and knowledge of JD as well as use of management practices related to herd biosecurity (NAHMS, 1994, 1999, 2010). An NAHMS study on beef in 1997 estimated that 92% of beef producers were either unaware of JD or only recognized the name (NAHMS, 1999) and this decreased to 69% in 2007-08 (NAHMS, 2010). The United States Voluntary Bovine JD Control Program (VBJDCP) was created in 2002 to provide minimum national standards for the control of JD and to educate veterinarians and producers regarding management, prevention and control of JD (VBJDCP, 2002). Beef producers with herds having low-risk of JD (Level 4) in the US-VBJDCP believe that a control program becomes economically beneficial as it progresses (Benjamin et al., 2009). A total of 59% of producers and 50% of veterinarians in Texas believed that losses in beef production due to JD are substantial (Benjamin et al., 2010). However, only 25% of producers with JD low-risk herds perceived a significant benefit of participation in control programs (Benjamin et al., 2009).

Veterinarians presumably influence opinions of producers regarding the estimation of JD associated costs, testing and other control measures as veterinarians are often involved in educating their clients on JD (Benjamin et al., 2010). The purpose of this study was to describe and compare the perceptions of producers and veterinarians in terms of economic aspects of MAP infection in beef cow-calf herds using responses from mailed questionnaires.

4.2 Materials and methods

The study protocol was approved by the Institutional Review Board at Texas A&M University (protocol number 2010-06666).

4.2.1 Questionnaire survey

Questionnaire surveys were developed to investigate the perceptions of producers and veterinarians regarding the economic impact of burden of JD and appropriate control measures being carried out. A mailed questionnaire survey of beef producers who had risk assessments and herd management plans for JD were administered in nine US states (FL, GA, IA, MO, ND, SC, SD, WI, and WV). At the time of the survey, producers were either actively participating or had participated at one time in a JD control program. Another questionnaire was mailed to veterinarians from the same nine states with active membership in a nationwide professional organization and who listed "bovine" as one of their practice types. The majority of questions for the veterinarian and producer questionnaires were designed to be comparable.

The Designated Johne's Coordinators mailed the questionnaires to all beef producers that had JD risk assessments performed and herd management plans developed for JD. Veterinarians were contacted with an introductory letter 12 days prior to the mailing of questionnaires. A business reply envelope and a $2 bill were included in each questionnaire packet as an incentive to improve response proportions (Bhattarai and Fosgate, 2010). Reminder post-cards were mailed eight days after the questionnaire.

Additional details on questionnaire development and administration has been explained in Section 3.2.

4.2.2 Analysis

Responses from the completed questionnaires were recorded using SelectSurvey (ClassApps.com, 2006, SelectSurvey.NET 1.5.1) on a secure server located at the College of Veterinary Medicine and Biomedical Sciences, Texas A&M University. Unsolicited personal information revealed by some producers in free text comments were not recorded in the database. Data were downloaded and analyzed using Stata® version 11.2 (StataCorp., College Station, TX) and OpenEpi (Dean et al., 2011). Descriptive statistics were stratified by veterinarians and producers. Statistical analysis was performed with categories of respondents: veterinarians with and without JD certification, seedstock producers, commercial cow-calf producers, and producers with both seedstock and commercial cow-calf operations. Continuous outcomes were reported with the mean, minimum, median, and maximum, or median and inter-quartile range (IQR). Wilcoxon rank-sum tests were used to compare continuous variables that were not normally distributed based on the Shapiro–Wilk test. Associations between categorical exposures and outcomes were evaluated using chi-square tests. Beliefs concerning risks of disease and categorical responses related to economic metrics were evaluated among producers and veterinarians using odds ratios. Crude and adjusted odds ratios were calculated for different groups within cow-calf producers and veterinarians. Potential confounding was controlled by including herd-size, herd infection status (infected or uninfected), and the perception of the respondent whether veterinary expense is higher for infected cows in the statistical models. Herd size was categorized as small (<50 head), medium (50-149) or large (150 or more). Two-sided statistical tests were performed and results were interpreted at the 5% significance level.

4.2.2.1 Economic losses

Survey data were used to estimate losses associated with MAP infected animals and predict overall herd-level monetary losses in typical cow-calf production scenarios. Pre-weaning losses were estimated using reduction in percent calving in infected cows and additional pre-weaning mortality of their calves. The loss in monetary terms was estimated based on the calf-crop at weaning and the prevailing price from the National Agricultural Statistics Service (USDA, 2012). Additional veterinary expenses for MAP infected cows reported by survey respondents were used as the loss due to additional cost of treating MAP infected cows. Total loss was the sum of component losses and reported in US$.

4.2.2.2 Parameter estimates

Triangular and beta distributions were used to model parameter inputs within the economic model (Table 11) using available software (@Risk, version 5.7, Palisade Corp, Ithaca, NY). Beta distribution parameters were estimated from survey data using available freeware BetaBuster (Su, 2006). Means and 95% credible regions (95% CR) were estimated for losses. Herd-level losses were projected to a cow-calf herd of 100 cows with an mean seroprevalence of 3% (Roussel et al., 2005), which corresponds to a 7% true prevalence after adjustment for the sensitivity and specificity of available serum ELISAs (Collins et al., 2006). Regression sensitivity analysis was conducted within @Risk by varying the value of each model input to estimate its impact on the total loss estimate. Sensitivity and robustness of models were evaluated using the relative values of the regression coefficients of model inputs.

Table 11: Cow-calf producer and veterinarian parameter estimates used to estimate losses associated with *Mycobacterium avium* subspecies *paratuberculosis* infected beef cows

	P	Distribution	Average (minimum, median, maximum) Producer[a]	Veterinarian[a]
A	Baseline calving percentage (all cows)	Beta P[b]:(36.7,2.9) V[b]:(28.8,3.3)	95(70,95,100)	90(10,90,100)
B	Percent point decrease in calving from infected cows	Beta P[b]:(1.3,5.7) V[b]:(1.5, 6.4)	15.5(2.3,9.7, 54.3)	14.6(0.9,9.4, 85.5)
C	Baseline pre-weaning mortality percentage (all cows)	Beta P[b]:(1.4,70.9) V[b]:(6.2,99.7)	1.7(0, 1, 15)	5.4(0, 5, 95)
D	Percent point increase in pre-weaning mortality in calves from infected cows	Beta P[b]:(1.0,33.1) V[b]:(1.3,55.0)	0.45(0.01,0.18,2.5)	0.9(0.1,0.5,9.5)
E	Baseline weaning weight (kg, all cows)	Triangular	258.8(35.4, 263.1, 351.5)	238.1(31.8, 249.5, 362.9)
F	Percent decrease in weaning weight in calves from infected cows	Beta[b] P[b]:(27.0,131.2) V[b]:(5.0,39.2)	12.45 (3.2, 10.26, 30.4)	11.36(0.83, 10, 40)
G	Decrease in weaning weight in calves from infected cows	E*F		
N	Number of cows	Fixed	100	100
P	Prevalence	Fixed	7	7
H	Weaning weight per exposed female (uninfected)	A*(1-C)*E		
I	Weaning weight lost by average infected cow	(A-B)*(1-C-D)*(E-G)		
J	Weaning weight per cow adjusted for prevalence	[(1-P)*A*(1-C)*E]+[P*(A-B)*(1-C-D)*(E-G)]		
K	Decrease in total weaning weight per cow in herd	H-J		
L	US$ value of weaning weight[c]	Triangular	2.7(2.4, 2.7, 3.1)	2.7(2.4, 2.7, 3.1)
M	Value of decrease in WW in infected herds	K*L		
R	Increased veterinary costs in infected herds cow	Triangular	33.4(0,22.5,100)	31.8(1,20,250)

[a] Producers estimated values in their own herds while veterinarians estimated values from client herds

[b] P denotes producers and V denotes veterinarians. Corresponding values in parenthesis were the parameters used in beta distribution. Proportions based on percentages reported in the table were used to estimate beta distribution parameters.

[c] USDA, NASS, five year average feeder calf price

4.3 Results

4.3.1 Description of respondents

Responses were received from160 of 989 (16%) contacted producers provided responses. The average (minimum, median, maximum) herd size was 155 head (1, 70, 2500). A total of 41% (66/160) of producers had only commercial cow-calf herds, 40% (60/160) had only seedstock and 19% (30/160) had both cattle types. All producers were considered to have participated in a control program at one point since they had completed a JD risk assessment or management plan in the past. A total of 95% (149/157) of producers had tested their herds at least once and 74% (117/158) were enrolled in a control program at the time of survey.

Of 1,080 questionnaires sent to veterinarians, 325 (30%) were completed and returned. A total of 41% (132/325) of veterinarians reported that they had been JD certified. Unregistered cow-calf operations were the most frequent type of clients (85%, 275/325) followed by registered commercial cow-calf (69%, 224/325), registered seedstock (58%, 189/325), and unregistered seedstock operations (32%, 107/325). There were veterinarians with other client types including feedlot (57%, 184/325) as well as clients with dairy, stockers, backgrounders, club-calf or non-bovine species (20%, 64/325).

Table 12: Comparison of producer estimates for their own herds and veterinarian estimates for client cow-calf herds

Variables	Producers	Veterinarians	P[a]
Herd Productivity (all cows): Average (min, median, max)			
Calving percentage	95.3 (70, 95, 100)	89.96 (10, 90, 100)	<0.001
Pre-weaning calf mortality percentage	1.7 (0, 1, 15)	5.36 (1, 5, 95)	<0.001
Weaning weight of calves, kg	259 (35, 263, 352)	238 (32, 250, 363)	<0.001
Productivity lost due to MAP infection: Average (min, median, max)			
Percent decrease in calving	15 (2, 10, 54)	14.5 (1, 9, 86)	0.588
Percent increase in calf mortality	23.5 (1,20,50)	16.3 (0.5,10,75)	0.243
Lost weaning weight, kg	30.9 (9.1, 22.7, 79.4)	26.6 (2.3, 22.7, 90.7)	0.098
Expenses: Average (min, median, max)			
US$ veterinary expense per cow	31.8 (0, 21, 150)	27.2 (2, 20, 200)	0.495
Additional veterinary expense per infected cow	33.4 (0, 22.5, 100)	31.8 (1, 20, 250)	0.465
Percent income lost due to presence of JD infected cattle in herd	3.24 (0, 0, 30)	7.19 (0, 5, 40)	<0.001

[a] P values based on Wilcoxon rank-sum

4.3.2 Economic metrics

Baseline calving percentage and weaning weight of calves were reported to be higher (P<0.001) by producers (Table 12). However, producers reported a lower pre-weaning calf mortality percentage (P<0.001). Income lost due to the presence of JD in an infected herd was perceived to be higher by veterinarians (P<0.001). Compared to veterinarians without JD certification, seedstock producers were six times more likely (P=0.002) to agree that there is genetic loss due to culling cows positive for MAP (Table 13). Seedstock producers were less likely to believe MAP infected dams wean lighter calves (P=0.006) or have higher pre-weaning mortality (P=0.020).

Table 13: Comparison of polar questions about economic metrics associated with *Mycobacterium avium* subspecies *paratuberculosis* infected herds reported by cow-calf producers and veterinarians

Respondent type	Crude odds ratio		Adjusted odds ratio[a]	
Calving percentage is lower	OR (95% CI)	P	OR (95% CI)	P
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.97 (0.54 to 1.77)	0.931	1.17 (0.58 to 2.37)	0.657
Producers with seedstock only	0.56 (0.23 to 1.39)	0.210	0.43 (0.14 to 1.28)	0.132
Producers with commercial cow-calf only	0.51 (0.21 to 1.25)	0.142	0.56 (0.20 to 1.64)	0.293
Producers with both seedstock and commercial cow-calf	0.43 (0.12 to 1.49)	0.183	0.29 (0.06 to 1.51)	0.142
Higher pre-weaning mortality				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.78 (0.43 to 1.42)	0.422	0.79 (0.40 to 1.58)	0.504
Producers with seedstock only	0.31 (0.11 to 0.85)	0.023	0.22 (0.06 to 0.79)	0.020
Producers with commercial cow-calf only	0.71 (0.30 to 1.67)	0.434	0.67 (0.25 to 1. 82)	0.436
Producers with both seedstock and commercial cow-calf	0.97 (0.31 to 3.06)	0.957	0.37 (0.08 to 1.81)	0.223
Lower average weaning weight				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.85 (0.35 to 2.04)	0.709	1.08 (0.40 to 2.94)	0.876
Producers with seedstock only	0.21 (0.77 to 0.58)	0.002	0.19 (0.06 to 0.62)	0.006
Producers with commercial cow-calf only	0.66 (0.21 to 2.01)	0.460	0.58 (0.15 to 2.24)	0.427
Producers with both seedstock and commercial cow-calf[b]	-	-	-	-

[a] Adjusted for herd-size, infection status, and the perception of the respondent whether veterinary expense is higher for infected cows

b No response in this category

Table 13 Continued

Respondent type	Crude odds ratio		Adjusted odds ratioa	
Genetic loss	OR (95% CI)	P	OR (95% CI)	P
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	1.07 (0.62 to 1.84)	0.811	1.07 (0.56 to 2.04)	0.832
Producers with seedstock only	5.00 (1.97 to 12.67)	0.001	6.15 (1.92 to 19.65)	0.002
Producers with commercial cow-calf only	1.02 (0.50 to 2.07)	0.960	1.66 (0.64 to 4.23)	0.291
Producers with both seedstock and commercial cow-calf	0.98 (0.41 to 2.36)	0.973	2.29 (0.58 to 8.96)	0.235
Higher veterinary expenses				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.75 (0.42 to 1.33)	0.325	0.76 (0.43 to 1.36)	0.358
Producers with seedstock only	0.90 (0.38 to 2.12)	0.810	1.00 (0.41 to 2.46)	0.996
Producers with commercial cow-calf only	0.81 (0.37 to 1.77)	0.595	0.79 (0.34 to 1.81)	0.582
Producers with both seedstock and commercial cow-calf	5.00 (0.62 to 40.41)	0.131	5.45 (0.66 to 45.05)	0.115

[a] Adjusted for herd-size, infection status, and the perception of the respondent whether veterinary expense is higher for infected cows

b No response in this category

Table 14: Estimates of economic metrics in beef cow-calf herds in presence and absence of *Mycobacterium avium* subspecis *paratuberculosis* (MAP) infection by cow-calf producers and veterinarians

Respondent type	n	Median (IQR[a])	P
Lowered percentage of calving by MAP infected cows			
Veterinarians without JD certification (reference)	72	10 (9.25, 20)	
Veterinarians with JD certification	58	10 (7.5, 20)	0.958
Producers with seedstock only	5	10(5, 20)	0.702
Producers with commercial cow-calf only	10	10(5, 30)	0.833
Producers with both seedstock and commercial cow-calf	5	10 (10, 15)	0.992
Higher percentage of pre weaning mortality risk in calves from MAP infected dam			
Veterinarians without JD certification (reference)	61	10 (7.5, 20)	
Veterinarians with JD certification	35	10 (5, 20)	0.522
Producers with seedstock only	1	10	0.819
Producers with commercial cow-calf only	7	25 (10, 50)	0.076
Producers with both seedstock and commercial cow-calf	5	10 (5, 20)	0.738
Lower weaning weight of calves from MAP infected dam (kg)			
Veterinarians without JD certification (reference)	97	23 (20, 34)	
Veterinarians with JD certification	57	23 (23, 34)	0.997
Producers with seedstock only	8	23 (20, 40)	0.660
Producers with commercial cow-calf only	22	24 (23, 45)	0.040
Producers with both seedstock and commercial cow-calf	9	23 (35, 32)	0.864
Additional veterinary expense per MAP infected adult cattle			
Veterinarians without JD certification (reference)	78	20 (10, 50)	
Veterinarians with JD certification	39	15 (10, 30)	0.065
Producers with seedstock only	10	22.5 (10, 50)	0.932
Producers with commercial cow-calf only	15	20 (10, 50)	0.563
Producers with both seedstock and commercial cow-calf	5	50 (40, 100)	0.104
Percentage of income lost due to presence of MAP infected cattle in herd			
Veterinarians without JD certification (reference)	130	5 (2, 10)	
Veterinarians with JD certification	86	5 (3, 10)	0.717
Producers with seedstock only	37	0 (0, 0.1)	<0.001
Producers with commercial cow-calf only	44	3 (0, 10)	0.004
Producers with both seedstock and commercial cow-calf	1	0 (0, 0)	<0.001

[a] Interquartile Range

Perceptions concerning JD-related economic metrics were generally not significantly different among respondent categories (Table 14). However, commercial cow-calf producers perceived a larger negative impact on weaning weight relative to veterinarians without JD certification (P=0.040). All producer categories reported a higher percentage of herd income lost due to presence of MAP infected cattle in a herd compared to veterinarians without JD certification (P≤0.004).

4.3.3 Risk of diseases / conditions

Compared to the reference category of veterinarians without JD certification, the perceived odds of lameness in MAP infected cattle were higher for producers with both seedstock and commercial cow-calf operations (P=0.021) (Table 15). Odds of neurologic diseases in MAP infected cattle were perceived to be lower by veterinarians with JD certification compared to those without (P=0.017). Producers with commercial cow-calf herds perceived four times higher odds of neurological disease (P=0.008) based on the crude model, but the association was not significant after adjustment for potential confounders. In general, perceptions of JD certified veterinarians and other producer categories did not differ regarding an increased risk of diseases and conditions in MAP infected cows.

Table 15: Comparison of perceptions about higher risk of diseases and conditions in *Mycobacterium avium* subspecies *paratuberculosis* infected cows reported by cow-calf producers and veterinarians

Respondent type	Odds Ratios (OR)			
	Crude		Adjusted[a]	
Mastitis	OR (95% CI)	P	OR (95% CI)	P
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	1.11 (0.63 to 1.97)	0.711	0.99 (0.49 to 2.00)	0.985
Producers with seedstock only	0.28 (0.07 to 1.07)	0.063	0.31 (0.07 to 1.34)	0.120
Producers with commercial cow-calf only	0.31 (0.11 to 0.89)	0.029	0.29 (0.07 to 1.25)	0.098
Producers with both seedstock and commercial cow-calf	0.26 (0.05 to 1.28)	0.097	0.16 (0.02 to 1.53)	0.112
Pneumonia				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	1.22 (0.67 to 2.20)	0.520	1.18 (0.58 to 2.44)	0.639
Producers with seedstock only	0.78 (0.30 to 2.04)	0.618	0.69 (0.21 to 2.24)	0.539
Producers with commercial cow-calf only	1.15 (0.46 to 2.83)	0.769	1.68 (0.46 to 6.13)	0.426
Producers with both seedstock and commercial cow-calf	1.21 (0.36 to 4.08)	0.763	0.96 (0.15 to 5.93)	0.962
Lameness				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	1.93 (1.05 to 3.54)	0.033	2.07 (0.96 to 4.43)	0.063
Producers with seedstock only	1.63 (0.50 to 5.38)	0.420	2.68 (0.67 to 10.73)	0.162
Producers with commercial cow-calf only	1.49 (0.57 to 3.91)	0.414	1.12 (0.25 to 5.01)	0.874
Producers with both seedstock and commercial cow-calf	4.18 (1.27 to 13.76)	0.019	8.30 (1.37 to 50.10)	0.021
Dystocia				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	1.00 (0.55 to 1.82)	0.993	1.29 (0.64 to 2.60)	0.469
Producers with seedstock only	1.47 (0.52 to 4.17)	0.465	1.39 (0.43 to 4.57)	0.580
Producers with commercial cow-calf only	1.90 (0.81 to 4.66)	0.136	1.77 (0.56 to 5.62)	0.333
Producers with both seedstock and commercial cow-calf	2.10 (0.64 to 6.96)	0.222	1.94 (0.35 to 10.84)	0.450

Table 15 Continued

Respondent type	Odds Ratios (OR)			
	Crude		Adjusted[a]	
Grass tetany	OR (95% CI)	P	OR (95% CI)	P
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.61 (0.28 to 1.32)	0.208	0.57 (0.22 to 1.44)	0.230
Producers with seedstock only	1.77 (0.55 to 5.76)	0.341	1.81 (0.43 to 7.60)	0.415
Producers with commercial cow-calf only	2.05 (0.80 to 5.29)	0.136	1.57 (0.43 to 5.68)	0.494
Producers with both seedstock and commercial cow-calf	3.72 (1.15 to 12.07)	0.028	1.98 (0.36 to 10.76)	0.430
Neurologic diseases				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.39 (0.18 to 0.86)	0.020	0.31 (0.11 to 0.81)	0.017
Producers with seedstock only	2.02 (0.68 to 6.05)	0.207	1.13 (0.27 to 4.73)	0.870
Producers with commercial cow-calf only	3.76 (1.42 to 9.94)	0.008	3.56 (0.85 to 14.95)	0.083
Producers with both seedstock and commercial cow-calf	1.16 (0.32 to 4.12)	0.823	0.49 (0.08 to 2.93)	0.435
Non-diarrheal digestive diseases				
Veterinarians without JD certification (reference)				
Veterinarians with JD certification	0.64 (0.34 to 1.21)	0.170	0.55 (0.26 to 1.19)	0.133
Producers with seedstock only	0.57 (0.21 to 1.54)	0.268	0.40 (0.12 to 1.27)	0.120
Producers with commercial cow-calf only	1.45 (0.51 to 4.12)	0.486	6.98 (0.83 to 58.46)	0.073
Producers with both seedstock and commercial cow-calf	1.08 (0.29 to 4.09)	0.906	0.30 (0.06 to 1.46)	0.136

[a] Adjusted for herd-size, infection status, and the perception of the respondent whether veterinary expense is higher for infected cows

4.3.4 Predicted losses

An annual loss of $235 (95% CR: $89 to $457) for each infected animal was estimated based on information from the producer survey (Figure 3). The analogous estimate using information collected from veterinarians was $250 ($82 to $486). Lowered weaning weight of calves from infected cows alone contributed an average of $87 ($28 to $213) or 40% (27 to 47%) of total loss per infected cow based on the data from producers, and $72 (18 to 176) or 32% (12 to 46%) based on the data from veterinarians.

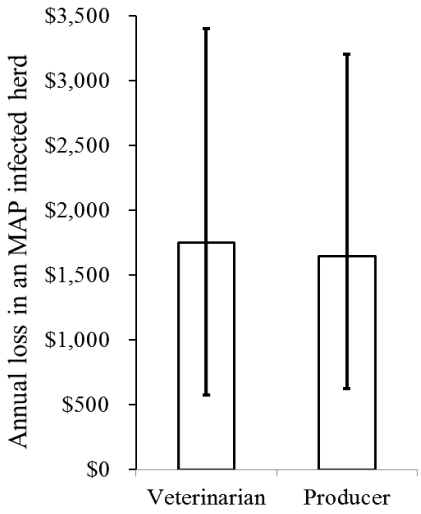

Figure 3. Mean (bar) and 95% credibility regions (whiskers) for estimated annual herd level losses in a 100 cow MAP infected beef herd at a prevalence of 7% estimated based on the responses of United States cow calf producers and veterinarians

Annual average loss in a 100 cow herd at 7% true prevalence for MAP was $1,644 (95% CR: $625 to $3,250) based on the information collected from the producers. Estimated average annual loss was $1,747 ($575 to $3,375) based on data from veterinarians. Regression sensitivity analysis suggested that the percent decrease in

calving proportion from an infected cow (regression coefficient, b = 0.68), baseline weaning weight (b = 0.63), and increased veterinary cost for infected cow (b = -0.23) were the most influential inputs for herd level losses based on the producer survey. Similarly, percent decrease in calving proportion from an infected cow (b =0.61), increased veterinary costs for infected cows (b = 0.55), and baseline weaning weight of calves (b = 0.49) were the most influential factors based on veterinarian survey data.

4.4 Discussion

Producers and veterinarians both perceived losses associated with JD in beef cow-calf operations due to lowered production and additional expenses. There were some differences in perceptions between producers and veterinarians regarding losses due to reduced calving proportions, higher calf mortality, lower weaning weight and higher veterinary expenses. The effects of JD within beef cattle may cause premature culling of affected animals, decreased milk production reducing the weaning weights of calves, reduced body weight of culled animals and loss of potential markets (Roussel, 2011). Some of these losses are analogous to MAP infected dairy herds having higher replacement costs (Johnson-Ifearulundu et al., 1999), lower milk production and additional feed costs (Ott et al., 1999; Raizman et al., 2009). Affected cows have higher mortality and there is a decrease in the weight of cows that are culled (Johnson-Ifearulundu et al., 1999). Subclinical MAP infection contributes to a decrease in total milk, fat, and protein over the lactation and a shorter productive lifespan (Gonda et al., 2007). Subclinical cows also have reduced fertility (Johnson-Ifearulundu et al., 2000) and receive lower slaughter prices (Benedictus et al., 1987) usually due to a decrease in the weight of cull cows (Johnson-Ifearulundu et al., 1999).

Between 0.4% and 9% of seropositive cows are estimated to be present in 8% to 63% of US beef herds (Thorne and Hardin, 1997; NAHMS, 1999; Dargatz et al., 2001; Hill et al., 2003; Roussel et al., 2005). Compared to veterinarians without JD certification, certified veterinarians and all classes of producers were generally less likely to perceive losses associated with calving, pre-weaning mortality and lowered

weaning weight of calves born to MAP infected cows. Commercial cow-calf producers perceived significantly lower weaning weights of calves by MAP infected cows. The magnitude of production related metrics reported by different producer classes were generally similar to veterinarians without JD certification. In spite of the differences in estimated medians, significant differences were not observed in some of the comparisons mainly due to low number of responses. Nevertheless, producers perceived significantly lower percentage of income lost due to MAP presence within the herd.

Lameness, pneumonia and mastitis have been reported to be the most common clinical diseases among fecal culture positive dairy cows in specific herds (Raizman et al., 2007). Except for mastitis, JD certified veterinarians and all producer classes were generally more likely to perceive higher risks of diseases and conditions in MAP infected cows. This is analogous to the perception that there is additional veterinary expense per infected cow. Significant differences were also observed as JD certified veterinarians perceived higher risk of lameness but lower risk of neurological diseases compared to non-certified veterinarians. Increased incidence of diseases and conditions in MAP infected cattle is a possible reason for the additional cost of treatment reported by 68% of producers and 64% of veterinarians. However, the perceived magnitude of losses varied among respondent classes. One of the reasons for mixed opinions is due to different burden of MAP infection in the respondent producer herds leading to a different degree of experience related to diseases and conditions. Another reason could be the higher premium of cows owned by seedstock producers, which is much different from commercial cow-calf producers.

Compared to the reference category of veterinarians without JD certification, seedstock producers were five times more likely to perceive a genetic loss when MAP infected cows are culled. This relates to the primary purpose of seedstock operations to improve the genetic value of their animals. While seedstock producers are more concerned about genetic determinants of production (weaning weight), commercial cow-calf producers are more concerned about the absolute weaning-weight loss because price received for weaned calves is the primary income for commercial cow-calf operations.

The perceived average loss in weaning weight of 31 kg and 27 kg by producers and veterinarians, respectively was fairly close to 27 kg lower weaning weight of calves from fecal culture positive beef cows (Bhattarai et al., 2013).

Return over total costs was negative for cow-calf producers during ten of the years between 1972 and 1989 (Krause, 1992) and for 26 of the 30 years between 1979 and 2008 in Kansas (Pope et al., 2011). This reflects, in part, the contribution of beef producers that choose to raise cattle for reasons other than as a primary source of income. Beef producers might be less concerned about the impact of JD due to a presumably lower within herd prevalence compared to dairy producers and lack of records to determine the true economic impact (Roussel, 2011). Of beef producers with Level 4 herds in the VBJDCP, 75% did not realize a significant benefit or realized only a marginal benefit from participation in the VBJDCP (Benjamin et al., 2009). However, dairy producers appear somewhat more concerned about the impact of JD. Level 3 and 4 (low-risk) dairy producers in the VBJDCP believed it was an economically beneficial strategy (Kovich et al., 2006). However, in a study of 40 dairies actively working to control JD on their operations, 15 (38%) producers perceived financial benefit while only five (13%) producers perceived an actual increase in revenue (Groenendaal and Wolf, 2008). In a previous study, 64% of veterinarians had educated beef producers on management strategies for the control or elimination of JD, but only 36% of veterinarians had received specific training regarding JD and 29% were JD-certified (Benjamin et al., 2010). In Canada, veterinarians had positive attitudes towards training for the prevention and control of JD and the majority also thought that training should be completed every few years (Sorge et al., 2010).

A limitation of this study was only selecting producers who had risk assessment and herd management plans from a subset of US states. These producers are therefore more likely than a typical producer to perceive benefits because they had voluntarily enrolled to control JD. Estimates of the effects of JD would have likely been different from a randomly selected population that had not been involved in a JD control program. Producers with infected cows might be less likely to respond or report about losses

despite the assurance that researchers would not collect any identifying information. A further limitation was the inability to evaluate whether responses varied by the geographic location of respondents. Important sources of losses are expected to vary by producer types and this was evidenced by the observation that only seedstock producers were concerned about the loss of valuable genetics. For the evaluation of perceived losses, most questions concerned directly measurable losses. Miscellaneous indirect costs could be substantial but are difficult to perceive. More comprehensive methods such as standardized performance analysis are necessary to account for all losses. Such estimates can account for different herd sizes, feeding practices, real estate, machinery, breeding stock investments, calving percentage, death loss and breeding-season length. Management-related costs are important to estimate profit in cow-calf herds. Awareness of the producers on the need of maintaining proper financial records is important to obtain such information inputs for accurate analysis. The herd level losses might have been underestimated using the 7% true prevalence derived from 3% seroprevalence (Roussel et al., 2005) because there are also reports of 5% (Thorne and Hardin, 1997), and 9% seroprevalence (Hill et al., 2003) in beef herds in other US states. Higher premium for animals was not accounted for in the analysis and this, can be substantial for the seedstock herds having cattle with superior genetics.

5. HERD-LEVEL ECONOMICS OF CULLING DECISIONS BASED ON MICROBIOLOGICAL AND SEROLOGICAL TEST RESULTS FOR JOHNE'S DISEASE IN BEEF COW-CALF OPERATIONS

5.1 Introduction

Johne's disease (JD) in cattle is a chronic and slowly progressing disease caused by infection with *Mycobacterium avium* subspecies *paratuberculosis* (MAP) that causes considerable production losses (Sweeney, 1996; Harris and Barletta, 2001; Manning and Collins, 2001). Economic losses in beef herds occur due to lower weaning weight of calves (Bhattarai et al., 2013), premature culling of affected animals, reduced body weight of culled animals and loss of potential markets (Roussel, 2011). The prevalence of JD in specific beef herds could be as high as 28% based on adjustment for sensitivity and specificity (Collins et al., 2006) of reported seroprevalence (Thorne and Hardin, 1997; Hill et al., 2003; Pence et al., 2003; Roussel et al., 2005). While the effectiveness of JD control measures are largely unknown, a voluntary JD control program was implemented in the US on 66 dairy herds and 22 beef herds in 17 states (Fossler, 2007). The participation of beef herds was considered to be low compared to dairy herds (Wells et al., 2008; Benjamin et al., 2010).

The majority of US beef producers as well as veterinarians and other stakeholders are unaware about the losses associated with JD. Despite being low overall, the percentage of beef producers who perceived a loss due to JD increased from 12% in 1994 (NAHMS, 1994) to 38% in 2010 (NAHMS, 2010). The economic impact of chronic diseases is typically greatest during the sub-clinical phase suggesting that early interventions may provide a higher return on investment due to increased production efficiency (Marsh, 1999). There is no mandatory JD control program in the US and herd level control is a choice that must be made by producers based on perceived benefits, economic or otherwise

Decision support systems are computer-based approaches that employ existing data and knowledge to facilitate decision making (Power and Sharda, 2009). Decision tree models can be useful for the estimation of overall economic return from a control

program. Models estimating losses and benefits associated with specific management alternatives to control JD have been developed for dairy cattle (Collins and Morgan, 1991; Collins and Morgan, 1992; Dorshorst et al., 2006). Studies evaluating the economic aspect of JD control strategies in beef cow-calf herds are limited. A deterministic cost-benefit model reported that improved management was able to reduce the prevalence but test and cull programs were not cost-effective (Bennett et al., 2010). Control rather than eradication was also identified as the preferred option for many commercial beef herds because eradication was only profitable in the longer term when discounts on the sale of stock from infected herds was high (Webb Ware et al., 2012).

Factors that must be considered when evaluating the benefit of JD control include reduced calving proportion, increased pre-weaning mortality, and lower weight of calves and cull cows among the infected stock. The objective of the present study was to compare the benefits of JD control for the scenarios of no-testing, serum ELISA testing, bacterial culture of feces (BCF) testing, and ELISA screening with BCF confirmation (EBCF) in an infected beef cow-calf herd using a decision tree model. A secondary objective was to estimate benefits over multiple years as MAP prevalence is reduced through the yearly test and cull with replacements obtained from low-risk herds.

5.2 Materials and methods

5.2.1 Data sources

The economic model was constructed using inputs from multiple sources (Table 16). Inputs for cow and herd level productivity were based on data obtained from a survey of beef cow-calf producers (Bhattarai et al., 2012) and presented in Sections 3 and 4 of this dissertation. Test costs were obtained from a paratuberculosis testing laboratory (TVMDL, 2013) and commodity values were based on 2012 statistics (USDA, 2012), and published reports (Apple, 1999). The effect on weaning weight of calves from infected cows was estimated from beef herds enrolled in a US national control program. Test sensitivity and specificity estimates were obtained from a published consensus report (Collins et al., 2006).

Table 16: Decision tree analysis inputs for JD control in a US cow-calf operation involved in a test and cull program

	Input	Distribution	Values / parameters
	Fecal culture: sensitivity	Beta	(162.65,108.77)[a]
	Fecal culture: specificity	Beta	(5752.3,6.8)[a]
	Serum ELISA: sensitivity	Beta	(60.7,140.4)[a]
	Serum ELISA: specificity	Beta	(560.7,6.6)[a]
P	True prevalence	0 to 100% with 1% increment	
	ELISA test cost ($)	Fixed	15[b]
	Fecal culture cost ($)	Fixed	23[b]
W	Live weight of cull cow (kg)	Normal	(481.1, 50.9)[c]
A	Value of test-negative replacement cow ($)	Triangular	1643 (1257 to 1833)[d]
U	Value of replacement from unknown herd ($)	Uniform	(A-389.85, A-371.42)[e]
L	Additional cost for low-risk replacement ($)	A-U	
B	Value of test-positive cull cow ($)	Uniform	W*(1.98, 1.92)[f]
C	Cull and replace cost ($)	A-B	
	Cull and replace cost – adjusted ($)	L*V + C*(1-V)	
V	Voluntary annual culling proportion	Beta	(3.9, 27.4) [e]
D	Calving proportion in non-infected cows	Beta	(36.7, 2.9) [e]
E	Calving proportion in infected cows	Beta	D- (1.3, 5.7) [e]
F	Price per kg calf ($)	Triangular	2.68 (2.38 to 3.13)[g]
K	Weaning weight: fecal culture negative (kg)	Normal	(249.8, 35.3)[h]
L	Kg lost per calf from test-positive dam: fecal culture positive	Normal	(33.26, 7.30)[h]
M	Additional pre-weaning mortality proportion in calves from infected cows	Beta	(1.03 , 33.12)[e]
Q	Lowered calving proportion in MAP infected cows	Beta	(1.3,5.7)[e]
R	Additional treatment cost for infected cows ($)	Triangular	22.5 (10 to 50)[e]
S	Adjusted weight lost per calf: fecal culture (kg)	L+(M/100)*(K-L)+(Q/100)*K	
T	Price received by calf from uninfected cow ($)	K*F	
U	Cost due to lost weight, calf mortality and lower calving ($)	F*S	
	Price received by calf from infected dam ($)	T-U	

a Collins et al. (2006)
b Texas Vet. Med. Diag. Laboratory data
c Cull cow at BCS 5 (Apple, 1999)
d 1-3 year female cattle (Meek et al., 1999), adjusted for 2012 cow-calf price (index = 1.6 times that of 1999)
e Survey of producers (Bhattarai et al., 2012)
f NASS: Cattle (excluding calves), price received, Kg
g NASS; Cattle, calves – price received, Kg
h NJDDHP(Bhattarai et al., 2013)

Model costs and the prices received for farm commodities include some important assumptions. A herd going through a test-based control program is assumed to get replacements from low-risk herds (Voluntary Bovine Johne's Disease Control Program, VBJDCP, Level 4 or higher herds with 1% or less infected cows), which are more expensive than a replacement from a herd of unknown JD status (Bhattarai et al., 2012). A non-testing herd is assumed to purchase less expensive replacements from herds of unknown JD status. Price received for a weaned calf was based on the weight of an average weaned calf (Bhattarai et al., 2013). Losses associated with an infected dam were attributed to reduced calving proportion, higher pre-weaning mortality, and lower weaning weight of calves. Cost of testing was estimated using standard laboratory fees with an estimated additional $5 labor cost per animal. Costs associated with treatment of infected cows (for other conditions at higher incidence in MAP infected cows) and cost of culling and replacement were also included. Additional details on steps used to calculate the model inputs have been presented in Appendix C.

5.2.2 Decision tree

A decision tree model was constructed within MS-Excel (Microsoft Corporation, Redmond, WA, version 2010) using Precision Tree (Palisade Corporation, Ithaca, NY, version 5.7). Decision trees provide a graphical structure of hierarchically linked decisions and chance events (Figure 4). The first node of the constructed tree was the producer's decision of whether or not to test all adult breeding cows (over two years of age) in the herd. The testing decision was structured to branch further into selection of test type: ELISA, BCF, or EBCF. Conditional probabilities for each branch of the chance (probability) node were calculated based on sensitivities, specificities and prevalence. Chance nodes were included for true infection status, test results, culling, and calving outcomes. Priority for voluntary culls was given to test-positive cows. Additional culls were obtained from test-negatives when test positive percentage was less than the voluntary culling percentage. All replacements for a tested herd were assumed to be purchased from low-risk herds. Price received for calves from uninfected

and infected calves varied based on lower calving probability and higher pre-weaning risk of mortality among infected cows.

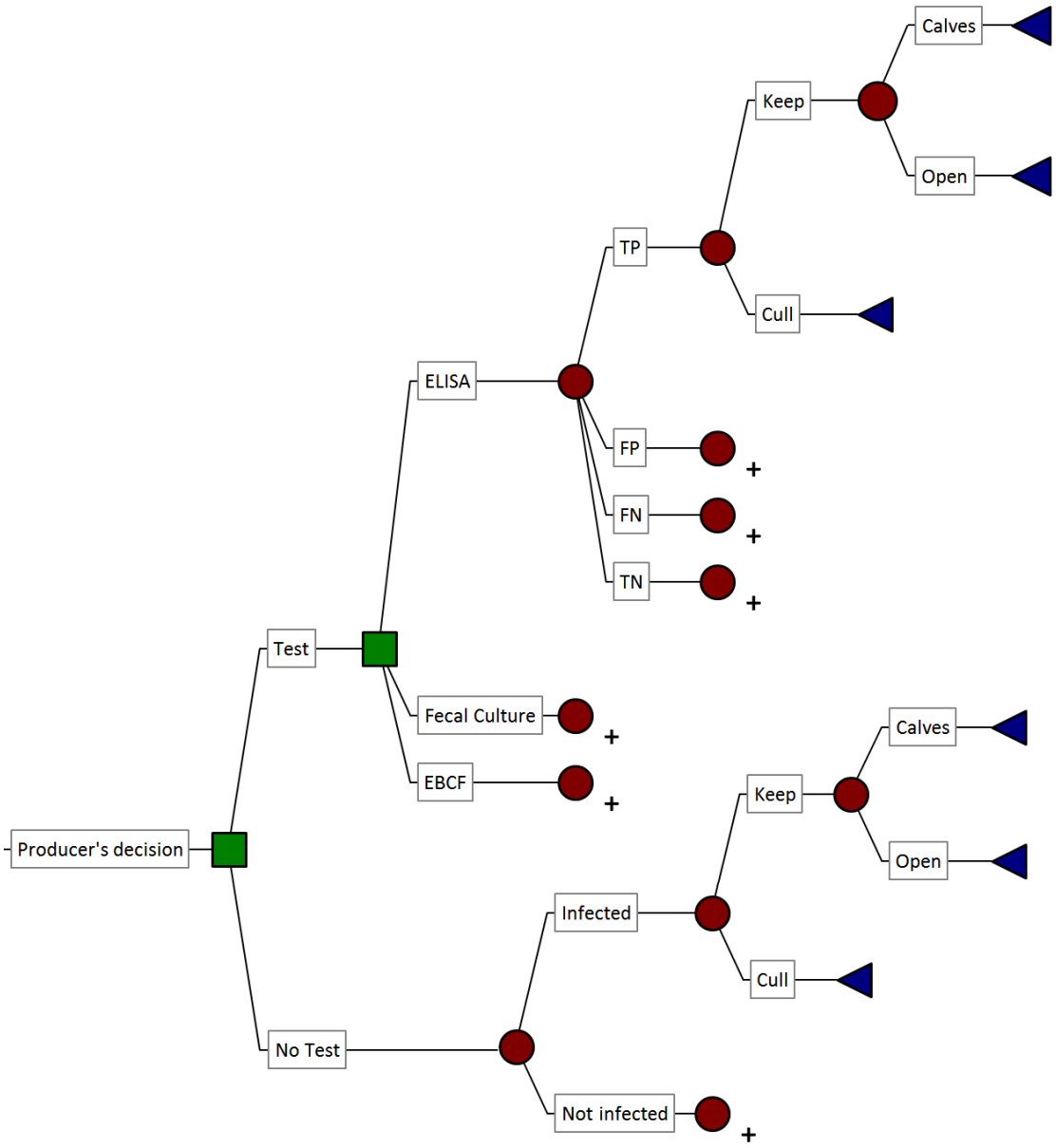

Figure 4. Decision tree for the economical evaluation of testing options for the control of *Mycobacterium avium* subspecies *paratuberculosis* in beef cow-calf herds.
+indicates sub branches analogous to alternative decision or chance.

The value of a specific decision branch is the probability-weighted average value of all corresponding terminal nodes. The economically prudent decision is the no-test, ELISA, BCF or EBCF decision option with the highest return (or lowest cost, benefit-cost) evaluated for each possible level of prevalence between 0 to 100% at a 1% increment. Latin hypercube sampling was used for model inputs.

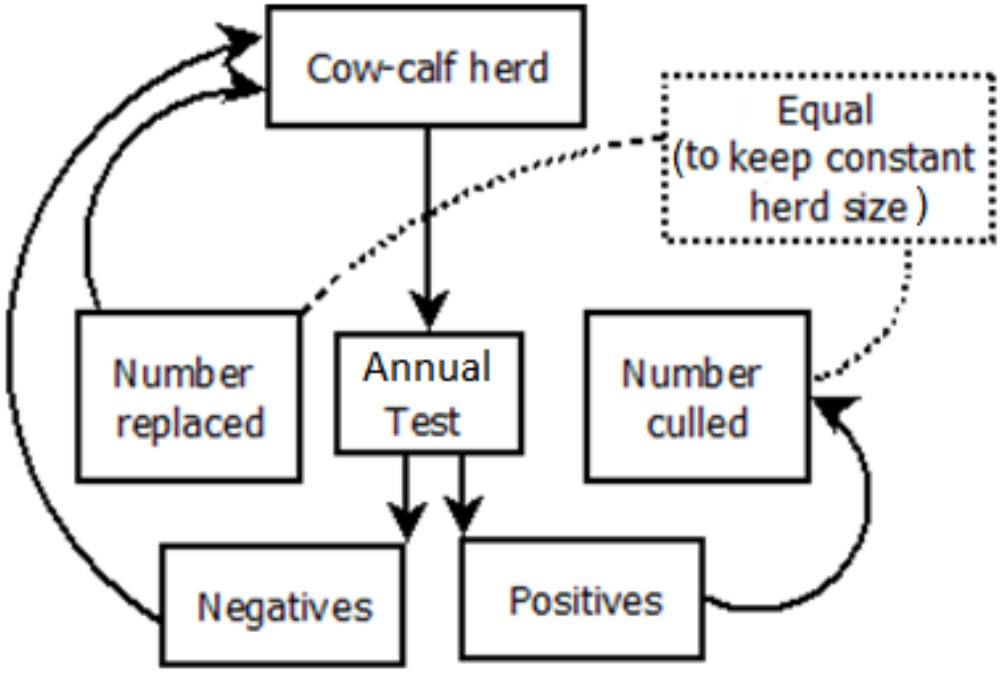

Figure 5: Test and cull with replacement cycle for the control of *Mycobacterium avium* subspecies *paratuberculosis* in beef cow-calf operations

5.2.3 Multi-year evaluation

An independent spreadsheet model was developed to estimate yearly changes in herd prevalence after implementation of a test and cull program (Figure 5). Spreadsheet assumptions included all test-positive cows being culled and replaced with cows from low-risk herds (Table 17). Replacements for voluntary culls were obtained from low-risk

herds for both testing and non-testing herds. All culls were assumed to be from test positives and the native herd stock allowing purchased low-risk replacements from earlier years to remain in the herd. There was a probability of 1% that replacements were infected with MAP, but within herd transmission was considered zero due to the sale of all weaned calves. The herd was assumed to have 100 cows with an initial true prevalence of 10%. Total yearly costs and cumulative costs over the control program were estimated based on test costs and production losses due to MAP infection. Uncertainties associated with outcomes were modeled using the stochastic probability distributions described for the single year evaluation. Farm costs based on no-test, testing with ELISA, testing with BCF, and testing with EBCF annually were calculated until the true herd prevalence was reduced to 0.5% (<1 infected animal in a 100 cow herd).

5.2.4 Sensitivity analysis

A regression sensitivity analysis was conducted using @Risk. The software varies the value of each model input and determines its regression coefficient for predicting return for each test decision branch. Critical variables for each decision were identified and ranked based on the relative values of regression coefficients. The most influential parameters contributing to total cost of MAP control in the multi-year test and cull scenario were also determined in a similar manner.

Table 17: Parameters and algorithm used to estimate yearly costs of MAP in a herd under test-based culling

	Input variables	Distribution and inputs[a]
N	Noumber of adult cows in herd	100 cows (for illustration)
P	Estimated number of infected cows	10 (initial 10% true prevalence)
	Test choice: ELISA, BCF or EBCF[b]	Choice of the producer
AP	No. of test positive cows	Based on sensitivity and specificity of chosen test (Collins et al., 2006)
A	Average weaning weight (kg)	Normal(249.8, 35.3)
B	Lowered weaning weight of calf from infected cow (kg)	Normal(33.26, 7.3)
C	Calving proportion	Beta(36.7,2.88)
D	Pre weaning mortality proportion	Beta(1.35,70.911)
E	Weaning proportion	C-D
F	Additional pre-weaning mortality – infected	Beta(1.03 , 33.1)
G	Lowered calving proportion - infected	Beta (1.3,5.7)
H	Adjusted weaning proportion for infected stock	E-F-G
I	Total calf crop weaning weight assuming all cattle are test negative (kg)	A*E*N
J	Total weaning weight adjusting for infected stock (kg)	I-(A-B)*P*H
L	**Lost weaning weight (kg)**	I-J
K	Annual average price per kg weaned calf ($)	$2.73
KL	**Lost weaning weight revenue over the year ($)**	K*L
R	Annual average replacement cost per cow ($)	Triangular (1257, 1643, 1833)
AP	Number of cows replaced / culled = test positives	AP
M	Average market price of a cull cow (received) ($)	NASS, from Table 16
S	**Additional replacement costs ($)**	(R-M)*AP
T	Average market price of a sick cow (culled due to Johne's disease) ($)	M*0.9 (10% lower weight)
U	Loss due to the cull being test positive ($)	M-T
X	**Lost revenue due to test positive culls ($)**	AP*U
Y	**Additional treatment cost for infected ($)**	Triangular(0,22.5,100)*P
Z	**Total yearly test and labor cost**	16.6 (ELISA); $23 (BCF)
	Total annual cost ($)	KL+S+X+Y+Z

[a] Derived from the inputs described in Table 16

[b] BCF (bacterial culture of feces), EBCF (ELISA confirmed by BCF)

5.3 Results

5.3.1 Herds testing for the first time

Herd-level returns decreased with increasing MAP prevalence when the herd was not tested (Figure 6). The annual return was lower for all testing options compared to no testing within the simulated beef herd with a regular culling and replacement cycle. The additional cost incurred for obtaining low-risk replacements was higher than the potential return recoverable by eliminating costs due to JD in the herd. Recovery of losses after the test based culling of an infected dam was highest at a true prevalence of 23% for BCF, 40% for ELISA and 70% for EBCF. Maximum returns at these thresholds were $374.9 (95% CR; -27.9 to 580.6) for BCF, $339 (95% CR -72.45 to 536.85) for ELISA, and $267.4 (95% CR (-138.68 to 487.59).

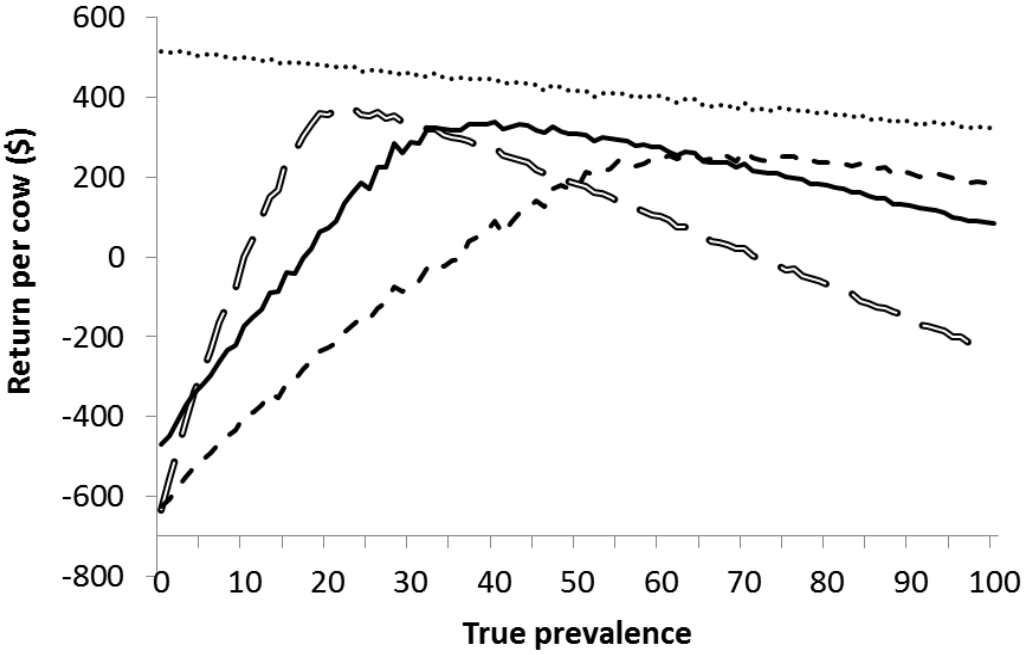

Figure 6: Average cow level return at different levels of prevalence based on tests for *Mycobacterium avium* subspecies *paratuberculosis* in beef cow-calf herds. Estimated based on the following options: no-test (dotted line), ELISA (solid line), bacterial culture of feces (long dash), and ELISA screening followed by bacterial culture of feces confirmation (short dash).

5.3.2 Multi-year testing

Culling BCF-positives and replacing with low-risk heifers annually caused a faster rate of reduction in herd prevalence compared to culling decisions based on ELISA alone or EBCF (Figure 7). A herd with 10% prevalence conducting a test and cull program based on BCF achieved a prevalence of less than 0.5% in five years while it took 11 years to reach the same prevalence with an ELISA-based control program and 18 years with EBCF-based control program. The median cumulative cost of MAP infection per cow until prevalence was reduced to less than 0.5% was $1,069 (95% CR: 505 to 2,241) for the ELISA-based control program, $548 (95% CR: 286 to 1,164) for the BCF-based control program, and $1,774 (95% CR: 880 to 3,648) for the EBCF-based control program. The prevalence in untested herds was 5% and the cumulative median cost was $1839 (95% CR: 932 to 3,807) after 20 years of obtaining replacements from low-risk herds.

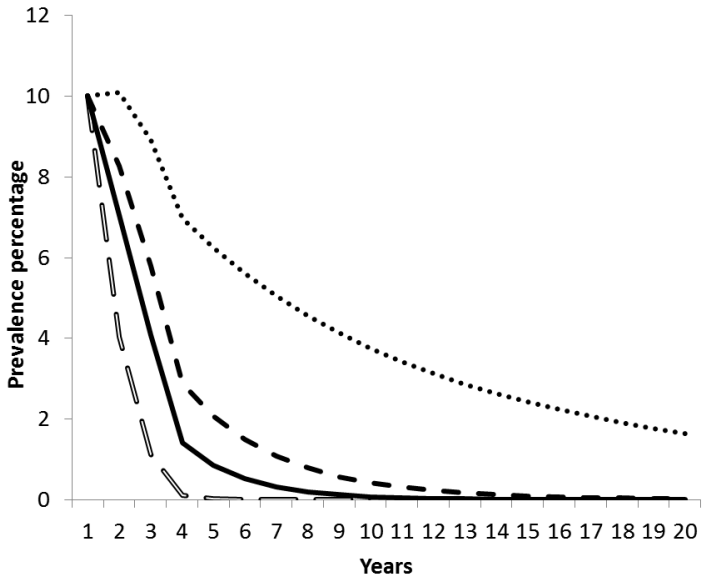

Figure 7: Prevalence changes after introduction of test based culling in a beef cow-calf herd with 10% initial prevalence of *Mycobacterium avium* subspecies *paratuberculosis.* Estimated based on the following options: no-test (dotted line), ELISA (solid line), bacterial culture of feces (long dash), and ELISA screening followed by bacterial culture of feces confirmation (short dash).

Costs associated with MAP infected cows were highest in the first year and decreased over time as the test and cull strategy removed infected cows (Figure 8).

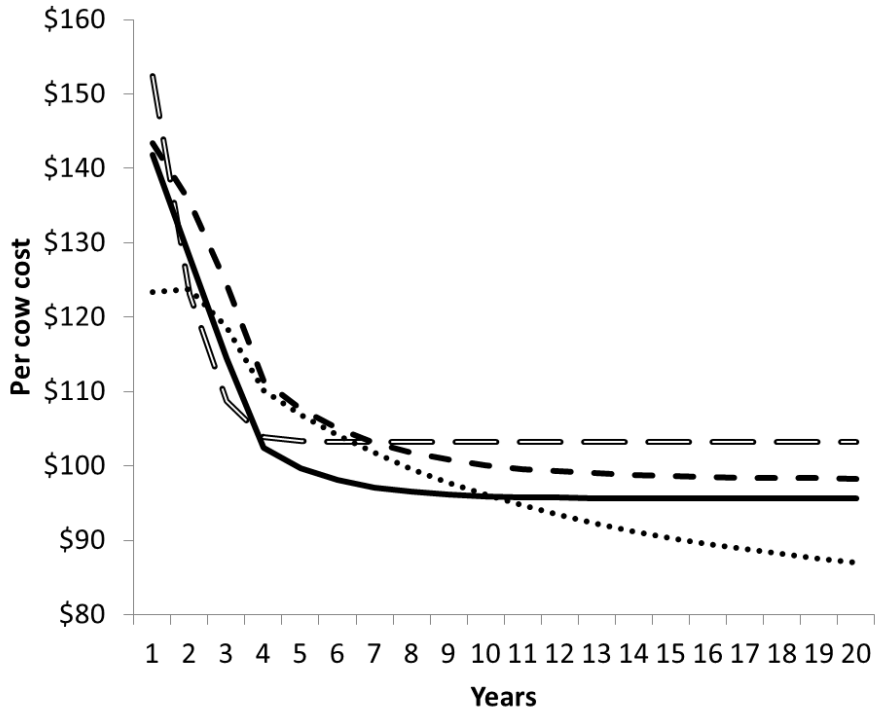

Figure 8: Cost changes after introduction of test based culling in a beef cow-calf herd with 10% initial prevalence of *Mycobacterium avium* subspecies *paratuberculosis*. Estimated based on the following options: no-test (dotted line), ELISA (solid line), bacterial culture of feces (long dash), and ELISA screening followed by bacterial culture of feces confirmation (short dash).

5.3.3 Sensitivity analysis

The most influential inputs on the value of the ELISA decision were the price of a low-risk replacement cow (b = -0.67), price of a replacement cow from a herd of unknown JD status (b = 0.55), and the voluntary culling rate (b = -0.38). The BCF decision was most sensitive to true prevalence (b=-0.30), weaning weight of a calf from an uninfected cow (b = 0.21), and the voluntary culling rate (b = -0.18). Similarly, the

EBCF decision was most sensitive to the true prevalence (b=0.67), price of a low-risk replacement (b=-0.58), and the price of a replacement from a herd of unknown JD status (b=0.46).

The most important factors for the cumulative cost were the voluntary culling rate, price of a low-risk replacement and the weight of a cull cow for all testing and not-testing options. Regression coefficients for the voluntary culling rate for ELISA, BCF, EBCF and no-test were 0.85, 0.87, 0.85 and 0.83, respectively. Regression coefficients for the price of low-risk replacement were 0.35, 0.35, 0.35, and 0.39, respectively. Similarly, weight of a cull cow was the third most influential factor with regression coefficients of -0.30, -0.29, -0.28, and -0.34 for ELISA, BCF, EBCF ,and no-test options, respectively.

5.4 Discussion

JD control in the US is voluntary and the primary reason is to improve herd productivity through reducing disease prevalence. The current study compared the benefits under the scenarios of no-testing, serum ELISA testing, BCF testing, or EBCF testing in an infected beef cow-calf herd. The decision tree modeled return after a single MAP test and culling cycle with purchased replacements from low-risk herds. The long term effect on MAP prevalence and MAP associated costs were also estimated. Total production decreased linearly with increasing prevalence. Compared to ELISA and EBCF, using BCF alone provided the fastest reduction in herd prevalence and was the least costly alternative based on long-term cumulative costs of an annual test and cull program.

There are only a limited number of studies evaluating the economic aspect of JD control strategies in beef cow-calf herds. Bennett et al. (2010) developed a deterministic cost-benefit model for the control of MAP in UK cow-calf herds under various control measures. Test and cull neither reduced the prevalence nor reduced the cost after 10 years. However, the current study estimated that culling BCF-positives and obtaining replacements from MAP low-risk herds annually can reduce a 10% initial prevalence to

less than 0.5% in five years. Eleven and 18 years were required to reach the same threshold using ELISA and EBCF, respectively. One of the major reasons for this difference is that within herd transmission was allowed in the Bennett et al. (2010) study while the current study assumed the sale of weaned calves and replacements exclusively obtained from low-risk herds. MAP transmission within the herd would hinder the effectiveness of a control program.

Results from the current study suggest that although testing provides faster progress, limiting within herd transmission by sale of all weaned calves and purchasing only low-risk replacements alone can also reduce the prevalence. Bovine JD control programs have two key strategies for preventing spread among and within herds. Strict biosecurity measures and not allowing infected cattle to enter the farm are important for uninfected herds (Roussel, 2011) because purchasing replacements from herds without known low-risk status increases the likelihood of transmission (Sweeney, 1996; Kovich et al., 2006). The herd replacement rate and contact between cows and calves are important parameters when MAP transmission is modeled. Obtaining replacements with zero risk of MAP infection might not be feasible due to current test limitations. Therefore, the current study assumed that replacements were obtained from herds with less than 1% chance of being infected (Level 4 in older JD classification system). The model by Collins and Morgan (1992) in dairy herds was sensitive to cow-calf contacts because that is considered the primary method of transmission. Some studies suggest that testing is not necessary when herd hygiene can be improved (Dorshorst et al., 2006; Lu et al., 2008). However, those results were based on observations from dairy herds, and the Lu et al. (2008) study did not employ empirical data.

Individual herd level costs may be important driving factors for an economic control program. Certain losses are recoverable by replacing test positives with low-risk cows. After the test based preferential culling, returns increased for a herd up to a certain threshold of true prevalence. Returns were lower for herds with true prevalence above these thresholds because, at a higher prevalence, the proportion of test positives is more than the typical culling percentage. Therefore, not all test positive cows are culled and

the loss due to presence of infected stock remains along with the additional cost of obtaining low-risk replacements. Such factors are important because the estimates of the cumulative multi-year cost of disease control were most sensitive to culling rate and also to the price of culls and replacements. A herd with an atypical culling rate or in which the price of culls and replacements is not typical will not have similar economic returns as reported in the current study. Control rather than eradication may be the economically preferred option for the majority of commercial beef herds. Eradication is possible by maintaining a strong commitment to these strategies for a long period of time (Sykes, 2000). Total herd depopulation with the removal of fecal materials has been recommended for small herds (Chiodini et al., 1984) although the feasibility is questionable. Selling of all calves, as assumed in this study, at least until the presence of MAP in the environment is no longer a risk might be a practical alternative. The high prevalence herds would otherwise progress slowly by annual testing due to the low sensitivity of available tests (Collins et al., 2006; Kudahl et al., 2007b; Kudahl et al., 2008). A Pennsylvania dairy farm with 60% apparent prevalence did not reach zero even after 20 years of semi-annual herd fecal culture tests followed by culling positives (Benedictus et al., 2008). Eradication in beef herds could be faster than dairy herds but low sensitivity and imperfect specificity would still hinder control programs as the herd approaches near eradication.

Specific and custumized control measures may be necessary for seedstock, or other specialized cow-calf herds, with an increased value of animals. Although test and cull decisions are not always profitable, control in seedstock herds might be important if restrictions were to be imposed on the sale of MAP-infected cattle (Kennedy and Allworth, 2000; Webb Ware et al., 2012). Factors that affect the decision to control JD on a herd include the discounts applied to sold animals, the duration of trading restrictions, and the adopted strategy (Webb Ware et al., 2012). Government or industry support might be necessary if market assurance was the reason for adopting control strategies.

Results of Webb Ware et al. (2012) for a self-replacing beef herd in Australia suggested that eradication is only profitable in the longer term when discounts on the sale of stock from infected herds are high. Purchasing low-risk additions accelerates the progress towards eradication. Although only three testing scenarios were compared in the present study, the most sensitive test (BCF) was the best choice for faster reduction of prevalence and reduced cost. BCF also has the highest specificity and specificity is important because false positive results cause an additional loss in test-based culling. Therefore, more specific tests are mainly important if culling false positive cows needs to be avoided for economic reasons. Another economic factor is the overall cost of testing. Evaluation of the trade-off between the number of years needed to reduce the prevalence below a certain threshold and overall cost to reach that threshold is important for decision making. BCF was the best choice based on both criteria.

Results from a dairy decision tree model by Dorshorst et al. (2006) suggested that a test-and-cull program is not always economically justifiable and the appropriate strategy depends on herd size, management types and initial MAP prevalence. Prior to this, Collins and Morgan (1991) developed a simulation model for JD control in dairy herds and concluded that test and cull was profitable when there was greater than a 6% prevalence. A modification of this model suggested that a test and cull program for JD was profitable at any prevalence over 1% (Collins and Morgan, 1992). The differences in these findings can be attributed to beef and dairy husbandry differences, particularly, the sale of calves and none retained as home-raised replacements. Another difference is that the ELISA and EBCF evaluated in the current study were assumed to have a lower sensitivity compared to a test sensitivity of 50% assumed by Collins and Morgan (1991). Test costs were also assumed to be greater in the present study, although this would be expected due to changes in costs over time.

Decision analysis models compare alternative courses while other factors are held constant. These comparisons should be limited to compare the relative impact of each course of action, but the estimated return may be affected by production parameters not included in the study. Lowered calving percentage, higher risk of pre-weaning

mortality, additional cost of treatment, and lower weaning weight of calves from MAP infected cows were considered in the current study. Other factors including indirect losses by reduced sales, loss of valuable genetic material due to premature culling, loss of export markets, lowered consumer confidence and the cost of litigation (Roussel, 2011) might also be important. Similarly, there are other losses due to lower production and higher management costs (Ott et al., 1999; Dorshorst et al., 2006; Kudahl et al., 2007a; Tiwari et al., 2008). Current estimates include additional veterinary expense per infected cows, but costs of morbidity and mortality due to diseases other than JD could be important additional indirect costs.

The estimates presented at the individual cow-level are likely to remain the same for herds at the same level of prevalence even if they are larger or smaller, but some inherent differences due to herd size may exist. Some large herds may have a lower cost for testing, labor, veterinary fees, handling and shipping samples for analysis. Data to validate model results were not available and this is an important limitation of the study. Precise inputs and use of primary empirical data are strengths of this study, but the model was sensitive to a number of inputs. Therefore, accurate estimation of these factors is important for model validity. While these values were collected from a producer survey and empirical data, caution should be taken while estimating losses in herds with production parameters markedly different than those used in this model. Cow parity and age were assumed to have no effect on production parameters and costs in effort to simplify the model. However, variation was included by using stochastic inputs and this is one of the reasons for wide CRs for economic estimates.Presented results are expected to benefit producers and other beef industry stakeholders to inform decisions concerning economically justifiable herd control strategies. It is very costly to control or eliminate MAP once the infection is established in a herd. While test and cull might be beneficial, proactive measures to reduce infection in herds are important. Future studies should evaluate other potential control measures including vaccination (Stabel, 1998; Kalis et al., 2001; Juste, 2012) and management options to reduce infection in calves (van Schaik et al., 1996; Groenendaal et al., 2002).

6. SUMMARY AND CONCLUSIONS

6.1 Conclusions

JD has been considered an economically important disease in cattle for over a century (Bang, 1906; Dunkin, 1936; Barkema et al., 2010). However, the majority of research has focused on dairy cattle (Benedictus et al., 1987; Collins and Morgan, 1991; Ott et al., 1999; Groenendaal and Wolf, 2008) and the disease has not been studied extensively in beef cattle operations. While there are some studies concerning the economic impact of JD in beef herds (Bennett et al., 2010; Webb Ware et al., 2012), this dissertation evaluates the specific economic consequences associated with JD in beef herds.

Weaning weight loss was significant in cows positive to the tests for MAP organism or antibody. Higher MAP shedders produced lighter calves compared to moderate and low intensity shedders. Similar results were also observed in ELISA positive cows. Calves from cows with higher levels of serum antibodies against MAP had lower weaning weights. The monetary losses associated with lower weaning weight of calves from test-positive cows was significant. Average monetary losses from a calf from heavy fecal shedder cow was $157 per calf. The loss was $58 for a calf from strong ELISA positive cow. True infection status could not be determined, but a higher response to ELISA or higher MAP shedding intensity both are likely representative of infected cows in more advanced stages of JD. Classification of tested cows in two categories (i.e., positive and negative) is less discriminating relative to impacts on adjusted weaning weight, especially for ELISA, presumably due to false-positive outcomes. This study focused on the loss associated with weaning weight, but additional losses, including premature culling of affected cows and lowered weight of culled animals, also contribute to the cumulative economic effect at the herd level.

The perceptions of beef producers and veterinarians concerning the burden of MAP infection in cow-calf herds and the measures for the control of new infections were also evaluated. Seedstock producers were more concerned with JD compared to other

producer groups. These producers were less likely to have an infected herd and more likely to enroll in a control program despite the fact that they purchased additions more frequently than other producer categories. However, it should be noted that the current study population consisted mainly (95%) of herds that were tested for MAP at least once. These producers presumably had better JD knowledge relative to the general cow-calf producers. Testing purchased additions was not a popular practice nor was serum ELISA based culling. One of the most important routes of transmission among herds is the addition of subclinically infected animals. This is also supported by the results that closed herds had lower perceived prevalence, test positive percentage, and also a lower risk of having animals with clinical JD. Larger herds were more likely to have test-positive cows, possibly due to a larger population being tested. A combination of tests and a 12-month testing interval was recommended by the majority of surveyed veterinarians. Educational activities regarding better management and control of JD should be directed at larger herds.

This dissertation also compared the perceptions of producers and veterinarians on the economic aspects of MAP infection in cow-calf herds. There were mixed opinions and differences in the production metrics perceived by veterinarians and producers. One of the most significant economic concerns of commercial cow-calf producers was a lower weaning weight of calves from infected cows. The loss of valuable genetics when an MAP infected cow was culled was an important concern to seedstock producers. Similarly, all producers reported a significantly higher percentage of herd income lost due to the presence of MAP infected cattle. Based on the reported losses, an annual loss of $235 for each infected animal was estimated using information from the producer survey. The analogous estimate using information from veterinarians was $250. Such losses, when translated into a 100 cow herd with an assumed true prevalence of 7%, totaled $1,644 based on information provided by producers and $1,747 based on the information from veterinarians. This indicates that MAP infection in beef herds is associated with substantial economic losses. These estimates provide useful background material to facilitate broad dissemination of control program benefits. Information

concerning the estimated cost might motivate producers with MAP infected herds to initiate a JD control program. This could also encourage low prevalence herds to continue JD control efforts to improve market opportunities.

The final study evaluated whether testing and culling MAP test-positive cows is economically justifiable to reduce herd-prevalence and to gain better productivity from replacement cows. A single test based culling was not profitable for a typical cow-calf herd at any level of prevalence. However, testing the herd annually effectively reduces the prevalence when the replacements are obtained from low-risk herds. BCF was the most sensitive and specific test, which caused the most rapid reduction in prevalence compared to ELISA, and ELISA confirmed by BCF. The cost to reduce the true prevalence from 10% to less than 0.5% was the lowest for BCF followed by ELISA and EBCF. BCF appears to be the most economic test for herds to reduce JD prevalence.

The overall results presented in this dissertation suggest that commercial cow-calf producers perceive a high loss due to lower weaning weight of calves born from MAP infected cows. Similar to the perception, observational data from cow-calf herds also demonstrated significantly lower weaning weight of calves from cows testing positive for MAP organisms or antibodies. For commercial cow-calf producers, minimizing the loss is the priority over reducing the prevalence per se. One way to minimize loss without aggressive investment in a control program is the implementation of management changes to reduce the spread of MAP within the herd. Selling all calves born in infected herds and obtaining replacements from low-risk herds to prevent further within-herd transmission results in a reduction in prevalence. For a quicker progress in reduction of prevalence, testing the entire herd by BCF is recommended.

Concern about lower weaning weight is also important for seedstock producers. Previous reports suggest that compensatory growth of cattle born with lower weight during calfhood is less likely. While test based culling results in additional cost to the seedstock producers due to the higher value of genetically superior animals, lowering the herd prevalence is a priority for better marketability of their cattle. Therefore, even the seedstock herds can test their herds with BCF for effective reduction in prevalence when

all calves are sold and replacements are obtained from low-risk herds. One of the major challenges for seedstock producers is to obtain genetically desirable replacements from low-risk herds. There is a necessity of nationwide effort to establish more low-risk herds so that animals with desired superior genetics can be obtained as replacements. Breed associations can also track herds for specific pathogens including MAP and keep information about herds with lower risk of JD.

Based on the perceptions and observed data, this dissertation concludes that herd level losses decrease with lowered prevalence. In a herd going through a control program, the number of better producing uninfected stocks increases after each culling and replacement. While there is usually additional cost associated with any control program, there is a potential of recovery of this cost with increased returns from increasing number of uninfected stocks as the herd progresses towards MAP eradication. For the herds going through a control program, total cost to reduce the true prevalence from 10% to less than 5% was lowest for BCF, followed by ELISA, and ELISA confirmed by BCF. Therefore, BCF is the recommended test for herds to reduce JD prevalence although it was the least frequently recommended test by the veterinarians for herds starting a control program to reduce MAP prevalence by test-based culling.

6.2 Proposed future studies

A comprehensive study using nationwide data on production metrics in beef herds would be an important step towards generating more accurate estimates of losses associated with JD in beef herds. Proper preparation and an effective data collection mechanism would provide more informative results. While several categories of losses were perceived to be important, producers probably did not formally evaluate farm records when providing questionnaire responses. Longitudinal data from different types of beef production units would be valuable to make more precise estimates. Additional surveys of producers including those who have not been enrolled in a control program or have tested herds would be beneficial to compare perceptions among all production types. Studies collecting actual farm data could be used in the decision tree model in

effort to improve the validity. The predictive ability of multi-year testing would be improved by incorporating data collected from producers over several years. Validation of decision tree and multi-year test-based culling will also be possible after the collection of the appropriate empirical data.

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APPENDIX A

QUESTIONNAIRE USED FOR VETERINARIAN SURVEY

Johne's Disease Survey

Perception of veterinarians on economic aspects of Johne's disease and its control

VETERINARY MEDICINE & BIOMEDICAL SCIENCES
TEXAS A&M UNIVERSITY

Information Sheet

You are invited to participate in a study to evaluate the perceptions of beef cow-calf veterinarians regarding aspects of the economic importance of Johne's disease and its control. It is widely believed that targeted control programs are important in controlling Johne's disease, but that the costs of implementing control strategies may interfere with the successful implementation of the program, particularly in light of the economic impact of the disease in cow-calf herds. Therefore, we would like to know how cow-calf veterinarians perceive the costs associated with Johne's disease and its control. We want to compare the perceived cost of Johne's disease with economic impacts measured in real life situations. This will enable us to identify if there is a difference between perception and reality when it comes to Johne's disease control programs.

The information obtained for this study will be confidential and all the physical records and data will be stored in locked file cabinets. Data submitted online via the electronic version of this survey will be stored in a secure server. All of the data associated with this study will be stored in password protected computers. Information that could potentially link a respondent to the questionnaire will not be included in any report that might be published. Research associated records will be accessible only to the researchers directly involved in this study.

This research study has been reviewed by the Institutional Review Board for Human Subjects in Research, Texas A&M University (protocol number 2010-0666). If you have questions about your rights, please contact the Institutional Review Board through http://researchcompliance.tamu.edu/contact, phone: (979) 458-1467.

Participation to this questionnaire survey is voluntary. You may choose to answer all of the questions or a portion of the survey, but we would encourage you to answer as many questions as possible to maximize the value of the results obtained from this study. We appreciate how valuable your time is and want to ensure that the study yields the best possible results and therefore provides the best possible information to help guide decisions that you will need to make in controlling Johne's disease in your client herds.

Please answer these questions based on your experience.

1. Were you ever a Johne's disease certified veterinarian? ☐ Yes ☐ No
   (An accredited veterinarian who has completed training for Johne's disease epidemiology and development of herd management plans approved by the designated Johne's disease coordinator.)

   If yes, initial year of certification_____

2. Have you ever performed a Johne's disease risk assessment for a cow-calf operation? ☐ Yes ☐ No

3. What type of production systems are represented within your practice clientele? (Please check all that apply)

   ☐ Commercial cow-calf (Registered)
   ☐ Seedstock (Registered)
   ☐ Commercial cow-calf (Not-registered)
   ☐ Seedstock (Not-registered)
   ☐ Feedlot
   ☐ Other
   (Please state) _____

4. What is the predominant breed or cross in your cow-calf practice clientele?
   _____
   (Please do not abbreviate)

5. Where is your current veterinary practice?
   _____
   (State / states)

6. Do you currently have cow-calf operation(s) as client(s)? ☐ Yes ☐ I had until_____ (Please enter the last year you had) ☐ Never had one

For the purposes of this survey, we define **herd** as a group of cattle managed as a separate and discrete unit not commingled with other groups of cattle. A herd may include two or more groups of cow-calves under common supervision that may be geographically separated, but have an exchange or movement of animals between units without regard to health status.

7. How many cow-calf herds do you serve as the primary veterinarian? _____ herds

8. What is the size of an average cow-calf herd you serve? _____ heads
   (Number of 2yr or older cows/herd)

9. What are the sizes of smallest and largest herds? _____ heads _____ heads
   (Number of 2yr or older cows/herd) (Smallest h

Following acronym and definitions have been used in the next part of this questionnaire

MAP = *Mycobacterium avium* subspecies *paratuberculosis*

Cow-level prevalence (%) = (Number of cows 2 yrs of age or older infected with MAP/ Total number of cows 2 yrs of age or older) x 100%

Herd-level prevalence (%) = (Number of herds with at least one MAP infected cow / Total number herds) x 100%

10. In your opinion, of all the cows 2 yrs of age or older among your practice clientele, what percentage of cattle are infected with MAP (i.e. cow-level prevalence)?

Best estimate _____% Likely between _____% (minimum) and _____% (maximum)

11. In your opinion, what percentage of your client herds has 1 or more animals infected with MAP (i.e., herd-level prevalence)?

Best estimate _____% Likely between _____% (minimum) and _____% (maximum)

12. Within MAP-infected cow-calf herds, what percentage of cattle do you believe is typically infected with MAP (i.e., within-herd prevalence)?

Best estimate _____% Likely between _____% (minimum) and _____% (maximum)

13. What is the basis of your estimates for cow-level, herd-level, and within-herd prevalence?
(Please check all that apply)

☐ Fecal culture tests performed in my client herds
☐ Animals with clinical signs of Johne's disease in my client herds
☐ ELISA tests performed in my client herds
☐ Based on regional or national data
☐ Other
(Please state) _____

14. In a typical year, what percent of cows 2 yrs of age or older will die on the farm in the following three sizes of cow-calf operations in your practice clientele?

	Small herd	Medium herd	Large herd
Mortality of cows due to any cause	_____ %	_____ %	_____ %
Mortality within MAP infected cows	_____ %	_____ %	_____ %

15. In a typical year, what percent of cows 2 yrs of age or older will die on the farm in the following three sizes of cow-calf operations in your practice clientele?

	Small herd	Medium herd	Large herd
Non-MAP infected cows culled	_____ %	_____ %	_____ %
MAP infected cows culled	_____ %	_____ %	_____ %

16. In a typical year in your cow-calf practice clientele, what percentage of cows will calve? (Please answer based on the major breed in your practice) _____ %

17. In general, do you believe cows infected with MAP have a different calving percentage than uninfected herdmates?

☐ Yes, the calving percentage in cows infected with MAP is different

If yes, the calving percentage is ☐ more ☐ less by _____ %
(Please check one)

☐ No, cows infected with MAP have a calving percentage similar to others

☐ I don't know

18. In a typical year in your cow-calf practice clientele, what percent of calves alive at birth die before weaning? (Please answer based on the major breed in your practice) _____ %

19. In general, do you believe calves from cows infected with MAP have a different pre-weaning risk of death than other calves?

☐ Yes, pre-weaning risk of death in calves from cows infected with MAP is different

If yes, the pre-weaning risk of death is ☐ more ☐ less by _____ %
(Please check one)

☐ No, pre-weaning risk of death in calves from cows infected with MAP is similar to others

☐ I don't know

20. In a typical herd in your cow-calf practice clientele, what is the average weaning weight of calves from second or higher parity cows? _____ lbs
(Please answer based on the major breed in your practice)

21. Do you believe that calves from cows infected with MAP have a different weaning weight than other calves?

☐ Yes, the weaning weight of calves from cows infected with MAP is different
If yes, the weaning weight is ☐ more ☐ less by _____ lbs
(Please check one)

☐ No, the weaning weight in calves from cows infected with MAP is similar to others

☐ I don't know

22. Do you believe there is an important loss of genetic potential when MAP infected cows are culled? ☐ Yes ☐ No ☐ I don't know

23. Based on your experience, do you believe that MAP infected cows are **more likely** to develop the following?

Mastitis	☐ Yes	☐ No	☐ I don't know
Pneumonia	☐ Yes	☐ No	☐ I don't know
Lameness	☐ Yes	☐ No	☐ I don't know
Dystocia	☐ Yes	☐ No	☐ I don't know
Grass tetany	☐ Yes	☐ No	☐ I don't know
Milk fever	☐ Yes	☐ No	☐ I don't know
Neurological disease	☐ Yes	☐ No	☐ I don't know
Diarrhea	☐ Yes	☐ No	☐ I don't know
Digestive disorders (excluding diarrhea)	☐ Yes	☐ No	☐ I don't know

24. Based on your experience, what other diseases are more likely to develop in MAP infected cattle?

_____

25. For a typical client's cow-calf herd, what is the average veterinary care expense per cow per year? $ _____ per cow per year
(for example - vaccination, deworming, treatment of sick animals, diagnostic tests for sick cows, routine diagnostic tests, service fees and farm calls)

26. Do you feel that the average veterinary expense for MAP infected cattle is different from uninfected herdmates?

☐ Yes, the expense for MAP infected cattle is different

If yes, the expense is ☐ more ☐ less by $ _____ per cow per year
(Please check one)

☐ No, the veterinary expense in MAP infected cattle is similar to others

☐ I don't know

27. In your opinion, how frequently do the cow-calf producers in your practice do the following with the sole or a partial intent of controlling Johne's disease?

a. Remove calves from dams suspected of being infected with MAP prior to nursing
(Please circle your choice)

Always Mostly Sometimes Seldom Never

b. Cull cows showing signs consistent with a diagnosis of Johne's disease prior to testing
(Please circle your choice)

Always Mostly Sometimes Seldom Never

c. Cull cows with signs consistent with a diagnosis of Johne's disease after laboratory testing
(Please circle your choice)

Always Mostly Sometimes Seldom Never

d. Cull calves from dams suspected or confirmed to be infected with MAP based on testing or clinical signs (Please circle your choice)

Always Mostly Sometimes Seldom Never

e. Early weaning of calves from dams with positive results from Johne's disease tests
(Please circle your choice)

Always Mostly Sometimes Seldom Never

f. Cull cows without clinical signs consistent with a diagnosis of Johne's disease, but positive serology (ELISA) (Please circle your choice)

Always Mostly Sometimes Seldom Never

g. Test purchased additions for Johne's disease
(Please circle your choice)

Always Mostly Sometimes Seldom Never

28. In percentage terms, what is your estimate of total income lost by the producer of a typical MAP-infected herd within your practice due to this infection?

Best estimate _____% Likely between _____% (minimum) and _____% (maximum)

29. Do you feel that the percentage of income lost by the producer attributed to having MAP infection in the herd depends on prevalence level? ☐ Yes ☐ No ☐ I don't know

30. For herds initiating a testing program, which test(s) would you recommend?

- ☐ Bacterial culture of feces for MAP
- ☐ Fecal PCR to detect MAP DNA
- ☐ Serology (ELISA) to detect MAP antibody
- ☐ Histology of tissue
- ☐ Combination of above tests
- ☐ Other (Please state)

31. Why do you prefer this test(s)? _____

_____

32. Which animals in the herd do you routinely recommend testing?
(Please check all that apply)

- ☐ Bull calves (pre-weaning)
- ☐ Heifer calves (pre-weaning)
- ☐ Heifers (weaning to first calving)
- ☐ First calf heifers
- ☐ Young bulls: weaning to 2 yrs of age
- ☐ Mature bulls (2 yrs of age or older)
- ☐ Cows (2 yrs of age or older)
- ☐ Other (Please state)

33. What should be the interval between successive testing in beef herds?

- ☐ Less than 6 months
- ☐ 6 months
- ☐ 12 months
- ☐ 18 months
- ☐ More than 18 months
- ☐ Never

34. How much would it cost to test a typical herd of 100 cows for Johne's disease?

	Minimum	Most likely	At the most
Veterinary costs	$_____	$_____	$_____
Test costs	$_____	$_____	$_____

35. What herd-level factors might influence these costs?_____

_____

Please return the completed survey in the postage-paid envelope in the survey packet

Thank you very much for your time to complete this survey!

APPENDIX B

QUESTIONNAIRE USED FOR PRODUCER SURVEY

Johne's Disease Survey

Perception of cow-calf producers on economic aspects of Johne's disease and its control

College of Veterinary Medicine and Biomedical Sciences
Texas A&M University

2010

DATE

Dear Cattle Producer:

Veterinarians at the Texas A&M University's College of Veterinary Medicine and Biomedical Sciences have conducted research on Johne's disease in beef herds for a number of years. This survey is a continuation of our long term goal to help understand and control Johne's disease in beef cattle. We hope that you will be willing and able to provide us with a little more data so that we can continue to work toward our goal. Your knowledge about the real losses associated with Johne's disease and its control is important to us and will be used to help answer key questions and guide future work. Our hope is that ultimately, we can deliver useful information to producers and veterinarians that will assist in the control of Johne's disease in beef cattle herds.

Completion of this survey is completely voluntary. This package contains a survey comprised of 31 questions and should take approximately 30 minutes to complete.

The identity of participants will not be recorded and any individual information obtained from this questionnaire will be strictly confidential. If you have any questions concerning this project then feel free to contact us.

We have also enclosed a pre-paid, self-addressed envelope for return of the questionnaire and an information sheet concerning the research. Alternatively, you may go to the following URL to complete this questionnaire online:

www.cvm.tamu.edu/selectsurvey and enter **L2LK472** into the survey ID box.

Thank you very much for your cooperation.

Sincerely,

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Dept of Large Animal Clinical Sciences
Phone: 979-845-3541
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Texas A&M University
College Station TX 77843

Information Sheet

You are invited to assist us in a study to evaluate the perceptions of beef cow-calf producers regarding some of the aspects of the economic importance of Johne's disease and its control. It is widely believed that targeted control programs are important in controlling Johne's disease, but that the costs of implementing control strategies may interfere with the successful implementation of the program, particularly in light of the economic impact of the disease in cow-calf herds. Therefore, we would like to know how cow-calf producers perceive the costs associated with Johne's disease and its control. We want to compare the perceived cost of Johne's disease with economic impacts measured in real life situations. This will enable us to identify if there is a difference between perception and reality when it comes to Johne's disease control programs.

The information obtained for this study will be confidential and all the physical records and data will be stored in locked file cabinets. Data submitted online via the electronic version of this survey will be stored in a secure server. All of the data associated with this study will be stored in password protected computers. Information that could potentially link a respondent to the questionnaire will not be included in any report that might be published. Research associated records will be accessible only to the researchers directly involved in this study.

This research study has been reviewed by the Institutional Review Board for Human Subjects in Research, Texas A&M University (protocol number 2010-0666). If you have questions about your rights, please contact the Texas A&M University Institutional Review Board through http://researchcompliance.tamu.edu/contact, phone: (979) 458-1467, email: bwhitney@vprmail.tamu.edu or mail:

Human Subjects' Protection Program Office
General Services Complex
750 Agronomy Rd, Suite 3501
TAMU 1186 (mailstop)
College Station, Texas 77843-1186.

Participation to this questionnaire survey is voluntary. You may choose to answer all of the questions or a portion of the survey, but we would encourage you to answer as many questions as possible to maximize the value of the results obtained from this study. We appreciate how valuable your time is and want to ensure that the study yields the best possible results and therefore provides the best possible information to help guide decisions that you will need to make in controlling Johne's disease in your herd.

Producers' Survey

Please answer the following questions about your cow-calf operation.

1. What type of cow-calf operation do you have? (Please check all that apply)

☐ Commercial cow-calf (Registered) ☐ Commercial cow-calf (Not-registered)

☐ Seedstock (Registered) ☐ Seedstock (Not-registered)

☐ Other

(Please state) _____

2. How many years have you been raising cattle for beef production? _____ years

If you have multiple herds please provide information about the herd for which you have the most information. However, if your animals in different herds routinely comingle, please consider all of them as a single herd

3. What breed(s) of cattle do you have? _____

(most common breed or cross)

_____

(other breeds or crosses, if any)

4. How many head of cattle do you typically add to your herd per year?

(please do not count home-raised replacements) _____ head/year

5. Estimate the number of animals that fit each category during **a typical year** over the last 5 years.

Categories	Total in herd	Culled	Sold	Died
Adult cows				
1st calf heifers				
Bulls > 2 yrs of age				
Bulls weaned-2 yrs of age				
Heifers weaned (replacements)				
Nursing heifers				
Nursing bulls/steers				

In the following questions, **MAP** refers to *Mycobacterium avium paratuberculosis*, which is the **organism that causes Johne's disease**

6. What is your estimate of the percentage of your herd infected with MAP today?

Best estimate _____ % Likely between _____% (minimum) and _____% (maximum)

What is the basis of your estimate? (Please check all that apply)

☐ Based on my veterinarian's opinion ☐ Personal experience with Johne's disease

☐ Estimate based on regional or national data ☐ Other : (Please state)_____

7. During the **past year**, how many animals in your herd had signs of Johne's disease?
(persistent diarrhea, very thin, unthrifty and weak without fever or loss of appetite) _____ head

8. Is your herd currently enrolled in any Johne's disease control program? ☐ Yes ☐ No (If no, then please go to question 9)

If yes, is it an official program (US Voluntary Bovine Johne's Disease Control Program) ☐ Yes ☐ No, my vet designed this program for my herd

How many years have you participated in the Johne's disease control program? _____ years

9. Have you ever tested your herd for Johne's disease? ☐ Yes ☐ No (If no, then please go to question 10 next page)

If yes, when was the most recent test? _____,_____ (month) (year)

Which test was used? ☐ ELISA (Blood test) ☐ Fecal Culture ☐ Other_____ (Please specify)

What percentage of your herd was positive by the test(s)? _____ %

10. During **a typical year** over the last 5 years, what percentage of cows calved? _____ %

11. In general, do you believe cows infected with MAP have a different calving percentage than uninfected herdmates?

☐ Yes, the calving percentage in cows infected with MAP is different

If yes, the calving percentage is ☐ more ☐ less by _____ %
(Please check one)

☐ No, cows infected with MAP have a calving percentage similar to others

☐ I don't know

12. During **a typical year** over the last 5 years, what percentage of calves alive at birth died before weaning? _____ %

13. In general, do you believe calves from cows infected with MAP have a different pre-weaning risk of death than other calves?

☐ Yes, pre-weaning risk of death in calves from cows infected with MAP is different

If yes, the pre-weaning risk of death is ☐ more ☐ less by _____ %
(Please check one)

☐ No, pre-weaning risk of death in calves from cows infected with MAP is similar to others

☐ I don't know

14. During **a typical year** over the last 5 years, what was the average weaning weight of calves from cows (not first calf heifers)? _____ lbs

15. Do you believe that calves from cows infected with MAP have a different weaning weight than other calves?

☐ Yes, the weaning weight of calves from cows infected with MAP is different

If yes, the weaning weight is ☐ more ☐ less by _____ lbs
(Please check one)

☐ No, the weaning weight in calves from cows infected with MAP is similar to others

☐ I don't know

16. Do you believe there is an important loss of genetic potential when MAP infected cows are culled? ☐ Yes ☐ No ☐ I don't know

17. Based on your experience, do you believe that MAP infected cows are **more likely** to develop the following?

Mastitis	☐ Yes	☐ No	☐ I don't know
Pneumonia	☐ Yes	☐ No	☐ I don't know
Lameness	☐ Yes	☐ No	☐ I don't know
Dystocia (calving difficulty)	☐ Yes	☐ No	☐ I don't know
Grass tetany	☐ Yes	☐ No	☐ I don't know
Milk fever or downer cow	☐ Yes	☐ No	☐ I don't know
Neurological disease	☐ Yes	☐ No	☐ I don't know
Diarrhea	☐ Yes	☐ No	☐ I don't know
Digestive disorders (excluding diarrhea)	☐ Yes	☐ No	☐ I don't know

Based on your experience, what other diseases are more likely to develop in MAP infected cattle?

_____

18. During **a typical year** over the last 5 years, what was the average veterinary care expense per cow? $ _____ per cow per year
(for example - vaccination, deworming, treatment of sick animals, diagnostic tests for sick cows, routine diagnostic tests, service fees and farm calls)

19. Do you feel that the average veterinary expense for MAP infected cattle is different from uninfected herdmates?

☐ Yes, the expense for MAP infected cattle is different

If yes, the expense is ☐ more ☐ less by $ _____ per cow per year
(Please check one)

☐ No, the veterinary expense in MAP infected cattle is similar to others

☐ I don't know

20. In percentage terms, what is your estimate of total income lost from your herd because of MAP infected cattle present in your herd?

Best estimate _____% Likely between _____% (minimum) and _____% (maximum)

21. How much would it cost to test your entire adult herd for Johne's disease this year?
(Do not include investment costs for new or upgraded facilities)

Item	Cost
Labor (include your own time)	$
Equipment	$
Veterinary costs (e.g., farm call, service fees)	$
Test costs	$
Other (Please state)	$

22. Please estimate how much money would be necessary for you to add the following facilities with the intent to test the adult animals in your herd for Johne's disease.

Item	Most likely cost	Minimum cost	Already have it in the operation?
Chute	$	$	☐ Yes
Head gate	$	$	☐ Yes
Alley system	$	$	☐ Yes
Corrals	$	$	☐ Yes
Holding area	$	$	☐ Yes

23. Based on your experience, please estimate the following costs:
(Please check the corresponding box if any item listed below is not feasible)

Item	Most likely	Minimum	
How much would it cost to build fence (per 100 ft) sufficient to separate groups of adult cattle?	$	$	☐ Not feasible
How much would it cost to hire an additional person to help manage the adult herd? (Per year)	$	$	☐ Not feasible
How much would it cost to dispose of an adult cow with Johne's disease on the operation (e.g., burial, composting) rather than send to slaughter?	$	$	☐ Not feasible
How much would it cost to build a separate area large enough to hold 5-10 cows separate from the rest of the herd to use as a quarantine facility for herd additions?	$	$	☐ Not feasible

If your cows calve on pasture, please skip question 24 and go to question 25 (next page).

24. What additional cost would you incur (over your regular expenses) if you were to implement the following changes with the intent to control MAP transmission?
(Please check the corresponding box if any item listed below is not feasible)

Item	Most likely	Minimum	
How much would it cost to build a separate calving area for MAP-infected cows?	$	$	☐ Not feasible
How much would it cost to build a separate nursing area for 5-10 MAP-infected cows?	$	$	☐ Not feasible
How much would it cost to build a new, separate manure disposal area and channel for younger or healthy stock?	$	$	☐ Not feasible
What would be the additional cost of labor to remove manure immediately from the calving area to avoid calf-manure contact?	$ /yr	$ /yr	☐ Not feasible
What would be the additional cost of labor to clean dirty udders at calving?	$ /yr	$ /yr	☐ Not feasible
What would be the additional cost of labor to clean pens or chutes where you assist with calving and provide immediate post-calving care?	$ /yr	$ /yr	☐ Not feasible

25. What additional cost would you incur (over your regular expenses) if you were to implement the following changes with the intent to control MAP transmission?
(Please check the corresponding box if any item listed below is not feasible)

Construction costs	Most likely	Minimum	
How much would it cost to add one water trough in the pasture?	$	$	☐ Not feasible
How much would it cost to build a fenced creep feeder for 20 calves?	$	$	☐ Not feasible

Additional labor costs	Most likely	Minimum	
What would be the additional cost of labor to move cow/ newborn calf-pairs to less crowded areas in your herd?	$ /yr	$ /yr	☐ Not feasible
What would be the additional cost of labor to move one hay ring (i.e. round bale feeder) 50-100 ft every week?	$ /yr	$ /yr	☐ Not feasible
What would be the additional cost of labor to avoid contamination of feed destined for youngstock with manure from older animals in your herd?	$ /yr	$ /yr	☐ Not feasible
What would be the additional cost of labor to manage one creep feeder for 20 calves?	$ /yr	$ /yr	☐ Not feasible

26. During the last 5 years, how many 2 year or older cows with **MAP-infection** (test-confirmed or suspected) did you cull from your herd? _____ head/5 years

27. During the last 5 years, how many 2 year or older cows with **MAP-infection** (test-confirmed or suspected) died within your herd (before they were sold)? _____ head/5 years

28. During the past 5 years, how frequently did you do the following with the sole or a partial intent of controlling Johne's disease?

a. Remove calves from dams suspected of being infected with MAP prior to nursing?
(Please circle your choice)

Always Mostly Sometimes Seldom Never

b. Cull cows showing signs consistent with a diagnosis of Johne's disease prior to testing?
(Please circle your choice)

Always Mostly Sometimes Seldom Never

c. Cull cows with signs consistent with a diagnosis of Johne's disease after laboratory testing?
(Please circle your choice)

Always Mostly Sometimes Seldom Never

d. Cull calves from dams suspected or confirmed to be infected with MAP based on testing or clinical signs? (Please circle your choice)

Always Mostly Sometimes Seldom Never

e. Early weaning of calves from dams with positive results from Johne's disease tests?
(Please circle your choice)

Always Mostly Sometimes Seldom Never

f. Cull cows without clinical signs consistent with a diagnosis of Johne's disease, but positive serology (ELISA)? (Please circle your choice)

Always Mostly Sometimes Seldom Never

g. Test purchased additions for Johne's disease?
(Please circle your choice)

Always Mostly Sometimes Seldom Never

29. Please estimate the cost to your herd in a typical year if you were to "always" perform **all** of these activities *(a to g above)* on your operation.

Estimated $ _____ Between $ _____ and $ _____
(Total yearly cost on your operation)

30. How much more would you be willing to pay for a bred-heifer from a herd known to have low risk for Johne's disease compared to a heifer from a herd of unknown status?

Estimated $ _____ Between $ _____ and $ _____
(Additional amount you are willing to pay for a bred-heifer from a low risk herd)

☐ I would not purchase

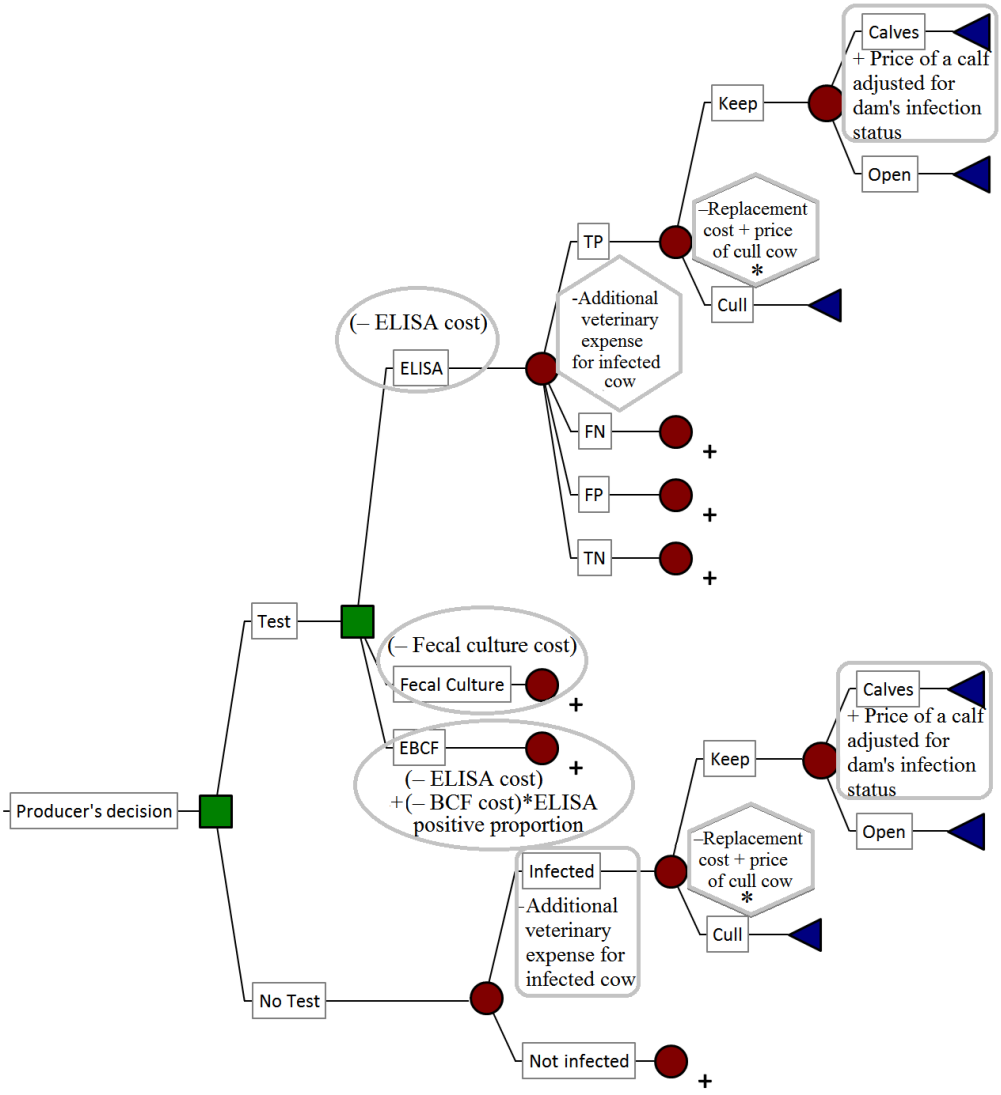
31. How much less would you be willing to pay for a bred-heifer from a herd known to be affected by Johne's disease compared to one from a herd of unknown status?

Estimated $ _____ Between $ _____ and $ _____
(Amount you would deduct when you pay for a bred-heifer from an infected herd)

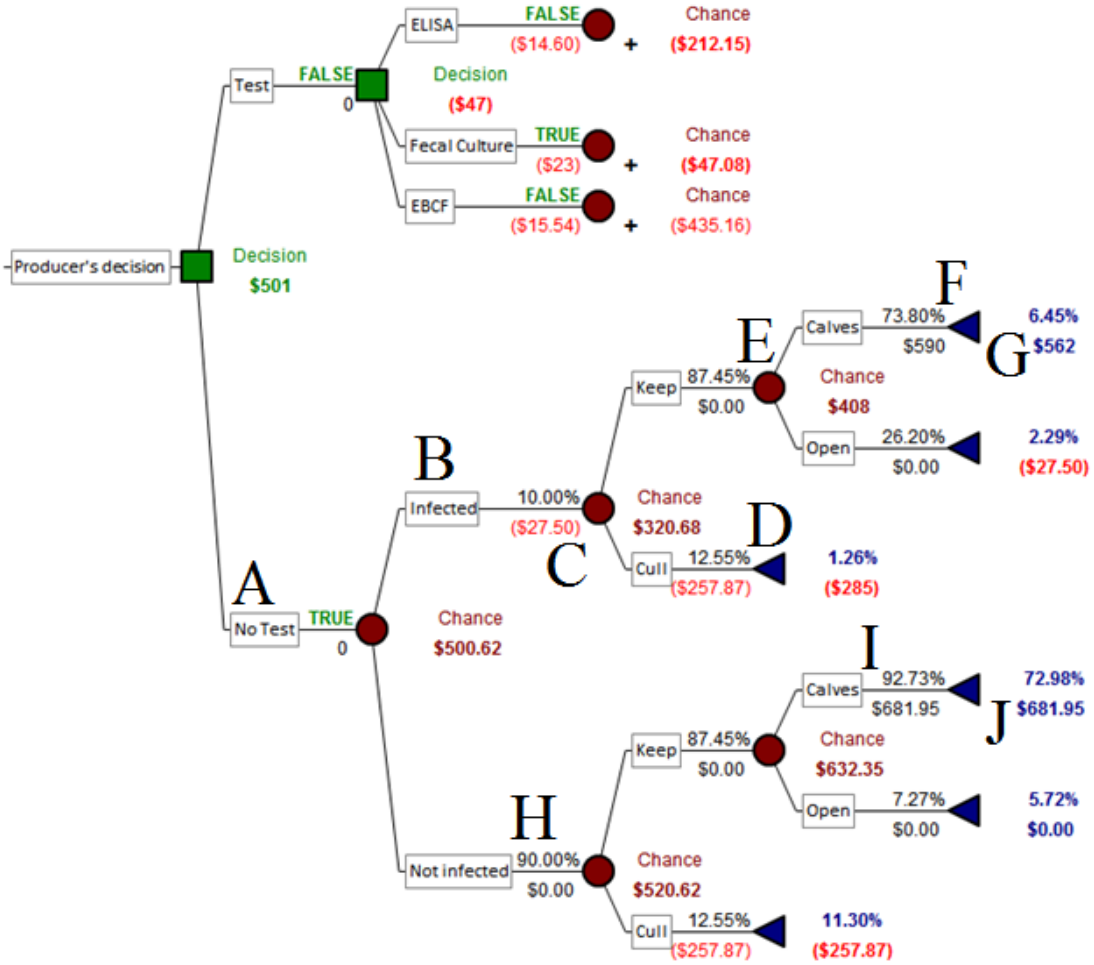
☐ I would not purchase

APPENDIX C

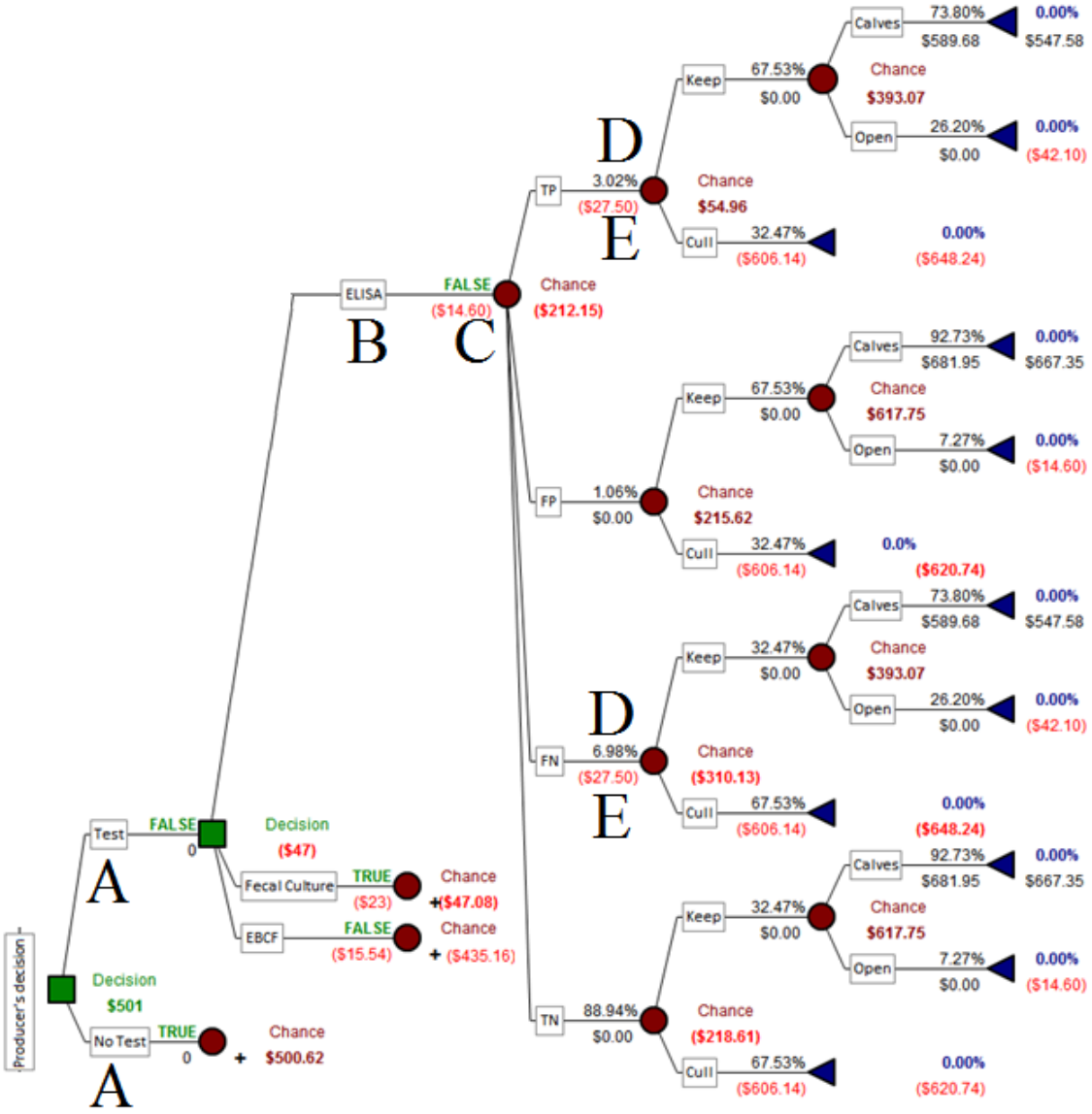
ESTIMATING THE OPTIMUM RETURN USING THE DECISION TREE MODEL



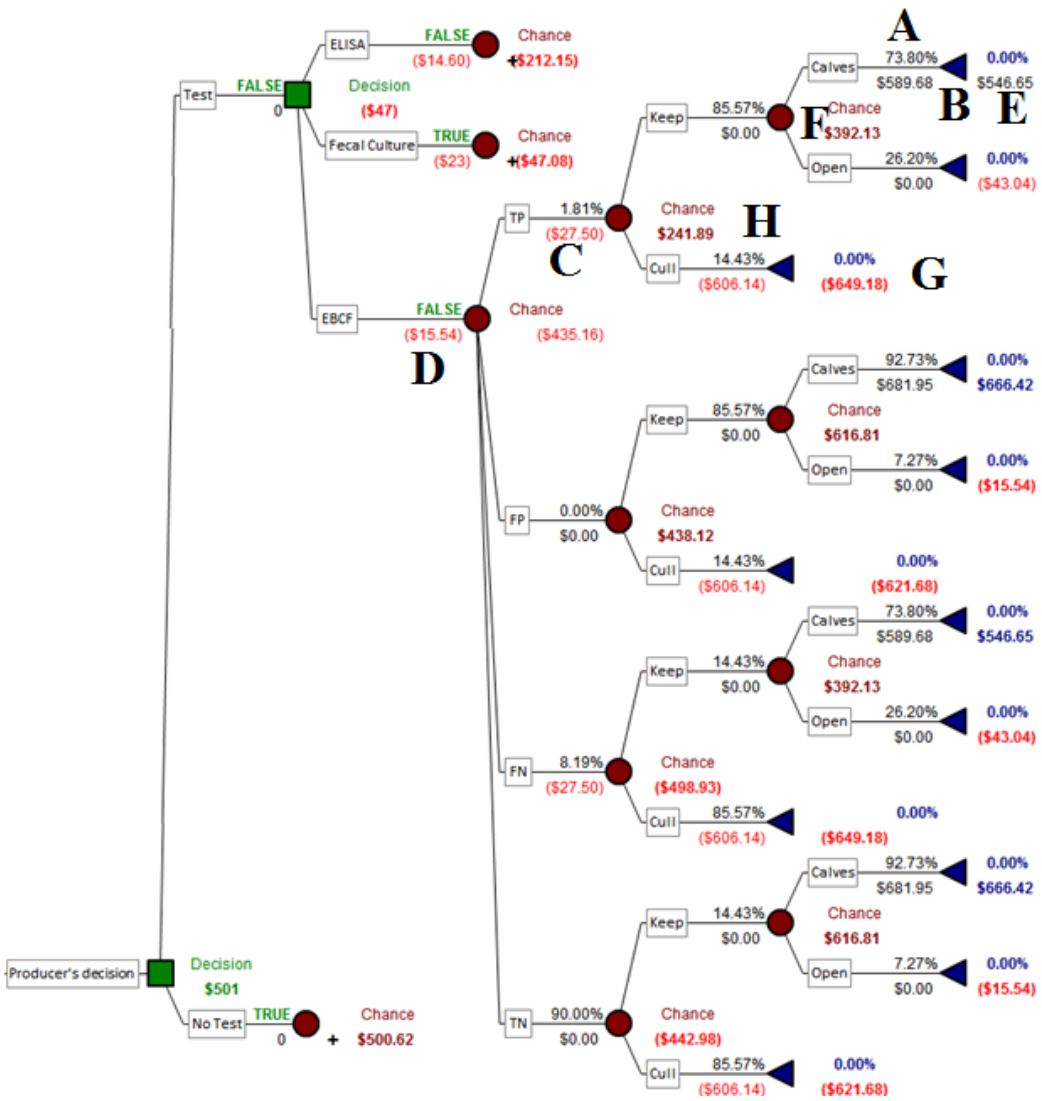
Apparent Prevalence (AP) = TP (Se + Sp – 1) +1– Sp, where Se = sensitivity and Sp = specificity.
True positive (TP) = Se. True prevalence
False positive (FP) = AP – TP
False Negative (FN) = True Prevalence –TP
True Negative (TN) = 1-True Prevalence – FP
* Testing herds obtain replacements from low-risk herds (expensive) compared to not-testing herds who have no preference to low-risk herds
+indicates sub branches analogous to alternative decision or chance.



This figure represents the node values associated probabilities in the decision tree. For example, a producer who decided to not test the herd (A) has cows with 10% probability (B) of being infected based on the assumption of 10% herd prevalence. Having an infected cow adds $27.5 (C) additional veterinary expense per year. At an annual culling rate of 12.55% (D), the probability of retaining an infected cow is 87.45% (E). Probability that an infected cow calves is 73.8% (F). A calf given by an infected cow provides a return of $562 (G). At the true prevalence of 10%, the probability of a cow in the herd being not infected is 90% (H). If an uninfected cow remains in the herd, it has a calving probabity of 92.73% (I), and thus provides a return of $681.95 (J) when it calves. Each cull is replaced to maintain a constant herd size and that cost was $257.87. +indicates sub branches analogous to alternative decision or chance.



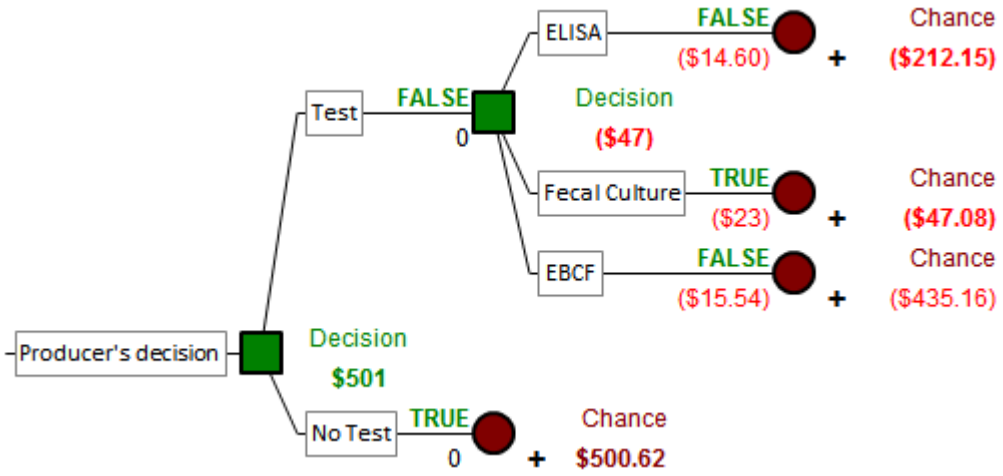
This figure shows all the branches from ELISA test decision expanded, while other options are collapsed. Starting from the base of the tree, the first decision of the producer is either to test or no test (A). For this illustration, ELISA is taken as the choice (B). The cost of ELISA test is $14.60 (C). The probabilities of a tested cow being true positive (TP), false positive (FP), false negative (FN) or true negative (TN) were estimated (D). The TP+FN make up the total infected cows or 10% in this example. An infected cow results an additional annual veterinary cost of $27.50 (E). Culling probabilities and calving probabilities were estimated as in the previous page. Apparent Prevalence (AP) = TP (Se + Sp – 1) +1– Sp, where Se = sensitivity and Sp = specificity. True positive (TP) = Se. True prevalence. False positive (FP) = AP – TP. False Negative (FN) = True Prevalence –TP. True Negative (TN) = 1-True Prevalence – FP



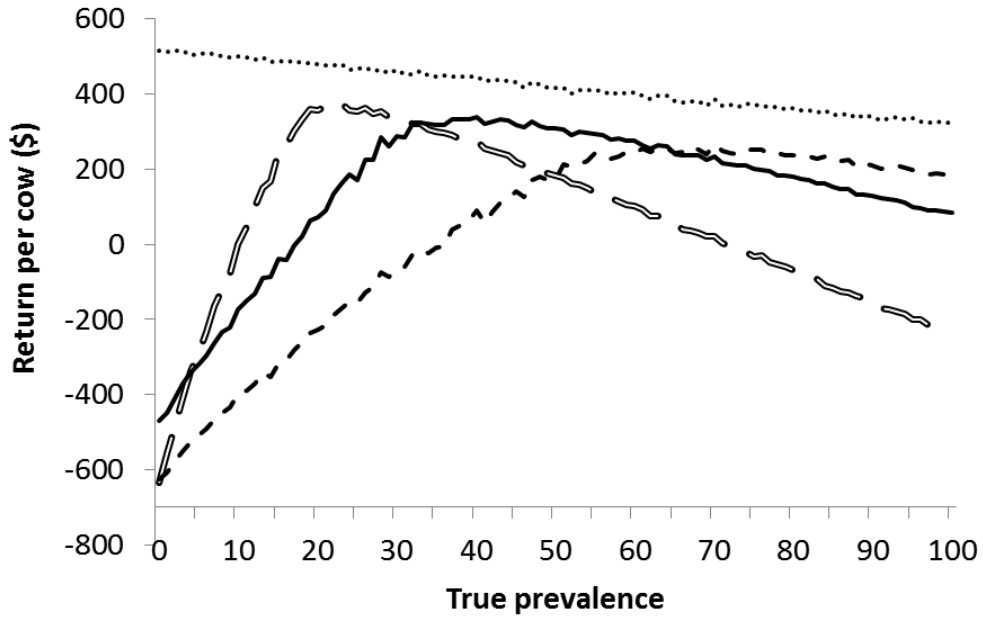
The return at each node is estimated based on the values and probabilities associated with the child branches. The software estimates these values by "averaging out and folding back." The calving probability at the topmost end node is 73.8% (A) and the probability of not calving (open) is thus 100%-73.8% 26.2%. The return from a calf given by that cow is $589.68 (B). When adjusted for the additional veterinary expense for infected cow ($27.5, C) and test cost (D, $15.54), The net return (E) can be calculated as: B-C-D= $589.68-$27.50-$15.54 = $546.65=E. Associated returns and probabilities when multiplied and added to get probability weighted average estimate the average return at that chance node as: (546.65*.738)-(26.2*0.4304) = $392.13 (F). Similarly, probability weighted average of F and G result in the value H = (14.43%)*(-649.18, G)+(87.57%)*($392.13, F)=$241.89. Further estimation in the same manner provides the value at all nodes up to the base of the tree

Annual return from a cow at specific permutation of producer's decision to test or not test, cow's infection status, test status and reproductive performance

Test	Infection	Test	Calved	Return per cow
ELISA	Infected	True positive	Calved	547.58
			Open	($42.10)
			Culled	($648.24)
		False positive	Calved	$667.35
			Open	($14.60)
			Culled	($620.74)
	Not infected	False negative	Calved	$547.58
			Open	($42.10)
			Culled	($648.24)
		True negative	Calved	$667.35
			Open	($14.60)
			Culled	($620.74)
Fecal culture	Infected	True positive	Calved	$539.18
			Open	($50.50)
			Culled	($656.64)
		False positive	Calved	$658.95
			Open	($23.00)
			Culled	($629.14)
	Not infected	False negative	Calved	$539.18
			Open	($50.50)
			Culled	($656.64)
		True negative	Calved	$658.95
			Open	($23.00)
			Culled	($1,464)
ELISA positives confirmed by fecal culture	Infected	True positive	Calved	$546.65
			Open	($43.04)
			Culled	($649.18)
		False positive	Calved	$666.42
			Open	($15.54)
			Culled	($621.68)
	Not infected	False negative	Calved	$546.65
			Open	($43.04)
			Culled	($649.18)
		True negative	Calved	$666.42
			Open	($15.54)
			Culled	($621.68)
No test	Infected		Calved	$562.00
			Open	($27.50)
			Culled	($285.00)
	Not infected		Calved	$681.95
			Open	$0.00
			Culled	($257.87)



Simplified version of decision tree with all child branches collapsed. The expected annual returns are negative for all test options with –$212, – $47 and –$435 for ELISA, fecal culture (BCF) and ELISA positives confirmed by BCF (EBCF), respectively. The decision among the test choices is fecal culture with the best return, or the lowest cost of $47 the given true prevalence of 10%. However, in the overall tree, the no-test option has a return of $501, and is the most economic decision in as shown in Figure 6 of the dissertation (reproduced below).



Copy of Figure 6: Average cow level return at different levels of prevalence based on tests for *Mycobacterium avium* subspecies *paratuberculosis* in beef cow-calf herds. Estimated based on the following options: no-test (dotted line), ELISA (solid line), bacterial culture of feces (long dash), and ELISA screening followed by bacterial culture of feces confirmation (short dash).