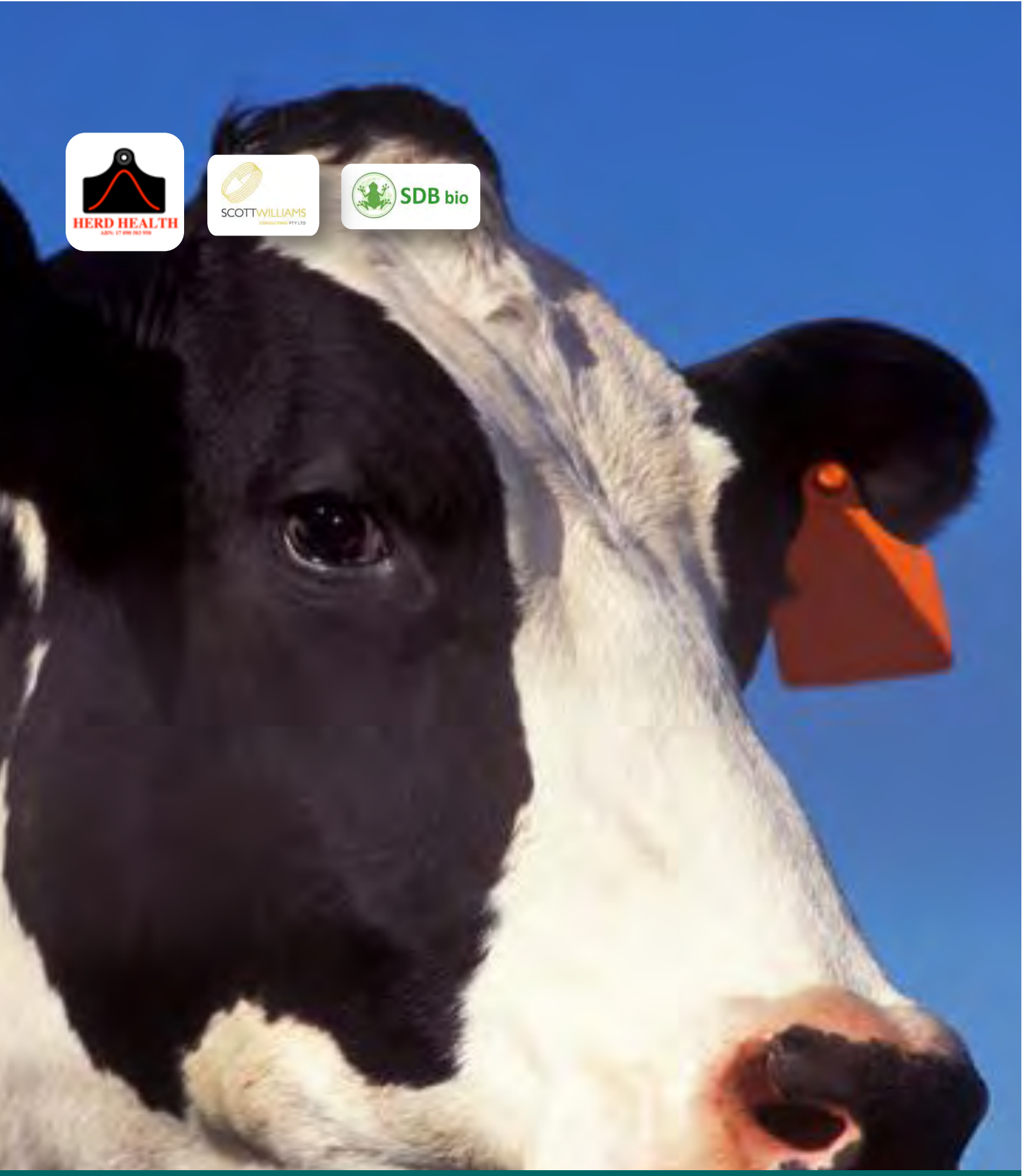

Review of On-Farm Bovine Johne's Disease Management Strategies for Victorian Cattle Herds

Project Report

October 2014

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CONTENTS

1 EXECUTIVE SUMMARY

This report presents the findings of a review of the control of bovine Johne's disease (BJD) in Victoria, with a particular focus on the Test-and-Control Program phase 3 (TCP3). The report includes the following elements:

- A comprehensive review of the literature on the epidemiology and control of BJD;
- An analysis of data from the Victorian TCP3;
- A review of the regulatory, trading and operating environment influencing BJD management, including state obligations under the national program;
- The findings from consultation with stakeholders, including producers, veterinarians, R&D managers, breeders, industry bodies and milk processors;
- A qualitative evaluation of BJD control components; and
- A detailed quantitative evaluation of a range of alternative control strategies for BJD using a purpose-built herd-level stochastic simulation model.

BJD is a complex disease that has proved difficult to control, given its long incubation period, its persistence within the environment and the generally poor accuracy of ante-mortem tests. TCP3 aims to disrupt the spread of infection from cow to calf by requiring a range of calf management practices, including removal of the calf from the cow within 12 hours of birth. This keeps calves from key sources of infection, such as the faeces of adults. All animals over the age of 4 years in the herd are tested every 2 years and any test-positive animals ('reactors') are culled. Herds 'graduate' from the program after a defined number of successive years without reactors or clinical cases.

Unfortunately, features of the disease and of the program itself serve to frustrate the aims of TCP3. The ELISA test has a very low sensitivity, so not all infected animals are detected. Infected animals shed bacteria for prolonged periods before testing positive to blood tests or showing clinical signs. Calves are exposed to adult faeces during the first 12 hours as they suck to gain colostrum, and the milk provided to calves may be sourced from unidentified shedding adults. Calves that pick up the organism can become transient shedders and spread this infection to other calves in their cohorts.

Since TCP3 commenced, only four herds have graduated to Tested to MAP Standard (TMS) status under the National Johne's Program BJD Standard Definitions, Rules and Guidelines (SDRGs) and only 10 participating TCP2 herds attained TMS status between 2000 and 2010. Twenty infected herds have withdrawn from TCP3 and continue to operate. The proportion of herds that have achieved at least one negative herd test (RD1 or RD2 status) has decreased, and the proportion of herds with a confirmed low herd prevalence (TLP) of reactors has increased slightly during TCP3 compared to TCP1 and TCP2.

Participation rates in TCP3 have declined dramatically since its introduction in late 2010. A total of 335 herds were enrolled in TCP3 (with only 237 possessing an up-to-date status) as at December 2013. This is less than 8% of all Victorian dairy herds and only 16% of the 2,000 infected herds estimated to be present in Victoria.

The figures show that TCP3 is not producing the desired objectives of reducing the spread of

BJD between farms. Too few infected farms are participating in, and too few participating farms graduate from, TCP3. The vast majority of participating herds do not eradicate disease or graduate from the program.

However, there is strong evidence that TCP3 has reduced the number of reactors and the prevalence of clinical disease in most participating herds. Experience in Australia and overseas has shown that if left unchecked, the prevalence of infected animals and the severity of disease will continue to rise within affected herds. The long-term prevalence of clinical disease in infected dairy herds not participating in TCP3 is predicted to average 2.5% whilst for herds participating in TCP3 the prevalence is predicted to be approximately 1.0%, as TCP1 is predicted to reduce clinical disease prevalence to 0.3% per annum. Most infected beef herds have a clinical disease prevalence of around 0.5% when first identified, and this rapidly reduces to a 0.25% (or less) in herds that participate in TCP3.

Economic modelling suggests that over the long term, TCP3 dairy participants can expect to gain approximately $1,450 per annum by participating in the program, while the benefit per farm net of Cattle Compensation Fund (CCF) and Department of Environment and Primary Industries (DEPI) costs is only $190 per annum. Corresponding figures for beef enterprises are $160 and -$890 per annum respectively. The benefit to dairy seed-stock breeders is similar to that of commercial producers. Beef cattle studs incur huge losses from a diagnosis of BJD infection and TCP3 has very little impact on these losses because it does not ameliorate the massive cut in trading income. Benefits for participants were greater for dairy farmers under TCP1 – a dairy farm would on average reduce BJD losses by $12,300 per annum and the benefit per farm after accounting for program costs would be approximately $10,600 per annum. Paradoxically, a beef farmer under TCP1 would experience slightly greater losses of $835 per annum, increasing to $1,400 per annum when the administrative costs of the program are included.

Stakeholders expressed varied opinions on the performance and future of TCP3. Consultations indicated that:

- The benefits of TCP have not been well communicated.
- Participants are realistic about the constraints of the program, but there is some frustration at not being able to graduate from it. False-positive reactions to the ELISA test, leading to expensive culling of apparently healthy animals, cause considerable angst.
- It is likely that complete cessation of TCP, without replacement by another, comparable (subsidised) program, would be met with widespread dissatisfaction. Regular testing would be largely abandoned.
- Program termination may also present a significant risk to future dairy disease control programs. DEPI and other authorities could lose credibility.
- There is widespread uncertainty over the value of vaccination, which is unsurprising given the lack of information that has been made available in Australia and globally. Views on vaccination are generally not extreme, but range from quite oppositional to quite supportive. The cautious introduction of vaccination, supported by evidence of likely benefit and appropriate 'fit' into existing frameworks (for example, declarations), should be reasonably well accepted.

The literature review and stakeholder feedback formed the basis of a qualitative evaluation of a range of possible elements of a future BJD control program. These elements included the use of new testing technologies such as the high-throughput PCR (HT-J-PCR) or herd environmental culture (HEC) tests, a return to the TCP1 testing regime, the use of calf milk replacer and the Silirum® vaccine.

This qualitative evaluation was then extended to a structured series of scenario analyses using a purpose-built herd-based stochastic simulation model. Each scenario represented a credible approach to the management of infected dairy herds. Outputs included changes over time in the prevalence of infection within the modelled herd, as well as the economic impact of the strategy at the farm and state level. Models offer advantages and disadvantages when used in this context. The major concern is that the model accurately predicts the outcomes from a given set of starting conditions (the scenarios). In this case, confidence in the model output of the model was gained from the close match between the predicted results of the TCP1 control scenario and the observed performance of TCP1, as well as the consistency of the modelled reproductive dynamics and the 2011 InCalf analysis of Dairy Australia.

The modelling showed that:

- The move from TCP1 to TCP3 has significantly reduced the disease control and economic outcomes (which could already be seen in the test data). The economic benefit for participating farmers was significantly reduced and the benefit for farmer participation in TCP3 was negligible over the longer term. When the costs of product administration and delivery were included, gains from participation were offset by the cost of the program to DEPI and CCF.
- Biosecurity alone (the Three-Step Calf Program without test-and-cull) would be essentially ineffective at reducing disease and product contamination and uneconomical for participating farmers. The absence of individual animal diagnostic tests with sufficient sensitivity also means there would be no way of assuring freedom from disease in replacement stock, including bulls.
- Vaccination may offer improved control over disease in infected herds but it is difficult to be definitive about Silirum® until the results of Australian dairy trials have been analysed and reported. Switching from test-and-cull to the vaccination of replacement calves is likely to at least provide for an equivalent level of disease control as TCP3 in the short-to-medium term. The effects of vaccination are likely to compound over time, although without concurrent test-and-cull, a number of generations would be required to break the in-utero transmission pathway and to reduce the prevalence of disease in the herd.
- Vaccination in combination with the TCP1 approach – but where the ELISA individual animal test is replaced with the HT-J-PCR test – would offer the highest level of disease control with a significant proportion of participating dairy farms expected to graduate from a combined TCP and vaccination program within 10 years. The cost of participation in a vaccination and TCP1 combined program would be higher than for other controls.

The choice for the future for BJD control in Victoria depends very much on the objectives of the key participants and on the availability of funds. The continuation of TCP3 is not supported under any argument – effectiveness, economics or current acceptance. If the

desire is to reduce the impact of BJD on the profitability of infected herds then disease control options may be employed. The effective options include a reversion to TCP1 or vaccination, or a combination of both.

Either TCP1 or vaccination alone is likely to minimise the economic impact of disease on participating dairy farms, prevent an increase in product contamination (milk and meat), and to be seen by trading partners as a reasoned approach to the control of disease. However, adopting one of these approaches alone is unlikely to reduce the prevalence of infected farms or to eradicate the disease on participating farms.

If a progressive BJD program is desired for which a high proportion of participating farms can successfully graduate within 10 years, then a combination of vaccination and TCP1 is the only real option. The majority of participating farms can be expected to graduate and leave the program within 10 years of deployment. For some producers (cattle studs in particular) the ability to graduate from a program and return to an operational and trading environment that existed before the diagnosis of disease in the herd may be the overarching priority. A program that combines TCP1 with vaccination is the strategy most likely to deliver this outcome for farmers. Changes to the SDRGs would, however, be required to allow individual animal testing of vaccinated animals. In particular, the HT-J-PCR (or similar) would need to replace the individual animal ELISA test in vaccinating herds. One alternative is to use a staged transition from TCP1 to vaccination that avoids any individual animal ELISA testing of vaccinates. The risk of re-introduction of disease into graduated herds would be significant – especially in regions with high herd prevalence – and all graduating herds should employ effective and vigilant biosecurity measures and consider regular HEC testing to promptly identify any re-introduction of disease.

The return on investment is likely to be greater for TCP1 on its own than for the combined TCP1 and vaccination program, assuming that vaccine use and administration is fully subsidised. This is because the marginal benefit from removing any of the few remaining diseased animals from the herd will likely be less than the cost of the program – TCP1 alone cost-effectively reduces the prevalence of disease in participating herds to a low level.

The conclusion of this study is that the ongoing management of BJD in Victoria might follow one of four possible pathways, depending on funds available:

1. Abandon the Victorian BJD control program (currently TCP3) and effectively deregulate the control of BJD, understanding that disease prevalence, incidence and economic impact will increase under this approach, and that there may be negative implications for future disease control programs as some current participants will feel abandoned;
2. Return to TCP1, understanding that a greater recruitment of infected farms will be necessary for real benefit to accrue at the state level;
3. Provide for subsidised vaccination, understanding that at least 10 years will be required for farms that have not undergone a test-and-cull prelude to vaccination to accrue observable benefit; or
4. Adopt TCP1 and vaccination, understanding that this will evoke the highest standard of control, benefit to producers but also the highest program cost. A staged conversion from TCP1 to vaccination may provide for fast, cost effective control whilst not compromising program graduation rates greatly compared to concurrent application of

both control arms.

Another growing concern acknowledged by this review is the increasing number of detections of ovine-strain Mptb in beef herds. Ovine-strain infection, whether associated with clinical disease or not, does not cause an animal or herd to be classified as 'Infected' with BJD (or ovine JD for that matter) under the SDRGs, but there is emerging evidence from Australia and New Zealand that ovine-strain Mptb infection may be more sustainable in cattle than previously thought. The definition of 'Beef Only' may need to be reconsidered and expanded under the SRDGs to recognise that cattle co-grazing with sheep may in some circumstances present a risk of JD infection to other cattle.

This review recommends that DEPI maintain a watching brief on the prevalence of ovine-strain infections in beef cattle herds and make appropriate representations to the national program should Victoria determine that this strain presents an unacceptable risk to the broader cattle population.

2 LITERATURE REVIEW: EPIDEMIOLOGY, DETECTION AND CONTROL OF BJD

2.1 Epidemiology of BJD

2.1.1 Introduction

Johne's disease, or paratuberculosis, is a chronic enteropathy of ruminants caused by *Mycobacterium avium subsp paratuberculosis* (Mptb). Distinct strains of Mptb are isolated in Australia from different ruminant species – and within species – but there is a strong pattern of sheep being infected with sheep strains and other species being infected with cattle strains (Whittington and Sergeant, 2001).

Bovine Johne's disease (BJD) was first detected in Victoria in 1925 and is now endemic in Victoria, New South Wales, South Australia and Tasmania (VIC DEPI, 2013). In Victoria, approximately 25% of dairy herds are known to be infected (1,017 herds in May, 2013) and another 25% are suspected of being infected. This is likely to be an under-estimate of the prevalence of BJD infected herds, given the insidious and chronic nature of the disease, and the likelihood of under-reporting. In contrast to the dairy sector, there are very few beef herds in Victoria known to be infected (VIC DEPI, 2013). In November 2012, Biosecurity Queensland confirmed that BJD was present in a Queensland stud beef cattle herd and identified 170 properties that had received cattle from the stud that would require investigation. This work is ongoing (QLD DAFF, 2014).

Bovine Johne's disease is a complex disease to manage in dairy and beef cattle herds as it has a generally long incubation period and the organism can survive for extended periods in the environment (Whittington *et al.*, 2004). Diagnostic tests are of a low sensitivity at most stages of the disease (Whittington and Sergeant, 2001) and within-herd prevalence is generally low (Craven, 2000). Collectively this means that managers do not often know precisely how or when infection entered a herd, or the key transmission events that occurred or continue to operate in the herd. Testing all animals and culling reactors can reduce the number of clinical cases (generally older animals) but may not identify many of the latently-infected and subclinically-infected animals. These may continue to contaminate the herd environment through infectious faeces or transmit the disease vertically to their offspring. Vaccination may reduce the susceptibility of young animals and the infectiousness of those that have the disease but have not been identified. Vaccination may also reduce the extent to which an environment is contaminated with viable bacteria in faecal matter or on pasture, and suppress clinical expression of the disease. Conversely, vaccination will cloud the interpretation of serological tests and may lead to a 'silent' increase in the prevalence of subclinically-affected animals within the herd.

These effects and others are well suited to analysis through computer modelling. Modelling studies are either mathematical, or based on the simulation of individual animals within a herd and the contact structures that would typically lead to exposure events. Individual-based models are in general more complex than mathematical models and require more parameters. However, they also allow researchers to examine more specific hypotheses

about the transmission or persistence of a disease within a closed system and more specific measures for its control.

The intent of this review was to provide the technical underpinning for the parameterisation of an individual-based simulation model based on the spread of BJD within Australian dairy herds. With this as the objective, the BJD modelling studies that have been undertaken to date were identified from the literature. These studies are listed below. The review placed greater emphasis on the more contemporary works of Lu *et al.* (2008, 2010, 2013a and 2013b), Marce *et al.* (2011) and Weber and Groenendaal (2012). The series of Lu *et al.* studies introduced a stochastic element, but otherwise built on the earlier modelling work of Mitchell *et al.* (2008). This paper was also consulted heavily. Whereas most of the models were mathematical, Kudahl *et al.* (2007) undertook their study using an individual-based simulation and this was examined closely. A systematic review of BJD modelling studies was undertaken by Marce *et al.* in 2010 and provided some useful grounding and analysis.

Collins and Morgan (1991)	*Simulation model of paratuberculosis control in a dairy herd*
Groenendaal *et al.* (2002)	*A simulation model of Johne's disease control*
van Roermund *et al.* (2002)	*Within-herd transmission of paratuberculosis and the possible role of infectious calves*
Groenendaal *et al.* (2003)	*Development of the Dutch Johne's disease control program supported by a simulation model*
Kalis *et al.* (2004)	*Certification of herds as free of* Mycobacterium paratuberculosis *infection: actual pooled faecal results versus certification model predictions*
Pouillot *et al.* (2004)	*A deterministic and stochastic simulation model for intra-herd paratuberculosis transmission*
Weber *et al.* (2004)	*Simulation of alternatives for the Dutch Johne's disease certification-and-monitoring program*
Ezanno *et al.* (2005)	*A modeling study on the sustainability of a certification-and-monitoring program for paratuberculosis in cattle*
Humphrey *et al.* (2006)	*A model of the relationship between the epidemiology of Johne's disease and the environment in suckler-beef herds*
Kudahl *et al.* (2007)	*A stochastic model simulating paratuberculosis in a dairy herd*
Mitchell *et al.* (2008)	*Simulation modeling to evaluate the persistence of* Mycobacterium avium subsp. paratuberculosis *(Mptb) on commercial dairy farms in the United States*
Lu *et al.* (2008)	*The importance of culling in Johne's disease control*
Weber *et al.* (2008)	*Milk quality assurance for paratuberculosis: simulation of within-herd infection dynamics and economics*
Lu *et al.* (2010)	*Stochastic simulations of a multi-group compartmental model*

	for Johne's disease on US dairy herds with test-based culling intervention
Marce *et al.* (2011)	*Predicting fadeout versus persistence of paratuberculosis in a dairy cattle herd for management and control purposes: a modelling study*
Weber and Groenendaal (2012)	*Effects of infectious young stock on results of certification, surveillance and control programmes for paratuberculosis in dairy herds*
Lu *et al.* (2013a)	*Impact of imperfect* Mycobacterium avium subsp. Paratuberculosis *vaccines in dairy herds: A mathematical modeling approach*
Lu *et al.* (2013b)	*Using vaccination to prevent the invasion of* Mycobacterium avium subsp. paratuberculosis *in dairy herds: A stochastic simulation study*

2.1.2 Pathogenesis and Disease States

Detailed discussions of the pathogenesis of BJD are given by Craven (2000), Whittington and Sergeant (2001), Crossley *et al.* (2005), van Roermund *et al.* (2007) and many other researchers and reviewers. To a variable extent, the discussions identify discrete disease states and correlate these with morphological changes in the intestine of affected animals, their immune responses and the extent to which the organism is likely to be shed in the faeces, milk or uterine fluids. Regardless of the modelling paradigm (mathematical or individual-based simulation), the computer models for the within-herd spread of BJD identified above were based on the characteristics of these delineated disease states and the transition of animals between them. For this reason, they are often termed 'state-transition' models. Marce *et al.* (2010) reviewed this aspect of BJD modelling in some depth, identifying and discussing the ramifications of the different state-transition schema and parameters that had been applied in the modelling literature.

A brief synopsis of each step in the disease process is given below. This includes references from the science literature and a brief account of how each step was approached in the key contemporary modelling papers. Following this is a discussion of our preferred disease state-transition framework (Figure 1).

Infection, passive and active transient shedding, and latency: following ingestion, Mptb passes close to the intestinal mucosa, attaches, evades dislodgement, resists innate defences in the mucosal barrier and penetrates the mucosa and M-cells overlying Peyer's patches. The organism is taken up by macrophages and acquires nutrients for growth and replication. It then replicates and disseminates in macrophages before localising in Peyer's patches within the intestinal lamina propria. At this stage, focal paucibacillary lesions become visible and cultures of tissues may be positive. The organism either succumbs to or resists the host's cell-mediated immunity and tests based on cell-mediated immunity (CMI) may be positive (Whittington and Sergeant, 2001).

This initial progression of events encompasses three separate disease states: (a) ingestion of the organism followed by passive shedding; (b) ingestion, followed by infection and then the onset of latency; and (c) ingestion and infection, followed by a period of transient active shedding and then the onset of latency. Transition from the latent state marks the commencement of subclinical faecal shedding.

Passive shedding describes the passage of Mptb through the gut of an exposed animal without multiplication. In this situation, the affected animal is simply a physical conduit for the bacteria. Passive shedding in cattle commences within 24 hours of ingestion and continues for up to a week after a single bolus dose (Whittington and Sergeant, 2001). Passive shedding is potentially significant as: (a) animals can amplify exposure in a geographic sense, re-distributing infectious material over a wider area; and (b) it can lead to the contamination of an otherwise clean environment. This applies in particular to the calf-rearing environment.

Transient active shedding was studied in the field by van Roermund *et al.* (2007), who showed that calves were infectious to other calves soon after they became infected and until approximately 6 months of age. This transient period of active shedding was known to be distinct from passive shedding as some of the affected calves continued to shed Mptb for approximately 3 months following removal of adult cows. Transmission from calf to calf occurred during this period. Infectivity declined to zero as the calves entered the silent subclinical phase. The authors remarked upon the substantial variation amongst exposed calves with respect to the pathogenesis of the disease and each animal's response to it.

Mitchell *et al.* (2008) referenced this work heavily, and appeared to be the first to include calf-to-calf transmission in computer modelling studies of BJD. In two separate experiments, these authors used a single deterministic value of either 6 or 12 months for the period of transient infection post exposure. These values were obtained from the early research of Rankin (1961) and are longer than the value obtained by van Roermund *et al.* (2007).

Animals completing a period of transient active shedding will move into the latent (or 'silent') phase of infection. At any point in time, approximately 30% of the infected cattle in an endemically infected herd are likely to be in the latent state (Whittington and Sergeant, 2001). Mitchell *et al.* (2008) used an unreferenced deterministic value of 1.5 years for the period of latency. This value was carried through to the work of Lu *et al.* (2008, 2010, 2013a and 2013b), who cited the primary research of van Schaik *et al.* (2003). Presumably the same research underpinned the Mitchell *et al.* (2008) estimate. In a separate paper evaluating the shedding of Mptb in calves, Mitchell *et al.* (2012) took a very different approach to transient infection and latency. In this paper, the authors delineated between a 'fast' latent period that follows transient active shedding, and 'slow' latency that follows directly from infection. In this model, 55% of infected animals did not develop early transient shedding but instead moved into a slow latent period. The highest risk of entry into early shedding was among the youngest animals and there was a zero risk of early shedding in adults. No other modelling teams have adopted this approach and it does not appear to have been discussed in the epidemiological research literature.

Citing van Roermund *et al.* (2007), Marce *et al.* (2011) specified an average transient state of 25 weeks, with the maximum age in this state being set by as the date of first calving. The

latent period was then an additional 52 weeks. Animals in a state of transient infection shed 10^6 × Beta(8.8,19) organisms per kg of faeces.

Based on the research of Weber *et al.* (2010), Weber and Groenendaal (2012) took a different approach to modelling the infectiousness of calves. These authors maintained that calves may be infectious, and that calf-to-calf transmission may be an important determinant in the persistence of infection within herds that employ a test-and-cull policy that includes clinically-affected animals. However, rather than include a transient period of infectiousness that precedes latency (as described above), Weber and Groenendaal (2012) appeared to suggest that some calves move directly from infection to subclinical shedding (below) and do so at an age determined by the force of infection within the herd and the age at which infection took place. This is discussed in the section below.

On balance, our preference for the Australian model was to include a period of transient active shedding, but to allow only a proportion of animals to enter this state. The Mitchell *et al.* (2012) estimate of 45% was chosen for this proportion. The length of the period of transient active shedding will be allowed to vary uniformly between 6 and 12 months. The ensuing latent period will not differ for animals that experienced transient active shedding. This period will have a minimum of 9 months, a most likely value of 12 months and a maximum of 18 months. A triangular distribution will be used to model this variation.

Subclinical shedding: in this phase, extensive multibacillary (or paucibacillary) lesions develop and Mptb is shed from the intestinal mucosa. This occurs in conjunction with the mounting of a humoral immune response (to which antibody tests may be positive) and the decline of CMI (Whittington and Sergeant, 2001). Marce *et al.* (2010) noted that most of the modelling studies they reviewed had divided the period of subclinical shedding into: (a) low shedding; and (b) high shedding. This group of studies included Kudahl *et al.* (2007), Groenendaal *et al.* (2002), Humphry *et al.* (2006), and van Roermund *et al.* (2002, 2005). Importantly, these authors also included a transition from high subclinical shedding to clinical disease. In contrast, Mitchell *et al.* (2008), and subsequently Lu *et al.* (2008, 2010, 2013a and 2013b), used a model that delineated between high and low shedding, but included clinically-affected animals within the high-shedding category.

The division of subclinically-affected animals into grades of shedding was examined by Crossley *et al.* (2005) in an analysis of 93 Pennsylvania dairies. These authors in fact observed three distinct groups of subclinically-infected faecal shedders. Most cows were light (<10 cfu[1]/tube[2], 51.4%) or high (>50 cfu/tube, 30.8%) faecal shedders with fewer cows in the moderate group (10-50 cfu/tube, 17.8%). Crossley *et al.* (2005) did not, however, draw conclusions as to whether individual animals moved from one group to another with the progression of the disease. Based on estimated infectious doses of about 10^3 bacilli, and estimates of the number of viable bacilli present in the faeces of a clinical case, 10^6 to 10^8/g,

[1] Colony-forming units

[2] One tube holds approximately 0.16g faeces (van Roermund *et al.*, 2007)

a small amount of faecal contamination is sufficient for infection of a large number of susceptible animals (Whittington and Sergeant, 2001).

Mitchell *et al.* (2008), and subsequently Lu *et al.* (2008, 2010, 2013a and 2013b), considered the entire subclinical phase to occupy a mean of approximately 3 years. Kudahl *et al.* (2007) maintained that low shedders are most likely to become high shedders around their second and third calving, and that high shedders are most likely to become clinically affected around third and fourth calving. Each of these estimates (Mitchell *et al.*, 2008; Lu *et al.* 2010, 2013a and 2013b; and Kudahl *et al.*, 2007) aligns approximately with Whittington and Sergeant (2001) who stated that most clinical cases in cattle occur in 2- to 4-year-old animals. Of note however, is the extremely long tail to the distribution of the overall incubation period which, assuming infection of neonates, can be up to 14 years.

Marce *et al.* (2011) describe a single subclinical state, where animals are infectious but not clinically affected. This state persists for 104 weeks on average. Within any given time step (1 week), subclinically-affected animals will shed Mptb in milk or colostrum with a probability of 0.4 and at a rate of 10^5 × Beta(8,8) bacteria per litre. Mptb will be shed in faeces at a rate of 10^6 × Beta(8.8,19) bacteria per kg. Rather than include a transient period of infectiousness that precedes latency (as described above), Weber and Groenendaal (2012) appeared to suggest that some calves move directly from infection to highly-infectious subclinical shedding (below) and do so at an age determined by the force of infection within the herd and the age at which infection took place. Weber *et al.* (2010) had found that in herds with an apparent prevalence of <0.05, 0.05-0.1, 0.1-0.2 and ≥0.2, the proportion (95% CI) of cattle with onset of faecal shedding before 2 years of age was estimated at 1% (0.5%; 2%), 4% (3%; 5%), 8% (5%; 10%) and 20% (11%; 32%), respectively. Extrapolating from this, the age at onset of highly-infectious subclinical shedding was parameterised in four ways by Weber and Groenendaal (2012), as shown in Table 1. Each of the distribution-sets (Tr1, Tr2, Wb1 or Wb2) was then examined using sensitivity analysis. Weibull distributions Wb1 and Wb2 were obtained from survival analyses of the age at onset of faecal culture positivity in herds with an apparent prevalence (AP) based on individual faecal culture of AP <0.05 and AP >= 0.20, respectively. It was not clear from the paper whether the authors maintained a preference for one or more of the approaches although differences were observed in the model output. Onset of the lowly infectious period was 2 years before onset of the highly infectious period.

Table 1: Age of onset of high-infectious subclinical state

Age and Route of Infection	Age at Onset of Subclinical Highly Infectious State			
	Tr1	Tr2	Wb1	Wb2
Congenital	Triang (1.5, 2.5, 20)	Triang (0, 2.5, 20)	2 + Weibull (2, 6)	2 + Weibull (0.75, 12)
At birth	Triang (2, 3.5, 20)	Triang (0.5, 3.5, 20)	2 + Weibull (2, 6)	2 + Weibull (0.75, 12)
0-6 months	Triang (2, 4, 20)	Triang (1, 4, 20)	2 + Weibull (2, 6)	2 + Weibull (0.75, 12)
6-12 months	Triang (4, 6, 20)	Triang (1.5, 6, 20)	2 + Weibull (2, 6)	2 + Weibull (0.75, 12)

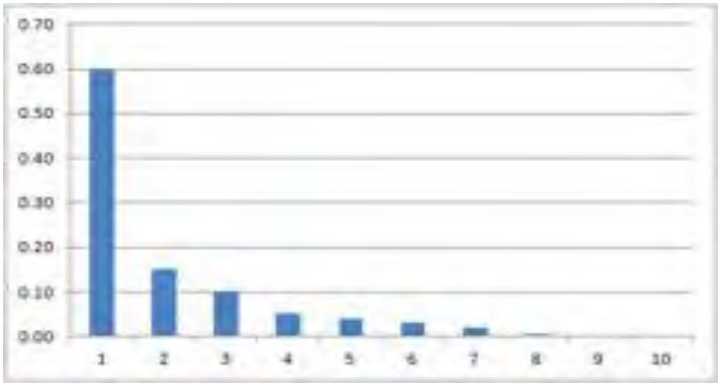
Source: adapted from Weber and Groenendaal (2012)

Jubb and Galvin (2004a) found that the average age of onset for sero-reactors amongst Victorian dairy cattle was 5.7 years, and for clinical disease was 5.9 years. This information will assist validation of the combined effects of each infection stage on disease expression and detection.

On balance, our preference for the Australian model was include two separate steps within a single period of subclinical disease. The first is a low-shedding phase and the second is a high-shedding phase. The transition from one phase to the next will occur midway through each animal's period of subclinical illness. The phases will correlate with the infectiousness of the faeces and milk from subclinically-infected animals, as discussed in Section 2.1.3.

For simplicity, the subclinical period for each individual will be drawn from the discrete distribution shown below.

Subclinical Period in Years	Probability
1	60%
2	15%
3	10%
4	5%
5	4%
6	3%
7	2%
8	0.5%
9	0.25%
10	0.25%



Clinical disease: this occurs as a result of the progressive extension and exacerbation of multibacillary lesions, and the impact of this on the function of the gastro-intestinal tract. These animals typically lose weight, have diarrhoea that is not responsive to antibiotic treatment, and are almost always culture and antibody positive (Crossley *et al.*, 2005). Many clinically-affected animals are culled as a result of their persistent symptoms or depressed performance. This will often take place in the absence of a definitive diagnosis (Crossley *et al.*, 2005). Kudahl *et al.* (2007) suggested that the ability of a farmer to detect and identify a

clinical case of BJD to be approximately 80%. During the clinical stage of pathogenesis, massive numbers of bacteria are excreted in the faeces. Most animals that are not culled will die as a result of the clinical effects of the disease (Marce *et al.*, 2010).

Because intervention generally takes place, models have not tended to parameterise a period for clinical illness directly. Rather, they include a rate of culling due to clinical BJD that is superimposed upon the baseline rate of culling (based on production or disease) for the herds under study. Mitchell *et al.* (2008), and subsequently Lu *et al.* (2008, 2010, 2013a and 2013b), used an additional culling rate of 0.7 per year for animals with clinical symptoms of BJD. Pouillot *et al.* (2004) believed that animals would on average be culled within 1 year. Groenendaal *et al.* (2002) placed an upper limit of 3 months for animals with clinical disease. Kudahl *et al.* (2007) found that high subclinical shedders were most likely to become clinically affected around third and fourth calving. This was result of their simulations, and not a parameter. These authors did, however, include a 50% risk of culling/death for animals that had remained in a clinical state for 3 months or more.

Marce *et al.* (2011) allowed clinically-affected animals to remain in the herd for 26 weeks on average before culling. During this time, Mptb was shed consistently in faeces and in the milk of 90% of animals (at any given time step). Weber and Groenendaal (2012) did not appear to provide any detail as to how they parameterised the period of clinical disease.

On balance, our preference for the Australian model was to specify a minimum clinical period of 1 month and a maximum of 6 months, with a most likely value of 3 months. In our estimation, it is extremely unlikely that clinically-affected animals would remain in a commercial herd for more than 6 months, and that most would be culled within approximately 3 months. Clinical disease is often precipitated by a stressful event with calving and the onset of lactation a common trigger. Weight loss, diarrhoea and reduced milk production in clinical animals are usually readily identified by farmers. The clinical period for individual animals will be drawn from a triangular distribution with these parameters.

Recovery and resistance: unlike many other infectious diseases, recovery from BJD is not generally considered to be a genuine possibility (Marce *et al.*, 2011). Whittington and Sergeant (2001) discuss isolated accounts where Mtpb may have been cleared from infected cattle or sheep, but were guarded about the delineation between the suppression of proliferating infection and true recovery. None of the models we reviewed included a 'recovered' state.

Most other state-transition schema did, however, allow for a 'resistant' state. This state was absolute, with no probability of infection, and was in general assigned to heifers and adult cattle. In the models reviewed by Marce *et al.*, (2010), susceptibility was age-based with a maximum age of infection at 0.5 years (van Roermund *et al.*, 2002) or at 1 year (Collins and Morgan, 1991; Groenendaal *et al.*, 2002; Pouillot *et al.*, 2004; van Roermund *et al.*, 2005; Humphry *et al.*, 2006; Kudahl *et al.*, 2007; Mitchell *et al.*, 2008). The same cut-point was used by Lu *et al.* (2008, 2010, 2013a and 2013b), Marce *et al.* (2011) and Weber and Groenendaal (2012). Mitchell *et al.* (2008), Lu *et al.* (2008, 2010, 2013a and 2013b), Marce *et al.* (2011) and Weber and Groenendaal (2012) specified a gradient in susceptibility such that this was highest at a week of age and decreased exponentially until 1 year of age. The

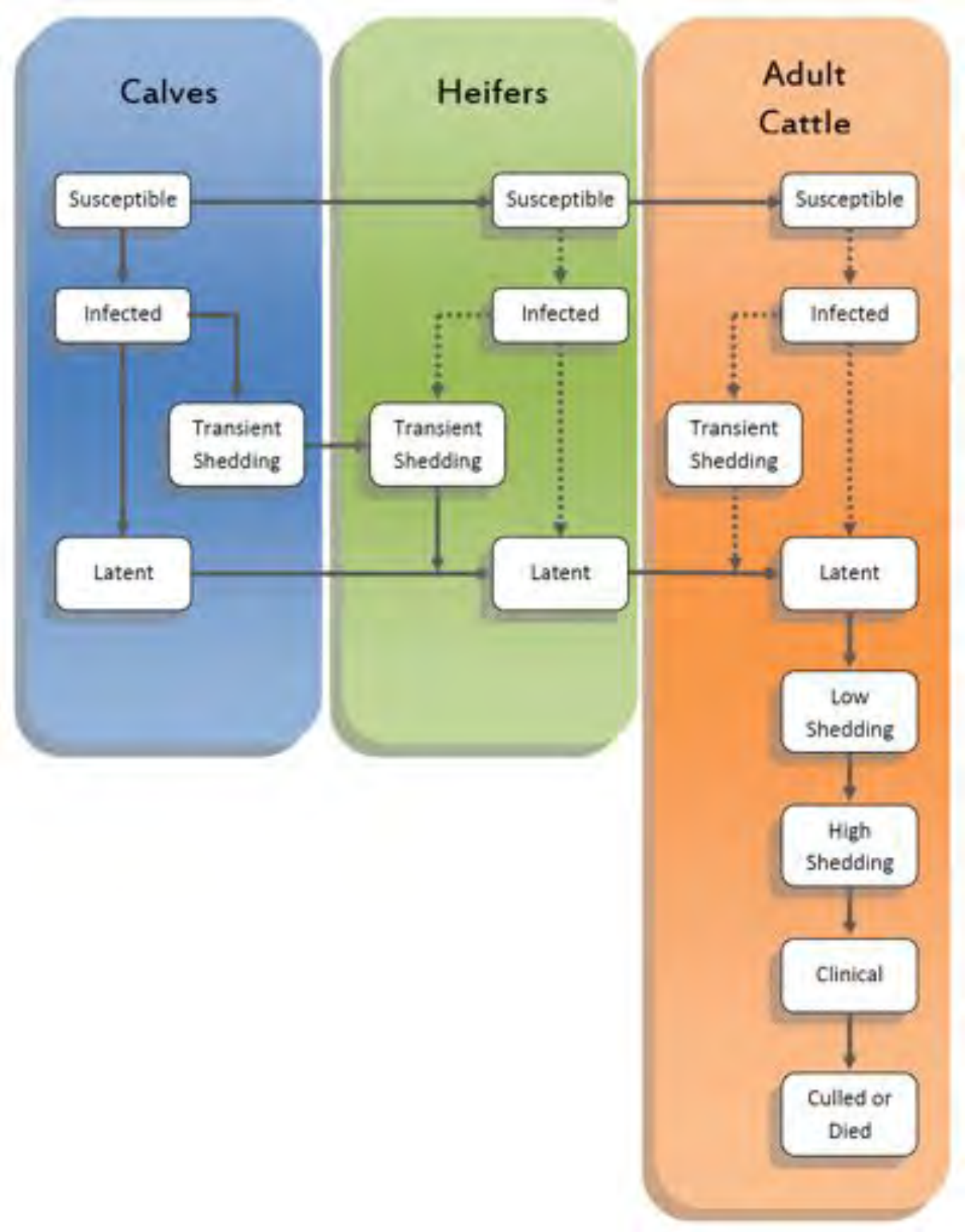
various papers cited different coefficients and formulae, but these are likely to reflect differences in time step and parameterisation rather than differences in the character of exponential decline in susceptibility.

Our preference for the Australian model was to allow all ages of animals within the herd to be equally susceptible. Importantly, this includes calves, growing heifers and adult cattle. The detail within the transmission pathways then allowed age-based opportunities for exposure to place calves at far greater risk than either heifers or adult cattle. These opportunities include suckling from infected mothers, consuming pooled milk and coexisting in a confined space with (potentially) other calves that may be excreting Mptb either passively or actively. By contrast, heifers and adult cattle will only be exposed to environmental contamination. Heifers and adult cattle will also have shorter life spans and, thus, decreased opportunity to develop the disease. One of the advantages of simulation modelling is that the number and proportion of undetected infected animals can be analysed and output by the model. In this way, it will be useful to understand whether a significant number of older animals may become infected, but not remain in the herd long enough to complete their latent period and period of low subclinical shedding. No animals are considered to be 'resistant' in an absolute sense.

Preferred state-transmission framework: based on the discussions above, the preferred state-transition framework is shown in Figure 1. This framework shares many common elements with the existing published modelling studies we identified for the review, but also has some differences.

The framework includes transient active shedding, as well as a direct pathway from infection to latency. There are also both low and high shedding states, with the former leading to the latter and preceding the onset of clinical symptoms. Animals will enter a period of transient active shedding probabilistically, with some moving directly from infection to latency. As noted above, the framework allows all animals within a herd to be susceptible. Importantly, this includes growing heifers and adult cattle.

Figure 1: Preferred state-transition framework



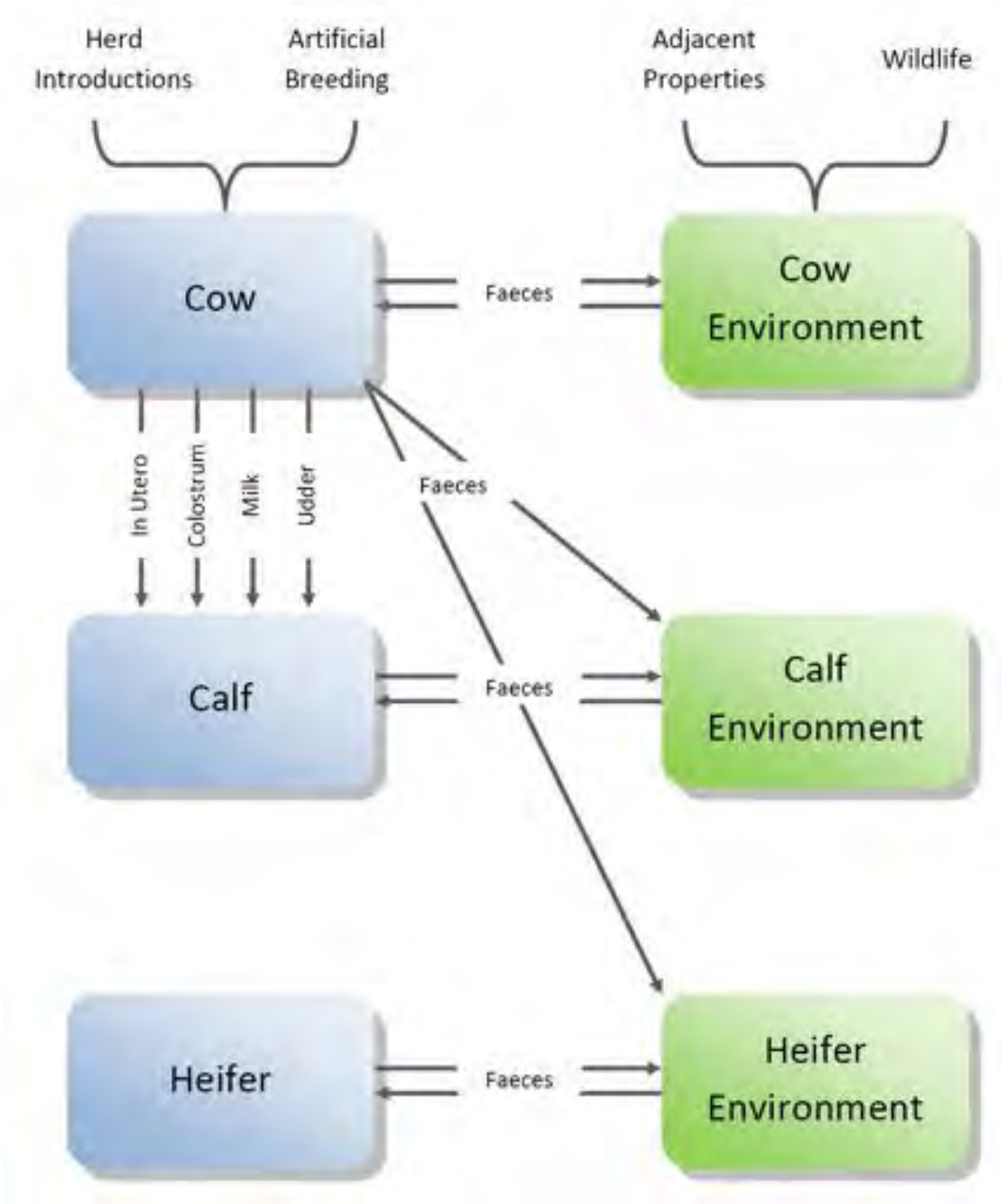
2.1.3 Transmission Pathways

The primary route of transmission for BJD is the ingestion of infectious faecal material adhered to a contaminated udder or teats, or on pasture, soil, water, contaminated surfaces or other parts of an animal's environment (Whittington and Sergeant, 2001). Less commonly, BJD may be transmitted through colostrum or milk (van Roermund *et al.*, 2007; Wilson *et al.*, 2010), in-utero (Whittington and Windsor, 2009) or through artificial breeding (Sergeant, 2005).

Because the disease has a long incubation period, adult cattle are the primary source of infection. That said, calves and young cattle may also shed Mptb passively or actively in the period following infection (Section 2.1.2). There is also a gradient in susceptibility, such that most animals become infected as calves (Section 2.1.4). To a lesser extent, wildlife have been implicated in the introduction of BJD into clean herds or its persistence in the face of control (Craven *et al.*, 2000; Greig *et al.*, 2002).

A schema illustrating the key pathways for the transmission of BJD is given in Figure 2. Individual pathways are discussed below.

Figure 2: Transmission pathways for bovine Johne's disease



Cow-calf transmission through faecal contamination of the udder or teats: one of the key pathways by which calves are exposed to Mptb is through faecal contamination of the udder or teats (Sergeant, 2005). The research that has demonstrated this has tended to do so by exclusion. Pithua *et al.* (2010), for example, showed that by removing calves from their mothers within 1 hour of birth, and depriving them of the opportunity to suckle, transmission from faecal-culture-positive dams was prevented. These calves were fed raw

colostrum collected from their mothers. The study was particularly powerful, as the group of calves was followed through to 90 days post-partum to examine whether infection that might have been transferred in-utero would be expressed as shedding in faeces, and whether transmission to other calves could be demonstrated. Neither of these events occurred. Johnson-Ifearulundu and Kaneene (1998) found that washing a dam's udder immediately prior to parturition, but failing to disinfect teats, resulted in a marked increase (OR^3=8.66, 95% CI 1.87-40.08) in the risk that Michigan dairy herds would be Mptb positive. These authors postulated that 'washing' an udder was, in this context, a curious proxy for poor udder sanitation as: (a) it tended to occur in herds where dams had accumulated substantial faecal material on their udders from a heavily contaminated environment; and (b) precluded the more effective practice of disinfecting the teats themselves. However, the link between exposure to a dam's udder and the transmission of BJD is not always demonstrated. Ridge *et al.* (2005 and 2010), for example, were unable to find an association between the removal of a calf from its dam within 12 hours of birth and the BJD status (positive or negative) of 137 Victorian dairy herds. The authors did not assess whether these calves had received colostrum by suckling, prior to removal from their dams.

Mitchell *et al.* (2008), and subsequently Lu *et al.* (2008, 2010, 2013a and 2013b), considered that susceptible calves could be infected through one of three direct transmission routes: calf-calf transmission, and susceptible calves infected by either low-shedding or high-shedding adult animals. These were mathematical modelling studies, rather than individual based simulation studies and, as such, were constrained in the amount of detail or complexity that could be included in their transmission elements.

Marce *et al.* (2011) considered vertical transmission (in-utero), horizontal transmission via the ingestion of contaminated colostrum or milk, and horizontal transmission via the ingestion of faeces in the environment. Separate pathways were implemented for the ingestion of contaminated faeces from adult cattle, as opposed to other calves. These authors were unique amongst those reviewed in that they parameterised the contamination of milk as a result of the faecal contamination of teats and udders (Table 2). This was a separate consideration to the secretion of Mptb in milk or colostrum, which is discussed in the following section.

[3] Odds ratio

Table 2: Faecal contamination of teats and udders (cfu per litre of milk)

	Minimum	Most Likely	Maximum	Modelled Distribution
Subclinically affected	0	40	2×10^{10}	$1 + 10^3 \times \text{beta}(1,25)$
Clinically affected	700	14×10^4	2×10^{10}	$10^{(3 + 10 \times \text{beta}(50,200))}$

Source: Marce *et al.* (2011)

Weber and Groenendaal (2012) also worked to the mathematical modelling paradigm and whilst these authors included a transmission pathway for animals infected at birth no further detail was provided.

On balance, our preference for the Australian model was to adopt the approach and basic parameters of Marce *et al.* (2011) when considering the faecal contamination of teats and udders.[4] This will be important to both: (a) the exposure of calves suckling from their dams in the peri-natal period; and (b) the contamination of pooled milk collected from peri-parturient cattle and subsequently fed to calves. However, rather than use the probability distributions adopted by these authors, our approach was to model the minimum, maximum and most likely values directly as the parameters for two betapert distributions. In this way, the contamination of teats and udders of low-shedding subclinically-affected animals is given by, betapert (0, 40, $2x10^{10}$). The companion distribution for high-shedding subclinically-affected animals, and for clinically-affected animals, is then, betapert (700, $14x10^4$, $2x10^{10}$). The bacterial counts per litre of milk reported by Marce *et al.* (2011) were assumed to represent the total bacterial load passed into milk due to teat contamination under the assumption that all adherent bacteria were removed into milk by the actions of calf suckling or machine milking.

Cow-calf transmission through colostrum and milk: most reviewers (for example, Çetinkaya *et al.*, 1997; Johnson-Ifearulundu and Kaneene, 1998; Craven, 2000; Sergeant, 2005; van Roermund *et al.*, 2007; Marce *et al.*, 2010) described the transmission of BJD by colostrum and milk as a pathway of lesser importance than faeces, but nevertheless significant to the overall epidemiology of the disease within a dairy herd. The secretion of Mptb in the milk of subclinically- and clinically-affected animals – and its dilution and inactivation as a result of milk processing – is also of key relevance to the debate about the role of the organism in the pathogenesis of Crohn's disease in humans (for example, Naser *et al.*, 2004).

Sweeney *et al.* (1992) found that 19%, 11% and 3% of high, medium and low-shedding subclinically-affected animals (respectively) had Mptb in milk. These results were significant ($P<0.05$), as was the trend from low to high shedding and its impact on the likelihood that

[4] The upper level of teat contamination was set at $2x10^8$ (not $2x10^{10}$ as described in Marce). This was to allow use of integer values in R ($2x10^{10}$ exceeds the maximum integer value allowed in R). The impact of this change is unlikely to be important as the model used limits on the maximum relative risk for infection following exposure.

Mptb would be found in milk. Similarly, Streeter *et al.* (1995) found that Mptb could be isolated from the colostrum of 22% of faecal-culture-positive cows, and from the milk of 8%. Cows that were heavy faecal shedders were more likely to shed the organism in the colostrum than were light faecal shedders. In a simulation of the impact of BJD on milk quality assurance, Weber *et al.* (2008) divided the infected portion of a dairy herd into latent, low-infectious, high-infectious and clinically-affected animals. Of these, only the high-infectious and clinically-infected animals shed Mptb in their milk (10^2 and 10^4 organisms per litre, respectively). However, these authors also parameterised the contamination of milk with faecal material. In this way, low-infectious animals had a total of 4 organisms per litre, while high-infectious and clinically-affected had totals of 6.4×10^4 and 4×10^7 organisms per litre, respectively.

Nielsen *et al.* (2008) took the analysis in a different direction, examining the role of colostrum and milk as risk factors for the development BJD in dairy herds. In a study of 808 Danish dairy farms, these authors found that calves fed colostrum from multiple cows had an odds ratio of 1.24 of being ELISA positive compared with calves fed colostrum from their own dam only. They also found that calves suckling with foster cows had an odds ratio of 2.01 of being ELISA positive compared with calves fed milk replacer. Feeding bulk tank milk and pooled milk from cows with high somatic cell counts did not increase the risk of being ELISA positive. Overall, the authors concluded that source of milk was not of great importance for the transmission of Mptb, but that colostrum should be fed only from the dam of that calf. Ridge *et al.* undertook a similar study in 2005 and found that the feeding of milk with antibiotic residue and other waste milk to calves was associated with a significantly increased risk of BJD for dairy herds participating in the test-and-control program ($P < 0.001$, with effect size not given). The same authors carried out a follow-up study in 2010 and found that whilst the effect remained significant, the direction of effect had reversed – that is, the feeding of waste milk now had a protective effect. This result was difficult to explain and the authors cautioned readers against its credibility.

Marce *et al.* (2011) included separate transmission pathways for animals consuming either colostrum or milk. These authors used a binomial infection parameter coupled with more complex algorithms for: (a) the amount of bacteria ingested by a calf during any given time step; and (b) the number of calves that might be infected. The infection parameter (shedding or not shedding) was 0.4 for colostrum or milk obtained from subclinically-affected animals and 0.9 when obtained from clinically-affected animals. The amount of bacteria (cfu) shed per litre of milk or colostrum from subclinically or clinically-affected animals ranged between a minimum of 2.2×10^4 cfu/l (clinically-affected animals only), a most likely of 5×10^4 cfu/l (clinically-affected only) and a maximum of $8.8 \times 10_4$ cfu/l (both clinically and subclinically-affected). Overall, these authors modelled the amount of Mptb in the milk or colostrum of both subclinically- and clinically-affected animals as $10^5 \times$ Beta(8,8) cfu/l.

Mitchell *et al.* (2008), and subsequently Lu *et al.* (2008, 2010, 2013a and 2013b), implemented a mathematical model that did not explicitly consider the exposure of calves through milk or colostrum. Weber and Groenendaal (2012) also used a mathematical model and claimed that separate transmission pathways for animals consuming either colostrum or

milk. Details about how these pathways were implemented, or their parameterisation, were not provided.

On balance, our preference for the Australian model was to derive parameters for the infectious load of Mptb in the colostrum and milk from the research of Sweeney *et al.* (1992) and the modelling work of Marce *et al.* (2011). The minimum and most likely amount of Mptb in the milk or colostrum of low-shedding subclinically-affected animals were considered to be zero, with 3% of animals shedding $5x10^4$ cfu/l. The minimum, most likely and maximum values for high-shedding subclinically-affected animals, and for clinically-affected animals, were considered to be $2.2x10^4$ cfu/l, $5x10^4$ cfu/l and $8.8x10^4$ cfu/l, respectively. The value for each individual will be drawn from a betapert distribution with these parameters.

Cow-calf transmission in-utero: the in-utero transmission of Mptb was examined in detail in a systematic review and meta-analysis carried out by Whittington and Windsor (2009) and much of what follows here has been adapted from that work.

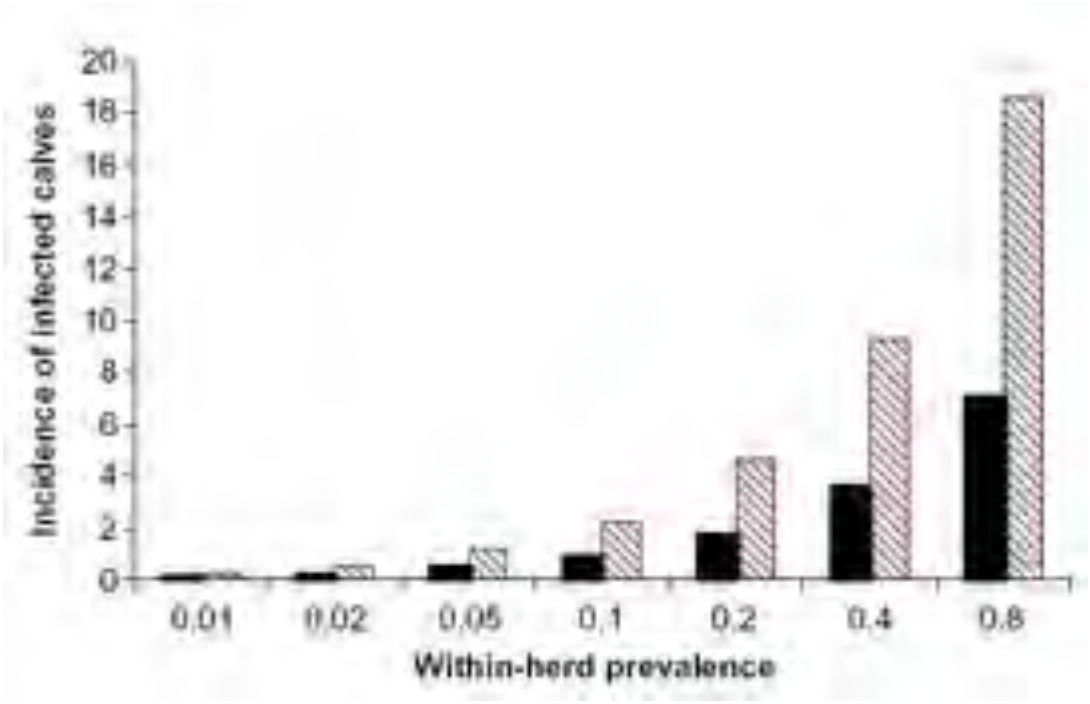
The prevalence of infected foetuses amongst cows with subclinical disease was found to be approximately 9% (95% confidence limits 6-14%). Corresponding figures for cows with clinical disease were 39% (20-60%), and for all infected cows 13% (9-18%). Of particular note is the fact that only two studies were identified in which the fate of infected foetuses was examined. One was in 1935 and provided shallow circumstantial evidence to effect that a bull calf infected in-utero developed clinical BJD as an adult bull without opportunity for horizontal transmission. The second study was published in 2003, and provides similarly circumstantial evidence to effect that a calf born by caesarean section to a clinically-affected mother developed BJD without opportunity for horizontal transmission. Neither of these studies is conclusive, and in each case only one animal was involved.

The sequelae to foetal infection with Mptb might potentially include: (a) progressive infection, manifest as faecal shedding then development of clinical disease; (b) immune tolerance with or without persistent infection, depending on time of infection in relation to the development of immunocompetence in the foetus and manifesting as either a lack of lesion development due to immunotolerance, failure to react to diagnostic tests, failure to respond to vaccination or possible shedding; or (c) recovery and elimination of the organism. It is unfortunate that evidence in support or denial of these possible sequelae does not at present exist. It can be said that infection with Mptb is unlikely to be lethal to the foetus in most cases, except where there has been massive exposure. Evidence for this includes the isolation of Mptb from foetuses in each trimester of gestation and at term. Further evidence is the observation that infertility due to early embryonic death and abortion are not considered to be signs of endemic Johne's disease in cattle or other species.

The incidence of calves infected as foetuses depends on the ratio of subclinical cases to clinical cases among infected cows and on within-herd prevalence. For a herd where 5% of cows are infected, between 0.44 and 1.2 infected calves per 100 cows per annum would be expected. Corresponding figures for within-herd prevalence of 40% are 3.5-9.3 infected calves per 100 cows per annum and values for other levels of prevalence can be determined from Figure 3. These estimates were not markedly affected by the value chosen for the proportion of infected cows that were clinical cases. For example, over an extreme range of

values (1-40% of infected cows being clinical cases) the estimated incidence of infected calves ranged from 0.47 to 1.05 per 100 cows per annum for a herd with 5% within-herd prevalence (Whittington and Windsor, 2009).

Figure 3: Impact of within-herd prevalence on in-utero transmission

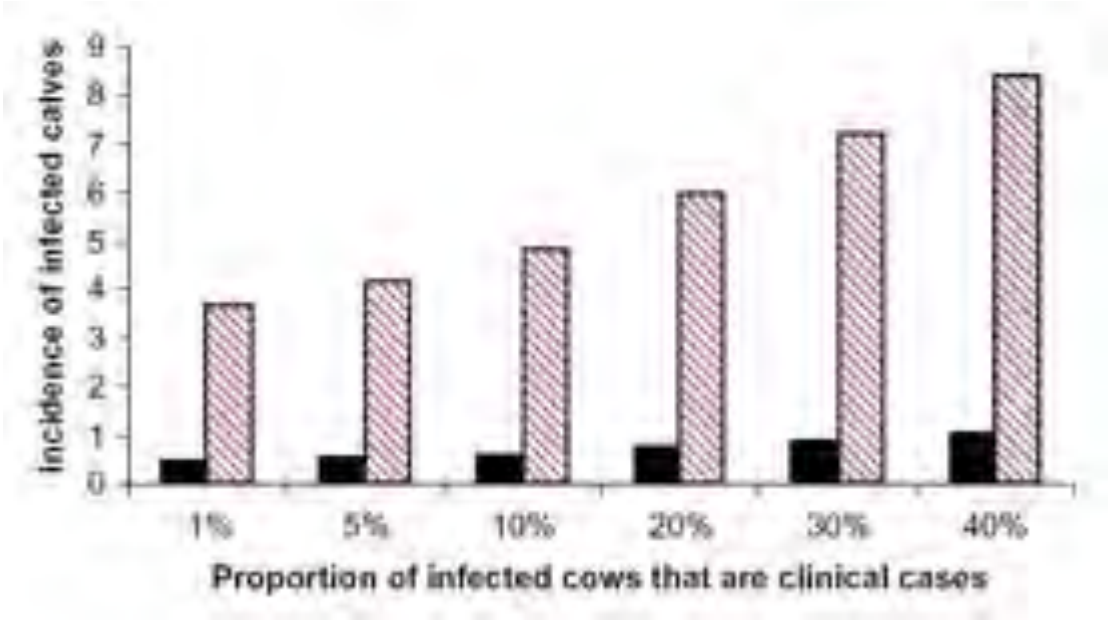


Source: Whittington and Windsor (2009)

Figure 3 shows the estimated incidence of calves infected via the in-utero route expressed as the number of infected calves per 100 cows per year for points within the reported range of within-herd prevalence. Incidence was estimated using 95% confidence limits (lower, black bars; upper, striped bars) assuming that 20% of cow infections were clinical.

Figure 4 shows the effect of the proportion of infected cows that are clinical cases on the estimate of incidence of calves infected via the in-utero route. The data were based on mean foetal infection rates for subclinically-infected cows (9%) and clinically-infected cows (39%) for two levels of within-herd prevalence: 5% (black bars); 40% (striped bars).

Figure 4: Impact of the proportion of clinical cases on in-utero transmission



Source: Whittington and Windsor (2009)

The risks associated with vertical transmission appear to have been first investigated in a modelling context through the mathematical modelling studies of Mitchell *et al.* (2008) and carried through to the work of Lu *et al.* (2008, 2010, 2013a and 2013b). Each of these papers describes vertical transmission and, to varying degrees, explains the parameters that were used throughout the study series. However, closer inspection reveals that the term 'vertical transmission' appears to have been expanded to include all forms of the transmission of infection directly from the dam to calf. Importantly this would include transmission by colostrum, as well as transmission by faecal material on the dam's teats or udder. In some places, the original Mitchell *et al.* (2008) discussion does introduce the phrase 'vertical or pseudo-vertical' but this qualification is not applied consistently and does not appear to have been carried through to the Lu *et al.* series of studies.

Marce *et al.* (2011) included in-utero transmission, giving transmission parameters of 0.149 for latently or subclinically-affected animals, and 0.65 for clinically-affected animals. Weber and Groenendaal (2012) parameterised the age of onset of a high-shedding subclinical state according to the route of infection (Table 1). One of these routes was termed 'congenital' and was explicitly distinct from 'at birth'. Animals infected congenitally had an earlier onset of subclinical shedding than animals infected by other routes and at a later age. This notwithstanding, the matter of congenital transmission is not discussed in the paper, and nor is it discussed in the research of Weber *et al.* (2010) upon which the later modelling was based.

On balance, our preference for the Australian model was to work with the values cited by Whittington and Windsor (2009) and précised at the start of this discussion. These authors maintained that the probability of in-utero transmission for cows with subclinical disease was approximately 9% (95% CI 6-14%) and for clinical disease was approximately 39% (95% CI 20-60%). We took these expected values and ranges to be the minimum, most likely and

maximum values for two triangular probability distributions, from which the in-utero transmission probability for an individual animal will be drawn. We specified the same transmission probability for high-shedding subclinical animals as for clinical animals – that is, Triangular (min=20%, mode=39%, max=60%). The distribution for low-shedding subclinically-affected animals was then given as Triangular (min=6%, mode=9%, max=14%).

Calf-calf passive and active transmission: the existence of a transient state of active infection, prior to the development of latency, was discussed in Section 2.1.2 and illustrated in the state-transition schema in Figure 1. This state may play an important role in the persistence of infection in a herd where clinical and test-positive animals are systematically removed (van Roermund *et al.*, 2007; Mitchell *et al.*, 2008 and 2012). Passive shedding was also discussed in Section 2.1.2. This describes the passage of Mptb through the gut of an exposed animal without multiplication, such that the affected animal is simply a conduit for the bacteria. Passive shedding in cattle commences within 24 hours of ingestion and continues for up to a week after a single bolus dose (Whittington and Sergeant, 2001).

Extending the modelling work of Mitchell *et al.*, (2008), Lu *et al.* (2008, 2010, 2013a and 2013b) used a transmission rate between transiently shedding animals and susceptibles of 0.01 per year per animal. This value was 'assumed' and not derived directly from the literature. Marce *et al.* (2011) modelled two types of environment in order to differentiate indirect adult-to-calf transmission from indirect calf-to-calf transmission. Their approach is discussed under Environmental Contamination and Persistence (below).

Weber and Groenendaal (2012) explicitly stated that the key the aim of their study was to evaluate the long-term effects of transmission of Mptb amongst young stock on the success of certification, surveillance, and control programmes for BJD in simulated closed dairy herds. These authors nested a modified Reed-Frost approach within their mathematical model for BJD. The nested model considered the number of effective contacts that calves might experience in a pen environment during each time step.

On balance, our preference for the Australian model was to take the similar approach as that used by Marce *et al.* (2011), such that transient shedding becomes one aspect of environmental contamination. This is discussed below.

Environmental contamination and persistence: in 2004, Whittington *et al.* undertook primary research and a systematic review of the survival of the sheep strain of Mptb in the Australian environment. These authors noted that questions as to how long the organism could survive outside the host had been raised as early as 1912. Mptb had been shown to survive for approximately 9 months when placed in an open bowl and left in an exposed site in London. Survival had been curtailed by ensilage, and by the presence of urine. These and many other experimental observations are referenced within the publication. The authors noted that these data were obtained in the northern hemisphere, where livestock are commonly housed indoors during winter on straw bedding, and where climates tend to be milder than in the temperate grazing regions of Australia. The authors were specifically interested in the Australian sheep strain of Mptb which they had found to have some difference cultural requirements to the cattle strain. The review concluded that Mptb could survive for up to 55 weeks in a fully shaded environment, with much shorter survival times in unshaded locations. Moisture and application of lime to soil did not affect survival. Whilst

UV radiation was an unlikely factor, infrared wavelengths leading to diurnal temperature flux may be the significant detrimental component that is correlated with lack of shade. The authors found that Mptb could survive for up to 24 weeks on grass that germinated through infected faecal material applied to the soil surface in completely shaded boxes; and for up to 9 weeks on grass in 70% shade. Most strikingly, they discovered evidence that suggested Mptb may enter a technically dormant state under some environmental conditions, with revival when placed in more suitable media.

Eisenberg *et al.* (2012) undertook a detailed analysis of the survival of Mptb within the environment of a single Dutch dairy farm. Because there are such striking differences between the husbandry of dairy cattle in the Netherlands and Australia (in particular, winter husbandry) the work must be interpreted with some caution. Interestingly, however, the study had a focus on bio-aerosols – specifically, viable Mptb associated with in aerosolised dust and faecal material. The authors found that Mptb could be recovered with equal frequency from samples of dust from air inlets when compared with material at animal level. Respiratory Mptb uptake had been implicated in the exposure calves under experimental conditions (Eisenberg *et al.*, 2011a). Outside the barn, most environmental samples tested negative, the exception to this was the doormat of the farm house itself, which was consistently positive.

Smith *et al.* (2011) examined the link between faecal shedding of Mptb by individual cows and herd-level environmental contamination using a cross-sectional analysis of longitudinally collected samples on three dairy farms in the northeast US. All sites and herds were cultured quarterly, providing 1,131 samples. Of these, 133 (11.8%) were culture-positive. All adult animals in the herds were tested biannually by faecal culture for 6 years. Of the environmental sites sampled, manure storage areas and shared alleyways were most likely to be culture-positive. Environmental sample results were compared to culture results from either the concurrent or previous sampling date at both the herd and the pen level. At the herd level, a 1-log unit increase in average faecal shedding increased the odds of a positive non-pen environmental sample by a factor of six, and increased the average amount of Mptb in non-pen samples by 2.9 cfu per gram of faeces. At the pen level, a 1-log unit increase in average faecal shedding in the pen increased the odds of a positive environment by a factor of 2.4, and the average amount of Mptb was increased by 3.5 per gram of faeces. The authors were not able to model the relationship between non-pen environmental sample status and the distance between shedding animals and the sample's location, and neighbouring pens did not significantly affect the results of the pen-level analysis. The amount of Mptb in pen-level samples and the probability of a pen testing positive for Mptb were both positively but non-significantly correlated with the number of animals in the pen shedding >30 cfu/g of Mptb. Interestingly, only 19 of 47 faecal-culture-positive sample instances also yielded positive environmental tests. This led to an apparent herd sensitivity of approximately 40% (95% CI: 26-54%), but may also have demonstrated the exposure of animals to high levels of Mptb in the environment may not be correlated with the point of highest shedding – that is, that the environmental persistence of Mptb, and the herd-level characteristics that dictate environmental exposure, may lead to the infection of susceptible animals at some point distant from the time of peak infectiousness within the herd.

Lombard *et al.* (2007) analysed a total of 483 environmental samples from 98 US dairy herds to investigate the efficacy of environmental samples as an identifier of herd infection. Of these, 218 (45.1%) farms were faecal culture-positive for Mptb by traditional means. Of the environmental samples, 52.3% of parlour exits, 49.1% of floors of holding pens, 48.8% of common alleyways, 47.4% of lagoons, 42.3% of manure spreaders and 41.5% of manure pits were culture-positive. The authors correlated the performance of environmental culture with that of serum and milk ELISA and traditional faecal culture. This analysis is outlined in Section 2.2.2. In the context of this discussion, the paper illustrates that viable Mptb is distributed throughout the environment of an operating dairy farm.

In their review of models for BJD, Marce *et al.* (2010) maintained that existing approaches could be improved by considering indirect transmission via the environment and taking account of the survival of Mptb and its relevance to the contact structure between animals in a herd. These authors suggested that the survival of Mptb in the environment might result in a delay between the shedding of Mptb by infectious animals and the exposure of susceptibles, and that this might influence the outcome of some control options.

Humphrey *et al.* (2006) developed a model focussed on the transmission of BJD within a Scottish beef suckler herd. In this context, environmental contamination provided the sole source of infection. Bacterial density in the environment (in units of 10^{13} bacteria per hectare) replaced the number of infected animals in a modified Reed-Frost equation for the force of infection. The number of bacteria in the environment at the end of a 6-month period was calculated from the number of bacteria produced during that period and those already surviving within the environment. The number produced was proportional to the number of subclinically- and clinically-infected animals. The amount of bacteria shed by subclinically-infected animals was lower than that shed by clinically-infected animals. The survival of bacteria in the environment followed an exponential decay with the survival rate in winter (0.01=the probability of a bacterium surviving six months) taken to be 10 times higher than that in summer. This study was the most detailed of the modelling papers in respect of its consideration of environmental contamination and persistence.

Mitchell *et al.* (2008), and subsequently Lu *et al.* (2008, 2010, 2013a and 2013b), did not explicitly consider environment as a source for Mptb on the grounds that the organism does not multiply in the environment and can therefore only serve as a mechanical vehicle. The authors considered the presence of Mptb in the environment to increase the number of contacts between infectious animals and susceptible animals and, thus, contribute to the persistence of the disease within a herd.

Marce *et al.* (2011) modelled two types of environment in order to differentiate indirect adult-to-calf transmission from indirect calf-to-calf transmission. These authors supplied the algorithms by which they estimated the amount of faecal contamination within calf pens, as a function of the number of calves within each pen and the number of these that are infected. The parameters used in these algorithms were also supplied. At time t, the quantity of Mptb in each environment compartment is updated, according to a removal rate (μ, reflecting cleaning of the barn and management of bedding) and the rate at which Mptb is shed into the environment by infectious animals. The removal parameter (μ) was 0.4 for the general environment of the farm, 0.67 for individual empty pens and 0.17 for collective

pens. The detail in this paper is tortuous, but may be sufficient to allow the approach to be replicated. When shedding animals were no longer present on the farm, but the environment was still contaminated, new infections as a result of residual Mptb in the environment occurred with a mean weekly probability of 3%. Weber and Groenendaal (2012) considered calf-calf spread (above) to be an outcome of environmental contamination. The persistence of Mptb was not considered explicitly.

The amount of Mptb added to a location at each time step can be calculated as the sum of the contributions from each infectious animal. The amount of Mptb that an infectious animal sheds into the environment varies with the stage of disease. The estimates we have chosen we adapted from Crossley *et al.* (2005). The daily production of faces for calves, heifers and adult cattle were taken from Marce *et al.* (2011). The existing burden in any given location is calculated as the burden at the previous time step, adjusted for exponential decline in the number of viable bacteria. Unpublished recent (2014) field study work on Mptb survival by the University of Sydney indicates that on average approximately 90% of environmental Mptb die each month (Eppleston and Whittington pers. comm., 2014). This translates to a daily exponential decline (death) rate estimate of 0.08 in summer, 0.07 in autumn and spring and 0.06 per day in winter.

Table 3: Daily Mptb environmental decline parameters

Season	Daily decline	Days until 90% gone	Days until 99% gone
Summer	8%	29	56
Autumn	7%	32	64
Winter	6%	38	75
Spring	7%	32	64

Source: Eppleston and Whittington (pers. comm. 2014)

On balance, our preference for the Australian model was to calculate the amount of Mptb shed into each location at each time step, add this to the burden already in that place, and from this determine the force of infection faced by animals at each location and time step. The model operates on a defined number of paddocks and calf pens, which the user defines at start-up. The herd is made up of mobs of adult cattle (lactating cows, dry cows and bulls), heifers and calves and, at each time step, each mob is assigned to a particular paddock or pen. This is based on defined herd management parameters. This means that at a given time step, a mob could be in the location that it was at the previous time step or it could be in a new location.

Table 4: Faecal contamination of the environment

Group	cfu/tube[2]	Kg faeces/day[3]	cfu/animal/day
Adults			
Transient[1]	10	30kg	1.88×10^6
Subclinical low	10		1.88×10^6
Subclinical high	50		9.38×10^6
Clinical	100[4]		1.88×10^7
Heifers			
Transient	10	10kg	6.25×10^5
Subclinical low	10		6.25×10^5
Subclinical high	50		3.13×10^6
Clinical	100		6.25×10^6
Calves			
Transient	10	0.5kg	3.13×10^4

[1] Values for transient shedders taken to be the same as for low subclinical shedders
[2] 1 tube is 0.16g
[3] Marce *et al.* (2011)
[4] Adapted from the standard deviation of values given in Crossley *et al.* (2005)

2.1.4 Individual-Level Risk Factors

Age-based susceptibility: one of the common threads of most accounts of the epidemiology of BJD in dairy herds is the emphasis placed on age-based susceptibility. Newborn and young calves are considered to be the most at-risk, with susceptibility declining through to adulthood. It is significant that none of the 18 modelling studies identified for this review considered adults to be susceptible (Section 2.1.2). This notwithstanding, some systematic reviews and meta-analyses (for example, Craven, 2000; Windsor and Whittington, 2010) and recent primary research (for example, Fecteau *et al.*, 2010; Weber *et al.*, 2010; Mitchell *et al.*, 2012; Mortier *et al.*, 2013) have challenged this view. The most robust conclusion would now appear to be that all ages of cattle are susceptible to infection with Mptb. Although age does impact on the establishment of the disease in an individual and characteristics of its ensuing pathogenesis, the key determinant is likely to be the size of the challenge dose of Mptb. This can be influenced by the route of exposure (for example, relatively higher numbers of bacteria are shed in faeces than in milk) as well as by aspects of animal behaviour and management. Repeated low-dose exposures may also be important. Calves have more opportunity for exposure than either heifers or adult cattle, and a longer lifespan during which to develop the disease. These and other key issues are discussed below.

Windsor and Whittington (2010) undertook a quantitative review and meta-analysis of the age-based susceptibility of cattle to infection with Mptb. These authors were cognizant of the difficulties associated with effectively managing calfhood exposure to Mptb – in particular, the removal of calves from the dam within 12-hours of birth. The study found a significant difference in age susceptibility to infection with Mptb between adults and calves <6 months of age ($P < 0.001$), and between adults and calves aged between 6 and 12 months of age ($P < 0.005$). Calves older than 6 months are less likely than younger calves to develop

BJD. However, at the high levels of exposure to Mptb used in these experiments significantly higher infection rates still occurred than for adult cattle. The authors also found that adult cattle can be infected by exposure to high levels of Mptb in a contaminated environment, but that they are less likely than calves to develop clinical signs of BJD. No direct evidence was found to support the commonly-held view that calf removal from the dam for a maximum period of 12 hours is preferable to 24 hours. However the studies examined did show that if exposure to infection occurs at birth, then the risk of infection progressing to BJD is high. Likewise, if it is likely that the dam is infected then any delay in immediate removal from the dam, such as provision of sufficient time for the calf to suck colostrum, would considerably increase the risk of infection with Mptb and should be avoided.

Windsor and Whittington (2010) also reviewed the pathobiology underpinning the increased susceptibility of calves to infection with Mptb. One theory is based on the mechanics of exposure, and linked to behaviour of calves. Another maintains that newborn calves have an 'open gut' which allows macromolecules such as colostral immunoglobulins to penetrate the mucosa. This may also enable Mptb to penetrate the mucosal barrier. It is also possible that the presence of a functional rumen in older animals may dilute or cause a detrimental effect on Mptb before they reach the intestine. None of these theories has been proven. A detailed review of age-based susceptibility was also undertaken by Craven (2000). Indeed, many passages within this paper appear to have been paraphrased subsequently by Windsor and Whittington (2010), and the author's conclusions are largely the same as those noted above.

Primary science demonstrating the susceptibility of all ages of cattle has been available since the 1960s. In general, this research showed that adult animals could become infected, albeit at a lower incidence and with less marked consequences. Rankin (1962), for example, found that of seven adult cows continuously exposed for 4 years to an environment naturally contaminated with Mptb, only one developed clinical BJD, but four of the remaining six harboured Mptb in the lymphatic system. Adult cattle would thus seem to be more resistant to Mptb than calves. Alternatively, Larsen *et al.* (1975) carried out an experiment in which two 1-month-old calves, four 9-month-old calves, and 4 adult (5 to 11 years old) cattle were exposed to Mptb. After 150 days all were slaughtered. Tissues of 1-month-old calves had more bacilli and lesions than those of 9-month-old calves or adult cattle. All cattle responded to immunological tests during the experiment.

More recently, Fecteau *et al.* (2010) followed a cohort of nine Jersey steers grazing pasture heavily contaminated by an infected herd of 80 milking cows. The steers commenced the trial at 15 months of age and were slaughtered at 28 months. The steers had been taken from their mothers prior to suckling, and had only received milk from ELISA-negative donor cows. Of the 80 lactating cows, 15 were culture-positive and four had been identified as heavy shedders. The lactating cows were divided into groups, and grazing then focussed on small pens. The steers were placed in a pen immediately following the removal of the adult cattle. This arrangement was not contrived for the purpose of the study – it is a common form of grazing practice in some parts of Canada. At post-mortem, six of the nine steers were Mptb tissue-culture-positive. As an aside to the study, the authors noted that Mptb antigen could be identified by PCR in the faeces of all nine animals during the grazing season – including those that were not tissue-culture-positive on post mortem. This finding was

considered good evidence in support of: (a) the consumption of Mptb by grazing animals, albeit observing these animals to avoid obvious dung piles; and (b) the redistribution role that passive shedding (Section 2.1.2) may play in the exposure of groups of animals grazing contaminated pasture.

In 2013, Mortier *et al.* carried out an experiment to investigate the dose-dependent susceptibility of dairy calves and young cattle to Mptb infection. Fifty-six animals from Mptb-negative dams were randomly allocated to 10 Mptb challenge groups (five animals per group) and a negative control group (six animals). The cattle were inoculated orally on two consecutive days at five different ages: 2 weeks and 3, 6, 9 or 12 months. Within each age group five animals received either a high (5×10^9 cfu) or low (5×10^7 cfu) dose of Mptb. The inoculum was placed in a syringe and expelled at the root of the tongue. All animals were then euthanised at 17 months of age. Macroscopic and histological lesions were assessed and bacterial culture was undertaken on various tissue samples. Twenty-eight of the 50 (56%) inoculated animals had at least one Mptb-positive tissue. Positive tissue culture results were present in animals of all age and dose groups. The proportion of animals with at least one Mptb-positive tissue culture was approximately equal (56%) between the low-dose and high-dose groups. However, all five animals with more than four culture-positive tissues were inoculated with a high dose. The proportion of animals with at least one culture-positive tissue was similar in the five age groups, ranging from 40-70%. The proportion of tissue culture-positive animals did not decrease with increasing age at inoculation, although all five animals with more than four culture-positive tissues were inoculated at less than 6 months of age. This study demonstrates that animals up to 12-months of age can be infected with Mptb without using an artificially raised challenge dose or unnatural exposure mechanism (for example, systemic injection). The study also shows that rapidity of pathogenesis and extent of the disease in each exposed individual is likely to be correlated with the amount of bacteria to which it is exposed.

It was noted in Section 2.1.2 that the models reviewed by Marce *et al.* (2010) used a maximum age of infection of either 0.5 years (van Roermund *et al.*, 2002) or 1 year (Collins and Morgan, 1991; Groenendaal *et al.*, 2002; Pouillot *et al.*, 2004; van Roermund *et al.*, 2005; Humphry *et al.*, 2006; Kudahl *et al.*, 2007; Mitchell *et al.*, 2008). The same cut-point was used by Lu *et al.* (2008, 2010, 2013a and 2013b), Marce *et al.* (2011) and Weber and Groenendaal (2012). Mitchell *et al.* (2008), Lu *et al.* (2008, 2010, 2013a and 2013b), Marce *et al.* (2011) and Weber and Groenendaal (2012) specified a gradient in susceptibility such that this was highest at a week of age and decreased exponentially until 1 year of age. The various papers cited different coefficients and formulae, but these are likely to reflect differences in time step and parameterisation rather than differences in the character of exponential decline in susceptibility.

On balance, our preference for the Australian model was to allow the detail within the transmission pathways governing age-based opportunities for exposure to place calves at far greater risk than either heifers or adult cattle. The opportunities include suckling from infected mothers, consuming pooled milk and coexisting in a confined space with other calves that may be excreting Mptb either passively or actively. By contrast, heifers and adult cattle will only be exposed to environmental contamination. Heifers and adult cattle will also

have shorter life spans and, thus, decreased opportunity to develop the disease. One of the advantages of simulation modelling is that the number and proportion of undetected infected animals can be analysed and output by the model. In this way, it will be useful to understand whether a significant number of older animals may become infected, but not remain in the herd long enough to complete their latent period and period of low subclinical shedding.

Breed-based susceptibility: Craven (2000) cited a 1959 reference that spoke to breed susceptibility for BJD[5] but did not identify any additional studies. Using a postal questionnaire sent out to farms in England and the border regions of Wales, Cetinkaya *et al.* (1997) found that herds where Channel Island breeds (Jersey and Guernsey) were predominant were more likely to report clinical disease than those in which Friesians or any other breeds were predominant. These authors maintained that Channel Island breeds had long been suggested to be more susceptible to Mptb. Citing the same 1959 research noted above (Withers, 1959), the authors pointed out that these breeds had higher incidence of clinical BJD than other breeds (5.8% in Channel Islands compared with 0.3% in Friesians). No further evidence was given. The authors conceded that the effect may be related to increased exposure rather than increased susceptibility, or otherwise confounded by management factors.

Other reviewers have not mentioned breed susceptibility at all. None of the 18 modelling studies identified in this review included the impact of breed-based susceptibility. Because there are very few dairies in Australia with uniquely Chanel Island breeds, our decision was to ignore breed-based susceptibility.

Genetics-based susceptibility: Koets *et al.* (2000) estimated genetic variation in susceptibility of Dutch dairy cattle to Mptb. Data from 3020 dairy cows collected during a vaccination trial (1984-1994) was used. Complete pedigree records and infection status at slaughter were available for analysis. The authors estimated the heritability of susceptibility to Mptb to be 0.06 across the study population. Continuing from that work, Koets *et al.* (2010) sought to identify the single nucleotide polymorphisms linked to susceptibility. The authors found that cows with a TLR2-1903 T/C mutation (termed the CT and CC genotypes) were at 1.7 (95% CI: 1.2, 2.8) times the odds of being infected than cows with the TT genotype. In in-vitro functional assays, monocyte-derived macrophages from animals with a TLR2- 1903 TT genotype produced more IL12p40 and IL1β when stimulated with Mptb compared to cells derived from TLR2-1903 CT and CC genotypes. Also, T-cell proliferative responses to mycobacterial antigens were higher in animals with a TLR2- 1903 TT genotype. Collectively these results show that genotypic differences amongst Dutch dairy cows are correlated with differences in the animal's ability to mount a competent response to challenge with Mptb and, thus, resist infection.

None of the 18 modelling studies identified in this review included the impact of genetics-based susceptibility. The Australian model is stochastic, and allows for some variance in the susceptibility of individuals and the outcome of direct or indirect challenges. Without an *a*

[5] Withers F (1959). Paratuberculosis II: Incidence of the disease. Vet. Rec. 71:1150-1156

priori reason for including additional genetics-based variance in susceptibility we considered this stochastic element to provide a sufficient representation of the variance that might be expected in the field.

2.1.5 Herd-Level Risk Factors

The factors that influence: (a) the likelihood that a herd will be infected with BJD; (b) the prevalence of infected animals within a herd; (c) the progress of a herd undertaking a control program; or (d) the force of infection applied to calves and other susceptible animals can be grouped as those relating to either herd size, within-herd prevalence of BJD, herd management and biosecurity, or livestock industry (beef or dairy). The principles underpinning these herd-level factors are linked to the epidemiology and pathogenesis of BJD and apply in a general sense to all countries and livestock systems. That said, the particular effect that a factor has in a given setting may be quite specific and, for this reason, the focus in this section is on Australian research and reviews with supplementary evidence from other works as required. The following key Australian papers were consulted: Ridge *et al.* (2005), Ridge *et al.* (2010), Jubb and Galvin (2000), Jubb and Galvin (2004a), Jubb and Galvin (2004b), Davis and Bell (2012), VIC DEPI (2013), and QLD DAFF (2014).

Herd size: fifty-four south Gippsland dairy herds participating in the Victorian BJD test-and-control program were visited between July and November 2002 and an audit of calf rearing practices was conducted (Ridge *et al.*, 2005). The results of testing completed under the program were analysed for each of the herds. Twenty-seven management factors were examined for a relationship with the presence of clinical cases of BJD or cattle with positive ELISA test results that were born after the completion of the second whole herd test. The authors noted that herd size was of *a priori* significance and, for this reason, included it as a covariate in their logistic regression on the impact of management factors on the occurrence of clinical cases or positive ELISA test results in animals born after the completion of the second whole herd test in a test-and-control program. The number of clinical cases and the proportion of test-positive animals at the initial test were also included as covariates. That said, the authors did not provide any quantitative detail about the significance of herd size in the final model nor its effect estimate. They did explain that at the start of the study the mean number of adult milking cows was 220 (range 63 to 802). At the time of the final audit, the average herd size had increased to 236 cows (range 76 to 1032).

Ridge *et al.* (2010) carried out a retrospective cohort study involving 137 dairy herds randomly selected from all 390 participating in the Victorian test-and-control program for BJD. This study was undertaken to gain insight into the relationships between calf rearing practices and the occurrence of BJD on infected dairy farms. Each study farm was visited between July 2005 and January 2006 and a structured survey examining herd management and calf rearing practices was completed. The resultant data, along with information from annual herd testing for BJD and records of clinical disease diagnosed in the herd, from May 1990 to March 2008, were analysed. The authors categorised herd size as less than 174 milkers (reference group), 174-242 milkers, 243-345 milkers and more than 345 milkers. These authors found that increasing herd size from less than 174 milkers to between 174 and 242 milkers had a protective effect. After this, increased herd size was associated with an increased daily risk of experiencing a home-bred clinical case BJD. The contrasts amongst

each level of herd size were not significant, but collectively the variable herd size was highly significant (P<0.01). The protective effect of increasing herd size from very small herds to herds of between 174 and 242 milkers is likely to reflect the raft of biosecurity and other management practices attributed to commercially-sized milking herds. As herd size then increased within this group of substantive commercial dairies, relatively more animals were likely to be shedding Mptb at any point in time and thus conveying infection directly to their offspring and indirectly to other susceptible animals through contamination of the herd environment. To this effect, the author stated that, "*a single highly infectious animal is capable of causing widespread environmental contamination and the odds of having one of these animals is likely to increase as herd size increases*".

Jubb and Galvin (2000) undertook a review of the Victorian test-and-control program for BJD. The paper describes changes in ELISA reactor rates and the number of clinical cases, and gives evidence for progress in the program. These authors noted that there was a marked increase in herd size from 1992 to 1998 in the 36 dairy herds that had completed 4 or more years of testing. These herds also had a higher initial prevalence than other dairy herds in the program (below). The authors suggested that the increase in herd size from 1992 to 1998 probably indicated that this group was comprised of more dedicated, progressive dairy farmers. The test-and-control program markedly reduced the number of clinical cases occurring in these larger herds, which had been seeing a rapidly increasing number of clinical cases each year. Heaviest environmental contamination, highest in-utero transmission and highest colostral and whole-milk transmission were likely to have occurred immediately prior to the start of the program.

Jubb and Galvin (2004a) reviewed the clinical histories and BJD testing data recorded by the [then] Department of Natural Resources and Environment for 542 dairy herds participating in TCP. The herds were required to conduct annual herd tests of cattle 2 years old and older with an ELISA, cull the reactors and manage the younger cattle to minimise infection. The authors found that there was an increase in average herd size from 216 at the first herd test to 780 at the 10th herd test. The authors did not offer any further comment on the impact of herd size on performance in the test-and-control program.

On balance, our preference for the Australian model was to run a series of scenarios using herds of differing sizes. This approach will allow the effect of herd size to be analysed directly, without a need for altering transmission parameters.

Within-herd prevalence of BJD: as was the case for herd size (above), Ridge *et al.* (2005) noted that the number of clinical cases and the proportion of test-positive animals at the initial test were of *a priori* significance and, for this reason, included them as covariates in their logistic regression. That said, the authors did not provide any quantitative detail about the significance of these variables in the final model nor their effect estimates.

Ridge *et al.* (2010) found that the rolling average percentage of sero-positive (ELISA) milking cows in the last two herd tests of their study significantly (P<0.01) influenced the daily risk of experiencing a home-bred clinical case BJD. This variable was coded as less than 0.2%

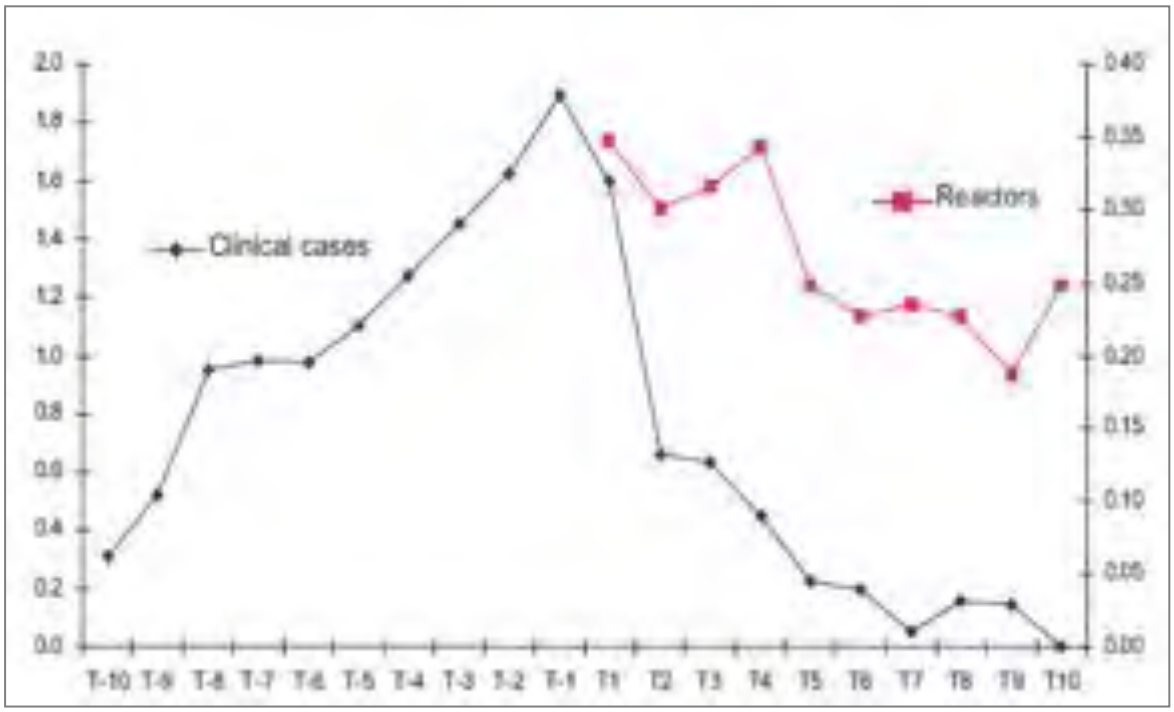
(referent group), 0.2% to less than 0.77% (HR[6]=2.20, 95% CI=1.162-4.153), 0.77% to less than 1.4% (HR=3.17, 95% CI=1.627-6.171) and 1.4% or greater (HR=2.55, 95% CI=1.334-4.892). As seen from the statistics cited (above) each contrast with the reference group was also significant (P<0.05). The result suggested that the risk peaked when sero-prevalence was as high as 1.4%, but declined thereafter. This result is difficult to explain on purely epidemiological grounds.

Jubb and Galvin (2000) examined the shift in prevalence of ELISA positive animals as herds moved through successive tests in the test-and-control program. These authors also commented on the shift in mean age of ELISA positive animals, and the implications this has as to the progress of a herd within the test-and-control program. The paper did not, however, explore the association between within-herd prevalence or sero-prevalence, and measures that indicate either the seriousness of the disease within the herd or the success of control.

Jubb and Galvin (2004a) plotted the prevalence (%) of ELISA reactors and clinical cases at various years before and after commencement of the test-and-control program (Figure 5). There was a relatively rapid increase in the rate of clinical disease before the program started and then it markedly declined. There was a slow and interrupted decline in reactor prevalence, with a marked peak occurring at the fourth herd test (T4). The pattern of interrupted decline in reactor prevalence was considered to be the result of a number of factors operating simultaneously. These included the establishment of infection in increasing numbers of animals before the program started, the long incubation period before sero-conversion, and the reduced exposure to infection of animals born after program commenced. There was also the possibility that test sensitivity might decline as repeated removal of positive animals caused retention of non-reacting, infected animals. This may have made the apparent reduction in infected animals an artefact of changing test sensitivity. The authors concluded that the program led to a marked decline in the number of clinical cases, probably because animals in which clinical disease was imminent were detected by testing and removed. A reduction in prevalence of reactors occurred only when most herd members were born after the program started.

[6] Hazard ratio

Figure 5: Clinical cases and reactors at different stages of a test-and-control program



Source: Jubb and Galvin (2004a)

Davis and Bell (2012) examined changes in sero-prevalence between 2003 and 2010, when stratified by retention rate and geographical region. The outcomes of this analysis are shown in Figure 6 and Figure 7, respectively. These authors concluded that throughout the period of study, mean sero-prevalence was higher in herds that took an early exit from the program. They also concluded that a dramatic improvement in herds in the southwest region of Victoria accounted for most of the observed improvement in mean sero-prevalence between 2003 and 2010. The authors did not undertake any analysis of the relationship between herd sero-prevalence and the likelihood that herds would move forward within the program.

Figure 6: Herd sero-prevalence as a function of program retention

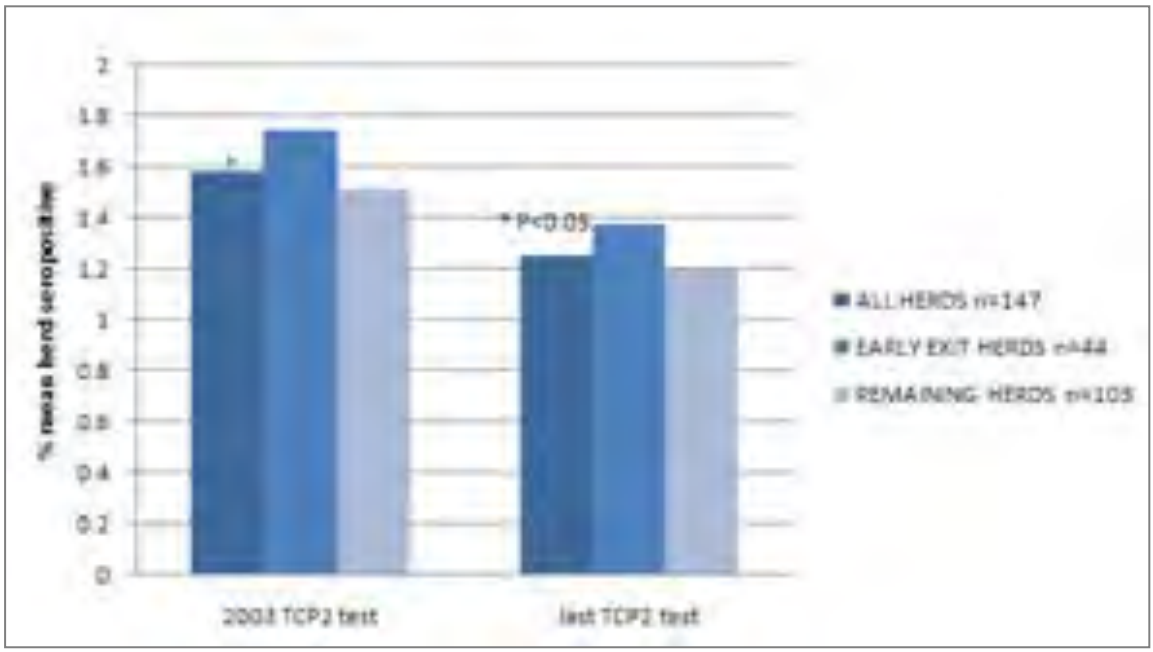
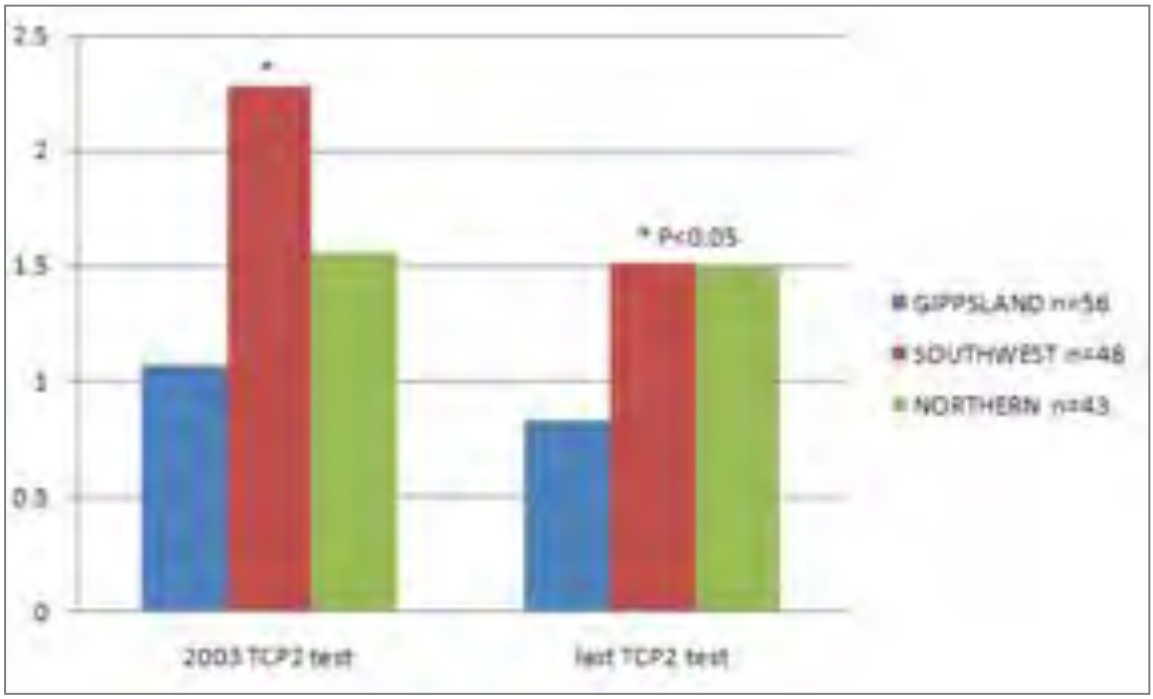


Figure 7: Herd sero-prevalence as a function of region



In their Project Report about future options for the Victorian program (TCP3), VIC DEPI (2013) suggested that TCP3 (and its predecessors) may be selecting for the survival of infected ELISA-negative non-reactor animals. The authors noted that this may help to explain the slow decline in reactor prevalence. This suspicion was based on data from 11 infected dairy and beef herds (termed the 'VIAS' research herds) that had been tested extensively during the 1980s and 90s. This research had shown that ELISA-positive and faecal-culture-

positive animals exist in almost separate groups in a herd. VIC DEPI (2013) also cited data that showed that as many as one third of clinical cases in TCP in 2000-2001 were negative on ELISA, while 12% of clinical cases were negative to the ELISA in non TCP herds.

Marce *et al.* (2010) discuss the matter of density-dependent and frequency-dependent infection dynamics, which may be more appropriate in the context of BJD. In this paper, the authors state that, "*In the first case (density-dependent), the number of cases is usually considered, whereas in the latter (frequency-dependent), the proportion of infected cattle in the population is considered*". This description is in fact in reverse of the truth, which is that density-dependent models are driven by the proportion of affected animals while frequency-dependent models depend on the number of affected animals in the population. In the context of an evenly mixed population, the force of infection applied to any individual can be understood by considering the proportion of infectious individuals. In the case of BJD, however, each additional infectious individual contributes to the burden of Mptb within the environment and the totality of this burden is experienced by susceptible animals. For this reason, a frequency-dependent model is preferred for the Australian model, to represent transmission events stemming from environmental exposure or the consumption of pooled milk. This includes a background rate of cow-calf, calf-calf and cow-heifer transmission via environmental contamination; as well as cow-calf transmission via contaminated pooled milk or colostrum. For other pathways, transmission is effected as an event arising from the contact of a particular infectious cow with its calf. This includes in-utero transmission, transmission via milk or colostrum, and transmission via faecal material on the udder or teats. In this situation, neither density-dependent nor frequency-dependent models will be used.

Herd management: Ridge *et al.* (2005) examined the effect of 27 management factors on the occurrence of clinical cases or positive ELISA test results in animals born after the completion of the second whole herd test in a test-and-control program. The analysis was adjusted for the effect of herd size, the total number of clinical cases that had ever been reported before the start of testing, the proportion of test-positive animals at the initial test, and the time over which farms were observed. A summary of the analysis is given in Table 5, which has been sorted by one-sided p-value. Feeding whole milk containing antibiotic residues was a highly-significant risk factor. This variable reflects the practice of providing calves with pooled milk from cows in the milking herd. Should any of these be infectious, then all calves drinking the milk will be exposed. Feeding once per day (as opposed to twice daily or ad lib feeding) was also a highly significant risk factor. This is difficult to explain from an epidemiological standpoint and presumably is heavily confounded with other management practices. Failure to separate calves from adult cattle was a risk factor, although fractionally non-significant (p=0.07). The direction of this result was not surprising, and its level of significance can be ignored. Having more than three workers on the farm is likely to be strongly correlated with herd size, which was included as a separate variable. The result can be interpreted as a higher risk associated with larger herds (discussion above).

A lower replacement rate was associated with a higher risk, which may signify the introduction of disease from replacements sourced from other infected farms. The provision of water for calves from birth onwards was associated with increased risk. This may reflect a

genuine environmental source of Mptb on some farms, or may be linked to persistently wet environments (for example, access to ponds or dams). Calving animals in a paddock (versus a calving pad or shed) was protective, and reflects a trend toward a lower level of exposure to environmental contamination.

Table 5: Impact of management on new clinical disease or ELISA positives

Management variable	Non-compliant controls associated with increased levels of disease	compliant control (comparator)	One-sided P
Milk type fed	Antibiotic milk	Milk Replacer, Mixed Colostrum and Whole Milk, Whole Milk	0.003
Feeding frequency	Once Daily	Ad Lib, Twice	0.032
Calf shed separation (from adult cattle, faeces or effluent)	No	Yes	0.070
Number of workers on the farm	≥ 3	< 3	0.072
Replacement rate	≤ 20%	> 20%	0.100
Water from birth	Yes	No	0.110
Calving area	Calving Pad, Paddock and Shed, Shed	Paddock	0.136
Calf removal	Not, Once day	Twice day	0.197
Bedding	Paddock, Straw	Rice Hulls, Sawdust, Slats,	0.200
Number of replacement calves	≥ 100	< 100	0.270
Age grazing adult pasture (months)	< 12	³ 12	0.348
Initial feed colostrum	No	Yes	0.357
Purchase replacements	Yes	No	0.376
Weaning age (weeks)	≥ 12	< 12	0.386
Rearer	Cow, Employee	Owner and Employee, Sharefarmer	0.479
Source of water	Dam, River	Bore, Rain, Spring, Town	0.585
Shelter	Paddock	Roof and sides	0.606
Source of water for weaned calves	Dam, Dam and Creek, River and Spring	Bore, Spring, Town	0.621
Heifer deaths in last 12 months	≥ 5	< 5	0.664
Grazing of weaned animals	Silage paddocks	Block, Calf paddocks,	0.724
Supplementary feed	Hay,	Grain, Grain and Hay, Pellets, Pellets and Hay	0.742
Correlation of mother and calf	Observation	Ear Tag, Neck Ear tag	0.782

Management variable	Non-compliant controls associated with increased levels of disease	compliant control (comparator)	One-sided P
Supplements introduced at day	≥ 7	< 7	0.880
Initial identification	Pen No, String	Ear tag, Tattoo	0.918
Supplements for weaned calves	Hay, Silage	Grain, Grain and Hay, Pellets and Silage	0.946
Source of hay	Home, Home and purchased	Purchased	0.968
Feeding method	Trough or bucket	Teat	0.979

Source: adapted from Ridge *et al.* (2005)

Ridge *et al.* (2010) carried out a logistic regression on data collected from the 137 survey herds in 2005, as well as a Cox proportional-hazards analysis on the daily risk of experiencing a home-bred clinical case (Table 6). These authors found that feeding concentrates only – as opposed to hay or straw alone or in combination with concentrates – was in both analyses significantly associated with increased risk. The mechanism by which this occurred was unclear, although might have been linked to a lower consumption of contaminated pasture or the buffering and pH adjustment provided by hay or straw. Feeding method was identified as a significant risk factor in the logistic regression, but the variable was not explained nor reported against elsewhere in the paper. The variable may refer to the feeding of antibiotic-contaminated milk, as discussed below. Feeding once daily as opposed to twice daily or ad lib feeding was associated with an increased risk in both analyses. This result mirrored that reported by Ridge *et al.* (2005).

Providing a water source was associated with an increased risk of new clinical cases or ELISA-positive animals, although the result was not significant (p=0.105). This result again mirrored that of Ridge *et al.* (2005). Feeding antibiotic contaminated waste was in both analyses protective, which is a contrast to the result observed in Ridge *et al.* (2005). The authors could not provide an interpretation for this finding and advised readers to view it with some caution. It is possible that the field was incorrectly coded, or the codes misinterpreted.

Table 6: Impact of management on new clinical disease or ELISA positives

Factor	P-Value
Supplement type for weaned calves	<0.001
Feeding method	0.037
Mortality in weaned calves	0.071
Feeding frequency	0.073
Water source for unweaned calves	0.105
Feeding antibiotic contaminated milk to calves	0.132
Feed (milk) type for unweaned calves	0.158
Source of hay for unweaned calves	0.158
Region within Victoria	0.193
Lime application to calf pens	0.202
Age of calves when supplements are introduced	0.243
Birthing area	0.259
Average weaning age	0.285

Source: adapted from Ridge *et al.* (2010)

Table 7: Impact of management factors on the daily risk of experiencing a home-bred clinical case

Variable	P-Value	Hazard Ratio	95% CI for Hazard Ratio
Birthing area			
Calving pad	<0.01	1.0	
Paddock		2.94	1.289-6.708
Shed		6.61	1.693-25.786
Daily feeding frequency for unweaned calves			
Twice per day	0.02	1.0	
Once per day		1.75	1.102-2.780
Feeding antibiotic and waste milk to unweaned calves			
No	<0.001	1.0	
Yes		0.42	0.247-0.720

Variable	P-Value	Hazard Ratio	95% CI for Hazard Ratio
Supplement fed to weaned calves			
Concentrates only	0.04	1.0	
Hay or straw alone or in combination with concentrates		0.60	0.366-0.983

Source: adapted from Ridge *et al.* (2010)

Some overseas research and modelling papers have included herd management factors in their analyses. These results, however, are either heavily couched in the broader herd management approaches followed in other countries or are quite dated.

On balance, our preference for the Australian model was to run a series of scenarios using herds with different characteristics. In some cases, these characteristics will reflect differing management approaches. In other cases the characteristics will be mitigation strategies directed specifically at BJD.

BJD in beef cattle herds: Larsen *et al.* (2012) carried out an analysis of the epidemiology of BJD in beef cattle herds in parts of Australia where the disease is endemic (New South Wales, Victoria, Tasmania and South Australia). Affected properties were identified, and jurisdictional officers then interviewed the herd owner or manager using a questionnaire about the management and physical characteristics of the herd. This included questions about the herd's association with dairy cattle; enterprise mix before and after the detection of BJD; breeds and numbers of cattle; details of cattle purchases and sales; grazing management; presence and management of any sheep enterprise; supplementary feeding practices; control or eradication methods that were used; factors that influenced the owner's decision to attempt control or eradication of the disease; and the physical characteristics of the farm and beef enterprise, including paddock size, stock watering systems and labour.

The analysis revealed that the purchase of dairy cattle was the most important risk factor determining the introduction of BJD into a beef herd. Index cases were most likely detected by veterinarians investigating clinical cases of scouring or ill-thrifty animals during winter, particularly bulls or aged cows. Most herds with clinical BJD had only a single case, with only one high-prevalence herd detected in the survey group. Over the period of observation, test-and-cull programs did not eradicate BJD unless combined with culling of known high-risk animals, but removal of high-risk cattle by partial or total destocking generally restored the trading status of affected herds. No other herd management practices were found to be significant risk factors.

In a study in beef cattle herds in Texas, USA, Roussel *et al.* (2005) found that risk factors for sero-positive animals included, the species of cattle (sero-prevalence was higher in *Bos indicus* than *Bos taurus*), the geographic location in the State of Texas, and water source (sero-prevalence was higher for cattle watered on a running stream or river).

2.1.6 Strains of Mptb

Whittington *et al.* (2000) investigated the distribution and prevalence of strains of Mptb amongst sheep, cattle and other species with Johne's disease in Australia. A total of 328 isolates were evaluated from farms in New South Wales, Victoria, Tasmania and South Australia. These isolates were classified as either cattle (C) or sheep (S) strains. These authors found that Johne's disease in sheep was always due to ovine strains, while cattle were infected only with bovine strains. This delineation has not been observed consistently, as discussed in Section 2.4 below.

Restriction fragment length polymorphism (RFLP) type S1 was the dominant strain in sheep in New South Wales (97% of isolates) and was the only strain found in sheep from Victoria. Seven RFLP types were present in cattle. RFLP types C3 and C1 were most common (collectively, 85% of isolates), but C1 was not found in New South Wales and C3 was present in dairy cattle but not in beef cattle in Victoria. These differences may be explained by restricted livestock trading patterns between different segments of the cattle industry. Up to five RFLP types were present in some geographic regions in Victoria, while up to three RFLP types were found among cattle on some farms. Individual cattle usually were infected with only one RFLP type, but one animal was infected with both C5 and C4. Two isolates from goats were C type as were three from alpacas, one from a rhinoceros, and two from a human with Crohn's disease. The prevalence of specific RFLP types in Australia differs from those reported in Europe and elsewhere.

2.2 Diagnostic Tests for BJD

A review of diagnostic tests and testing strategies for BJD was provided in Whittington and Sergeant (2001). Cursory updates to this were given by Sergeant (2005). With two exceptions (herd environmental culture and the high-throughput direct faecal PCR assay) there have been few substantive advancements in the field since 2005.

Sergeant (2005) pointed out that the one of greatest difficulties in understanding the epidemiology of BJD lies in the fact that ante-mortem tests are of generally low sensitivity. This is particularly problematic at early stages of the disease process. Similarly, Whittington and Sergeant (2001) noted that the different types of test are better applied to animals in different stages of the disease. This is summarised in Table 8. In this table, the terms 'early', 'middle' and 'late' are descriptive only, but approximate weeks, months and years, respectively. The terms low, moderate and high indicate sensitivity or specificity in the ranges <40%, 40-70%, >70% and <80%, 80-95% and >95%, respectively.

Table 8: Characteristics of diagnostic tests for BJD

Test	Stage of pathogenesis	Potential sensitivity	Potential specificity
Tests for cell mediated immunity	Early, middle	Moderate to high	Moderate
Culture of intestinal tissues	Early, middle, late	High	High
Histopathology of intestinal tissues	Early, middle, late	Moderate to high	High
Culture of faeces	Middle, late	Moderate to high	High
Tests for serum antibody	Middle, late	Low to high	Moderate to high
Gross pathology	Late	Low to moderate	Low to moderate
Clinical signs	Late	Low to moderate	Low to moderate

Source: adapted from Whittington and Sergeant (2001)

Whittington and Sergeant (2001) explain that meaningful comparisons between the diagnostic tests for BJD can only be made when the stage of disease in animals in the sample is understood. The comparisons may be invalid if this information is lacking, if case definitions are not equivalent and if inefficient or non-standardised methods have been used. For these reasons the data from different studies cannot generally be compared reliably. This notwithstanding, the comparative table of Timms *et al.* (2011) provides a useful point of reference and has been reproduced in Table 9 below. References for each of the estimates cited in this table were given by Timms *et al.* (2011), but have been removed here for brevity. Cited heavily by Timms *et al.* (2011), Alinovi *et al.* (2009) found that with a prevalence of infection of 24%, the mean sensitivity of solid culture, liquid culture and real-time PCR across the herd were 72%, 65% and 72%, respectively. The specificities were 98%, 98% and 99%, respectively. Using the same herd, these authors estimated mean serum ELISA sensitivity to be 26% and specificity to be 100%.

It is important when interpreting the test characteristics cited in these and other research and review papers to delineate between the sensitivity or specificity of a test when applied: (a) to a whole herd infected at a given prevalence (herd sensitivity or specificity); (b) to an individual animal selected at random from a herd infected at a given prevalence (mean sensitivity or specificity); or (c) to an individual animal at a particular stage in the pathogenesis of BJD.

Table 9: Performance of diagnostic tests for BJD

	Sensitivity	Specificity
Culture		
Bovine milk	16%-37%	100%
Bovine tissue	60%	100%
Bovine blood	10 bacterial cells / ml of whole blood	100%
Faeces sheep	8%	100%
Faeces goat	25% -0.38	0.9
Faeces bovine(pre-clinical)		
Liquid media	54%-65%	95%-99%
Solid media	45%-72%	98%-100%
Faeces bovine (late stage)		
Liquid media	93%	95%
Solid media	91%	100%
Molecular		
DNA nested IS900 PCR	0.01 pg of DNA (10 genomic copies)	100%
Conventional IS900 PCR	0.1 pg of DNA (100 genomic copies)	100%
f57 PCR	0.1 pg of DNA (100 genomic copies)	100%
IS900 PCR (bovine faeces)	96%	100%
RT-PCR (bovine faeces)	72%	96%
Serology		
Bovine ELISA serology	26%	100%
Bovine ELISA in bulk milk	30%-97%	83%
Hircine ELISA serology	1.5-76.6%	44.6-97.6
Complement Fixation test (CFT)	21-52%	96.9%
Histology		
Histology of bovine biopsies	90 ±5%	100%

Source: adapted from Timms *et al.* (2011)

2.2.1 Serum and Milk ELISA

Timms *et al.* (2011) cited the individual-level sensitivity of the serum ELISA to be 87% for clinical cases, 75% for subclinical heavy faecal shedders and 15% for subclinical light faecal shedders. Whittington and Sergeant (2001) suggested that the usual mix of animals in a subclinically-infected herd would render the herd-level sensitivity of ELISA to be approximately 45% and faecal culture 45-55%. These authors noted, however, that their stated herd-level estimates may be too high, and that the work of Whitlock *et al.* (2000) indicated that the actual figure for the herd-level sensitivity of both faecal culture and ELISA in cattle may be about 35%.

As noted above (and illustrated in Table 9) the mean individual-level sensitivity and specificity for the serum ELISA applied in a herd with prevalence of 24% were found by

Alinovi *et al.* (2009) to be approximately 26% and 100%, respectively. The importance of prevalence in this context is that it is known to influence the force of infection. This, in turn, impacts upon the aggressiveness of disease in most affected animals and, thus, the sensitivity of different tests.

Another important caveat when interpreting the results of a serum ELISA applied in a herd setting is the presence or absence of an ELISA-based test-and-cull policy. Where that occurs, animals that have a detectable humoral response will tend to be selected for removal and leave behind within the herd a relatively higher proportion of latently-infected or low-antibody animals. The overall ability of subsequent ELISA herd tests is then likely to be progressively diminished. For this reason, older animals are generally selected for testing, with repeated negative tests spaced at regular (for example yearly) intervals and combined with management to minimise the risk of introducing infection. The passage of time allows infected animals to advance in the disease process and reach positive thresholds in diagnostic tests (Whittington and Sergeant, 2001).

Of the contemporary modelling studies included in this review, only Lu *et al.* (2008) and Weber and Groenendaal (2012) specifically included a serum ELISA. A summary of the estimates used by these authors is given in Table 10 below. The serum ELISA has a 2-3 day turnaround (VIC DEPI, 2013) and has a laboratory processing cost of less than $7 (VIC DEPI, 2013).

Table 10: Model estimates for the sensitivity and specificity of serum ELISA

Study	Sensitivity	Specificity
Lu *et al.* (2008)	20-40% (low shedding) 75% (high shedding)	100%
Weber and Groenendaal (2012)	1% (latent infected) 10% (low infectious) 60% (high infectious) 80% (clinical disease)	99.7%

Bovine Johne's disease ELISAs have also been applied to individual and bulk milk samples. Sergeant (2005) noted that although this application shows promise as an alternative individual animal test to serology, it is likely to be of limited value as a bulk milk test for surveillance purposes. Somewhat at odds with this, Timms *et al.* (2011) reported that the bulk milk ELISA had a herd-level sensitivity of approximately 97% (Nielsen *et al.*, 2000) and an individual sensitivity of 30% (Hendrick *et al.*, 2006; Singh *et al.*, 2007). These authors noted, however, that the milk ELISA was substantially hampered by sampling, milk handling and treatment issues, all of which can have a marked impact on its performance.

In a study of 32 small Canadian dairy herds with a median herd size of 66 animals followed over 2 years, Lavers *et al.* (2014) evaluated the performance of three different commercial milk ELISAs. In this study, faecal and milk samples were collected from all milking cows at 6-month intervals. Faecal samples were pooled by cow age, with five cow samples per pool. Individual faecal culture was then undertaken on samples from the positive pools. Herd-level BJD status was defined as positive if, at any point during the study, a pooled faecal culture

from the herd was positive. The authors found the herd-level sensitivity of the three ELISAs to be: ELISA A, 59% (95% CI 36-78%); ELISA B, 56% (95% CI 32-77%); and ELISA C, 63% (95% CI 41-81%). Herd specificity for ELISA A, B, and C was 80% (95% CI, 71-88%), 96% (95% CI, 89-98%) and 92% (95% CI, 86-96%), respectively. Within this result, herd-level sensitivity was found to vary markedly with herd prevalence. In herds with a mean Mptb prevalence of 1%, for example, the herd sensitivity of ELISA B fell to approximately 11%. When herd prevalence was 5%, the sensitivity of the same ELISA was approximately 62%. The authors concluded that although milk ELISA worked well to establish the herd Mptb status of high-prevalence herds, it was an unreliable test for low-prevalence herds. Sergeant *et al.* (2008) noted that the sensitivity of milk ELISAs for BJD varies with the age of the animal and stage of infection, but lay in the range of <10% in young animals to >80% in older animals with clinical disease or high levels of faecal shedding of Mptb. Specificity estimates also vary considerably, but are generally >95% and often >99%.

On balance, our preference for the Australian model was to use the individual-level sensitivities and specificities for serum ELISA given by Weber and Groenendaal (2012) and cited in Table 10. Robust estimates for individual-level sensitivity and specificity of milk ELISAs at different stages of the disease were not identified in the literature, although Sergeant *et al.* (2008) suggested that they would be very similar to those of the serum ELISA. Our approach was to follow the recommendation of Sergeant *et al.* (2008) and use the Weber and Groenendaal (2012) estimates mentioned above. All diagnostic tests were parameterised at the individual level, allowing herd-level sensitivity and specificity to be calculated from the simulation.

2.2.2 Faecal Culture in Solid or Liquid Media

Timms *et al.* (2011) noted that Mptb could be cultured from bovine tissue, milk, faeces or blood. The sensitivity depended on many factors, including the stage of clinical disease, the type of media used, the decontamination protocol, the age of the sample and what type of sample is used. For pre-clinical animals, faecal culture from liquid media and solid media was reported to have a sensitivity of approximately 54%-65% and 45%-72%, respectively. For clinically-affected animals the sensitivity for liquid media and solid media increased to approximately 93% and 91%, respectively. In all cases, the specificity approached 100% (Table 9). Timms *et al.* (2011) noted that faecal culture could detect infected animals six months before they started showing clinical manifestations, identifying between 30-42% of all infected cattle. Therefore, although the method is technically demanding and time consuming, it was considered a useful tool in abating the spread of BJD. Culture from bovine blood has received little attention, but one study reached a sensitivity of 10 Mptb cells per mL of whole blood and this could also be used as an epidemiological tool (Bower *et al.*, 2010).

Sergeant (2005) noted that the pooling of faecal samples for culture had been researched or applied in a number of countries for detection of Johne's disease in both sheep and cattle. Pooled culture is primarily useful as a tool for the identification of infected herds or flocks, or for certification of low-risk herds and flocks. Environmental sampling has also been used as an alternative to faecal sampling for the identification of high-risk areas on dairy farms, and for evaluating the effectiveness of control programs.

Lombard *et al.* (2007) investigated the correlation between the culture of environmental samples (approximately 5 per farm) and the results of individual serum and milk ELISAs and individual faecal cultures. Of the 98 operations tested with the environmental sample culture, 97 had individual serum ELISA results, 60 had individual faecal culture results, and 34 had individual milk ELISA results. Sixty-nine of the 98 operations (70.4%) had at least one environmental sample that was culture-positive. Of the 50 herds classified as infected by faecal culture, 38 (76.0%) were identified by environmental culture. Two of the 10 operations classified as not infected based on individual animal faecal culture were environmental-culture-positive. Of the 80 operations classified as infected based on serum ELISA-positive results, 61 (76.3%) were identified as environmental-positive, whereas 20 of the 28 (71.4%) operations identified as infected based on milk ELISA were detected by environmental sampling. Environmental sample culturing is less costly than individual animal sampling, does not require animal restraint and identified more than 70% of infected operations. Environmental sampling is another diagnostic tool that veterinarians and dairy producers can use to determine herd infection status for Mptb.

A special case of environmental sampling is Herd Environmental Culture, or HEC. This test was described in the two Victorian Project Reports for TCP3 circulated by the Victorian Government in 2011 (VIC DPI, 2011) and 2013 (VIC DEPI, 2013). A search of the literature failed to identify any subsequent analysis of the HEC test and much of what is written below is paraphrased from the two Victorian Government documents.

The HEC test was approved in 2011 for use in dairy herds. A representative herd faecal sample is collected by a veterinarian from the dairy yard for culture. The aggregated faecal sample required for performing a HEC test is convenient and quick to collect, and the sample collection process does not interfere with other farm activities. The minimum turnaround time for a HEC test sample with no bacterial growth is approximately 9 weeks. Samples with microbial growth may take 9-16 weeks for the culture to be completed. The HEC test is reported to have higher herd-level sensitivity than the ELISA test (45.8%), although this will depend on the prevalence of infection within the herd. Specificity is considered to be 100%.

Under the SDRGs[7] the HEC test can be used: (a) as a Check Test (Maintenance Test) for herds not known to be infected; and (b) for assessing progress in eradication programs. The HEC test cannot currently be used to progress from an infected herd status. The higher sensitivity of the HEC test means that latent infection is likely to be found in herds from which the owners think that BJD has been eradicated (or deemed non-infected) based on results of ELISA testing.

The above notwithstanding, VIC DEPI (2013) maintained that the HEC test has limited application in TCP3 as it is a herd-level test that does not identify individual infected animals. The test has the potential through repeated negative tests to be highly sensitive, and could have application in TCP3 by replacing the ELISA test for progressing status of RD1 and RD2

[7] The nationally agreed Standards, Definitions, Rules and Guidelines for BJD provide guiding principles, upon which industries and state/territory governments formulate disease control and management programs to suit their circumstances (VIC DEPI, 2013).

herds. A majority of herds currently participating in TCP3 have not attained a status of at least RD1 and therefore still require testing of individual animals using the ELISA test. The HEC test may have an important role in vaccination programs if the owner/manager wishes to prove that disease has been reduced to negligible or undetectable levels.

Excluding collection costs, the cost of a single HEC test is approximately $150. The test can be completed in 9 weeks.

Of the contemporary modelling studies included in this review, only Marce *et al.* (2010) and Lu *et al.* (2013b) did not include faecal culture. A summary of the estimates used by the balance of authors is given in Table 11 below.

On balance, our preference for the Australian model was to parameterise individual-level faecal culture and the HEC tests separately. The sensitivity of faecal culture was conservatively taken to be 45% for transiently infectious and low-shedding subclinically-affected animals, and 93% for high-shedding and clinically-affected animals. This was adapted from Timms *et al.* (2011). The herd-level sensitivity of the HEC test was taken to be 45%. This was the single example where herd-level estimate was parameterised rather than calculated from the simulation. The specificity of the individual-level faecal culture and the HEC test were taken to be 100%.

Table 11: Model estimates for the sensitivity and specificity of faecal culture

Study	Sensitivity	Specificity
Mitchell *et al.* (2008)	20% (low shedding with one culture) 25% (low shedding with two cultures)	Not given
Lu *et al.* (2008)	40-60% (low shedding) 90% (high shedding)	100%
Lu *et al.* (2010)	50% (low shedding) 90% (high shedding)	Not given
Lu *et al.* (2013a)	50% (low shedding) 90% (high shedding)	Not given
Weber and Groenendaal (2012)	Individual faecal culture 0% (latent infected) 40% (low infectious) 95% (high infectious) 90% (clinical disease) Pooled faecal culture 0% (latent infected) 36% (low infectious) 95% (high infectious) 90% (clinical disease)	100%

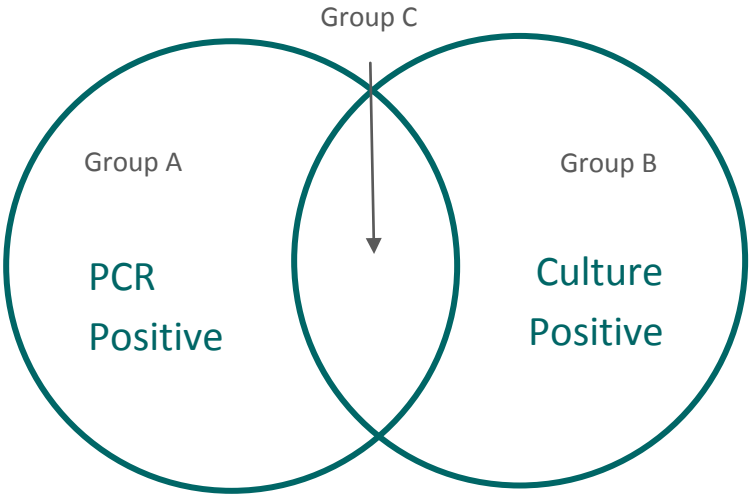
2.2.3 PCR on Faeces, Milk or Tissue Samples

Most PCR tests for Mptb are based on a gene called IS900 which exists in 15-20 copies in each Mptb genome. This gene is quite specific for Mptb, but related genes exist in obscure species of mycobacteria which tend to be found in the farm environment. These organisms occasionally find their way into faeces (presumably after ingestion with fodder) and may cause cross-reactions with IS900 (Whittington *et al.*, 2013). For this reason, careful design and validation of PCR assays for Mptb is critical. The f57 segment is found only in Mptb (single copy), and does not occur in other mycobacteria – including other species of the M. avium complex. The presence of f57 is usually ascertained using a standard PCR and is an ideal backup to the IS900 assay (Timms *et al.*, 2011).

PCR tests can be applied to faeces, tissues and other types of samples. Whittington *et al.* (2013) explained that a PCR will detect a set of animals that overlaps with that detected by culture. The principle of this is shown in Figure 8. Whittington and Sergeant (2001) suggested that a comparison of the faecal PCR test with faecal culture, tissue culture and histopathology is required to better understand the nature of positive results in the two faecal tests. It is already known that many animals with positive tissue culture results are negative in faecal culture because of stage of infection. However it is not yet known whether it is these animals that test positive in the faecal PCR assay. PCR detects DNA, regardless of whether the organism from which it was extracted was alive or dead. Culture detects only living Mptb. Approximately 90 to 99% of the living Mptb in a faecal sample is destroyed during decontamination of the sample prior to culture. For this reason there must be >200 live Mptb per gram of faeces to ensure successful culture. The losses of Mptb during preparation of a sample for PCR are probably less than the losses during culture (Whittington *et al.*, 2013). Conversely, there may be substances in clinical samples like faeces which inhibit PCR. These may vary from sample to sample, and may be affected by diet.

For these reasons, culture results and PCR results for a given sample may differ, and so both tests work best at herd level. The PCR, which may be more sensitive than culture, is especially appropriate as a herd test because it may detect passive shedding of dead Mptb. On an endemically infected farm, there may be high levels of pasture contamination with Mptb, but over time most of the Mptb cells on pasture die (about 90% of bacteria die each month). DNA persists intact within these dead cells for many months and possibly for years. These robust but dead cells can be ingested and pass through the gut, appearing in faeces. A low signal from these may thus be seen in the PCR result (Whittington *et al.*, 2013).

Figure 8: Overlap of PCR-positive and culture positive animals



Source: adapted from Whittington *et al.* (2013)

A PCR test for BJD, termed the High-Throughput Real-Time PCR (HT-J) Test for the direct detection of Mptb in faeces, has recently been developed. Although the test has been approved for use by laboratories in Australia for testing individual cattle faecal samples, its use and application is yet to be agreed to and incorporated into the SDRGs (VIC DEPI, 2013). An analysis of the HT-J test was given in Whittington *et al.* (2013), and is summarised below.

In order to validate the HT-J test, samples were sourced from more than 20 beef herds where a diagnosis of Mptb infection had been made in at least one animal. The herds were located in New South Wales, Tasmania and Victoria. Samples were collected from across the herds and were not biased in favour of older animals, clinical cases or ELISA reactors. Faecal samples were also obtained from unexposed properties from Queensland and Western Australia. Approximately 1,300 bovine faecal samples were tested in two laboratories.

The apparent sensitivity of the PCR was 60-70% when compared with faecal culture. However, approximately three times as many culture negative samples were detected in the faecal PCR test compared to faecal culture positive samples that were not detected in the PCR. Thus, in the exposed herds that were tested, there was a greater number of PCR-positive samples than faecal-culture-positive samples (more than half as many again). The specificity of the test at both laboratories was greater than 99%. Overall, the sensitivity of the PCR appeared to be greater than faecal culture because more animals from infected flocks and herds tested positive in faecal PCR than in faecal culture. However, the true infection status of the majority of these animals was not able to be determined in this project.

The HT-J test has a fast turnaround time of approximately one week and is estimated to have a laboratory cost of about $100-155 per test (VIC DEPI, 2013).[8] The cost of this test is likely to reduce if increased uptake occurs in Australia. Like the HEC test, the HT-J test could

[8] A minimum number of tests may be specified by some laboratories. Gribbles Veterinary for example has a cost of approximately $100 per sample with a minimum of 10 samples (VIC DEPI, 2013).

potentially have application in TCP3 for progressing herds with a status of RD1 or RD2. The higher sensitivity of the HT-J test means that latent infection is likely to be found in herds where the owner thinks they have eradicated the disease or are free of disease based on results of ELISA testing. Likewise, non-infected passive shedding animals may be identified as infected animals using this test and unnecessarily culled (VIC DEPI, 2013).

Of the contemporary modelling studies included in this review, only Lu *et al.* (2008) included estimates for the characteristics of faecal PCR. These authors used a sensitivity of 4% for low shedders and 80% for high shedders. The specificity was 99%.

On balance, our preference for the Australian model was to adopt the estimates of Lu *et al.* (2008) as the parameters for the HT-J PCR test. That is, a sensitivity of 4% for low-shedding subclinically-affected animals and 80% for high-shedding subclinical and clinically-affected animals. The specificity will be taken to be 100%.

2.3 Vaccination for BJD

VIC DEPI (2013) noted that Zoetis (formerly Pfizer Animal Health) is currently in the process of registering a BJD vaccine (Silirum®) with the Australian Pesticides and Veterinary Medicines Authority (APVMA) and expects to have the product on the market in early 2014. Silirum® is a killed vaccine similar to Gudair, which is currently used across the Australian sheep industry to reduce the prevalence of ovine Johne's disease in affected flocks and to minimise the risk of new introductions.

In general terms, a vaccine against BJD might act in the following ways:

- Reduce susceptibility to infection;
- Reduce the infectiousness of affected animals, resulting from
  - Reduced faecal excretion of Mptb,
  - Reduced excretion of Mptb in milk and colostrum, and
  - Reduced in-utero transmission of Mptb; and
- Reduce clinical symptoms and production effects, with the possibility of complete recovery.

With some or all of these effects, vaccination might be used to reduce the prevalence of infection in infected herds or to minimise the risk of introducing Mptb with the purchase of replacement animals. When combined with hygienic calf rearing and a systematic reduction in the number of older animals in the herd, it might be possible to reduce the prevalence of infection to an undetectable level. Conversely, a small proportion of animals vaccinated as 3-10 week old calves may test positive on the ELISA blood test. Vaccination of older age classes in endemically infected herds may also result in a higher proportion of animals testing positive on the ELISA blood test. The vaccine may not therefore be entirely compatible with Victoria's current test-and-control program (TCP3) and vaccinated animals may also be excluded from some overseas export markets.

These effects are discussed in turn. At the close of the section are accounts of two contemporary modelling studies that have considered the impacts of vaccination on the control of BJD.

Silirum® is likely to cost approximately $20 to $25 per dose. A single dose is initially administered to calves at around the time of weaning, and no booster is required. For an average TCP herd of 350 cows with a 25% annual heifer calf replacement rate, the cost of vaccination for the 87 heifer calves at $25 each would be approximately $2,200 annually (VIC DEPI, 2013).

Protection of susceptible animals from infection with Mptb: Little *et al.* (2012) undertook an evaluation of the field efficacy of Silirum® in two Australian dairy herds. The principal author of this study was an employee of (then) Pfizer Animal Health and co-authorship was provided from the (then) Victorian Department of Primary Industries. The paper covered the initial part of the study, which was planned to progress through until at least 2012. A follow-up paper was not identified in the literature but may have been produced as an in-house report. As data were limited, the authors of the interim paper declined to report statistical significance.

All classes of female cattle in two herds (including adult cows, 2 year-old heifers, yearling heifers, autumn-born calves and newborn calves) were enrolled in the study at its commencement in 2005, and these animals were randomly allocated to an unvaccinated control group (group NTX) and a Silirum®-vaccinated group (group T01). In the four subsequent years (2006-2009) newborn female calves were also enrolled in the study and randomly allocated to one of the two groups. A total of 1,351 animals were enrolled in 2005 (675 controls, 676 vaccinates) and a further 1,009 newborn calves were enrolled between 2006 and 2009 (502 controls, 507 vaccinates). Blood and faecal samples were collected twice a year from animals more than 15 months of age.

In all age groups vaccinated in the first year of this study, including newborn calves vaccinated at 3-6 weeks of age, administration of a single dose of Silirum® induced a cell-mediated immune response, as measured by the mean γ-IFN response to both avian tuberculin PPD and Johnin PPD. Vaccination also induced a humoral (antibody-mediated) immune response in all age groups except newborn calves. This study did not investigate the response of vaccinates and control animals to challenge with Mptb, although the immune responses suggest that some protection would have been afforded.

In a study spanning 14 years, Muskens *et al.* (2002) examined the efficacy of a killed vaccine for Mptb in two Dutch dairy herds with a history of clinical BJD. At the start of the study, at least 5% of cattle in both herds showed clinical symptoms of BJD annually. The B-cell response was evaluated using CFT and ELISA and the CMI response was evaluated using the γ-interferon assay. The study showed a marked and prolonged effect on both humoral and cellular immune responses. The authors did note, however, that responses were highly variable amongst individual animals.

Munoz *et al.* (2005) evaluated the efficacy of Silirum® in calves experimentally challenged with Mptb. Ten calves from a total of 18 were injected subcutaneously when 2 months old with a single dose of the vaccine. The remaining 8 calves were controls. Two months after vaccination eight and six calves from the vaccinated and control groups (respectively) were challenged with six doses of 6.9×10^{10} cfu of Mptb. Peripheral cellular and humoral immune responses were assessed as well as Mptb faecal shedding between 0 and 330 days post vaccination. Three vaccinated and two control calves were slaughtered at 180 days and the

remaining 13 calves at 330 days. Pathologic and bacteriologic evaluation of intestine and lymph nodes samples were undertaken. The number of granulomas was counted in sections from both locations. Humoral responses appeared in vaccinated groups at 90 days, whereas cellular responses were detected at 30 days, reaching the highest values at 120 days. A significant reduction in the number of granulomas present in the tissues was observed in vaccinated calves. These calves showed either no or only focal lesions confined mainly to the lymphoid tissue, except in one case of the diffuse form of infection. In unvaccinated control calves, diffuse lesions extended to the intestinal mucosa. The authors concluded that the administration of a single dose of Silirum® in calves was able to control the progression of disease. Vaccinated calves had fewer and less severe lesions and a lower tissue burden of Mptb than unvaccinated calves.

Kohler *et al.* (2009) undertook a systematic review and meta-analysis of research into the effects of vaccination against Mptb and its significance in the control of BJD. Experimental (n=12) and field studies (n=14) were separated. The paper was scant and difficult to interpret and was not published beyond the proceedings of the 10th International Colloquium on Paratuberculosis (2009). Results appeared to indicate that experimental studies had shown a reduced likelihood of a positive pathological or histological results (OR=0.35), or a positive organ culture result (OR=0.35), for animals vaccinated prior to infection. By comparison, field studies showed a reduced rate of identifying Mptb using histopathology (OR=0.17), organ culture (OR=0.40) and faecal culture (OR=0.24). Collectively, these results led the authors to conclude that vaccination resulted in a lower risk of infection.

Our preference for the Australian model was to use sensitivity analysis to examine the impact of reduced susceptibility of vaccinates on the development and maintenance of BJD within a dairy or beef herd. This analysis compares vaccines that reduce susceptibility to infection by 25%, 60% and 75%. There is not currently sufficient published evidence about the efficacy of Silirum® or comparable vaccines to enable us to parameterise the model with confidence.

Reduced infectiousness of affected animals: a précis of the Little *et al.* (2012) Australian field evaluation of Silirum® was given at the start of this section. At the 5-year study time point, the authors reported a lower proportion of animals with Mptb-positive faecal cultures in vaccinates compared to controls, across all age groups (Table 12). A comparison of ante-mortem faecal cultures and post-mortem histopathology data indicated strong agreement between animals with at least two Mptb-positive cultures and a subsequent positive histopathology classification. Data for this result were not provided. The proportion of animals with at least two Mptb-positive faecal cultures during the first 5 years of the study was lower in vaccinates compared to controls for all age groups except adult cows (Table 13). Collectively these results suggest that vaccinated animals are likely to be less infectious than controls.

Table 12: Animals with Mptb-positive faecal culture

Age group at enrolment	Negative control group (NTX)		Silirum®-vaccinated group (T01)	
	Rate	Percentage (%)	Rate	Percentage (%)
Adult cows (2005)	4/39	10.3	1/30	3.3
1-2 year old heifers (2005)	11/90	12.2	5/88	5.7
Newborn calves (2005-08)	27/365	7.4	5/372	1.3

Table 13: Animals with two or more Mptb-positive faecal cultures

Age group at enrolment	Negative control group (NTX)		Silirum®-vaccinated group (T01)	
	Rate	Percentage (%)	Rate	Percentage (%)
Adult cows (2005)	39/313	12.5	41/315	13.0
1-2 year old heifers (2005)	25/182	13.7	6/180	3.3
Newborn calves (2005-08)	10/417	2.4	4/427	0.9

Kalis *et al.* (2001) undertook two studies of 58 Dutch dairy herds to: (a) determine whether vaccination with a killed vaccine prevented faecal shedding of Mptb; (b) compare the effectiveness of a culture and cull program in vaccinated and unvaccinated herds; and (c) compare paratuberculosis-related preventive management in vaccinated and unvaccinated herds. The first study was cross-sectional study analysis of vaccinated (n=25) and unvaccinated (n=29) herds. Faecal samples were obtained from adult cows in herds with and without a history of vaccination with a killed vaccine and management measures were evaluated. The authors found that Mptb could be cultured from 4.4% of the 29 vaccinated herds and 6.7% of the 29 unvaccinated herds, although the difference was not significant. The second study was a longitudinal analysis of vaccinated (n=2) and unvaccinated (n=2) herds. In this study, faecal samples were obtained four times at 6-month intervals from cows older than 6 months. Cows that had positive test results were removed from the herd directly after the outcome of the culture. Here the authors found that the percentage of positive results on culture decreased from 10.9% and 5.7% to 3.5% and 0%, respectively, in the two vaccinated herds. In the two unvaccinated herds, percentages decreased from 6.1% and 16.5% to 0% and 2.3%, respectively. These results were not significant. The authors also noted that the owners of herds that were not vaccinated tended to follow more preventive management procedures and practiced less feeding of raw milk to calves.

Juste *et al.* (2009) examined the effect of vaccination with Silirum® on faecal shedding in six dairy herds in the Basque region of Spain. These authors found that vaccination led to a reduction in the prevalence of faecal shedders of 100% in three of the four farms. The total amount of Mptb shed in faeces was reduced by 77%. The paper was in poor English and could not be reviewed with complete confidence.

Bastida and Juste (2011) undertook a systematic review and meta-analysis of research into the effects of vaccination against Mptb and its significance in the control of BJD. These authors categorised research outcomes as 'production effects', 'epidemiological effects' or 'pathogenetic effects'. Under this categorisation, production effects relate to the frequency of clinical cases or mortality rates, epidemiological effects described the frequency or amount of Mptb shed in faeces or recovered from tissue cultures, and pathogenetic effects were the frequency or severity of histopathological lesions. The second category is most relevant to this part of the review. The authors reported a reduction in epidemiological effect of Mptb of approximately 73%, when averaged across 25 research papers. The rigour or robustness of this metric could not be determined from the detail provided in the paper, and nor was it clear how best to apply the result other than to conclude that most studies appeared to show a reduction in the amount of faecal shedding.

Alonso-Hearn *et al.* (2012) collected faeces and gastrointestinal tissues at slaughter from 50 cows vaccinated with Silirum® and 38 unvaccinated cows. The authors found that vaccination was associated with a significant reduction of the frequency of Mptb in faeces and gut tissues compared with the unvaccinated animals. In addition, the frequency of vaccinated animals with heavy bacterial load in gut tissues was 40% lower than the frequency of the unvaccinated animals with the same load of Mptb.

Knust *et al.* (2013) used 200 vaccinated and 195 unvaccinated dairy cows from three herds in Wisconsin to evaluate the effects of a killed whole-cell vaccine on faecal shedding, the development of clinical BJD, milk production, measures of reproduction, and within-herd longevity of dairy cattle. The first of these effects is relevant here. The balance is discussed in the section below. In this study, every second heifer calf born in each herd received the Mptb vaccine. Bacteriologic culture of faecal samples was performed annually for 7 years and the results confirmed with histology and PCR. This study found that vaccinates had a significantly lower likelihood of testing positive for Mptb by faecal culture (HR=0.57; 95% CI 0.34 to 0.97) and that, in all herds, the prevalence of faecal shedding decreased over time. The authors concluded that vaccination appeared to be an effective tool as part of a program to control the spread of BJD in dairy cattle.

Our preference for the Australian model was to use sensitivity analysis examine the impact of reduced infectiousness of vaccinates on the development and maintenance of BJD within a herd. This analysis compares vaccines that reduce infectiousness by 25%, 60% and 75%. In this context, reduced infectiousness applies to all transmission pathways, including in-utero transmission, peri-natal transmission through contaminated teats or udder, transmission through contaminated colostrum or milk, and transmission through contact with a contaminated environment.

Reduction in clinical symptoms: a précis of the Little *et al.* (2012) Australian field evaluation of Silirum® was given at the start of this section. The authors found that approximately 50% of animals enrolled between 2005 and 2008 were removed from the study during its first 5 years. These animals had died, or were culled sold. For each age group, the proportion of animals removed was similar between vaccinates and controls. Overall, 42 animals were culled from both herds due to clinical signs of BJD. Twenty-six (62%) of these were controls and 16 (38%) were vaccinates. The authors suggested that because these animals were

enrolled in the study as adult cows or 1-2 year-old heifers, they were likely to have been infected prior to vaccination. This position is difficult to corroborate from the evidence given as it would seem quite plausible that a proportion at least might have been infected during the course of the study. Post-mortem specimens of the gastrointestinal tract from 269 animals were submitted for histopathology and tissue culture. It is not clear, however, if this sample of 269 animals was drawn at random from the study population or whether these animals were targeted for post-mortem examination on the basis of clinical symptoms. A total of 101 animals were then classified as positive or equivocal for BJD. The authors state that only 49 of these 101 animals were definitively positive on histopathology – that is, 27 (55%) controls and 22 (45%) vaccinates. It is difficult to understand why only 49 of 101 purported positives were conclusively positive although the result appeared to indicate a reasonably even spread of disease amongst vaccinated and control animals. On balance, it was difficult to draw robust conclusions from this study as to the effect of Silirum® on the clinical expression of BJD.

In a study of five Holstein-Friesian dairy farms and one Jersey dairy farm in the Basque region of Spain, Alonso-Hearn *et al.* (2012) found that the peak age of BJD-associated culling was from 4.5 to 5 yr old (21%) in animals vaccinated with Silirum® and from 3 to 4.5 yr old (60%) in unvaccinated animals. The vaccinated and unvaccinated animals with suspected BJD were culled at an average age of 4.7 and 3.7 years, respectively. This suggested that vaccination led to an increase in average productive life. The authors also found a positive effect of vaccination on the carcass weights of the animals with severe histopathological lesions at slaughter, when compared with the unvaccinated animals. The authors concluded that vaccination was likely to be having a therapeutic effect, with attenuation of pre-existing infection in cows naturally infected with Mptb.

The systematic review and meta-analysis of Bastida and Juste (2011) was discussed above. These authors reported a reduction in the 'production effects' (the frequency of clinical cases or mortality rates) and 'pathogenetic effects' (the frequency or severity of histopathological lesions) of Mptb of approximately 96% and 58%, when averaged across the studies included in the review. As noted previously, the rigour or robustness of these metric could not be determined from the detail provided in the paper, and nor was it clear how best to apply the results other than to conclude that most studies appeared to show a reduction in the amount of clinical disease and the frequency or severity of histopathological lesions.

Knust *et al.* (2013) used 200 vaccinated and 195 unvaccinated (control) dairy cows from three herds in Wisconsin to evaluate the effects of a killed whole-cell vaccine on faecal shedding, the development of clinical BJD, milk production, measures of reproduction, and within-herd longevity of dairy cattle. These authors found that overall within-herd longevity, total milk production, and calving-to-conception intervals were similar between vaccinates and controls. The study reported a reduction in faecal shedding (discussion above) and on that basis concluded that vaccination appeared to be an effective tool as part of a program to control the spread of BJD in dairy cattle.

Our preference for the Australian model was to use sensitivity analysis examine the impact of reduced clinical expression in vaccinates on the development and maintenance of BJD

within a dairy or beef herd. This analysis compares vaccines that reduce clinical expression by 25%, 60% and 75%. There is not currently sufficient published evidence about the efficacy of Silirum® or comparable vaccines to enable us to parameterise this aspect of the model with confidence.

Modelling studies of the efficacy of vaccination: of the contemporary modelling studies examined in this review, only the works of Lu *et al.* (2013a and 2013b) included a focus on the efficacy of vaccination.

Lu *et al.* (2013a) carried out a series of simulations experiments to investigate the impact of an imperfect vaccine on the persistence of BJD in dairy herds. These authors considered that vaccination might act to: (a) reduce the susceptibility of exposed animals; (b) reduce the infectiousness (shedding) of infected animals at different stages in the pathogenesis of the disease; (c) prolong the latent period; (d) slow the progression from low to high shedding; and (e) reduce the cumulative incidence of clinical cases. Each of these effects was parameterised individually with a value that could be ranged between 0 and 1. The default value of each parameter was 0.9, or 90%. The parameter acted to apply (as relevant) a reduction of diminishment of the underlying transmission of state-transition process. The mathematical model of Lu *et al.* (2013a) was based on that of Mitchell *et al.* (2008), as was also the model used by Lu *et al.* (2008, 2010 and 2013b). This mathematical model did not allow for the elaborate implementation of individual transmission pathways – as might have been expected of an individual-based simulation model. The detail was, however, sufficient for the authors to run a series of simulation experiments and show that vaccination is likely to have more complex and unpredictable effects on the epidemiology of the disease in a dairy herd than might have been expected from its five simple modes of action (labelled (a) to (e) above).

The authors concluded that the overall effect of vaccination on the proportion of infected animals at the population level may be beneficial, negligible, or detrimental, depending on the parameter assigned to each mode of action and the use of concurrent use of test-based culling. Amongst all evaluated vaccines, the authors found that high-efficacy vaccine aimed at reducing susceptibility by as much as 90% would be the most effective in reducing the proportion of infected animals.

Lu *et al.* (2013b) extended the work above to investigate the effect of herd vaccination in the ability of BJD to establish and persist through the introduction of infected animals. The authors modelled as separate considerations: (a) the efficacy of the vaccine as a safeguard against infection; and (b) the proportion of animals that mount an effective immunologic response when challenged with vaccination.

The simulation experiments showed that vaccination could only be effective if it was assumed to be both highly successful in safeguarding against new infections and able to produce an immune response in a high of proportion of vaccinated calves. The authors interpreted the term 'high' in this context to imply a value of approximately 90%. Even with such efficacy, they found that there was a small chance (<15%) that the disease would persist in herds over a period in excess of 10 years on the strength of vertical transmission. The authors concluded that a reduction in the rate of disease transmission from high shedders (>50 cfu per culture tube)(Crossley *et al.*, 2005), the number of infected heifers

initially introduced to herds, and vertical transmission, are important to further decrease the probability the Mptb will become endemic in a herd and the overall number of infected animals.

As noted within each of the discussions above, our preference for the Australian model was to take a similar approach to that of Lu *et al.* (2013b) and use sensitivity simulations to examine the impact of a vaccine with ranging efficacy (susceptibility, infectiousness and clinical expression) on the development or maintenance of BJD in dairy or beef herds.

2.4 Infection of Beef Herds with Ovine Strains of Mptb

Whilst the infection of beef cattle with ovine strains of Mptb is not currently considered to be a form of BJD, it is nevertheless an important consideration for both the farming and regulatory communities. Beef cattle are generally exposed to ovine strains of Mptb on properties where both sheep and beef cattle are raised, and where OJD is endemic in the sheep flock. Exposure is likely to be a result of grazing contaminated pasture, although it is possible that other pathways exist. Fahy and Ridge (2008), for example, noted that routine hand-feeding or the supplementation of stock during drought may result in transmission. Alternatively, Stone and McLaren (2008) postulated that the exposure of a beef herd may have occurred when heavy rains washed infectious sheep pellets (faeces) from one area to another.

The frequency of transmission of ovine strains of Mptb from sheep to beef cattle, and the role that beef cattle may play in the epidemiology of OJD on Australian mixed or beef-only properties, is not currently well understood. Sergeant (2013) explained that the prevalence of infection of beef cattle with ovine strains of Mptb is currently being monitored using data collected through the Cattle Council of Australia's (CCA) National BJD Financial and Non-Financial Assistance Package (FNF package). Owners of beef herds that are known or are suspected of being infected with BJD are eligible for assistance to investigate and resolve the status of their herd. Established in 2003, the FNF package is not a compensation arrangement to cover losses. Instead, it provides assistance for producers to: (a) undertake a situation assessment, including testing; (b) develop a property disease management plan; and (c) identify and remove high-risk animals from within the herd.

Data collected through the FNF package is maintained in a centralised database. This includes herd details, as well as events such as changes to herd status or strain-typing and the outcomes of tracing forward and backward (Sergeant, pers. comm., 2014). It is important that only beef herds that enrol in the FNF package are included in this database. The herds of producers who have not sought assistance are not included. These may include those who judge that the diagnosis will have no impact on their business, or those who feel that the assistance offered will be of little value. Similarly, dairy herds are not included, although some beef herds that have introduced dairy or dairy-cross animals are. These caveats are important, as data from the FNF package is not considered to be either a census or a completely unbiased random sample of infected Australian beef herds. That said, it is a useful database and its analysis will continue to provide relevant insights.

A summary analysis of the FNF package data is given in Table 14. It can be seen that ovine strains of Mptb were identified in 20 beef herds across four states. Both ovine and bovine strains were identified from a further four herds. Collectively this means that ovine strains of Mptb were identified from approximately 14% of the 176 herds that applied for assistance.

Table 14: Summary of strain typing by state

State	Bovine strain	Ovine strain	Both strains	Un-typed*	Total
NSW	0	6	2	64	72
SA	2	1	1	18	22
Tas	1	3	0	6	10
Vic	6	10	1	55	72
Total	9	20	4	143	176

* Some un-typed cases may have been typed as bovine strain but not recorded in the data

Source: Sergeant pers. comm. (2014)

New South Wales cases can be classifieds regionally as either 'coastal' or 'central and southern' New South Wales (Sergeant pers. comm., 2014). The coastal area has few sheep and few if any cases of OJD, and a significant dairy industry, whereas the central and southern parts of the state are predominantly pastoral or mixed farming and cover much of the former high and medium prevalence OJD areas. There were no cases in inland New South Wales outside this general regional description. Victorian cases were summarised by region according to Victorian DPI classification of North-East, North-West, Gippsland and South-West. With relatively few cases and limited geographic distribution, cases in Tasmania and South Australia were not allocated to regions. When summarised by region, there were no ovine strain infections in the major dairying areas of Gippsland and the New South Wales coastal area and approximately 50% in central and southern New South Wales and south-western Victoria (Table 2). South Australia had two cases (9%), of which at least one was introduced from western Victoria, north-east Victoria also had two (9%) and Tasmania had three (30%)(Table 15).

From this analysis, Sergeant (pers. comm., 2014) concluded that the majority of cases of Johne's disease in beef herds were probably due to a cattle strain, and that many (particularly in dairying areas) are likely to be spill-over from the dairy industry. However, in areas where OJD is endemic, and where mixed farming operations are common, ovine strain infection comprised approximately 50% (or more) of cases. Although not shown in these data, Sergeant also noted that approximately one third of the ovine cases identified were seedstock producers, and could potentially spread infection through sales of stud stock.

Table 15: Summary of strain typing by state and region

State	Region	Ovine strain	Bovine strain or un-typed	Total	% Ovine strain
NSW	Central-South	8	7	15	53%
	Coastal	0	57	57	0%
SA	State	2	20	22	9%

State	Region	Ovine strain	Bovine strain or un-typed	Total	% Ovine strain
Tas	State	3	7	10	30%
Vic	North-west	0	4	4	0%
	Gippsland	0	28	28	0%
	North-east	2	20	22	9%
	South-west	9	9	18	50%
Total		24	152	176	14%

Source: Sergeant pers. comm. (2014)

The infection of beef cattle with ovine strains of Mptb was also been considered by Fridriksdotti *et al.* (2000), Moloney and Whittington (2008), Fahy and Ridge (2008), Stone and McLaren (2008) and Verdugo (2013).

Fridriksdotti *et al.* (2000): these authors reported on the development of Johne's disease and maedi-visna in Iceland following the importation of Karakul sheep from Halle, Germany, in 1933. The ovine strain of Mptb associated with these sheep was shown to be transmitted to Icelandic cattle, although with lower pathogenicity than observed in sheep. Aggressive regionalisation and movement controls, and the slaughter of 102,000 affected sheep, were employed in an effort to rid Iceland of Mptb. The disease re-appeared, however, when farms were restocked with clean sheep 12 months following. The authors maintain that infection was likely to have persisted within the cattle population, and transmitted to the clean sheep. This is possible, although it is also possible that Mptb either persisted within the environment or that the sheep introduced after these measures were not completely free of the disease. In a control program in Australia, for example, 41 sheep farms were depopulated for 15 to 21 months and restocked with low risk animals. Three years after restocking, 28 of the 41 flocks were again Mptb-positive (Taylor and Webster, 2005).

It is noteworthy that the Icelandic experience is often cited in the literature as an example of the persistence of ovine strains of Mptb within beef cattle herds. This may be the case, but it is clear that alternative hypotheses are also quite feasible.

Moloney and Whittington (2008): these authors undertook a prospective survey of 1,774 cattle from 12 New South Wales properties that managed both beef cattle and sheep. Each property was selected on the basis of significant prevalence of Johne's disease infection in sheep (estimated at an average of 4% clinical disease with a range 1% to 9%) at a time when the young cattle included in the trial were present. These cattle had contact with infected sheep, or sheep faeces, from less than 6 months of age. The cattle were at least 2 years of age at the time of testing by ELISA and faecal culture. Almost all animals were home-bred and were on the property all their lives.

All animals in the survey returned negative results on serology, while one animal from a herd of 349 gave a positive faecal culture result. Follow-up faecal culture, post-mortem and histopathology on this single animal were negative, suggesting that it was a passive faecal shedder or carrier. The authors concluded that the risk of transmission of ovine strains of Mptb from sheep to cattle was low, and infections sporadic. The authors also concluded that the upper limit of the prevalence of infection of beef cattle with the ovine strain of Mptb in

New South Wales is approximately 0.8%. It is difficult to correlate this estimate with the results obtained by Sergeant (2013), as the latter's analysis was based only on the sample of herds seeking assistance from the FNF package.

Fahy and Ridge (2008): these authors undertook a detailed analysis of a single beef herd from the Ballarat region of Victoria. The property had a history of clinical Johne's disease in sheep during the period 1998 to 2002, and the owner of the herd elected to remove (for slaughter) all the cattle on the property. In total, 73 cattle were sampled before and after slaughter. Fifteen (15) animals (20.5%) returned positive results to at least one of the non-serological tests, and 14 animals (19.2%) returned positive results to histology or tissue culture. Initial ante-mortem testing in the herd using ELISA and faecal culture had suggested that infection was confined to cows in the 5- and 6-year old age groups. Further investigation, including thorough post-mortem examination and testing, revealed that infection was widespread throughout the herd with infected animals ranging from 15 months to 6 years. All animals from which organisms could be cultured were shown to be infected with a single ovine strain of Mptb.

The property reported co-grazing cattle (in particular calves) with OJD-infected sheep – both concurrently and in succession. There was also water run-off from OJD-infected neighbouring flocks and the hand-feeding of both sheep and beef cattle during drought. The authors postulated that cattle may have contributed to the spread of the disease on this farm, although there was no evidence to support this.

Stone and McLaren (2008): these authors investigated a second property in the Ballarat region of Victoria. The study was undertaken following the diagnosis of Johne's disease in a 7-year-old cow due to an ovine strain of Mptb. The stud beef herd was at CattleMAP MN2 status and did not run sheep. The remaining 55 animals on the property were slaughtered, but, in contrast to the work of Fahy and Ridge (2008), Stone and McLaren (2008) found that the index case was the only infected animal within the herd. The index case was not exhibiting clinical signs, and would probably not have been diagnosed if the producer had not elected to enter the CattleMAP program. The index case was, however, found to be shedding Mptb in faeces at the time of slaughter. The authors postulated that high rainfall experienced in the November 1998, when the index case was approximately 7 months old, could have washed infected sheep faecal pellets from a neighbouring property onto this property.

Verdugo (2013): this author prepared a doctoral thesis investigating the epidemiology of Mptb in New Zealand sheep, beef cattle and deer farms. In New Zealand, it is common practice to co-graze sheep, cattle and deer both concurrently and in succession. Although this practice may increase the risk of transmission of infectious diseases across ruminant species, it is thought to improve pasture management, control noxious weeds and reduce the burden of internal parasites. Farms in New Zealand are generally small, with a high stocking density. In the North Island, where the highest prevalence of Mptb-infection is observed, conditions are generally cool and moist.

Faecal and blood samples were taken from a total of 11,089 animals from 350 mixed species farms. Management and other epidemiological data were also collected. The author found that the herd-level prevalence was higher for sheep, beef cattle or deer in mixed-species

farms when compared to herds or flocks on single-species farms. It is difficult to know whether this reflected greater exposure to Mptb as a direct result of multi-species shedding, or whether the management of mixed farms in some other respect resulted in increased exposure. The authors also found that most (80%) of the Mptb isolates from beef cattle were of Type I, which is commonly considered an ovine strain. By contrast, isolates from dairy farms were of Type II. This result was interpreted as implying that Johnes disease in New Zealand beef cattle tends to result from ovine strains. The result differs from the Australian situation, but is not unexpected as the farming systems within New Zealand are very different. In the New Zealand context, beef cattle do not appear to be exposed to infection as a result of the purchase of dairy animals but, as noted, are commonly co-grazed with sheep under very intensive conditions. The result is interesting, but does not necessarily indicate that the Type I strains are being maintained within beef herds in the absence of sheep. The author also observed regional differences in the aggressiveness of the disease and raised the possibility of variance in pathogenicity, both between and within Type I and Type II strains. This is possible, but the study's results might also be explained by regional differences in environment and farming systems and, as a result of these, opportunities for exposure.

Conclusions: retrospective examination of archival samples and historical data suggests that ovine strains of Mptb have been infecting beef cattle as far back as the 1980s, and possibly the 1960s (Sergeant pers. comm., 2014). Over that period, the prevalence of infected sheep flocks throughout Australia has risen, and vigilance for ovine-strain Johne's disease in beef cattle has increased, with the result being a steady rise in the reported prevalence of infection within the national beef herd. Primary researchers and reviewers agree that ovine strains of Mptb are less infectious for cattle than bovine strains, and generally result in a less aggressive disease. That notwithstanding, there is very strong evidence to show that beef cattle co-grazed with sheep (either concurrently or successively) can be exposed to a sufficient burden of Mptb to initiate infection in some animals. It is also generally accepted that passive carriage of the organism within the gastrointestinal tract can occur, with the organism redistributed elsewhere on the farm.

The role that beef cattle may play in the on-farm and between-farm epidemiology of ovine-strain Johne's disease is less clear-cut. Passive redistribution of the organism is likely to increase on-farm opportunities for the continued exposure of both sheep and cattle. Beef cattle tend to congregate and over-graze particular areas within paddocks, resulting in heightened exposure to faeces. A beef animal passively carrying the organism would be likely to contaminate these areas leading, potentially, to the exposure of its herd-mates. Passive transfer might also result in the infection of additional properties, if beef animals carrying the organism are moved directly or through saleyards.

As noted, active infection of beef cattle with ovine strains of Mptb may progress to clinical disease and the shedding of the organism in faeces. Breeding male and female beef animals are more likely to have a lifespan sufficient for the realisation of this process. Stud animals can be particularly at-risk, as the reproductive inefficiency that generally accompanies increasing age may be tolerated in view of their genetic merits. The larger proportion of commercial beef animals does not, however, live long lives and within this sector the

progression to clinical disease is unlikely unless individual animals are exposed to an ovine strain of Mptb in-utero or as calves. Most peri-natal exposure of cattle to Mptb stems from advanced disease within an infected dam (Section 2.1.3). However, with a very low proportion of animals progressing to advanced disease, the majority of exposure opportunities for beef cattle are likely to result from the less efficient environmental route. This route is also less specifically targeted at peri-natal calves. When coupled with the reduced infectiousness of ovine strains of Mptb for cattle, a reduction in the efficacy of transmission within a beef herd may mean that the disease is not generally self-sustaining without the continued contamination of pasture by infected sheep – in particular, on more extensive properties in warmer and drier environments.

This position has not been conclusively supported or disproved, and remains the key question for management of ovine-strain Johne's disease in beef cattle. The current national rules allow cattle herds that have reactors – or cases of clinical disease that are subsequently infected to be the ovine strain only – to remain as non-assessed or uninfected status. Ovine strain-confirmed herds are therefore not eliminated from CattleMAP nor required to enter TCP3. Eradication of Johne's disease from beef herds was shown not to be economical unless the herd was a beef stud and the loss of stud animal sales was significant or the annual clinical mortality rate exceeded 5% in a commercial herd (Webb Ware, 2012). Prevention of spill-over of disease from the dairy industry to the beef industry has, to-date, been regarded as the most cost-effective way to protect the beef industry.

3 BJD IN VICTORIA

3.1 Background

The August 2103 discussion paper on the future of TCP3 provided the following herd-level summary of the program (DEPI, 2013) (Table 16)

Table 16: Victorian herd BJD status as at May 2013 (DEPI, 2013)

Herd BJD status	Herd status sub- category	No. dairy herds	No. beef herds	Total no. herds
Suspect[9]	-	1107	16	1123
Infected	Infected	560	20	580
	Restricted 1 (RD1)	41	4	45
	Restricted 2 (RD2)	67	2	69
	Tested High Prevalence	23	0	23
	Tested Moderate Prevalence	52	2	54
	Tested Low Prevalence	160	2	162
	Total infected	**903**	**30**	**933**

The status of Victorian herds as at December 2013 is presented in Table 17.

[9] Whilst DEPI has continued to trace BJD within the beef sector, tracing within the dairy sector ceased many years ago, leading to little change to the number of known suspect herds

Table 17: Victorian herd BJD status as at December 2013

Herd BJD status	Herd status sub-category	No. dairy herds	No. beef herds	Total no. herds	Change since May 2013
Suspect	-	1106	22	1128	+5
Infected	Infected	565	17	582	+2
	Restricted 1 (RD1)	35	3	38	-7
	Restricted 2 (RD2)	57	3	60	-9
	Tested High Prevalence	25	0	25	+2
	Tested Moderate Prevalence	55	0	55	+1
	Tested Low Prevalence	156	1	157	-5
Total infected		893	24	917	-16

Source: DEPI (2013)

There were approximately 335 dairy herds participating in TCP3 in 2013. Of these, only 237 had a current status as at the 31st December 2013. This equates to around 7.8% of Victorian dairy herds (4,284 herds in total). It was estimated that at least 50% of Victorian dairy herds are likely to be infected with BJD (2,140 herds) therefore only 15.7% of (suspected) infected Victorian herds are currently participating in TCP3. The location of the TCP3 herds as at October 2013 is presented in Figure 9. Most participants are located in the south.

Figure 9: Location of Victorian TCP3 herds in 2013

Only four herds have achieved TMS (tested to CattleMAP standard) status since TCP3 started.[10] A total of 20 herds have withdrawn from TCP3 and continue to operate as a cattle farm, and almost all of these remain confirmed infected with BJD. Only 10 participating TCP2 herds attained TMS status in the ten-year period from 2000 to 201011. Since TCP3 began in 2009 the number of infected herds and the number of suspect herds has remained stable (Figure 10) but the percentage of infected dairy herds and the percentage of suspect dairy herds have increased over this time reflecting the ongoing contraction of the Victorian dairy industry. The number of TCP3 herds that have achieved at least one negative herd test (RD1 or RD2 status) has decreased whereas the number of herds with a confirmed low herd prevalence (TLP) of sero-reactors has increased slightly since the inception of TCP3 (Figure 11).

[10] TMS requires at least one (negative) herd test undertaken approximately 24 months after attaining RD2 status

[11] TCP2 was the current version for the most years within this period

Figure 10: Victorian dairy herds infected or suspected of being infected with BJD

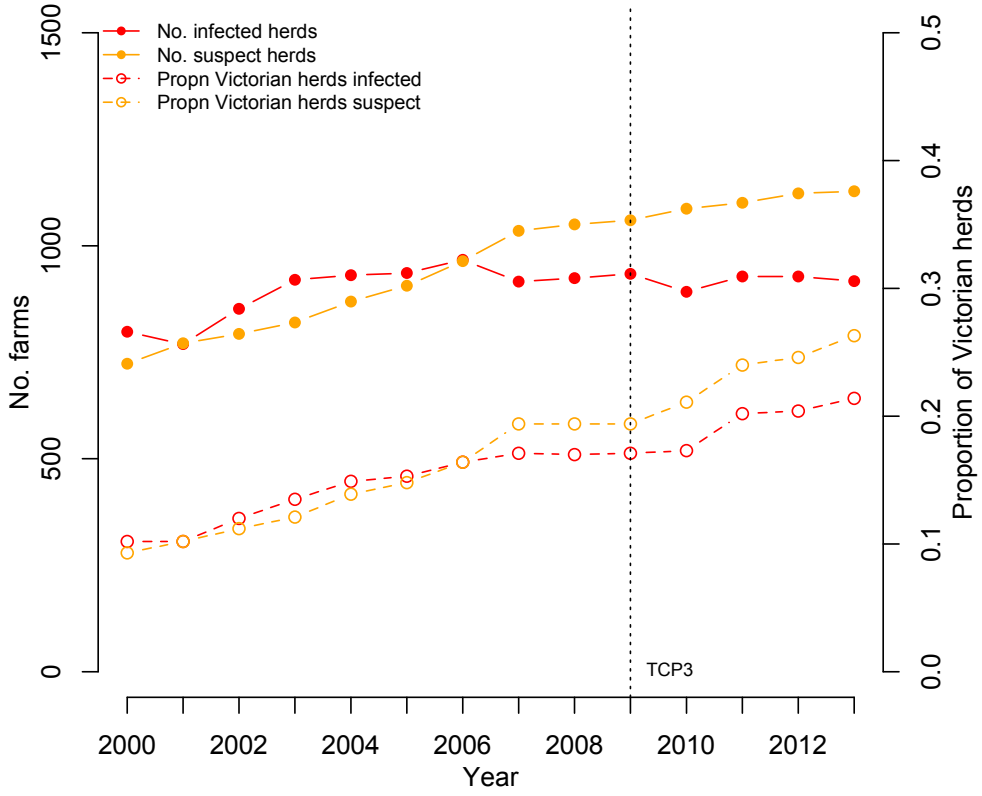
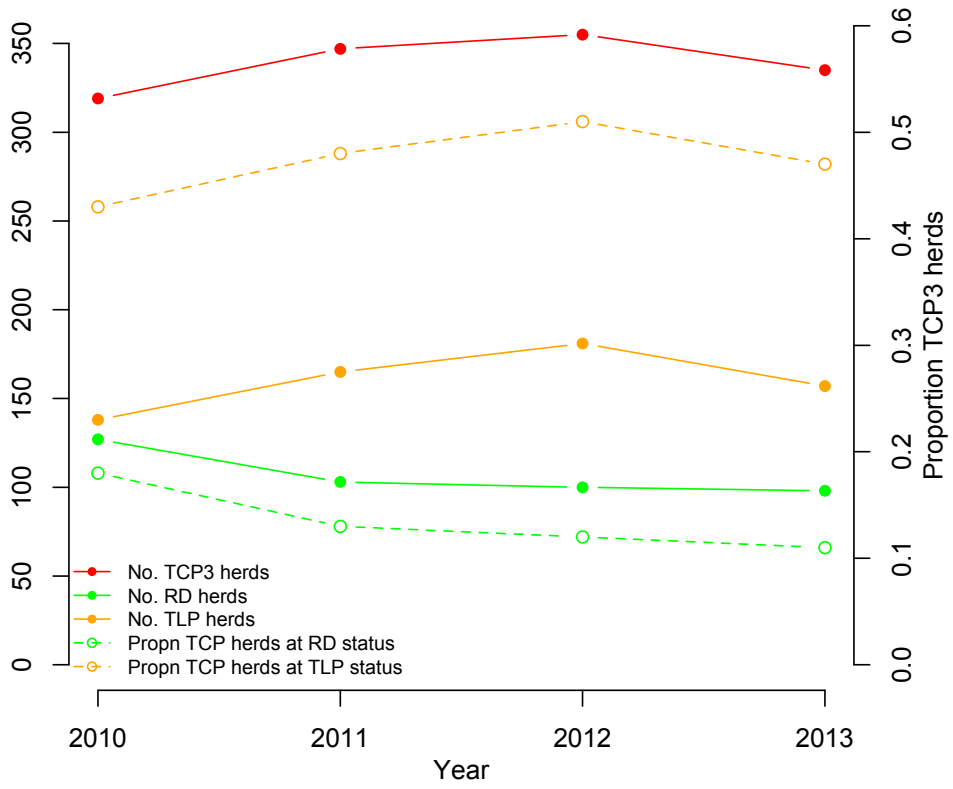


Figure 11: TCP3 herds at RD (RD1 and RD2) status or TLP status by year



3.2 Summary of TCP3

It is apparent that TCP3 is not producing the desired objectives of reducing the spread of BJD or the prevalence of disease in the state herd. Too few infected farms are participating and too few participating farms are experiencing ongoing reduction in the prevalence of disease. Whilst TCP3 appears to be stabilising BJD prevalence within infected and participating herds to a low level, the overall impact of the program on the prevalence of disease in the state herd is minimal due to the low and declining participation rate.

The (known) BJD status of Victorian beef producers is: 22 suspect, 17 infected, one TLP, three RD1 and three RD2 herds. This is a total of 46 herds or which only seven are participating in TCP3.

4 BJD REGULATORY, OPERATING AND TRADING ENVIRONMENT

4.1 BJD Control in Australia

4.1.1 The National Framework

NJDCP and BJD Strategic Plan: the National Johne's Disease Control program (NJDCP) is the overarching agreement between governments and industries for the management of Johne's disease in *susceptible species* in Australia. The NJDCP has three principal components:

1. National Standard Definitions, Rules and Guidelines (SDRGs) for zoning, inter-zone movement controls and official disease control programs in the respective states. There are separate OJD and BJD editions of this manual.
2. The voluntary Australian Johne's Disease Market Assurance Program, comprising the Cattle Market Assurance Program (Mptb), SheepMAP, GoatMAP and AlpacaMAP.
3. The Australian and New Zealand Standard Diagnostic Procedures for Johne's Disease (ANZSDPs), which describes tests that are approved for use in Australia. The ANZSDPs are maintained by the Sub-Committee on Animal Health laboratory Standards (SCAHLS).

Bovine Johne's disease is specifically addressed by the National BJD Strategic Plan 2012-20. Note that the scope of this Plan is the bovine strain of Mptb, which can affect cattle but also goats, alpaca and deer. It does not include cattle infected with ovine, bison or other strains of Mptb. A circular describing the changes in the 2012 revision of the previous plan notes that governments and industries have "*reaffirmed their commitment to protect the north and west of the country, and the beef and alpaca sectors, from BJD while allowing dairy and goat producers greater control over how they manage the infection in their herds*".[12]

The plan refers to the three components of the NJDCP – that is, the BJD SRDGs (Edition 8, May 2012), the CattleMAP and the ANZSDPs.

The Plan has the following objectives:[13]

- Minimise contamination of farms and farm products by Mptb
  - Minimise contamination of animal products with Mptb
  - Minimise exposure of humans to Mptb from infected cattle
  - Minimise Mptb. contamination of the farm environment.
- Protect non-infected herds while minimising disruption to trade
  - Reduce the spread of BJD between regions and production sectors while minimising disruption to trade.

[12] There is no specific program yet in place for the deer industry

[13] See: www.animalhealthaustralia.com.au/programs/jd/jd_home.cfm

- Minimise the social, economic and trade impact of BJD at herd, regional and national levels
  - Provide assistance to affected producers
  - Reduce prevalence of BJD in both the dairy and beef sectors
  - Remove the stigma associated with BJD infection and reduce emotional stress.

Dairy-specific sub-programs: the dairy sector has a primary focus on minimising the risk of contamination of product by Mptb. This is addressed generically through the dairy companies' on-farm quality assurance programs. All of these now include the Three-Step Calf Plan, which involves:

1. Removal of calves from dams before 12 hours after birth;
2. Managing the calf rearing area to ensure calves have no contact with the effluent of susceptible species; and
3. Rearing of calves to 12 months of age on pastures that have not carried adult stock or known BJD-infected stock during the past 12 months.

The Three-Step Calf Plan does not otherwise exist as a 'program' per se. It is designed to maximise uptake of calf-rearing fundamentals where producers are not prepared to follow all of the dictates of a more rigorous calf hygiene program, the Johne's Disease Calf Accreditation Program (JDCAP). The JDCAP adds numerous provisions to the Three-Step Calf Plan – for example, the requirement to calve cows in an area free of dairy effluent. The JDCAP is supervised by a veterinarian and accredited herds are listed in a public register.

The other important dairy-specific element of the national BJD program is a voluntary risk assessment tool called the National Dairy BJD Assurance Score. The Dairy Assurance Score takes account of CattleMAP status, history of BJD infection, test results, participation in approved BJD control programs, herd geographic location and implementation of BJD-minimising calf-rearing programs (JDCAP or Three-Step Calf Plan). A higher score represents a lower risk.

The Dairy Assurance Score may be declared on the National Vendor Declaration (NVD) or, if an NVD is not required, on a stand-alone Dairy BJD Assurance Score Declaration Form. The Scheme is audited.

Beef-specific sub-programs: the Strategic Plan recognises the much higher incidence of BJD in dairy cattle than in beef cattle and describes a sectoral approach to control of the disease. An important element of this approach is the 'Beef Only' Scheme. The designation 'Beef Only' may be claimed by any herd provided that it meets all of the following criteria (AHA website, SRDGs):

- The cattle are not dairy cattle. Dairy cattle are defined as any cattle of a dairy breed or first-generation dairy cross breeding, or 'any other cattle that have been born, reared, or run on a property that included a registered dairy herd at the time those cattle were present';
- The cattle do not include animals that have been part of a herd classified as Infected (IN), Suspect (SU) or Restricted (RD), according to the SRDGs;

- The cattle are from a beef herd that has not grazed with dairy cattle at any time during the previous 5 years, unless those dairy cattle were from a herd enrolled in the CattleMAP or of equivalent status;
- The cattle are from a beef herd that has not, at any time in the past, grazed on land that had been grazed by dairy cattle aged 2 years old or older during the 12 months before the arrival of the beef herd, unless those dairy cattle were part of a CattleMAP herd;
- Any cattle that have been introduced into the herd or onto the property(s) have come only from herds of the same Beef Only or higher status for BJD and have come with a Cattle Health Statement or BJD vendor declaration; and
- The cattle are identified under the National Livestock Identification Scheme (NLIS).

The CCA provides assistance to owners of infected or suspect beef cattle herds through an initiative called the National BJD Financial and Non-Financial Assistance Package (FNF package). The FNF Package provides non-financial assistance in the form of advice from a BJD Counsellor, including the conduct of a situation assessment and identification of future options. Financial support is also available for the development and implementation of an Enhanced Property Disease Management Plan, including testing costs, to a maximum of $11,000 per property.

CCA also provides a rebate to beef producers for BJD testing for the purposes of meeting interstate movement requirements, or maintaining or progressing status within the CattleMAP. The maximum amount claimable is $550 per annum.

Zoning and movement controls: under the BJD Strategic Plan, Australia is divided into Free and Protected Zones, a Beef Protected Area and a Management Area (Figure 12). WA is a Free Zone, while the NT, Queensland and the northern pastoral region of SA are Protected Zones. Any detection of BJD in these jurisdictions will trigger vigorous control or eradication measures.

Figure 12: BJD zones in Australia

The Beef Protected Area (BPA) is new to the 2012 Plan. Dairies within the BPA are considered to be within a 'Dairy Compartment', which is not geographically-defined but includes all herds that supply milk to a dairy factory, including all the land on which the cattle run. Victoria and Tasmania make up the Management Area (MA). In these states, BJD is well established in dairy cattle. The emphasis in the MA is on voluntary control and restriction of spread of BJD.

There are restrictions in the movement of cattle towards zones of higher status. In each case there is the requirement to provide a health certificate (the National Cattle Health Statement) and, depending on the specific movement, to demonstrate a level of assurance of freedom from BJD (CattleMAP status, test results, origin and history of herd, Dairy Assurance Score or Beef Only status). CVOs may approve exemptions for any cattle moving to immediate slaughter at an approved abattoir or to an approved feedlot, or for steers or spayed heifers from non-assessed or better herds to any property.

There are no restrictions on movement within zones, except from 'Infected' or 'Suspect' herds where these have been identified. In the BPA, Dairy Compartment herds must declare their Dairy Assurance Score. In the MA, voluntary declaration of the Dairy Assurance Score, CattleMAP or Beef Only status is encouraged.

4.1.2 Victoria in the National Context

Trading restraints on Victorian cattle producers: because Victoria is part of the Management Area, there is an emphasis on voluntary control and restriction of spread of BJD, and applicable within-state regulations are somewhat less onerous on producers than in other zones. BJD is a notifiable disease but 'competent investigation of suspected infection' and associated tracing are only required for infected or suspected herds where they are Beef Only or CattleMAP herds. Control measures for infected herds are encouraged (especially Beef Only or CattleMAP) but voluntary. Use of the Dairy Assurance Score for movement within the MA and to/from the Dairy Compartment of the BPA is also voluntary.

Cattle from Victoria can be traded freely with Tasmania, which is also in the MA (Flinders Island is excepted – it forms part of the Protected Zone). The export of Victorian cattle to other zones is more restricted. The requirements for the movement of dairy and beef cattle from Victoria to other states are shown in Table 18.

Table 18: BJD movement requirements by state, zone and sector of destination

Destination state/territory	Beef or dairy	BJD requirements	State requirements
Tas (excl Flinders Island)	Both	Nil	Tas requires Tas Health Certificate If herd is infected or suspect, purchaser or recipient must be informed
NSW / ACT / SA (BPA)	Beef	Mandatory health certificate / statement MN1 CattleMAP or Beef Only status Check Test status with negative test last 12 months, Tested to Mptb Standard or Tested Four-Years-Old and Over	SA and NSW require National Cattle Health Statement Female beef breeders that do not qualify for Beef Only require a permit
	Dairy	To Dairy Compartment only Mandatory health certificate / statement and declaration of Dairy Score	SA requires National Cattle Health Statement NSW does not
SA (PZ) / Flinders Island / Qld / NT	Beef	Mandatory health certificate / statement MN1 CattleMAP or Beef Only status (SA: or Check Test status)	SA requires National Cattle Health Statement Qld requires Qld Certificate of Health (plus NCHS if Beef Only) NT requires NT Health Certificate and Waybill

Destination state/territory	Beef or dairy	BJD requirements	State requirements
	Dairy	Mandatory health certificate / statement MN1 CattleMAP status or Dairy Score 8[14]	SA requires National Cattle Health Statement Qld requires Qld Certificate of Health NT requires NT Health Certificate and Waybill
WA	Both	Mandatory health certificate / statement MN3 CattleMAP status	WA requires WA Health Certificate

Victoria's TCP3: the SDRGs set out the criteria applicable to each of the national BJD zones. Essentially, these are the minimum biosecurity provisions required for each zone.

Table 19 lists the criteria applicable to cattle and notes the extent of Victoria's fulfilment of each one. The table shows that the Victorian Government and cattle industry, through the CCF and in association with industry bodies such as CCA and Dairy Australia, exceed the jurisdiction's obligations under the National BJD Strategic Plan.

Table 19: Cattle BJD control criteria as described in SDRGs and Victoria's compliance with national requirements

Criterion	MA requirement	Victoria
BJD is a notifiable disease	Yes	BJD is notifiable
Awareness program is in place to advise producers about recognising and reporting the disease	Beef and dairy cattle	Program in place
Competent investigation of suspected infection	*Beef Only* and CattleMAP	Competent investigation is carried out
Thorough tracing of suspected infection utilising NLIS or other methods	*Beef Only* and CattleMAP	Tracing is carried out
Industry awareness program regarding the national BJD program	Yes	Program in place
Vaccination	Vaccination is permitted with CVO approval	Vaccination is permitted with CVO approval

[14] A score of 8 requires herd to be of known BJD status and at RD1 and to follow JDCAP

Criterion	MA requirement	Victoria
Awareness program is in place to advise producers that there are movement requirements for introducing cattle into the zone or area	Yes	Program in place
Obligation of owners of cattle to meet the conditions for importation, with penalties for non-compliance and for false declarations	Yes	Relevant regulations in place
A risk-based trading approach utilising Vendor Declaration of Dairy Assurance Score for the movement of Dairy Compartment cattle within and between the Beef Protected Area and the Management Area	Voluntary	Voluntary program in place
A formal risk assessment is used for amendment of movements between zones and areas	Yes	Formal risk assessment is used
Industry led advisory program to encourage hygienic calf rearing practices in the dairy industry	Yes	Program in place, led by Dairy Australia
Official movement restrictions in IN and SU herds	Not required	No restrictions in place
Official control measures in IN herds	Encouraged in *Beef Only* and CattleMAP herds	No official control measures in place – control and participation are now voluntary
Voluntary control measures in IN herds	Encouraged, especially in formerly *Beef Only* and CattleMAP herds	Encouraged and supported through the provision of TCP3, available to all herds
There is active investigation of SU herds to determine if infection is present	*Beef Only* and CattleMAP herds	Active investigation undertaken in *Beef Only* and CattleMAP herds
Cattle industry provides assistance for affected cattle producers (IN, RD and SU herds)	Beef herds	Assistance provided by TCP3 (above); also CCA through FNF Assistance Package
Surveillance, monitoring and compliance activity is reported to AHC annually	Yes	Surveillance, monitoring and compliance activity reported to AHC annually
NLIS monitoring from IN dairy herds on a regular basis with follow-up action taken	Not required	Not undertaken

Criterion	MA requirement	Victoria
Industry-funded independent audits of Vendor Declarations that utilise assurance status or scores (e.g. dairy score, goat health score and *Beef Only)*	Yes	Independent audits undertaken
Effective information management system to effectively collate and report on surveillance, monitoring and compliance activity	Yes	Information management system (ADMIS) in place
Monitoring of compliance with importation conditions using NLIS or other methods	Not required	Not undertaken
Monitoring of movements from high-risk herds/sectors within zone or area	Not required	Not undertaken

It is notable that Tasmania, which is the other state in the Management Area, does not have a program equivalent to TCP3. Neither does New South Wales in the BPA.

South Australia, however, has a program called 'Dairy ManaJD', funded by the Cattle Industry Fund, equivalent to Victoria's CCF. Dairy ManaJD comprises the following key components:

- Enrolment: with a private, APAV veterinarian. The veterinary services provided as part of the program are subsidised. On enrolment producers receive a manual designed for compatibility with the on-farm QA manual. Enrolled herds with infected status are exempted from quarantine.
- Testing: of all cattle over 2 years of age using the ELISA test. Testing is subsidised. The testing leads to herds being assigned Dairy Scores. Infected herds (scores 0-6) can choose to attempt eradication by test-and-cull and hygienic calf rearing, or to use management to minimise BJD. Compensation is paid for reactors and high-risk offspring of reactors that are slaughtered.
- Audit: provided free by the South Australian Dairy Authority in conjunction with on-farm food safety audits. On the basis of the audit and his/her own observations, the veterinarian issues a Dairy Score and a Dairy ManaJD Certificate is issued by PIRSA.
- Scrutiny of calf rearing practices: JDCAP and Three-Step Calf Plan.

According to Rogers *et al.* (2012) and pers. comm. (2014), Dairy ManaJD had recruited more than 97% of SA dairy farmers by 2011. Twenty-eight herds eradicated BJD between 2004 and 2011. These were generally closed, small-to-medium sized herds (1-300) with very low initial prevalence, clean neighbours and operating in relatively dry climates. Many of these herds had also been applying test-and-cull for some years before Dairy ManaJD was introduced and also feed milk replacer to calves. Eradication was confirmed as per the SDRG requirement of three consecutive negative whole-herd tests over 5-6 years, with 30-50% of herds actually undertaking both ELISA and faecal culture testing of all animals over 2 years of age.

Dairy ManaJD is continuing in 'maintenance' mode. There are 56 infected herds. Ten are RD1 or RD2 (score 5-6) and are continuing with TCP. These are small, closed herds and they expect to eradicate BJD. There are two known infected beef herds, one of which uses Silirum®.

Rogers (pers. comm., 2014) indicated that, while the results from Dairy ManaJD have been very satisfactory for South Australia, they may have limited application to the Victorian situation. Prevalence of BJD in SA herds in 2012 was reported to be 19%. This is much lower than the Victorian prevalence. Also, South Australian herds are much smaller and fewer in number than those of Victoria. One of the success factors for Dairy ManaJD was an initial recruitment campaign by an experienced veterinarian who personally contacted every dairy producer. Such an approach could conceivably be adopted in Victoria, but it would be expensive and would have to be distributed across a number of vets, meaning that the value of a single 'champion' would be diluted.

Finally, environmental conditions in South Australian dairy regions may be less supportive of Mptb bacteria than those of Victoria. This may have contributed to the high rate of BJD eradication from participating SA herds and suggests that eradication of disease may be a more feasible prospect in South Australia than it is in Victoria.

4.2 On-Farm Management of BJD

Specific aspects of BJD management within the dairy and beef sectors in Victoria are presented below.

4.2.1 Dairy Enterprises

The dairy industry, through Dairy Australia and supported by national and state peak industry bodies and processors, provides extensive resources for dairy producers on the prevention and control of BJD. Many of these resources relate directly to the programs described above such as the JDCAP. The Dairy Australia publication 'Dairy BJD Technotes' explains in detail the best practice recommendations for managing BJD.

As noted above, the Three-Step Calf Plan is incorporated into on-farm QA programs required by milk processors of their suppliers. Most milk processors have quality assurance systems that have a food safety focus – designed to manage risks and to limit contamination of food products with chemicals, microbiological contaminants and physical contaminants. Murray-Goulburn's MilkCare is an example of a compulsory audited program applied to all suppliers.

4.2.2 Beef Enterprises

BJD is far less prevalent in beef than dairy herds. It is therefore a much less prominent priority among best practice health recommendations in beef than it is in dairy. Meat and Livestock Australia's 'More Beef from Pastures' manual recommends purchasing cattle from low-risk zones or high-status herds (Beef Only, CattleMAP); implementing grazing management strategies to prevent disease spread within the herd; weaning early; and vaccinating sheep.

DEPI makes recommendations for managing situations in which an infected animal is introduced (cull all animals from the same source, cull calves exposed to the manure from those animals, restrict access of calves to potentially contaminated land for at least 12 months) or where BJD is detected in an animal bred on the property (consider control through culling of high-risk animals and calf management, test-and-cull, progressive depopulation or total depopulation).

Anecdotally, very few if any commercial beef producers adopt any BJD minimisation measures unless the disease has been diagnosed in the herd. Economic evaluation of the impact of disease by the University of Melbourne Mackinnon Project veterinarians found eradication of BJD to be uneconomic unless the prevalence of clinical disease exceeded 5% per annum (Webb Ware *et al.*, 2012).

4.3 Impact of BJD and Control Programs on Farm Profitability

4.3.1 Methodology

In 1994 the (then) Victorian Department of Agriculture estimated the economic impact of BJD at farm level for infected Victorian dairy and beef farms (DAV, 1994). A whole-farm computer model was developed to mimic the year-on-year herd structure and workings of dairy and beef herds in Victoria. This partial-budget model was run across a 15-year horizon to allow the effects of changes to herd size and structure arising from premature loss of animals and reduced production to be determined by comparison between 'with' and 'without' simulation runs.

Commercial losses due to BJD were assumed to arise in two ways: (a) early removal of clinical animals; and (b) production losses in subclinical animals prior to becoming clinical (this was mostly reduced milk production in the preceding lactation). The ratio between subclinical and clinical animals was fixed with the subclinical period lasting 2 years resulting in 6% and 17% reduced milk production in the years immediately preceding clinical disease. Latently-infected animals experienced no loss. The losses due to early removal of clinical animals were estimated at 75% of total loss, with production losses from subclinically-affected cows providing the remaining 25% (Brett, 1998). Other losses arose from livestock movement restrictions resulting in livestock trading limitations and losses. The sale of elite genetics is an important source of income for stud producers. The presence of confirmed BJD prevents the sale of stud animals effectively reducing the realisable value of the stud animal to meat value.

Farm level: the partial-budget marginal response methodology captures changes in profit arising from the loss of a diseased animal and the subsequent change in herd management structures and costs (replacements, animal health, etc.) and income (sale of surplus and cull animals and product such as milk). However, the authors also stated that operating costs were constant (fixed) for each farm. If this is the case then feed savings arising from animals

lost early due to disease were not considered, as feed is a variable cost. This would result in an overestimation of economic losses arising from early removal of a clinical case.[15]

The economic impact of disease was calculated as the change in profit (income minus costs) between a herd without BJD and one with BJD. The economic impact calculated this way included the losses in the year of culling (cull sale value and milk production for dairy animals) as well as the discounted future losses arising from premature removal of the animal (lost future production and fewer offspring). In order to use this approach to estimate the economic impact of the test and control program the cost of testing and compliance along with the cost of premature removal of ELISA reactors and their contacts must be added. The simulation was run over a 15-year period to estimate the long-term average cost to a farming enterprise of a clinical case of disease. Separate scenarios were examined for commercial dairy herds, stud dairy herds (that sell elite genetics to artificial breeding companies), commercial beef herds and stud beef herds (that sell bulls to other beef farmers for mating). The costs at the farm level for infected beef and dairy farms were then aggregated to state level to determine the cost to Victoria arising from BJD.

The DAV (1994) model estimated the enterprise loss arising from a single clinical case of BJD to be $1,803 for an average dairy herd and $800 for a beef herd in 1994. The loss was the combined effects of decreased product (milk or meat) and reduced number of calves born (due to loss of the dam).[16] There was an extra source of loss experienced by stud herds arising from inability to sell elite genetics for breeding. This was calculated as $1,675 for each elite animal sale that was blocked due to the presence of BJD on the farm. We have assumed that the premature loss of a reactor is the same as for a clinical case. Examination of TCP1 data indicates that sero-reactors and clinical cases both had an average age of 5 years at detection.

Whilst these cost estimates are now 20 years old, the basic systems of dairy and beef production have not changed significantly and the use of a whole-farm approach to estimating economic impact is commendable and sound. However, the reduced costs of production from prematurely culled animals do not appear to have been considered, and this might inflate the estimates of loss. These costs were updated to 2013 prices by adjusting for inflation in the ensuing 20-year period and for the introduction of the 10% Goods and Services Tax (GST) in 2000. The 2013 losses for a single clinical case of BJD in a dairy herd were adjusted to $3,307 and for a beef herd adjusted to $1,467. The 2013 opportunity loss for a stud animal whose sale is blocked due to declared presence of BJD on the farm was adjusted to $3,072.

Cattle trade between jurisdictions: the 1994 economic modelling also assessed the impact of BJD-based movement controls for cattle leaving Victoria for other states, and to international destinations. The authors cautioned that movement restrictions resulted in a

[15] Pasture subsequently not consumed by culled clinical cows is now available for herd mates. Grain not consumed by culled clinical cows represents a saving in feed cash expenditure.

[16] Because the ratio between subclinical and clinical cases and the transition pathway from subclinical to clinical disease was fixed the economic effect can be summarized as the annual losses per case of clinical disease

redistribution of cattle, and that it was difficult to quantify the losses accurately and to determine who incurred them. For example, buyers of store cattle (re-stockers, feedlots, etc.) in Victoria might enjoy lower prices because of the restrictions on movement of cattle to other states arising from the presence of BJD, whereas sellers of cattle in other states may obtain higher prices because supply of competing cattle from Victoria is limited due to BJD and movement restrictions. The high prevalence of infection within the Victorian dairy herd also implies that removal of movement restrictions (by elimination of the disease or removal of the requirements for freedom) would substantially alter the supply of cattle for various markets. The equilibrium price for the individual market would then change, and the market would be substantively altered. Given this, and because none of the three options under consideration for the future of TCP provide a feasible way to eradicate disease, we have not extended the economic assessment to include the effects of restricted trade between jurisdictions. A similar economic analysis conducted on the impact of BJD in New Zealand did not include trade-related effects for these reasons.

TCP3 impacts: the 1994 DAV model was extended to include the economic effects of participation in TCP3. The average herd size in 2013 for dairy farms was estimated at 252 milkers and, for beef farms, 184 breeders.[17] The average farm losses due to BJD were estimated using the updated 2013 loss estimates for individual cases, the average 2013 herd size for dairy and beef producers in Victoria, and the estimated level of Johne's disease in infected herds that either participate in TCP3 or take no control over Johne's disease in the herd.

In order to assess the impact of TCP3 on farm profitability the costs of compliance and management of TCP3 were estimated along with the impact of the program on the level of disease within participating herds. The August 2013 discussion paper (DEPI, 2013) stated that there were 3,966 Victorian dairy farms. Of these there were approximately 1,100 dairy farms suspected to be infected with BJD and another 644 dairy farms confirmed infected (but not within TCP3). Approximately 335 confirmed infected dairy farms had a valid TCP3 status at the time of this report. Therefore 25% of Victorian dairy farms are infected with BJD, with at least another 28% likely to be infected. The authors suggested that the suspect list is most probably an underestimate. This means that, conservatively, at least 60% of Victorian dairy farms are likely to be infected with BJD.

At the time of writing, 24 Victorian beef herds were confirmed infected and 22 beef herds were listed as suspect. The Australian Bureau of Resource Economics and Sciences (ABARES) lists Victoria as having 3,926 beef enterprises carrying a total of 722,000 breeder cows with a state beef herd size of 1.55 million head in 2012 (DAFF, 2014). This provides an average herd size of 184 breeder cows and 396 animals in total for the average Victorian beef producer.[18] Therefore, 1% of Victorian beef herds are known infected with BJD, but only 0.2% of beef herds are known infected and participating in TCP3. These are again likely to be

[17] See: http://apps.daff.gov.au/MLA/mla.asp

[18] This is likely to be a highly skewed distribution with many small holder beef producers and a few very large producers

underestimates, so we have assumed that 1% of Victorian beef herds may be infected and would participate in TCP3 (given favourable circumstances), another 1% of herds are confirmed infected but opt not to participate in TCP3 and another 5% of beef herds are suspect for BJD (infection not confirmed).

For our model, the background prevalence of disease in infected dairy herds that undertake no control was set at 8.8%, with an annual clinical incidence of around 2.6%. We have assumed that the ELISA prevalence would be approximately twice the clinical incidence rate – setting this parameter at 5.2% (if testing was undertaken).[19] Recent assessments of the performance of the various manifestations of TCP have shown a reduction in the ELISA reactor rate and in the incidence of clinical cases in herds that participated in TCP. Jubb and Galvin (2000) demonstrated that the clinical case rate post implementation of TCP1 was 0.4%. This represents an approximately 90% reduction in annual clinical incidence. Analysis of the birthdate of reactors indicated a marked reduction in the number of reactors born on TCP3 farms after the start of the program. A subsequent assessment of TCP conducted by the same authors in 2004 found a similar reduction (approximately 67%) in the incidence of reactors and clinical cases in participating farms (Jubb and Galvin, 2004a). Whilst few farms have eradicated BJD though TCP, there is strong evidence that TCP has reduced both the prevalence and incidence of reactors and disease in most participating herds. Therefore we have assumed that the long-term prevalence of disease is 8.8% and of clinical disease is 2.6% for infected dairy herds not participating in TCP3, whilst for herds participating over the long term in TCP3 the average prevalence is predicted to be 4.1% and annual clinical incidence is predicted at 1.1%. The comparable estimates for long-term TCP1 herds were 1.7% prevalence and 0.3% annual clinical case incidence.[20] For beef herds we have assumed that infected herds not participating in TCP3 have a baseline reactor incidence of 1% and a clinical disease incidence of 0.5%, consistent with the findings of Larsen *et al*. (2012). For infected herds participating in either TCP1 or TCP3 we have assumed a reactor incidence of 0.5% and a clinical disease incidence of 0.25%.

This reduction in incidence of clinical and subclinical cases will likely confer long-term economic benefits to the farmer (DAV, 1994). However, TCP3 program costs must also be considered in order to determine if a net benefit from TCP participation occurs for the average participant. Costs and assumptions for participation (dairy and beef) in TCP3 are presented in Table 20.

[19]The baseline prevalence of disease in infected and uncontrolled herd was based on the results of modeling – see Chapter 8 for details.

[20]See results of modeling disease in infected herds – Chapter 8. TCP1 appears more effective at reducing the level of BJD than does TCP3. Modelled TCP1 results also provide good fit to reports of Jubb and Galvin (2004a)

Table 20: TCP3 costs (farm level)

Program component	Affecting	Who pays?	Cost	Comment
Dedicated calf paddocks	Dairy	Farmer	$0[F]	Farmers are required to separate calves from other age groups for management. It can be argued that the use of 'fixed' calf rearing areas incur no extra cost year on year as an equivalent area must be set aside for calves irrespective of involvement in TCP3/JDCAP or not.
Twice-daily calf removal	Dairy	Farmer	$1,722[F]	An extra calf collection visit each day has been assumed across a 42-day calving period when replacements are being born (i.e. twice-daily removal instead of once-daily removal). Two workers with a vehicle will take around 1 hour to capture calves and process them and their dams on a typical dairy farm. This has been costed.
Calf feeding	Dairy	Farmer	$0[F]	The majority of dairy farmers remove calves from cows and feed waste milk supplemented with milk from the vat. TCP3 and JDCAP have not resulted in fundamental changes to calf feeding practices; few farmers use milk replacer.
Blood testing adults 4 years and older (every 2nd year)	Dairy, Beef	Farmer	$60[F]	Extra workers to assist cow flow at milking (dairy) or to yard beef cows are required to be supplied by the farmer. Testing occurs every second year on average.
Inspection and audit	Dairy, Beef	Farmer	$100[F]	The farm manager is required to attend the inspection.
Inspection and audit	Dairy, Beef	CCF[C]	$200[F]	The annual audit fee is paid to the TCP veterinarian.
ELISA testing costs	Dairy, Beef	CCF[C]	$12.95[V]	The collection fee is paid to the TCP veterinarian. Comprised of $6.35 collection fee + $6.60 laboratory fee per sample.
Clinical case confirmatory testing	Dairy, Beef	CCF[C]	$40[V]	Clinical sample collection and processing (per case).
DEPI admin	Dairy, Beef	DEPI[K]	$360[F]	Three professional hours per farm per year is assumed by senior DEPI staff.

F – fixed cost (per farm), V – variable cost (per animal), C – cash costs (CCF) and K – in-kind costs

Stud herds: significant emphasis was placed on the impact of (confirmed) disease on the losses incurred by stud herds. A stud herd has the option to sell individual elite animals for breeding at prices well in excess of trade or slaughter prices. The confirmed presence of BJD limits the capacity to sell animals to other farmers and participants in TCP3 are prohibited from selling high-risk animals anywhere except for direct slaughter. The proportion of herds that operate as studs differs markedly between the beef and dairy industries. Within the dairy industry there is now only one local buyer of elite genetics (Genetics Australia) and it purchases approximately 50 elite male calves per year from approximately 15 stud farms. A small number of farmers with highly-regarded herds sell pure-bred dairy breed bulls to farmers who do not use artificial insemination, or who attempt to sell home-bred surplus pure-bred dairy heifers into the live export market. We have assumed that 1% of dairy farms operate as studs and that only 1% of the annual calf drop is sold as elite animals. We have also assumed that losses arising from the foregone sales of elite dairy animals are three times the inflation-adjusted estimate used by DAV in 1994. This is a figure of $9,216 per elite animal – a typical value for an elite stud dairy bull calf.

We have also assumed that approximately one in 50 beef producers sells elite bulls to other commercial producers, and that 50% of the annual male calf drop of these producers are elite, surplus and available for sale. This estimate would provide approximately 3,000 new beef bulls for sale each season which would imply that each bull survives for an average of four mating seasons and operates at a cow-to-bull ratio of 60:1. These are sensible operating numbers. We have adjusted the loss estimate from 1994 for inflation, and have estimated the losses from a foregone sale of an elite beef bull to be approximately $3,072 per lost opportunity.

4.3.2 Results

Farm level: the average economic losses experienced by average Victorian dairy farms (252 milkers) are presented in Table 21 (TCP3) and Table 22 (TCP1) and for beef farms (184 breeders) in Table 23 (TCP3) and Table 24 (TCP1), respectively. Participation by dairy farmers in TCP1 is likely to have reduced farm losses due to BJD whereas participation in TCP3 appears to have resulted in marginally reduced losses when compared to non-participation. Disease is predicted to produce average annual losses of approximately $21,700 per annum in infected and uncontrolled herds, whereas the reduction in prevalence provided by TCP1 participation reduces losses to around $9,300 per annum (a net gain of $12,300 over non-participation). The losses from participation in TCP3 average around $20,200 per annum (a net reduction in loss due to disease of $1,450 over non-participation). When the additional cost of TCP program compliance and participation (borne by DEPI) is included, there was a net benefit of approximately $10,600 per year for TCP1 participants but only a net gain of approximately $200 for TCP3 participants compared to non-participation.

For commercial beef farms the average cost of disease is estimated at $1,350 per annum for infected herds. Participation in TCP1 would increase cost to $2,200 (TCP1) whereas TCP3 participation would increase losses to $1,500, providing a participating farmer with a net

loss of around $840 (TCP1) and $160 (TCP3) per year from participation.[21] However, when the DEPI costs of compliance and participation in TCP are included the net losses per participating farm increase to $3,600 (TCP1) and $2,200 (TCP3) per year resulting in an increased losses of $2,200 (TCP1) and $890 (TCP3) compared to non-participation in the program.

Because few dairy herds sell stud animals – and the number of animals sold for stud from participating herd is very small (often only one elite male animal) – the losses for a stud dairy herd are similar to those of a commercial herd. If disease is confirmed in a stud dairy herd, thereby restricting the sale of stud animals, the average annual loss for a non-participating herd increases to $26,300. This reduces to $24,900 if the herd is participating in TCP3 (reduced loss of $1,450 over non-participation) and reduced to $15,700 if the herd remained in TCP1 (resulting in a reduced loss of $10,600 compared to non-participation). For stud herds, the losses are greater than for non-stud herds.

The losses for beef stud herds are markedly greater from a confirmed infected status than for non-stud or dairy herds. An average-sized stud beef herd with BJD may experience annual losses of around $285,000. Like non-stud beef herds, participation in TCP3 (or TCP1) results in a small increase in loss. The loss of trading income due to elimination of stud sales in herds that participate in TCP dwarf the costs of administering the program. It is the stud beef farm that has the greatest potential to experience major economic harm from BJD if disease is identified. Reducing disease movement into the beef sector should be of high priority for any future BJD management programs.

Farm-level sensitivity analysis: TCP1 was estimated to reduce the clinical annual incidence and reactor rate by around 80% whereas TCP3 is estimated to reduce the clinical annual incidence rate by around 60%. A reduction of 60-70% effectively equalises the participation cost with the benefit. TCP3 is therefore not returning sufficient benefit to justify continuation.

The break-even value for losses arising from premature culling of a clinical case was estimated at $530 (dairy cow) – being around 15% of the estimated value. This implies that any error arising from failure to control for feed cost changes in the methodology are not influencing outcome and therefore are not important.

Dairy farmers may argue that use of dedicated calf paddocks involves costs. For example, the emergence of drench resistance in cattle worm and fluke populations may be encouraged by use of dedicated calf rearing paddocks. This sensitivity analysis demonstrates that even small reductions in the incidence of disease in infected herds – especially the incidence of clinical disease – will return significant benefit to producers. TCP1 returned real (if intangible) benefits to the majority of farmer participants.

[21]The cost of testing is greater than the benefits accrued from reduced prevalence in beef herds. Therefore TCP3 invokes less cost and less loss than TCP1 because it has fewer animal tests and less frequent testing than TCP1

Table 21: Average farm level economic losses due to BJD on Victorian dairy farms – TCP3 program

Component	Commercial dairy (99.0%)				Stud dairy (1.0%)			
	Uninfected (40%)	Suspect (35%)	Non-TCP3 (16%)	TCP3 (9%)	Uninfected (40%)	Suspect (35%)	Non-TCP3 (16%)	TCP3 (9%)
Farmer costs								
Cows	251.9	251.9	251.9	251.9	251.9	251.9	251.9	251.9
JD reactors	0	13.1	13.1	2.8	0	13.1	13.1	2.8
Clinical	0	6.5	6.5	2.8	0	6.5	6.5	2.8
Losses – Reactors	$0	$0	$0	$9,162	$0	$0	$0	$9,162
Losses – Clinicals	$0	$21,656	$21,656	$9,162	$0	$21,656	$21,656	$9,162
Losses stud sales	$0	$0	$0	$0	$0	$0	$4,642	$4,642
Costs TCP/ JDCAP compliance	$0	$0	$0	$1,882	$0	$0	$0	$1,882
Total	***$0***	***$21,656***	***$21,656***	***$20,206***	***$0***	***$21,656***	***$26,298***	***$24,849***
CBA (c.f. uninfected)	-	$21,656	$21,656	$20,206	$0	$21,656	$26,298	$24,849
CBA (TCP c.f. non-TCP)				-$1,450				-$1,450
TCP Program costs								
Blood test[c]	$0	$0	$0	$245	$0	$0	$0	$979
Clinical confirmatory tests[c]	$0	$0	$0	$554	$0	$0	$0	$554
Annual report[c]	$0	$0	$0	$200	$0	$0	$0	$200
Internal DEPI admin[k]	$0	$0	$0	$360	$0	$0	$0	$360
Total	***$0***	***$0***	***$0***	***$1,259***	***$0***	***$0***	***$0***	***$1,259***
Combined costs								
Total	***$0***	***$21,656***	***$21,656***	***$21,465***	***$0***	***$21,656***	***$26,298***	***$26,108***
CBA (cfuninfected)	-	$21,656	$21,656	$21,465	$0	$21,656	$26,298	$26,108
CBA (TCP c.f. non-TCP)	$0	$0	$0	-$191	$0	$0	$0	-$191

c – cash costs (total CCF cash costs = $899); k – in-kind contributions by DEPI

Table 22: Average farm level economic losses due to BJD on Victorian dairy farms – TCP1 program

Component	Commercial dairy (99.0%)				Stud dairy (1.0%)			
	Uninfected (40%)	Suspect (35%)	Non-TCP1 (16%)	TCP1 (9%)	Uninfected (40%)	Suspect (35%)	Non-TCP1 (16%)	TCP1 (9%)
Farmer costs								
Cows	251.9	251.9	251.9	251.9	251.9	251.9	251.9	251.9
JD reactors	0	13.1	13.1	1.5	0	13.1	13.1	1.5
Clinical	0	6.5	6.5	0.8	0	6.5	6.5	0.8
Losses – Reactors	$0	$0	$0	$4,998	$0	$0	$0	$4,998
Losses – Clinicals	$0	$21,656	$21,656	$2,499	$0	$21,656	$21,656	$2,499
Losses stud sales	$0	$0	$0	$0	$0	$0	$4,642	$4,642
Costs TCP/ JDCAP compliance	$0	$0	$0	$1,882	$0	$0	$0	$1,882
Total	***$0***	***$21,656***	***$21,656***	***$9,378***	***$0***	***$21,656***	***$26,298***	***$14,021***
CBA (cfuninfected)	-	$21,656	$21,656	$9,378	$0	$21,656	$26,298	$14,021
CBA (TCP c.f. non-TCP)				-$12,278				-$12,278
TCP Program costs								
Blood test[c]	$0	$0	$0	$979	$0	$0	$0	$979
Clinical confirmatory tests[c]	$0	$0	$0	$151	$0	$0	$0	$151
Annual report[c]	$0	$0	$0	$200	$0	$0	$0	$200
Internal DEPI admin[k]	$0	$0	$0	$360	$0	$0	$0	$360
Total	***$0***	***$0***	***$0***	***$1,690***	***$0***	***$0***	***$0***	***$1,690***
Combined costs								
Total	***$0***	***$21,656***	***$21,656***	***$11,068***	***$0***	***$21,656***	***$26,298***	***$15,710***
CBA (cfuninfected)	-	$21,656	$21,656	$11,068	$0	$21,656	$26,298	$15,710
CBA (TCP c.f. non-TCP)	$0	$0	$0	-$10,588	$0	$0	$0	-$10,588

c – cash costs (total CCF cash costs = $899); k – in-kind contributions by DEPI

Table 23: Average farm level economic losses due to BJD on Victorian beef farms - TCP3

Component	Commercial beef (98.0%)				Stud beef (2.0%)			
	Uninfected (93%)	Suspect (5%)	Non-TCP3 (1%)	TCP3 (1%)	Uninfected (93%)	Suspect (5%)	Non-TCP3 (1%)	TCP3 (1%)
Farmer costs								
Cows	184.0	184.0	184.0	184.0	184.0	184.0	184.0	184.0
JD reactors	0	1.8	1.8	0.5	0.0	1.8	1.8	0.5
Clinical	0	0.9	0.9	0.5	0.0	0.9	0.9	0.5
Losses – Reactors	$0	$0	$0	$675	$0	$0	$0	$675
Losses – Clinicals	$0	$1,350	$1,350	$675	$0	$1,350	$1,350	$675
Losses stud sales	$0	$0	$0	$0	$0	$0	$282,624	$282,624
Costs TCP/ JDCAP compliance	$0	$0	$0	$160	$0	$0	$0	$160
Total	**$0**	**$1,350**	**$1,350**	**$1,510**	**$0**	**$1,350**	**$283,974**	**$284,134**
CBA (cfuninfected)	-	$1,350	$1,350	$1,510	$0	$1,350	$283,974	$284,134
CBA (TCP c.f. non-TCP)				$160				$160
TCP Program costs								
Blood test[c]	$0	$0	$0	$179	$0	$0	$0	$179
Clinical confirmatory tests[c]	$0	$0	$0	$92	$0	$0	$0	$92
Annual report[c]	$0	$0	$0	$200	$0	$0	$0	$200
Internal DEPI admin[k]	$0	$0	$0	$360	$0	$0	$0	$360
Total	**$0**	**$0**	**$0**	**$731**	**$0**	**$0**	**$0**	**$731**
Combined costs								
Total	**$0**	**$1,350**	**$1,350**	**$2,240**	**$0**	**$1,350**	**$283,974**	**$284,864**
CBA (cfuninfected)	$0	$1,350	$1,350	$2,240	$0	$1,350	$283,974	$284,864
CBA (TCP c.f. non-TCP)	$0	$0	$0	$891	$0	$0	$0	$891

c – cash costs (total CCF cash costs = $899); k – in-kind contributions by DEPI

Table 24: Average farm level economic losses due to BJD on Victorian beef farms - TCP1

Component	Commercial beef (98.0%)				Stud beef (2.0%)			
	Uninfected (93%)	Suspect (5%)	Non-TCP1 (1%)	TCP (1%)	Uninfected (93%)	Suspect (5%)	Non-TCP1 (1%)	TCP1 (1%)
Farmer costs								
Cows	184.0	184.0	184.0	184.0	184.0	184.0	184.0	184.0
JD reactors	0	1.8	1.8	0.9	0.0	1.8	1.8	0.9
Clinical	0	0.9	0.9	0.5	0.0	0.9	0.9	0.5
Losses – Reactors	$0	$0	$0	$1,350	$0	$0	$0	$1,350
Losses – Clinicals	$0	$1,350	$1,350	$675	$0	$1,350	$1,350	$675
Losses stud sales	$0	$0	$0	$0	$0	$0	$282,624	$282,624
Costs TCP/ JDCAP compliance	$0	$0	$0	$160	$0	$0	$0	$160
Total	**$0**	**$1,350**	**$1,350**	**$2,184**	**$0**	**$1,350**	**$283,974**	**$284,808**
CBA (cfuninfected)	-	$1,350	$1,350	$2,184	$0	$1,350	$283,974	$284,808
CBA (TCP c.f. non-TCP)				$835				$835
TCP Program costs								
Blood test[c]	$0	$0	$0	$715	$0	$0	$0	$715
Clinical confirmatory tests[c]	$0	$0	$0	$92	$0	$0	$0	$92
Annual report[c]	$0	$0	$0	$200	$0	$0	$0	$200
Internal DEPI admin[k]	$0	$0	$0	$360	$0	$0	$0	$360
Total	**$0**	**$0**	**$0**	**$1,367**	**$0**	**$0**	**$0**	**$1,367**
Combined costs								
Total	**$0**	**$1,350**	**$1,350**	**$3,551**	**$0**	**$1,350**	**$283,974**	**$286,175**
CBA (cfuninfected)	$0	$1,350	$1,350	$3,551	$0	$1,350	$283,974	$286,175
CBA (TCP c.f. non-TCP)	$0	$0	$0	$2,202	$0	$0	$0	$2,202

c – cash costs (total CCF cash costs = $899); k – in-kind contributions by DEPI

State level: the total projected losses due to BJD in the state of Victoria by production sector and BJD herd status for 2014 are presented in Table 25. The expected loss due to BJD by the Victorian dairy industry in 2014 was estimated at $22.2m and for the Victorian beef industry at $795,000.

The cost of TCP3 for DEPI and the CCF for 2014 is predicted to be $450,000. This comprises expenditure of $422,000 on dairy herds and $28,000 on beef herds. Currently this expenditure is not resulting in significant net benefit to participating dairy or beef farmers.

The maintenance of TCP3 in its current guise is therefore not supported by economic analysis. A return to TCP1 (with increased investment and increased recruitment of farmers) or the diversion of TCP funds into alternative control programs is warranted.

Table 25: Victorian BJD losses by industry and status – under TCP3

	Commercial				Stud			
Dairy	Uninfected (1,583 herds)	Suspect (1,374 herds)	Non-TCP3 (638 herds)	TCP3 (332 herds)	Uninfected (16 herds)	Suspect (14 herds)	Non-TCP3 (6 herds)	TCP3 (3 herds)
Farmer costs	$0	$29.7M	$13.8M	$6.7M	$0	$0.3M	$0.17M	$0.08
TCP costs[a]	$0	$0	$0	$0.4M	$0	$0	$0	$0
Total costs	$0	$29.7M	$13.8M	$7.1M	$0	$0.3M	$0.17M	$0.09M
Beef	Uninfected (3,578 herds)	Suspect (192 herds)	Non-TCP (38 herds)	TCP (38 herds)	Uninfected (73 herds)	Suspect (4 herds)	Non-TCP (1 herd)	TCP (1 herd)
Farmer costs	$0	$0.26M	$0.05M	$0.06M	$0	$0.01M	$0.22M	$0.22M
TCP costs[a]	$0	$0	$0	$0.03M	$0	$0	$0	$0
Total costs	$0	$0.26M	$0.05M	$0.09M	$0	$0.01M	$0.22M	$0.22M

a – includes cash (CCF) and in-kind (DEPI) costs of program delivery

4.4 Cost of BJD Control to the Regulatory Agencies

The expenditure by the CCF on TCP1 – TCP3 is shown in Table 26 (source: DEPI).

Table 26: Expenditure by year on TCP2 and TCP3 by the Cattle Compensation Fund

Year	Herd advice	Vet collection	Lab	Compensation.[22]	Admin	Total
2003/04	$71,370	$250,269	$248,712	$327,200		$897,550
2004/05	$70,205	$277,094	$273,790	$272,200		$893,289
2005/06	$68,175	$303,833	$283,361	$384,000		$1,039,369
2006/07	$62,766	$298,501	$270,332	$377,300		$1,008,898
2007/08	$55,335	$267,100	$234,637	$292,100		$849,173
2008/09	$55,107	$271,679	$230,672	$392,900		$950,358
2009/10		$772,585		$348,300		$1,120,885
2010/11		$901,138		$167,935	$150,000	$1,219,073
2011/12		$627,255		$17,400	$150,000	$794,655
2012/13		$457,220		$0	$150,000	$607,220
2013/14						$450-500,000 est.[a]

a – with an additional estimated $100,000 for program administration and reporting

The estimated costs for 2012/13 and the predicted costs for 2013/14 were obtained from updating and extending the 1994 BJD economics estimated (DAV 1994) are reasonably consistent – given the reduced testing due to farmer drop-out, the reduced testing of animals in participating TCP3 herds when compared to TCP1, and an unaccounted estimate of approximately $100,000 for administration of the program. The total CCF expenditure on all TCP variants is estimated at more than $15M since program inception in 1996.

[22] Principally but not exclusively related to BJD

5 STAKEHOLDER PERCEPTIONS

5.1 Approach

The approach to gathering stakeholder perceptions of TCP and possible future options for BJD control in Victoria was as follows:

- A brief Discussion Paper was prepared, and provided a summary of:
  - Whether TCP3 is doing what it was intended to do;
  - What new knowledge, tools and other developments might be changing the BJD landscape;
  - What Victoria is obliged to do under the national program, and whether it is fulfilling those obligations; and
  - What questions might need to be considered as possible alternatives to TCP3 are developed.

  After a review of accuracy by the DEPI project managers, the paper was circulated to potential interviewees, who were asked to consider responses to them prior to discussion with the consultants.
- A two-hour dairy industry workshop at the offices of United Dairy Farmers of Victoria was held on 7 May, 2014. There were 13 participants at the workshop, representing different organisations from the following sectors:
  - Production;
  - Breed societies;
  - Processing;
  - R&D;
  - Food safety; and
  - Biosecurity.

  The workshop comprised a short re-presentation of key elements of the Discussion Paper followed by a semi-structured discussion of the questions.
- Telephone and farmer discussion group interviews with approximately 20 dairy and beef producers and telephone interview with follow-up email discussions with eight leading cattle veterinarians were conducted. Informal feedback on the program in general was also gathered from a dairy farm discussion group meeting in Warragul.

5.2 Summary of Workshop Feedback

It was difficult to distil key messages from the workshop, particularly as the discussion was not as balanced as might have been preferred. The following observations appeared to be sufficiently significant to warrant follow-up during the subsequent consultations and analysis:

- The information presented in the Discussion Paper on the positive economic benefit of TCP3 for dairy participants was surprising, and needed to be more widely promulgated to counter negative views about the program.
- There are differing perceptions, accurate or otherwise, as to what TCP originally set out to achieve and currently aims to achieve – for example eradication, or to provide a pool of BJD-free farms.
- Dairy ManaJD (SA) should be more closely examined, if its success is genuinely as claimed.
- False-positive reactors are a major source of frustration for program participants and do not receive enough attention. They are a major reason people leave the program.
- There are mixed and generally scattered views on the imperatives for a continued program to control BJD – including the emergence of sheep strain, satisfying trading partners, meeting interstate requirements, obligation to existing participants.
- The Dairy Assurance Score has been poorly promoted and under-utilised.
- One of the participants held a strong view that vaccination will not be a substitute for calf management and may even be detrimental to BJD control except in high-prevalence herds. Others pointed to the high cost of vaccine.

5.3 Summary of Producer and Veterinarian Feedback

The sentiments expressed regarding TCP and possible future programs were summarised as follows:

- Participants interviewed for the project understood that TCP is about control, rather than the eradication of the disease. Most veterinarians believed that their producer clients see TCP as a control rather than eradication program. However, there were false expectations at the outset of the scheme that eradication was feasible. One veterinarian reported that his clients were aiming to eradicate BJD, and were very close to having three negative tests.
- Producers participating in the program did not believe that they were disadvantaged by their involvement. This was especially true of those who had a high number of clinical cases prior to TCP. Some producers who were not participating thought that the participants were disadvantaged. As for the producers, veterinarians had mixed views about where the value of TCP accrued, but most said that producers participated for private benefit.
- Notwithstanding the point above, producers understood the rationale for BJD control but the disease was generally not seen as a major issue in their businesses.
- Veterinarians generally maintained that TCP has a poor image across the industry. The fact that TCP herds do make progress, and realise benefits from this, was not well understood. The risk associated with false-positive test results, and the lack of compensation for (sometimes) highly-productive cows, were major disincentives. The paperwork of TCP3 (especially listing at-risk cattle) was also mentioned.
- There was a general expectation amongst participants that some sort of BJD program would continue to be made available. However, veterinarians had differing views as to whether their clients would (or, indeed, should) care if TCP itself ceased. Producers and

veterinarians agreed that ceasing subsidies will virtually 'kill' testing. Producers would not continue to pay for a test they knew to be highly inaccurate, and would drop back to simply raising calves under JDCAP.

- There were mixed views about vaccination amongst the producers, at least partially reflecting a lack of good information on which to form a judgement. Those producers with years of experience in TCP were generally unenthusiastic about vaccination. Veterinarians had differing views. Some are supportive, while others are sceptical. This was again based largely on a lack of information with which to estimate the benefit, although costs, OH&S concerns, low producer compliance, a lack of auditability and interference with diagnostics were all noted.

5.4 Implications of Stakeholder Feedback

The implications of the stakeholder feedback were summarised as follows:

- The benefits of TCP have not been well communicated. This represents a lost opportunity to recruit participants and to generate kudos for animal health programs generally.
- It is possible that those who were unrealistically hopeful of eradicating BJD at the outset of the program have since departed, leaving the 'realists' as the ongoing participants. The transition from TCP2 to TCP3 may have exacerbated this. This might suggest that the participation rate has bottomed out or will at least decline more slowly. This effect will be countered, though, by frustration at not being able to graduate from the program.
- The issue of false positives needs to be neutralised as far as is possible given the constraints of the tests. Provisions such as the discretion to re-test individuals using culture or PCR should be examined.
- It is likely that complete cessation of TCP without replacement with another, comparable (subsidised) program would be met with widespread dissatisfaction. Certainly it seems that regular testing as used in the current program would be largely abandoned. Participants would stand to lose a hard-earned status, but the clear message is that this would not be sufficient incentive to start to pay for testing. Contributing to this withdrawal would be the lack of a clear drive in the industry to control the disease.
- Because current TCP participants are likely to be quite progressive in relation to biosecurity and industry responsibility, program termination may also present a significant risk to future dairy disease control programs. The 'authorities' such as DEPI could lose significant credibility.
- There is widespread uncertainty over the value of vaccination, which is entirely unsurprising given the lack of information available. Views on vaccination appear to range from quite oppositional to quite supportive. With the exception of one particularly negative view, extreme views at either end of the spectrum were not noted, suggesting that the cautious introduction of vaccination supported by evidence of likely benefit and appropriate 'fit' into existing frameworks (declarations etc.) should be reasonably well accepted. It will be important to complete the analysis of the Australian Silirum® field study data to determine the effectiveness of the vaccine on susceptibility to new

infection, and for infected vaccinates the rate of progression of disease, rate of shedding and the incidence of clinical disease. Introduction will require longitudinal monitoring of the impact of vaccination on within-herd prevalence of disease.

- A future option may be to provide the option of vaccination or test-and-cull, with a standard rebate for either, with vaccinators agreeing that vaccination data must be made available for the purposes of further analysis.

6 EVALUATION OF BJD CONTROL COMPONENTS

Specific components of on-farm BJD control were evaluated for their application, effectiveness, strengths and weaknesses and the attitude of the various Victorian stakeholders. A special focus was placed on those components that are integral parts of TCP or JDCAP. The process essentially broke each component down into a building block for a BJD control program, and thereby provided insight into the necessary and essential components of a working and workable BJD control program for Victorian cattle farmers.[23]

6.1 Dedicated Calf Paddocks

TCP/JDCAP: this is a mandatory component of JDCAP component. It states that paddocks must not have grazed adults or other high-risk species for a minimum of 12 months prior to young stock grazing. Run-off from irrigated paddocks to paddocks grazed by adults must also be avoided.

Application: minimise faecal-oral exposure in calves by eliminating contact by young stock to faeces of adult animals.

Effectiveness: likely to be effective against contacting Mptb derived from infected adults.

Strengths: prevents young stock from directly contacting faeces from adult animals.

Weaknesses: transient shedding of Mptb in newly infected calves is common (< 50%). Failure to cull calves from infected dams or new infections in calves arising from contaminated calf milk can produce calf infections with subsequent shedding of Mptb onto dedicated calf paddocks. This can result in an 'internal' paddock contamination and infection cycle. Dedicated calf paddocks are also risk factor for the emergence of drench resistance (worms and flukes) because worm-resistant adult cows are unavailable to 'vacuum' pasture larvae. This leads to rapid larvae build up on pastures and high calf exposures necessitating increased use of drench. This combined with the limited ability to provide new safe pasture after drenching promotes selection for resistant parasites. Irrigation run-off and reuse systems also present a direct risk for transfer (introduction or recirculation) of Mptb onto dedicated calf paddocks on flood irrigated dairy farms. The calving paddock presents a small but important breach in the separation of calves from adults – most farms use the same calving paddocks (close to facilities) so the potential for Mptb build-up on calving areas is often high.

Stakeholder attitudes: the dairy industry has accepted the ancillary advantages arising from JDCAP calf management practices. The principles of early removal, individual calf colostrum management and dedicated rearing facilities are now well accepted by the dairy industry as essential practices for rearing healthy and thriving calves.

Alternatives: none identified.

[23] Please note that the material in this section was previously described to DEPI as an 'information matrix'

6.2 Twice Daily Calf Removal

TCP/JDCAP: mandatory JDCAP component.

Application: minimises faecal-oral/contaminated teat/contaminated colostrum spread of Mptb to newborn calves.

Effectiveness: early removal is effective at minimising exposure risk of calves to Mptb from adult faeces.

Strengths: early removal and individual focus on colostrum intake offer significant calf health and welfare benefits that extend beyond BJD control.

Weaknesses: no clear advantage of 12-hourly removal over 24-hourly removal has been demonstrated. Twice-daily removal may be difficult to consistently achieve over time – especially on large farms. Early calf removal is ineffective at preventing direct spread from the dam to the calf via colostrum or contaminated teats.

Stakeholder attitudes: see above.

Alternatives: none identified. Early removal of calves is an essential pillar of breaking the faecal-oral infection cycle on dairies.

6.3 Calf Feeding

TCP/JDCAP: JDCAP states that milk must not be contaminated by manure from adult cows and that milk from low risk individuals should be used to supply calves if calf milk replacer is not used.

Application: minimises faecal-oral spread risk to unweaned calves through milk.

Effectiveness: questionable efficacy when non-sterilised whole milk is fed to calves on commercial dairy farms. Few farmers feed milk replacer.

Strengths: effective exclusion of Mptb from calf milk eliminates this minor but important pathway of infection.

Weaknesses: subclinical lactating shedders cannot be identified with confidence and be reliably eliminated from the calf supply. Clinical cases are also more likely to be in the 'blue milk' calf group before disease is suspected or confirmed. A single super-shedder provides significant exposure risk to the whole calf cohort. Faecal contamination of calf milk supply cows (the 'blue' herd) may be more likely than for factory milk as these are typically the fresh cows and sick cows in the herd. There is a significant and persistent risk of mass exposure of calves to contaminated pooled calf milk from feeding of non-pasteurised calf milk in infected herds and this risk increases as herd size increases and as calving becomes more compressed (seasonal versus split calving). A 1% clinical disease incidence suggests at least 3-5% of the herd are shedders. As herd sizes increase beyond 100 milkers the likelihood becomes greater than 50% that a shedder is providing calf milk to replacements.

Stakeholder attitudes: few Australian dairy farms feed calf milk replacer. Disposal of waste milk poses an environmental issue that most farmers avoid by feeding this milk to calves.

The cost of and time required to pasteurise calf milk is likely to be unacceptable to most farmers – especially smaller farms.

Alternatives: milk replacer. Calf milk sterilisers – such as pasteurisers reduce risk of infection from feeding waste milk from cows to calves.

6.4 Young Stock Water Supply

TCP/JDCAP: JDCAP states that ideally water for young stock will come from dedicated rain-water tanks or bores.

Application: minimise faecal-oral spread to young stock.

Effectiveness: questionable due to the low levels of compliance – but the level of risk is unlikely to be great.

Strengths: dedicated rainwater or bore water supply eliminates risk of transfer.

Weaknesses: unlikely to be deployed on the majority of dairy farms – especially irrigation dairy farms where the majority of farms have reticulated stock watering systems that source from the irrigation supply. Irrigation channels also present a direct opportunity for exposure.

Stakeholder attitudes: farmers are unlikely to invest in dedicated calf stock water supply systems.

Alternatives: dedicated watering systems. This is unlikely to be deployed.

6.5 Dedicated Young Stock Machinery and Worker Clothing

TCP/JDCAP: JDCAP states that vehicles and clothing that has had contact with adults should not be used.

Application: minimise faecal-oral spread to young stock.

Effectiveness: questionable due to low levels of compliance – but the level of risk is unlikely to be great.

Strengths: eliminating vehicle transfer from paddocks reduces transfer risk to calf paddocks.

Weaknesses: unlikely to be adhered to on large dairy farms.

Stakeholder attitudes: farmers are unlikely to invest in dedicated calf machinery and equipment.

Alternatives: dedicated machinery and personnel. This is unlikely to be deployed.

6.6 ELISA Blood Testing Adults ('Test-and-Cull')

TCP/JDCAP: TCP1 – all adults 2 years of age and older tested annually. TCP3 – all adults 4 years of age and older tested biennially.

Application: early removal of Mptb shedders. The objective is to minimise pasture and milk contamination with Mptb by (ideally) removing infected animals before they enter the

heavy shedding phases of disease. This reduces the infection risk and rate of new infection on infected farms.

Effectiveness: the ELISA test has low sensitivity. This is in turn dependent on the stage of infection when tested – ranging from <10% in early shedding stages to approximately 80% in clinical cases. The test has imperfect specificity resulting in false positives. (TCP rules expressly forbid retesting of positive animals).

Strengths: TCP1 was more effective at identifying and eradicating shedding animals from the herd and reducing farm contamination levels.

Weaknesses: TCP1 was more effective at identifying and eradicating shedding animals from the herd than TCP3 – however not all shedders were identified or removed in a timely manner in either forms of the program. Test-and-cull using ELISA is unable to drive eradication of disease on most farms (when used in combination with targeted culling of high-risk animals and JDCAP). This may have been partly due to disease maintenance via secondary pathways (in-utero and infected calf milk) but identification and removal of shedders by ELISA testing and culling was not effective enough to remove all diseased animals from the herd. TCP3 appears to have been markedly less effective than TCP1 – too many shedding animals avoid detection for too long resulting in little effective change to pasture and milk contamination rates. The high but imperfect specificity of the ELISA test produces around one false positive per 200 uninfected and tested animals. This rate of false positives makes it unlikely for medium to large sized dairy herds to return consecutive all negative herd tests. The implication is that few farms move from low prevalence (TLP) to tested negative (RD1-RD2, TMS) even if truly free of disease.

Stakeholder attitudes: the culling of apparently clinically unaffected reactors (and high-risk contacts – preferential culls) remains a sticking point for many farmers. Removal of compensation for reactors has increased farmer frustration. This is enhanced by the poor participation rate in TCP – a few dedicated farmers are suffering seemingly unreasonable and apparently unnecessary losses to eradicate a disease and observe many of their neighbours not taking similar action against BJD or in some cases actively concealing the presence of disease within their herds. Many interviewed veterinarians identified the policy failure in TCP for both acknowledging and investigating potential false-positive ELISA tests as a major flaw.

Alternatives: use of more sensitive tests for infection such as individual faecal culture or HT-J-PCR may identify more infected animals earlier if used annually on adult stock. There is a risk of culling of transient passive shedders (not infected; but having recently grazed contaminated pasture and ingested Mptb). Cost of testing is likely to be higher than for ELISA testing of individuals. HT-J-PCR is not (yet) an accepted test in SDRGSs. The HEC test may provide a means of investigating potential false-positive ELISA results in low sero-prevalence herds. However, current SDRGs do not allow a herd to progress to an uninfected status from an infected status. A policy for dealing with potential false-positive ELISA results in long-term low prevalence herds is necessary to re-engage sceptical farmers and veterinarians if TCP is to continue as a valid program. The HEC test may provide a valid approach to investigating low reactor rates in these herds.

6.7 Herd Records

TCP/JDCAP: all variants of TCP (TCP1 – TCP3) state that calves and dams of clinical cases and ELISA positive animals should be culled (slaughter) within 12 months. Cohorts of clinical cases and reactors should be marked for preferential culling.

Application: to control the vertical transmission pathway (in-utero and colostrum).

Effectiveness: likely to be high. Less than 50% of clinical and pregnant cases transfer infection into the unborn foetus.

Strengths: good records allow control over secondary transmission pathways (in-utero and colostrum) and early removal of high-risk individuals

Weaknesses: inaccuracies in calf records are common. Incomplete records – especially in amalgamated herds – can make identification of preferential culling lists difficult and incomplete. Large scale culling can impact upon farm income, especially in the early stages of the program on individual farms.

Stakeholder attitudes: most farmers regard the culling of apparently normal (non clinical) preferential contacts as a significant economic cost. The risk of large scale culling is a major deterrent for entering TCP in its current format.

Alternatives: none identified. Preferential culling of dam-calf infected lines is essential to break the vertical transmission pathway.

6.8 Notification and Immediate Culling of Clinical Cases

TCP/JDCAP: all variants of TCP (TCP1 to TCP3).

Application: eradicate high-shedding clinical cases from herd and exclude from human food chain (direct to knackery).

Effectiveness: clinical cases are unlikely to be profitable so removal is inevitable. Delayed removal may result in significant contamination of paddocks.

Strengths: removal of clinical cases at first opportunity reduces farm contamination levels.

Weaknesses: there may be a period of up to 6 months before clinical cases are detected. Sale instead of removal to a knackery may occur in early clinical cases. The farm owner must pay any veterinary fee for investigation of the case. Direct disposal without notification is likely to occur in a proportion of cases.

Stakeholder attitudes: many farmers with infected herds discussed the increasing losses due to clinical disease in uncontrolled herds. The (eventual) reduction in the incidence of clinical disease following successful participation in TCP was seen as a benefit. However, this benefit is likely to have been apparent only in moderate or high prevalence herds that successfully reduced the new infection rate as a result of TCP participation and only after a number of years of participation – a small subset of infected herds in Victoria.

Alternatives: none identified.

6.9 Faecal Culture Test

TCP/JDCAP: not used as part of the standard TCP.

Application: potential to identify active shedders of Mptb with high confidence. This test has a potential application in investigating ELISA reactors in low prevalence herds to separate false-positive reactors from true positive cases.

Effectiveness: the faecal culture test has high sensitivity (45% for transient/low-shedding infected animals; increasing to 93% for high-shedding and clinical animals). The test is regarded to have perfect specificity (no false positives) if sample integrity is maintained.

Strengths: the test has high sensitivity and has perfect specificity. The test can detect shedders with moderate to high sensitivity before clinical signs of disease become apparent.

Weaknesses: culture is technically demanding and requires experienced microbiologists and dedicated laboratory facilities. Costly and slow — minimum turnaround time exceeds 2 months. Cross contamination can be a problem.

Stakeholder attitudes: the failure of TCP to recognise false positives on ELISA is a flaw in the current program. The strategic application of individual animal faecal culture tests may provide an acceptable way to investigate potential false positives in tested low prevalence herds. A false-negative culture test indicates that faecal shedding rates are low or absent at the time of sample collection and this is in line with the objectives of the ELISA test-and-cull component of TCP.

Alternatives: HT-J-PCR (at herd level).

6.10 HEC (Herd Environmental Culture) Test

TCP/JDCAP: not used.

Application: potential to identify persisting infection in low prevalence herds. Potential application in demonstrating herd freedom from disease. May have use in investigating false-positive ELISA sero-reactors in long-term low prevalence herds. May be used to confirm eradication of disease in testing herds.

Effectiveness: the HEC test has higher sensitivity than the current ELISA test and is regarded to have perfect specificity (no false positives). It is cheap and easily undertaken.

Strengths: the test is easy to apply in dairy herds (sample collection from dairy yard). It has high sensitivity and perfect specificity.

Weaknesses: the test is harder to apply in beef herds (require yarding and pool collection). The HEC test is a herd-level test only; it cannot identify infected individuals. Turnaround can take up to 16 weeks. No (current) capacity in SDRGs to allow herds to move from infected to uninfected status based on a series of negative HEC tests. The prolonged pre-shedding period that can occur in some infected animals may necessitate up to 10 years of annual (negative) HEC tests to demonstrate freedom with confidence.

Stakeholder attitudes: the failure of TCP to recognise false positives on ELISA is a flaw in the current program. The HEC test may allow a reasoned approach to investigating potential false positives in tested low prevalence herds.

Alternatives: HT-J-PCR (at herd level).

6.11 HT-J-PCR (High-Throughput Real-Time PCR) Test

TCP/JDCAP: nil.

Application: potential higher sensitivity substitute for the individual animal ELISA test used within TCP (test and cull).

Effectiveness: the HT-J-PCR has high sensitivity (60-70%) – but this is still < 10% for early infected and low shedding animals. The aggregate sensitivity is higher than the HEC test. The HT-J-PCR does not have perfect specificity (estimated at 99%). The test has fast turnaround times (one week).

Strengths: high sensitivity, rapid turnaround.

Weaknesses: not incorporated into SDRGs. Expensive ($100-$150 per test at present). Potential for DNA fragments from ingested dead Mptb to provide a positive result in uninfected animals (passive shedders). False positives are likely to be an issue (as per the current ELISA test).

Stakeholder attitudes: the failure of TCP to recognise false positives on ELISA is a flaw in the current program. The HT-J-PCR test may allow a reasoned approach to investigating potential false positives in tested low prevalence herds.

Alternatives: none identified.

6.12 Vaccination (Silirum® Killed Mptb Vaccine)

TCP/JDCAP: not used.

Application: to reduce the prevalence of infection in infected herds

Effectiveness: Silirum® is still under field trial evaluation in Australia. Final data analysis by Zoetis has not been undertaken. Early examination of culture data suggests a reduction in clinical cases of around 60% and delay in the progression of disease (10% older at first positive faecal culture). The impact of vaccination on susceptibility and shedding has not been calculated but interim company data suggests 80% fewer shedders amongst cattle vaccinated as calves. Detailed modelling studies have shown that low-efficacy vaccines (<50% effective) must: reduce susceptibility, slow the rate of progression of infection, reduce Mptb shedding and reduce the number of clinical cases if vaccination is to hold prevalence at low levels in the herds. Lowly effective vaccines that do not impact on each aspect presented above will paradoxically result in a marked increase in the prevalence of disease. Highly effective vaccines (>50% effective) can assist eliminate infection from herds over 10-20 years even if not (or less) effective in any one area.

Strengths: effective vaccines can be used to reduce prevalence of disease and over time eliminate disease in herds.

Weaknesses: Silirum® has not been fully evaluated to determine efficacy against risk of infection, time and rate of Mptb shedding, time and rate of progression of infection and incidence and time of onset of clinical disease in Australian dairy herds. Some vaccinates will provide (false) positive TB tests. Some vaccinates will provide positive ELISA tests (TCP regards ELISA+ vaccinates as infected). There are human health risks from accidental self-administration.

Stakeholder attitudes: some veterinarians are dubious about vaccination. Lack of efficacy information, OH&S issues with use, likely low economic benefit to producers, potential impact of vaccination in enabling infected animals to remain in herds for longer before breaking down with disease (or being tested and removed), likely poor farmer compliance, difficulty in assessing progress in control, cross-reactivity with TB tests (exclusion from export), and increasing dissatisfaction of farmers with 'yet another vaccine' were listed as reasons by veterinarians that may limit acceptance and uptake. Other veterinarians perceive built-up frustration by farmers participating in TCP (due to no progress) and many of these clients turned to vaccination (as part of the limited release trial) as a way of getting out of TCP – despite the increased cost of participating. Most veterinarians believe that vaccination cannot be used alone and one concern is that vaccinating farmers will ignore the other pillars of control (JDCAP). Some veterinarians state that JDCAP must be compulsory in vaccinating herds. Producers are wary of the vaccine. All want more information – many feel that they already administer too many vaccines to their cows. Farmers in TCP with low prevalence of clinical cases especially doubt there will be a cost-benefit from vaccination – especially at the price of $25 per dose.

Alternatives: non-reliance on vaccination. Focus on removal of shedding animals and reduction of exposure of animals to Mptb in and between infected herds.

6.13 Future Research

The knowledge gaps that exist and warrant further research depend in part upon the desired future direction of BJD control in Victoria. The major gaps are summarised below.

6.13.1 Diagnostic Tests

The absence of individual animal diagnostic tests with high sensitivity, high specificity, short turn-around times and low cost is a key factor contributing to the persistence of BJD within the jurisdictions that undertake control or eradication programs.

New tests – such as the HT-J-PCR and HEC test – are in the latter stages of development. However, these tests are currently not approved for use in the SDRGs or cannot be used to allow an infected herd to move to uninfected on the basis of a series of negative tests. The final validation and verification of these tests and the inclusion into the SDRGs is recommended.

The failure of BJD control programs to formally acknowledge the occurrence of false-positive ELISA results on individual animal tests has damaged the credibility of TCPs.

Research to confirm ELISA specificity and to develop acceptable ways (perhaps using HT-J-PCR) to investigate ELISA positives from low prevalence herds is recommended.

Modelling of the application of the HEC test in infected, low prevalence and eradicating herds to determine pool sizes and testing frequency (for beef herds) and the serial application of tests and the confidence in freedom from BJD after consecutive negative tests for both dairy and beef scenarios is recommended

6.13.2 Vaccination Performance

As previously discussed, the performance of the Silium® vaccine on the four essential performance parameters – response rate, susceptibility to infection, reduction in shedding and prolongation of pre-clinical phases of disease – must be clarified. This can be partly achieved by the completion of the two-farm Silirum® field study sponsored by Zoetis and DEPI but supported by the implementation of a longitudinal study on a proportion of vaccinating herds.

6.13.3 Environmental Persistence

The prevalence of transient shedding in animals less than 12 months of age, and the contamination levels in calf pens and calf paddocks for herds adhering to the JDCAP component of TCP, will identify the importance of this route in persistence of infection in TCP herds. A cross-sectional study with faecal culture of calf drop cohorts and calf pens and paddocks will provide insight into the role of this pathway in disease persistence on farm.

Examination of the contamination rates and levels of irrigation water on TCP herds with irrigation reuse systems may be required to determine the potential role of irrigation water in the spread of disease into the calves.

The effectiveness of eradication of BJD bison strain from northern extensive properties infected as a result of purchase of infected Rockley Brahman stud bulls must be monitored. If disease becomes established in Queensland there will need to be a re-consideration of both the risk factors for occurrence of disease in extensive grazed environments – such as beef farms – and the likely effectiveness (or purpose) and any disease control/eradication program in the south.

6.13.4 Strain Specificity

The increased isolation of ovine-strain Mptb in beef cattle needs to be investigated in the Australian environment. This may be due to increased awareness and investigations of disease in beef cattle but may also (most likely) be contributed to by an increase in the prevalence of OJD in the co-grazed sheep population. The ability of the ovine strain to persist in the beef herd after contact with the sheep host population has ceased is unknown in the Australian environment. Longitudinal studies of infected beef herds may be warranted to determine the capacity for ovine strain to self-sustain in beef herds.

7 A SIMULATION MODEL FOR BJD IN AUSTRALIAN DAIRY AND BEEF HERDS

It can be difficult to predict performance of integrated control programs that have many components – especially when individual control components are known or suspected to be of moderate efficacy. Computer simulation modelling can provide a useful approach to investigating disease and controls within and between herds if herd and disease dynamics and control components can be successfully and accurately represented by computer code.

Johne's disease is complex. Not all exposures result in disease, disease progression is slow and variable; diagnostic tests have modest and variable sensitivity; the disease agent can persist in the environment for prolonged periods; and individual control components provide incomplete protection. Johne's disease is therefore a strong candidate for computer modelling. It is essential that dairy herd population dynamics, disease infection pathways and disease dynamics are accurately coded for computer modelling to be useful. The careful construction and validation of model performance (where possible) is essential before findings from interpretation of model output can be trusted with any confidence.

7.1 Model Overview

A simulation model of BJD in Australian cattle herds was constructed in the R programming environment (version 3.0.1: R Core Team, 2014). Individual animals were modelled, and the herd was structured to present the common makeup of Victorian dairy herds. Individuals moved through the time horizon in discrete (daily) steps. Animals were held in logical farm management groups and were subjected to farm management and intervention practices according to farm production system and management practices, the physiological status of the animal and its age and sex, the time of the year, and the animal's current and historical performance in the herd. Where appropriate, animal and herd events were modelled stochastically. This allowed for uncertainty to be included and the model's outputs to be interpreted probabilistically.

Individual modules were developed for particular farm-level and animal-level events, including culling of surplus stock, mating, calving, milk production, mastitis, infection and shedding of pathogens. Modules were called according to the management practices of the herd (user input). Key parameters for modules were set by the user or derived from literature. The specific BJD parameters were coded as described in the review of the published literature given in Section 2.

Animal mortality, culling, reproductive performance and milk production were validated against existing industry data. Model outputs for which such data did not exist, or were not accessible, were partly validated against expected performance. Baseline levels of disease (including both mastitis and BJD) were validated using this approach. The TCP database provided a key means by which key characteristics of BJD within the modelled herd could be validated. These characteristics included the importance of transmission pathways, the incidence of clinical disease, and the average age of sero-reactors and clinical cases.

Model output was written to file at the individual animal level (events, lifetime performance, physiological and infection status), day, month and year level (e.g. herd milk production) and at site level (e.g. paddock Mptb contamination level). The outputs for 'non-visible' variables, such as the source and route of each infection and the daily site risk of new infection, were also written to file.

7.2 Structure and Parameterisation of the Dairy Herd Model

Parameters used by the simulation model are given in Table 33 and Table 34 (Appendix 1).

Both seasonal and a split-calving Victorian dairy herds scenarios were simulated. The seasonal herd began calving in August with all cows calved before the end of December and mating from November to the end of January.[24] The split-calving herd calved 60% of cows as above and the remaining 40% of cows calved in April or May following a short mating in July and early August.

For all calving patterns, unweaned calves, weaned calves, heifers, milking cows (lactating), dry cows and bulls are managed in separate groups. A set number of sites (paddocks and pens) are present on the farm. Depending upon the adherence or otherwise to JDCAP principles, weaned calves and heifers (< 2 years of age) use paddocks that are separate from paddocks used for adult cattle. If the farm does not adhere to JDCAP only the weaned calf pen(s) and calving paddock are removed from the general rotation. Milkers change paddocks on a daily basis. Non-lactating stock are set to change paddocks on a monthly basis. The next paddock in any grazing sequence is the paddock that has been un-grazed for the longest period and is eligible for the class of stock (and JDCAP program adherence). The level of Mptb contamination of each site is updated daily and this is used to modify the daily risk of a faecal-oral infection in uninfected animals that occupy the paddock or site.

Animals move through the respective stock class group based on age (calves are weaned at 42 days of age, yearlings become heifers around 365 days of age) or on physiological status (heifers join the lactating cow group of milkers on calving). Milkers join the dry cow group at the completion of the lactation. Artificial insemination is used early in the mating period. Bulls are used after AI. The reproductive performance of individuals is determined by the combined influence of the animal age, previous calving history, number of days calved and herd heat detection efficiency. The 2011 InCalf data was used to determine baseline performance (i.e. submission, conception) for individuals and model output was validated against this data.

Cows that are not pregnant at the end of the mating period are marked for culling at the end of the current lactation in the seasonal calving system. A proportion of non-pregnant cows may be moved from the spring to the autumn calving group (or vice-versa) if milk production and age characteristics of the animal support extended lactation. Cows may swap calving group once only and if they remain empty after a second mating period are marked for culling at the end of the current lactation.

[24] Reflective of the increase in the spread of calving occurring in the majority of Victorian herds

Mortality and culling events occur according to industry standard risk. For calves and cows, most mortality occurs in the month after calving. This reflects the high risk of these phases of life. These parameters were derived from the HiCo MISTRO database. Model output for mortality and culling was validated against this source.

Each animal has lifetime constants generated at introduction to the herd. These determine cow-level performance in production, reproduction, infection, response to vaccination (if administered), length of time at each stage of infection (if infected) etc. Pregnant animals generate a newborn calf (if carrying an AI heifer) and the newborn calf has the sire and dam recorded at simulated birth. This allows lines of cattle to be identified and traced.

Management events are coded to occur at certain times of the year (vaccination, blood testing, etc.), or when certain individual animal or herd criteria are attained (milk production and the number of days until calving for drying off, size of the shortfall of replacement heifers for purchasing of extra replacements). Most individual animal events are stochastic and appropriate probability distributions determine occurrence and fate. For example, a heat may be detected and subsequently may be served using AI or a bull if detected. A conception may ensue and the sex of the foetus is randomly assigned.

The derivation of calf milk for unweaned replacement calves was specifically modelled to mimic the potential exposure of unweaned calves to milk from BJD infected and Mptb shedding milking cows. Where possible, calf milk was obtained from lactating cows that were excluded from the factory supply vat for various reasons. The primary reason was the industry-required exclusion of fresh cows for the first eight milkings post calving. Cows with clinical mastitis were also used to provide calf milk as the milk from antibiotic-treated cows was withheld from factory supply. Where insufficient milk from naturally factory-excluded cows was available to meet calf demand, extra milk was taken from the vat. The average load of Mptb in the milk was determined from individual milk shedding rates and from teat contamination rates in infected and shedding cows. The daily requirement for calf milk and the average Mptb load in calf milk was calculated and updated on a daily basis. This determined the level of exposure in unweaned calves. For scenarios where calf milk replacer was used (or calf milk pasteurisation was undertaken), the calf milk Mptb load was set to zero each day. It should be noted that all calves obtained colostrum directly from suckling their dam so all replacement calves had at least one day of exposure to their dam's milk and teat Mptb contamination. Calves were assumed weaned at 42 days of age and were provided 6 litres of milk or milk replacer each day until weaning.

7.3 Simulating the Within-Herd Transmission of BJD

Disease parameters used by the simulation model are given in Table 34 (Appendix 1).

The following five transmission pathways were modelled:

- In-utero infection of the foetus by an infected dam;
- Infection of the new-born foetus through suckling the dam via contaminated teats;
- Infection of the new-born calf by suckling contaminated colostrum from the dam;
- Infection of unweaned calves following consumption of contaminated calf milk; and
- Faecal-oral transmission following grazing exposure to Mptb on contaminated pasture.

In-utero infection pathway: pregnant and infected dams pose a risk to the unborn calf. The baseline probability of infection for the foetus carried by early subclinical, late subclinical and clinical dams is described in Table 34 (no. 25). This provides average probabilities of in-utero infection of 0.09 for early subclinical and 0.39 for late subclinical and clinical cows respectively matching the direct foetal infection risks as described by Whittington and Windsor (2009) in their meta-analysis (page 25). It should be noted that the dam can also infect the newborn animal immediately after birth (before calf removal) via the contaminated teat or milk. This is an additional pathway and is described below. A single random binomial draw determines if the foetus is infected. If infected, the modality of infection and time of infection is recorded

Contaminated teat infection pathway: if a calf is born uninfected to an infected dam (i.e. it avoided becoming infected in-utero) it may become infected as a result of suckling Mptb-contaminated teats of the dam. The probability of infection from Mptb contaminated teats is assigned according to the teat excretion function described below. It is assumed the calf ingests all teat Mptb when consuming colostrum from the dam after birth. The total load of Mptb ingested by the calf on the day of birth is the sum of teat load and the (direct) colostrum Mptb burden. The Mptb load is used to determine the probability of new infection for the calf and a random binomial draw is used to determine the new-born calf fate.

Contaminated dam colostrum infection pathway: if the calf was not infected in-utero (but the dam is infected) there remains a risk of infection as a result of drinking contaminated colostrum. The contamination of colostrum is subtly different to the (additional) teat-based contamination of milk. Teat-based contamination is effectively transfer of gut derived Mptb to the teat surface and then into milk whereas direct colostrum and milk contamination reflects Mptb infection of the mammary lymph nodes and tissues whereby bacteria directly spill into the udder and into the milk. The effects of contamination of the teats and direct contamination of the milk are therefore additive.

The Mptb bacterial load of colostrum is described above (Table 34, item 25). The Mptb load in colostrum is used to determine the probability of new infection for the calf and a random binomial draw is used to determine the new-born calf fate.

Contaminated pooled calf milk infection pathway: calves are reared on either pooled milk or calf milk replacer until weaning (set at 42 days) but both the source of feed and the time of weaning can be changed by the user. Calf milk obtained from the herd is first sourced from lactating cows that cannot be included in the vat collection. These are fresh cows (the first eight milkings must be excluded from the vat) and also from clinical mastitis cows – clinical cases are withheld from the vat for seven days from onset in this model. The volume required to feed calves is calculated (it is assumed that 6L per calf per day is required) and the volume of supply determined. If the amount of milk supplied is insufficient the deficit is taken from the vat.

The daily Mptb excretion into milk of individual lactating cows is calculated using the lactation module (which determines daily individual volume – see Table 33, item 13) and the Mptb excretion function for infected animals (Table 33, item 28). This is determined by the infection stage of the animal and a draw from the Mptb milk excretion distribution for each

stage. The daily Mptb excretion of infected and lactating cows is described in detail on page 25 and the method for determining the Mptb load of pooled calf is described on page 111. There is an option to feed milk replacer, which sets the calf milk new infection probability back to zero. This can be used to isolate the effects of calf milk on herd infection maintenance pathways.

Faecal-oral contamination infection pathway: infected animals may shed Mptb into the environment. The amount of Mptb that is shed each day is determined by the infection stage of the animal and the size of the animal (juvenile versus adult). All of these parameter estimates were obtained from literature and are presented in Table 4 (page 32) and again in Table 34 (item 27). The Mptb contamination level at any given site is a function of the amount excreted that day by animals grazing or occupying the site, and the surviving bacteria in the historic load for the site. The existing load undergoes an exponential decay that is determined primarily by the season. The parameters for the decline and the impact of the chosen rate of decline on Mptb survival in the environment summarised in Table 34 (item 30). Loads are adjusted to a count per hectare to provide a measure of exposure density for grazing animals. This process moderates the frequency-based exposure level by the stocking density of the farm – an essential adjustment to more effectively model the impact of herd and farm size on disease transmission.

The level of exposure of individuals to environmental Mptb is determined by the level of contamination of the various sites on the farm and the grazing rotation that is in operation on the farm. The grazing rotation and grazing rules are set by the user and for each management group. Weaned calves, heifers, milking cows, dry cows and bulls are grazed in separate paddocks. The user has the option of following JDCAP rules. This determines which (dedicated) paddocks are used only for yearlings and rising-two-year-old heifers and which for adult stock. If the farm does not follow JDCAP rules, all paddocks are available for grazing by all classes of stock.

The Mptb load (density) of pasture is used to determine the probability of new infection in grazing and uninfected animals on the sire each day.

7.4 Simulating the Mitigation of BJD

Mitigations parameters used by the simulation model are given in Table 34 (Appendix 1).

Three-Step Calf Plan control: this control consists of: (a) removal of calves from dams before 12 hours after birth; (b) managing the calf rearing area to ensure calves have no contact with the effluent of susceptible species; and (c) rearing of calves to 12 months of age on pastures that have not carried adult stock or known BJD-infected stock during the past 12 months. The Three-Step Calf Plan control provides the following impact on the transmission pathways described above:

- In-utero risk pathway: unchanged; this control has no impact on direct transmission across the placenta from the dam to the calf.
- Colostrum (and contaminated teat) pathway: all calves are assumed to have drunk colostrum directly from their dam and therefore this control has no impact on this pathway.

- Calf milk pathway: there are no restrictions on the feeding of pooled milk from herd cows to the calves. Whilst feeding of milk replacer is recommended it is not compulsory. Most farmers do not feed calf milk replacer therefore no impact on this transmission pathway has been assumed.
- Faecal-oral pathway: the earlier removal of the calves from the calving paddock effectively reduces their exposure to environmental Mptb in the grazing sites. The control therefore halves the probability of faecal oral infection whilst occupying the calving paddock. The Three-Step Calf Plan control effectively isolates all young stock from the adult sites and therefore exposure of young stock to the faeces of shedding adults is prevented. It must be noted, however, that transient shedding in infected calves (either infected in-utero infection, by colostrum, contaminated dam teats, environmental exposure in the calving paddock, or from contaminated calf milk infected) can result in shedding into and environmental contamination of the young stock paddocks. This exposure risk is not prevented by this control for the young stock.

Test-and-cull control: the test-and-cull component represents the herd testing component of both TCP1 and the current program (TCP3). For TCP1 participating farms, all adults at or over 2 years of age are tested every February (annually) and for TCP3 participating farms, all adults at or over four years of age are tested every second February (to match program requirements and the common timing of testing in spring-calving herds). In both variants, positive animals (reactors) are immediately culled. The reactor's dam and any of her offspring are marked for immediate culling (if present in the herd). A requirement of TCP1 and TCP3 is that any clinical animal that is confirmed (noting that clinical animals may be lost or culled before diagnosis is confirmed) will also have their dam and any offspring marked for preferential culling. In the model, all preferential culls occur at the time of removal of the reactor or clinical. The ELISA test is used for identifying reactors. The sensitivity and specificity of the serum ELISA test is as described in Table 10. The test-and-cull component provides the following impact on the transmission pathways described above:

- In-utero risk pathway: unchanged. Whilst there is no direct effect the regular removal of sero-reactors from the herd will (theoretically) reduce the number of infected and pregnant animals that will calve down with an in-utero infected calf.
- Colostrum (and contaminated teat) pathway: also unchanged. Like above, the regular and early removal of sero-reactors will reduce the prevalence and level of Mptb shedding into milk (directly and via contaminated teats).
- Calf milk pathway: unchanged, as above.
- Faecal-oral pathway: unchanged – but the regular and early removal of sero-reactors will reduce the prevalence and level of Mptb shedding onto pasture. Whilst the Three-Step Calf Plan control effectively isolates all young stock from the adult sites, the test-and-cull component may also operate by reducing the incidence of infected calves (either directly or indirectly infected) and therefore the subsequent exposure of young stock to a contaminated environment.

Vaccination control: this assumes that all replacement calves are vaccinated with Silirum® at 21 days of age. The model ensures that immunity is not obtained until 15 days after

vaccination. The effectiveness of the Silirum® vaccine has not been fully elucidated from field studies. A proportion of vaccinates are assumed protected (where protection if it occurs is absolute). This is currently set to an arbitrary 75%. Non-responders to vaccination are at equal risk and suffer equivalent sequelae following infection as infected non-vaccinates. Vaccinates that respond have a relative reduction in risk of new infection (by all routes), of rate of Mptb shedding (if infected) and of duration or pre-clinical phases (if infected). The relative risk reductions were modelled as 60% (most likely), 25% (pessimistic) and 75% (optimistic). The extension in pre-clinical phase duration was modelled as 10% (most likely), 0% (pessimistic) and 25% (optimistic) increases in stage duration (Table 34).

The vaccination component provides the following impact on the transmission pathways described above:

- In-utero risk pathway: vaccinated (and responsive) pregnant cows have a reduced risk of in-utero transfer of infection to the calf – if infected and pregnant. If vaccination is effective it should reduce the number of infected and pregnant animals that will calve down with an in-utero infected calf. The unborn calf has the same susceptibility to infection following exposure as an unborn calf in non-vaccinated cows (i.e. no effect of the vaccine on the unborn calf).
- Colostrum (and contaminated teat) pathway: vaccinated (and responsive) calving cows have a reduced rate of excretion of Mptb (milk, teats and faeces) and therefore there is a reduction in risk of colostrum/teat transfer to the calf – if infected. The calf has the same susceptibility to infection following exposure to contaminated colostrum and calf milk as a calf born to an unvaccinated cow, as vaccination does not occur until the calf is three weeks of age and immunity is not attained in vaccine responders until 15 days after vaccination.
- Calf milk pathway: as per colostrum/teat pathway described directly above.
- Faecal-oral pathway: vaccinated (and responsive) cows have a reduced rate of excretion of Mptb in faeces and a prolongation of latent/subclinical phases. Therefore fewer infected and vaccinated cows will shed Mptb in their faeces and the rate of shedding of Mptb for an infected (and responsive) vaccinate will be less than for an infected non-vaccinate at the same stage of disease. Vaccinated calves that have had sufficient time to mount an immunological response and who mount an effective immunological response are at reduced risk of infection following exposure to environmental Mptb than for a non-vaccinate of the same age and level of exposure.

7.5 Model Outputs and Comparisons

The performance of each control scenario was assessed by determining the changes to the incidence and prevalence of BJD over time, and the impact upon the various transmission pathways (in-utero, colostrum and calf milk in calves and by faecal-oral spread in cattle at pasture). The economic impact of each control scenario was assessed using the economic template presented in Section 4.3. To ensure valid comparisons, and to represent uncertainty in parameter estimates, each scenario was repeated multiple times within a simulation run. Each repetition of a scenario used an identical herd structure (including

calving patterns, sizes, starting herds etc.). Output was examined to assess the effectiveness of the program in controlling disease and the economic impact on farm profitability.

The model was used to examine the passage and sequelae of bovine-strain Mptb in dairy herds. Beef herds and ovine-strain Mptb were not modelled, as there is insufficient information about the infectivity of the ovine strain for cattle, the sequelae following infection of cattle with the ovine strain and the ability of the ovine strain to sustain itself in cattle herds in the absence of co-grazing with infected sheep to support model development. These issues are discussed in Section 2.4.

8 SIMULATION OF CONTROL STRATEGIES FOR BJD IN VICTORIA

8.1 Model Scenarios

Ten start-up herds were generated for each herd size and calving pattern by running the model for 10 years and with 10% of the herd initially infected. No BJD controls were implemented. This provided a steady-state herd with representative herd age structure and with BJD distributed throughout the age classes at appropriate disease stages. The average prevalence of infection in the start-up herds remained around 10% after the 10-year burn-in. The model used typical herd management criteria to maintain herd size. All herds were closed (i.e. no replacements were purchased). This ensured that the effectiveness of the control program was not confounded by the purchase of pre-existing infection.

The dairy BJD model was used to examine eleven scenarios. These are described in detail below.

8.1.1 Baseline Scenario

The scenario had the following characteristics:

- No BJD control was undertaken.
- Calf rearing did not follow TCP rules. Calves were removed after 24 hours, placed into rearing pens and fed waste milk supplemented with milk from the vat. On weaning they were allowed to graze paddocks that had been grazed by adults. Yearlings and heifers shared paddocks in the grazing rotation with adults.
- No BJD ELISA testing of animals was undertaken.
- Clinical cases of BJD were culled when identified (clinically-affected), but preferential culling of contacts with a clinical case (dam and offspring) did not occur.

This scenario provided the baseline level of disease. Comparison against the various control programs gave insight into the overall effectiveness of the control programs. The baseline scenario allowed the economic losses that might be expected by infected farms that exert no control over BJD to be estimated, and a cost-benefit assessment of the individual control programs to be undertaken.

8.1.2 Test-and-Control Program 1 (TCP1) Scenario

This scenario was identical to the BJD baseline scenario, with the following exceptions:

- Calf rearing was undertaken according to the JDCAP/Three-Step Calf Plan rules. These include: (1) removal of calves from dams before 12 hours after birth; (2) managing of the calf rearing area to ensure calves have no contact with the effluent of susceptible species; and (3) rearing calves to 12 months of age on pastures that have not carried adult stock or known BJD-infected stock during the past 12 months.
- Each year all animals aged 2 years or older were submitted for individual ELISA testing. Positive reactors were culled immediately as was the reactor's dam and offspring.
- Clinical cases of BJD were culled when identified, along with their dam and offspring.

Analysis of output from this scenario was used to validate the model performance by assessing the predicted prevalence of reactors and clinical cases in TCP1 herds over time against actual field data.

8.1.3 Test-and-Control Program 3 (TCP3) Scenario

This scenario was identical to the TCP1 scenario (Section 8.1.2) but with the following exceptions:

- Animals aged 4 years and older only were submitted for individual ELISA testing every second year.

Analysis of output from this scenario provided a comparison between the performance of TCP3 and TCP1. This gave insight into the relative merit of TCP under its current guise.

8.1.4 Vaccination Scenario – Median Efficacy

This scenario used 'most likely' parameter settings for the efficacy of vaccination. These settings were considered to lie between pessimistic and optimistic settings used for the scenarios in Sections 8.1.5 and 8.1.6, respectively. A snapshot comparison of the three vaccination scenarios is provided in Table 27.

The scenario was identical to the BJD baseline scenario but with the following exceptions:

- Calves were vaccinated with Silirum® at 3 weeks of age. Immunity following vaccination was assumed to take 15 days to develop. Only a proportion of vaccinated (and uninfected) calves were assumed to respond to the vaccine – i.e. not all were protected. Only those animals that responded were (partially) protected, once sufficient time (15 days) had passed since vaccination for the development of a competent immune response. The proportion of vaccinated calves that responded to the vaccine was set at 75%. Infected vaccinated non-responders experienced the same sequelae following infection as non-vaccinates.
- Vaccinated responders became partially immune to infection, and had reduced rates of Mptb shedding if subsequently infected. The risk reduction for both of these components was set at 60%, this being the relative reduction in risk compared to non-vaccinated animals. Infected vaccinated responders were also coded to have a 10% increase in the duration of each phase of disease up to, but excluding, the clinical phase. The magnitude of risk reduction, and the extension of pre-clinical phases of disease in vaccinates, was based on estimates obtained from interim analysis of Zoetis Silirum® clinical vaccine trial data.
- Vaccinating herds continued to follow the Three-Step Calf Plan and keep calves separate from adults for the first years of life – especially as vaccination must occur a number of weeks after birth. Calves were fed milk from the vat (i.e. no milk replacer). Calf rearing was undertaken according to the JDCAP/Three-Step Calf Plan rules.

Analysis of output from this scenario provided an assessment of the likely performance of the Silirum® vaccine following field deployment in Victoria.

8.1.5 Vaccination Scenario – Pessimistic Efficacy

This scenario was identical to the vaccination scenario with median settings (Section 8.1.4) but with the following adjustment to vaccine response and efficacy performance:

- Vaccinated responders were assumed to be partially immune to infection and had reduced rates of Mptb shedding if they became infected. The risk reduction for both of these components was reduced to 25%, this being the relative reduction in risk compared to non-vaccinated animals.
- Infected vaccinated responders did not have any increase in the duration of any phase of disease. This included the clinical phase.

Analysis of output from this scenario (along with the optimistic scenario) provided insight into the sensitivity of outcome to vaccine performance.

8.1.6 Vaccination Scenario – Optimistic Efficacy

This scenario was identical to the vaccination scenario with median settings (Section 8.1.4) but with the following adjustment to response and efficacy performance:

- Vaccinated responders were assumed to be partially immune to infection and had reduced rates of Mptb shedding if they became infected. The risk reduction for both of these components was increased to 75%, this being the relative reduction in risk compared to non-vaccinated animals.
- Infected vaccinated responders had a 25% extension in the duration of each phase of disease up to, but excluding, the clinical phase (increased from 10% in the median scenario).

Analysis of output from this scenario provided insight into the sensitivity of outcome to vaccine performance.

Table 27: Parameters for vaccination scenarios

Parameter	Scenario		
	Median	Pessimistic	Optimistic
Age at vaccination	3 weeks	3 weeks	3 weeks
Time to development of immunity	15 days	15 days	15 days
Proportion of responders	75%	75%	75%
Reduction in risk of infection in responders	60%	25%	75%
Reduction in rate of shedding in responders	60%	25%	75%
Increase in duration of disease phases (except clinical) in responders	10%	0%	25%

8.1.7 Three-Step Calf Plan (BJD Biosecurity) with Vat Milk for Calves Scenario

This scenario was identical to the TCP1 scenario described above (Section 8.1.2) but with the following exceptions:

- No individual animal ELISA testing was undertaken, and therefore no preferential culling of (identified) subclinical cases occurred.
- Clinical cases of BJD were culled when identified, as were the preferential contacts of the clinical cases.

Analysis of the output from this scenario provided insight into the relative effectiveness of the main pillar of TCP – the hygienic rearing of calves and replacement stock.

8.1.8 Three-Step Calf Plan (BJD Biosecurity) with Milk Replacer for Calves Scenario

This scenario was identical to the Three-Step Calf Plan (BJD biosecurity) with vat milk for calves scenario (Section 8.1.7), but with the following exception:

- Calf milk replacer was fed to the calves instead of waste milk.

Analysis of the output from this scenario provided insight into the role of feeding contaminated waste milk to calves in the maintenance of disease within herds.

8.1.9 Three-Step Calf Plan (BJD Biosecurity) with Vaccination Scenario

This scenario was identical to the Three-Step Calf Plan (BJD biosecurity) with milk replacer for calves scenario (Section 8.1.8) but with the following exception:

- Calves were vaccinated with Silirum® at 3 weeks of age.
- Vaccine performance was the same as described in the vaccination scenario with median settings (Section 8.1.4).

Analysis of the output from this scenario provided insight into the relative effectiveness of combining vaccination with the main control arm of TCP – the use of milk replacer with hygienic rearing of calves and replacement stock.

8.1.10 Vaccination with TCP1 Scenario

This scenario was identical to the TCP1 scenario (Section 8.1.2) but with the following exceptions:

- Calves were vaccinated with Silirum® at 3 weeks of age. Vaccine performance was the same as described in the Vaccination scenario with median settings (Section 8.1.4).
- It was assumed that a test with an equivalent efficacy to the current ELISA test could be used. This might be an ELISA, as low rates of cross reactivity have been reported in vaccinates. Alternatively, it might be the high-throughput real-time PCR (HT-J PCR), as discussed in Section 2.2.3. This scenario was therefore considered to be hypothetical given current test limitations and existing bovine SDRGs.

This scenario was modelled to determine the impact of dual approaches to control of BJD that combined: (a) early identification and removal of infected individuals and high-risk contacts with; (b) the increased resistance of the population to infection by the use of vaccination. Analysis of the output from this scenario provided insight into the effectiveness of addition of vaccination to TCP1 for BJD.

It should be noted that this is at present a theoretical scenario. The ELISA is at present the only feasible test for individual animals and it is expected that ELISA testing of vaccinated

animals will result in an increase the number of false-positive results. This scenario would require use of a rapid and cost-effective PCR or culture-based test for individual animals to replace the ELISA test. Currently the only feasible way to combine individual animal ELISA testing with vaccination would be to terminate any ELISA test-and-cull component before the first vaccinated animals became eligible for testing.[25]

8.1.11 Vaccination with TCP3 Scenario

This scenario was identical to the vaccination with TCP1 scenario (Section 8.1.10) but with the following exception:

- Animals aged 4 years or older only were submitted for individual ELISA testing every second year.

This scenario was included to evaluate the impact of dual approaches to control of BJD that combined: (a) early identification and removal of infected individuals and high-risk contacts with; (b) the increased resistance of the population to infection by the use of vaccination. Analysis of the output from this scenario provided insight into the effectiveness of the addition of vaccination to TCP3 for BJD.

8.2 Herd Caving Pattern and Herd Size Scenarios

Two calving patterns were modelled.

- Seasonally calving herds, with a single calving period that is typically completed within 12 weeks.
- Split calving herds, with two calving periods. The majority of cows (60-70%) calved in the main calving period (lasting up to 12 weeks), with the remaining cows calving within a typically shorter (7-9 week) calving period that is timed to begin approximately 6 months before the start of the main calving period.

The majority of Victorian dairy herds are either split or seasonally calving. The key difference between the two systems is the number of calf rearing periods and, therefore, the typical calf stocking density. Seasonally-calving herds tend to batch-rear a greater number of calves than similar sized split calving herds, which will typically raise two smaller batches of calves.

Three herd sizes were simulated: (a) 180 milking cows; (b) 320 milking cows; and (c) 450 milking cows. These herds averaged approximately 40, 70 and 100 replacement calves each year, respectively. The impact of herd size on BJD would reflect the intensification and management of calf rearing. Larger calf drops require more cows to provide calf milk, thereby presenting a greater opportunity for the mass contamination of all calves. Larger calf drops are also more likely than smaller calf drops to contain an infected (and transiently shedding) individual in infected herds at a given BJD prevalence. Larger herds are therefore at consistently greater risk of having one or more Mptb shedders in the calf pen.

[25] See Appendix 2 where the effectiveness of staged (and terminating) ELISA test-and-cull with calf vaccination programs are evaluated

Using the above specifications, six calving pattern and herd size combinations were simulated for each test scenario to allow the combined effect of calving pattern and herd size on control scenario performance to be examined.

8.3 Model Results

The aggregated performance (across all calving patterns and herd sizes) for each scenario is summarised below.

- The key disease parameters are presented in Table 28.
- The distributions of within-herd BJD prevalence across time for each control scenario (with line of best fit) are presented in Figure 13.
- The distributions of within-herd BJD shedder prevalence across time for each control scenario (with line of best fit) are presented in Figure 15.
- The distributions of within-herd BJD clinical prevalence (annual adult incidence) across time for each control scenario (with line of best fit) are presented in Figure 16 and in combination with the within-herd prevalence of infection in Figure 16.
- The distributions of incidence rates for infection pathways across time for each control scenario are presented in Figure 17.

Table 28: Model output at 5 years and 10 years after initiation of control scenario

Scenario	Parameter	Year 5		Year 10	
		Mean (range)	Median (IQR)[26]	Mean (range)	Median (IQR)
Baseline	Avg. no. infected	41.89 (0.00-151.00)	27.00 (11.00-68.25)	34.21 (0.00-155.00)	15.50 (3.00-58.50)
	No. new infections	13.03 (0.00-57.00)	7.00 (3.00-21.00)	11.80 (0.00-62.00)	5.00 (1.00-21.25)
	No clinicals (year)	5.47 (0.00-29.00)	3.00 (1.00-8.00)	6.83 (0.00-37.00)	3.00 (1.00-11.00)
	Avg. no. shedders	34.76 (0.00-127.67)	22.50 (9.71-56.25)	27.68 (0.00-125.67)	12.63 (3.17-46.27)
	Prevalence (%)	9.70 (0.00-21.97)	9.46 (4.99-13.95)	8.78 (0.00-24.95)	7.39 (2.04-15.07)
	Incidence (%)	2.92 (0.00-9.09)	2.69 (1.11-4.55)	2.96 (0.00-10.55)	2.21 (0.37-5.35)
	Clinical incid. (adults - %)	1.80 (0.00-5.65)	1.70 (0.91-2.70)	2.56 (0.00-9.41)	2.09 (0.64-4.12)
	Shedder prev. (%)	8.07 (0.00-18.35)	8.00 (4.22-11.60)	7.14 (0.00-20.14)	6.05 (1.87-12.19)
Three-Step Calf Plan (vat milk)	Avg. no. infected	41.33 (0.00-148.00)	26.00 (11.00-70.00)	32.98 (0.00-161.00)	17.00 (3.00-58.25)
	No. new infections	12.52 (0.00-62.00)	7.00 (2.75-21.00)	11.11 (0.00-50.00)	5.00 (1.00-20.00)
	No clinicals (year)	5.31 (0.00-32.00)	3.00 (1.00-8.00)	6.36 (0.00-34.00)	3.00 (0.00-11.00)
	Avg. no. shedders	34.43 (0.00-119.42)	21.58 (9.69-58.63)	26.77 (0.00-131.42)	14.38 (2.98-48.60)
	Prevalence (%)	9.64 (0.00-23.11)	9.42 (4.99-14.12)	8.65 (0.00-26.77)	7.32 (1.89-14.37)
	Incidence (%)	2.81 (0.00-8.30)	2.64 (1.05-4.51)	2.85 (0.00-10.55)	1.98 (0.36-5.02)
	Clinical incid. (adults - %)	1.75 (0.00-5.65)	1.64 (0.86-2.55)	2.43 (0.00-9.14)	2.13 (0.00-4.00)
	Shedder prev. (%)	8.07 (0.00-19.61)	7.96 (4.16-11.83)	7.06 (0.00-21.49)	6.10 (1.59-11.71)

[26] Inter-quartile range

Scenario	Parameter	Year 5		Year 10	
		Mean (range)	Median (IQR)[26]	Mean (range)	Median (IQR)
Three-Step Calf Plan (milk replacer)	Avg. no. infected	39.30 (0.00-163.00)	24.00 (10.75-67.25)	31.57 (0.00-148.00)	11.00 (3.00-53.25)
	No. new infections	12.10 (0.00-59.00)	7.00 (3.00-20.00)	10.69 (0.00-56.00)	4.00 (0.00-18.00)
	No clinicals (year)	5.07 (0.00-28.00)	3.00 (1.00-7.00)	5.96 (0.00-33.00)	3.00 (1.00-10.00)
	Avg. no. shedders	32.80 (0.00-136.42)	19.67 (8.92-57.17)	25.61 (0.00-120.08)	9.79 (2.81-41.92)
	Prevalence (%)	8.99 (0.00-21.15)	7.89 (4.24-13.65)	8.04 (0.00-24.41)	5.81 (1.88-13.79)
	Incidence (%)	2.69 (0.00-9.51)	2.39 (0.96-4.11)	2.68 (0.00-10.15)	2.22 (0.00-4.73)
	Clinical incid. (adults - %)	1.65 (0.00-5.34)	1.58 (0.79-2.42)	2.19 (0.00-8.86)	1.74 (0.46-3.56)
	Shedder prev. (%)	7.52 (0.00-17.67)	6.66 (3.83-11.27)	6.56 (0.00-20.71)	4.66 (1.65-11.19)
Three-Step Calf Plan (vaccination)	Avg. no. infected	29.48 (0.00-128.00)	18.00 (8.00-47.25)	16.04 (0.00-85.00)	6.00 (1.00-27.00)
	No. new infections	6.98 (0.00-34.00)	3.00 (1.00-11.25)	4.43 (0.00-32.00)	1.00 (0.00-7.00)
	No clinicals (year)	3.94 (0.00-20.00)	3.00 (1.00-5.25)	3.06 (0.00-19.00)	1.00 (0.00-5.00)
	Avg. no. shedders	25.06 (0.00-109.92)	15.58 (6.90-40.08)	13.05 (0.00-68.08)	5.17 (1.00-21.19)
	Prevalence (%)	6.73 (0.00-20.36)	6.17 (3.29-9.63)	3.80 (0.00-14.38)	2.99 (0.56-6.34)
	Incidence (%)	1.50 (0.00-5.84)	1.26 (0.56-2.38)	1.01 (0.00-4.79)	0.56 (0.00-1.74)
	Clinical incid. (adults - %)	1.29 (0.00-4.76)	1.21 (0.58-1.87)	1.06 (0.00-5.98)	0.74 (0.00-1.83)
	Shedder prev. (%)	5.78 (0.00-19.05)	5.39 (2.90-8.34)	3.10 (0.00-11.86)	2.42 (0.49-5.26)
TCP1	Avg. no. infected	14.70 (0.00-60.00)	9.00 (4.00-23.00)	6.03 (0.00-34.00)	2.00 (0.00-10.00)
	No. new infections	4.07 (0.00-23.00)	2.00 (0.00-6.00)	2.07 (0.00-18.00)	0.00 (0.00-3.00)
	No clinicals (year)	0.99 (0.00-8.00)	1.00 (0.00-1.00)	0.72 (0.00-9.00)	0.00 (0.00-1.00)
	Avg. no. shedders	12.24 (0.00-51.00)	7.42 (3.42-18.40)	4.68 (0.00-26.67)	1.50 (0.00-8.27)

Scenario	Parameter	Year 5		Year 10	
		Mean (range)	Median (IQR)[26]	Mean (range)	Median (IQR)
	Prevalence (%)	3.87 (0.00-10.99)	3.48 (1.83-5.95)	1.65 (0.00-7.50)	1.02 (0.00-2.96)
	Incidence (%)	1.01 (0.00-4.07)	0.82 (0.00-1.56)	0.57 (0.00-4.68)	0.00 (0.00-0.91)
	Clinical incid. (adults - %)	0.39 (0.00-2.64)	0.27 (0.00-0.63)	0.29 (0.00-2.47)	0.00 (0.00-0.56)
	Shedder prev. (%)	3.23 (0.00-8.63)	2.93 (1.61-4.91)	1.29 (0.00-5.67)	0.78 (0.00-2.25)
TCP3	Avg. no. infected	23.54 (0.00-93.00)	14.00 (7.00-40.00)	15.39 (0.00-73.00)	5.50 (1.00-25.00)
	No. new infections	6.53 (0.00-36.00)	4.00 (1.00-11.00)	5.76 (0.00-35.00)	2.00 (0.00-9.00)
	No clinicals (year)	2.09 (0.00-16.00)	1.00 (0.00-3.00)	2.85 (0.00-20.00)	1.00 (0.00-4.25)
	Avg. no. shedders	19.19 (0.00-74.92)	11.42 (5.98-33.56)	12.53 (0.00-58.25)	4.96 (1.00-19.88)
	Prevalence (%)	5.87 (0.00-13.95)	5.38 (2.76-8.70)	4.06 (0.00-15.09)	2.72 (0.77-7.11)
	Incidence (%)	1.55 (0.00-5.47)	1.27 (0.41-2.54)	1.47 (0.00-5.93)	0.92 (0.00-2.64)
	Clinical incid. (adults - %)	0.73 (0.00-3.34)	0.62 (0.00-1.16)	1.09 (0.00-4.76)	0.82 (0.00-1.82)
	Shedder prev. (%)	4.80 (0.00-11.74)	4.55 (2.39-7.06)	3.33 (0.00-12.32)	2.37 (0.62-5.70)
Vaccination	Avg. no. infected	31.13 (0.00-117.00)	19.00 (8.00-52.00)	17.43 (0.00-86.00)	6.50 (1.00-30.00)
	No. new infections	7.93 (0.00-37.00)	4.00 (1.00-13.25)	4.92 (0.00-30.00)	1.00 (0.00-8.00)
	No clinicals (year)	4.03 (0.00-19.00)	3.00 (1.00-6.00)	3.43 (0.00-20.00)	2.00 (0.00-6.00)
	Avg. no. shedders	26.38 (0.17-106.92)	16.04 (6.73-43.94)	14.32 (0.00-74.58)	5.58 (1.06-24.31)
	Prevalence (%)	7.19 (0.00-16.03)	6.50 (3.60-10.86)	4.22 (0.00-14.66)	2.90 (0.80-7.73)
	Incidence (%)	1.76 (0.00-5.44)	1.54 (0.65-2.81)	1.17 (0.00-5.39)	0.76 (0.00-2.10)
	Clinical incid. (adults - %)	1.33 (0.00-5.26)	1.21 (0.59-2.00)	1.22 (0.00-5.26)	0.94 (0.00-2.09)
	Shedder prev. (%)	6.12 (0.15-14.85)	5.52 (3.11-9.12)	3.48 (0.00-12.22)	2.57 (0.71-6.25)

Scenario	Parameter	Year 5		Year 10	
		Mean (range)	Median (IQR)[26]	Mean (range)	Median (IQR)
Vaccination (optimistic)	Avg. no. infected	28.35 (0.00-121.00)	16.50 (7.75-47.25)	14.21 (0.00-74.00)	5.00 (1.00-26.25)
	No. new infections	6.52 (0.00-33.00)	3.50 (1.00-12.00)	3.46 (0.00-20.00)	1.00 (0.00-6.00)
	No clinicals (year)	3.50 (0.00-18.00)	2.00 (1.00-5.00)	2.55 (0.00-15.00)	1.00 (0.00-5.00)
	Avg. no. shedders	24.14 (0.00-100.50)	13.92 (6.42-40.46)	11.85 (0.00-65.75)	4.33 (1.00-21.79)
	Prevalence (%)	6.53 (0.00-18.01)	6.09 (3.16-9.63)	3.44 (0.00-14.88)	2.35 (0.55-5.99)
	Incidence (%)	1.41 (0.00-5.47)	1.31 (0.33-2.15)	0.81 (0.00-5.00)	0.45 (0.00-1.41)
	Clinical incid. (adults - %)	1.16 (0.00-5.15)	1.06 (0.50-1.73)	0.89 (0.00-4.14)	0.63 (0.00-1.48)
	Shedder prev. (%)	5.62 (0.00-15.39)	5.18 (2.73-8.29)	2.87 (0.00-12.17)	2.08 (0.46-5.10)
Vaccination (pessimistic)	Avg. no. infected	36.86 (0.00-143.00)	21.50 (10.00-61.25)	26.86 (0.00-150.00)	11.00 (3.00-47.00)
	No. new infections	11.04 (0.00-55.00)	6.00 (2.00-18.25)	8.70 (0.00-55.00)	3.00 (0.00-14.25)
	No clinicals (year)	4.89 (0.00-23.00)	3.00 (1.00-8.00)	5.35 (0.00-29.00)	3.00 (0.00-9.00)
	Avg. no. shedders	31.02 (0.25-117.00)	18.29 (8.42-51.52)	21.79 (0.00-121.58)	9.00 (2.31-36.58)
	Prevalence (%)	8.50 (0.00-21.79)	7.49 (4.28-12.58)	6.77 (0.00-21.80)	5.32 (1.61-11.35)
	Incidence (%)	2.47 (0.00-9.77)	2.31 (0.85-3.88)	2.12 (0.00-8.36)	1.66 (0.00-3.75)
	Clinical incid. (adults - %)	1.62 (0.00-5.63)	1.50 (0.74-2.42)	1.96 (0.00-8.16)	1.60 (0.00-3.30)
	Shedder prev. (%)	7.20 (0.14-18.74)	6.40 (3.65-10.55)	5.51 (0.00-17.67)	4.20 (1.29-8.97)
Vaccination (TCP1)	Avg. no. infected	10.37 (0.00-40.00)	6.00 (3.00-16.00)	2.09 (0.00-17.00)	0.00 (0.00-3.00)
	No. new infections	2.25 (0.00-17.00)	1.00 (0.00-3.00)	0.50 (0.00-9.00)	0.00 (0.00-0.00)
	No clinicals (year)	0.59 (0.00-4.00)	0.00 (0.00-1.00)	0.27 (0.00-4.00)	0.00 (0.00-0.00)
	Avg. no. shedders	8.88 (0.00-34.83)	5.50 (2.40-14.00)	1.69 (0.00-14.50)	0.17 (0.00-2.75)

Scenario	Parameter	Year 5		Year 10	
		Mean (range)	Median (IQR)[26]	Mean (range)	Median (IQR)
	Prevalence (%)	2.73 (0.00-7.95)	2.54 (1.17-4.00)	0.55 (0.00-4.72)	0.00 (0.00-0.95)
	Incidence (%)	0.55 (0.00-3.97)	0.40 (0.00-0.86)	0.13 (0.00-2.34)	0.00 (0.00-0.00)
	Clinical incid. (adults - %)	0.21 (0.00-1.30)	0.00 (0.00-0.43)	0.09 (0.00-1.18)	0.00 (0.00-0.00)
	Shedder prev. (%)	2.35 (0.00-6.33)	2.25 (1.01-3.46)	0.45 (0.00-3.30)	0.07 (0.00-0.78)
Vaccination (TCP3)	Avg. no. infected	16.95 (0.00-80.00)	10.00 (4.00-27.00)	6.14 (0.00-40.00)	2.00 (0.00-10.00)
	No. new infections	3.60 (0.00-21.00)	2.00 (0.00-5.25)	1.77 (0.00-14.00)	0.00 (0.00-3.00)
	No clinicals (year)	1.56 (0.00-10.00)	1.00 (0.00-2.00)	1.13 (0.00-11.00)	0.00 (0.00-2.00)
	Avg. no. shedders	14.26 (0.00-63.67)	8.96 (3.90-22.35)	5.17 (0.00-33.33)	2.04 (0.00-8.19)
	Prevalence (%)	4.19 (0.00-11.46)	3.83 (2.06-6.18)	1.56 (0.00-7.09)	1.02 (0.00-2.48)
	Incidence (%)	0.84 (0.00-3.96)	0.69 (0.00-1.40)	0.43 (0.00-3.76)	0.00 (0.00-0.72)
	Clinical incid. (adults - %)	0.58 (0.00-4.07)	0.51 (0.00-0.95)	0.42 (0.00-3.32)	0.00 (0.00-0.70)
	Shedder prev. (%)	3.56 (0.00-9.74)	3.19 (1.73-5.14)	1.32 (0.00-6.09)	0.92 (0.00-2.10)

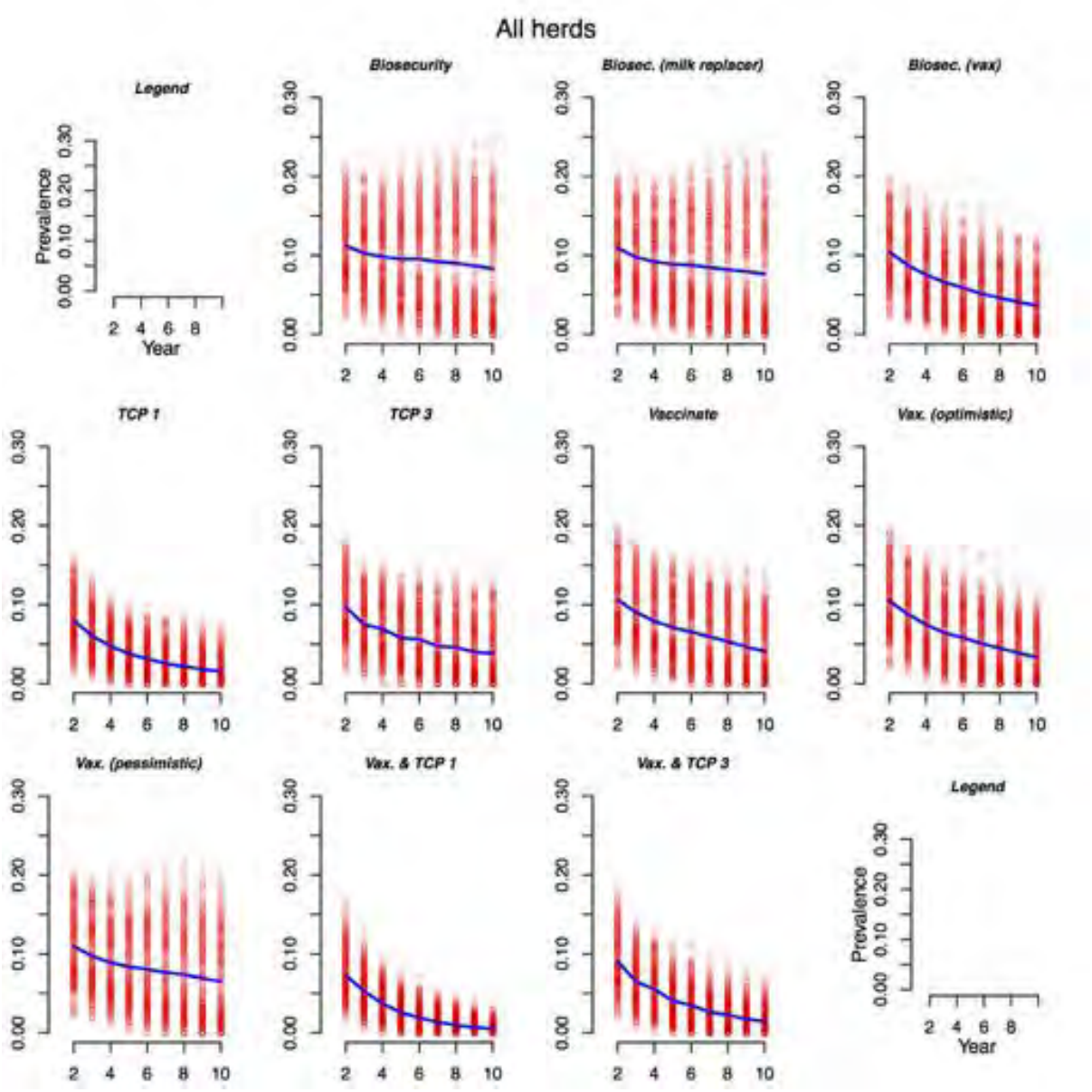


Figure 13: BJD prevalence (all animals) and trend line by time since initiation of control scenario

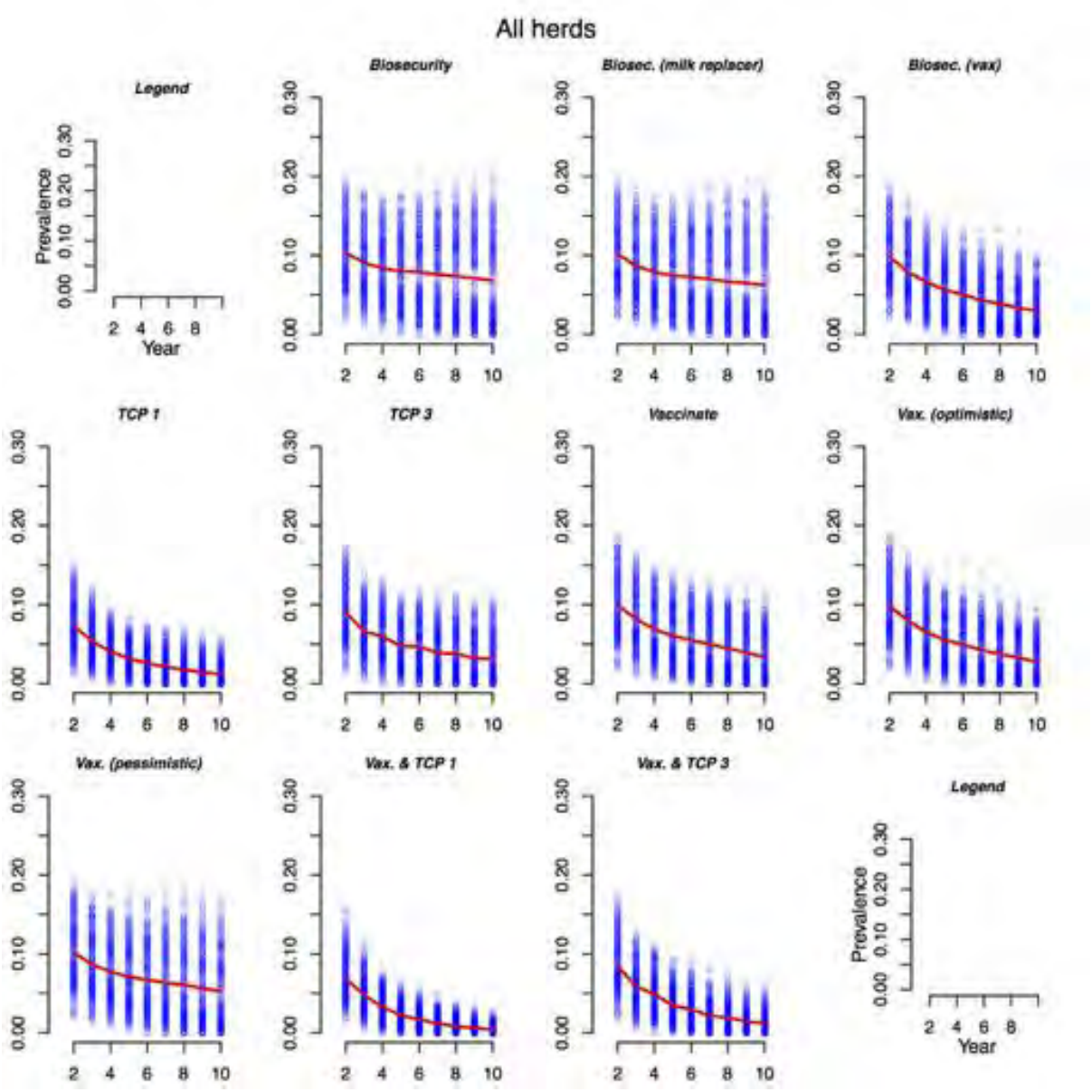


Figure 14: BJD shedder prevalence (all animals) and trend line by time since initiation of control scenario

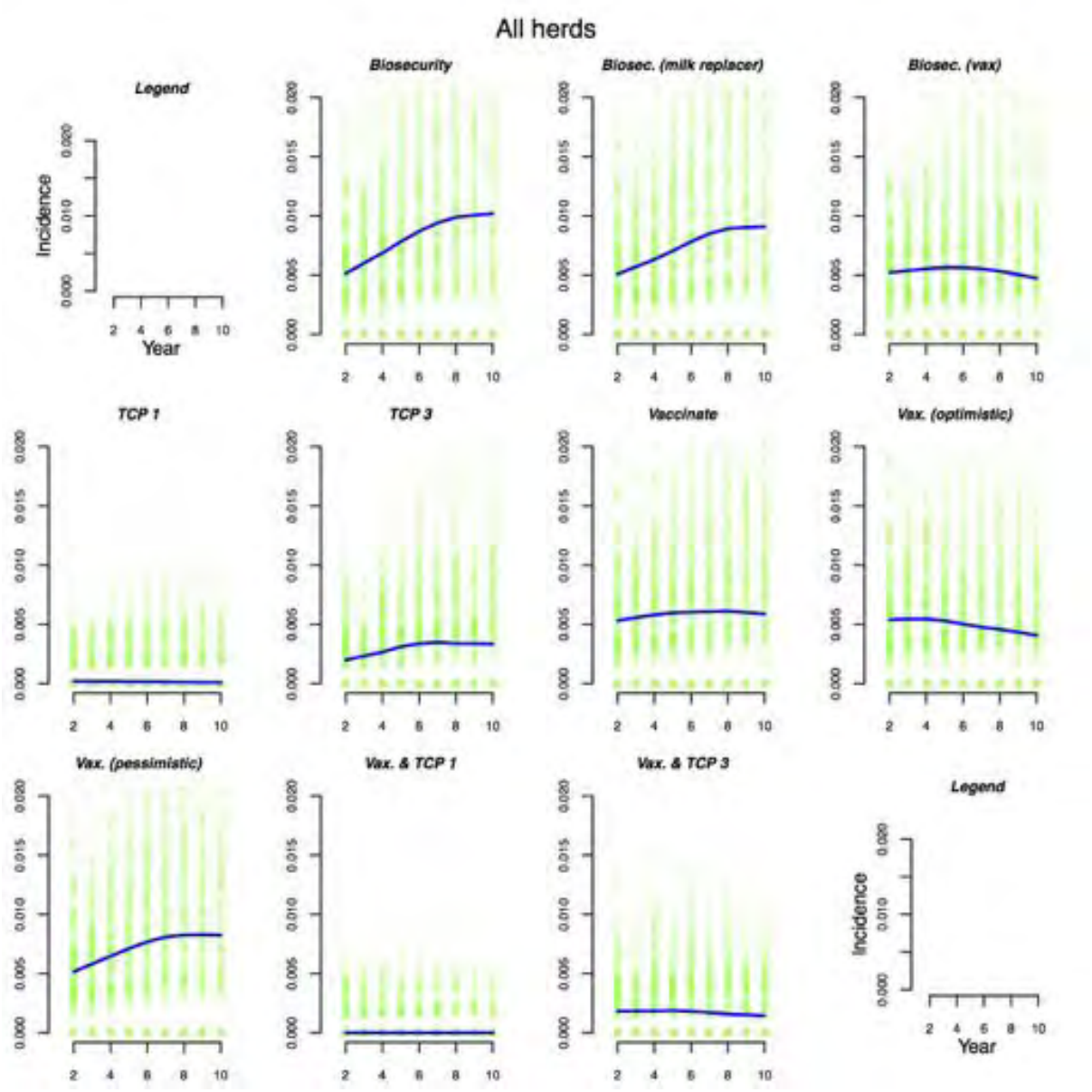


Figure 15: BJD annual clinical incidence (adult herd) and trend line by time since initiation of control scenario

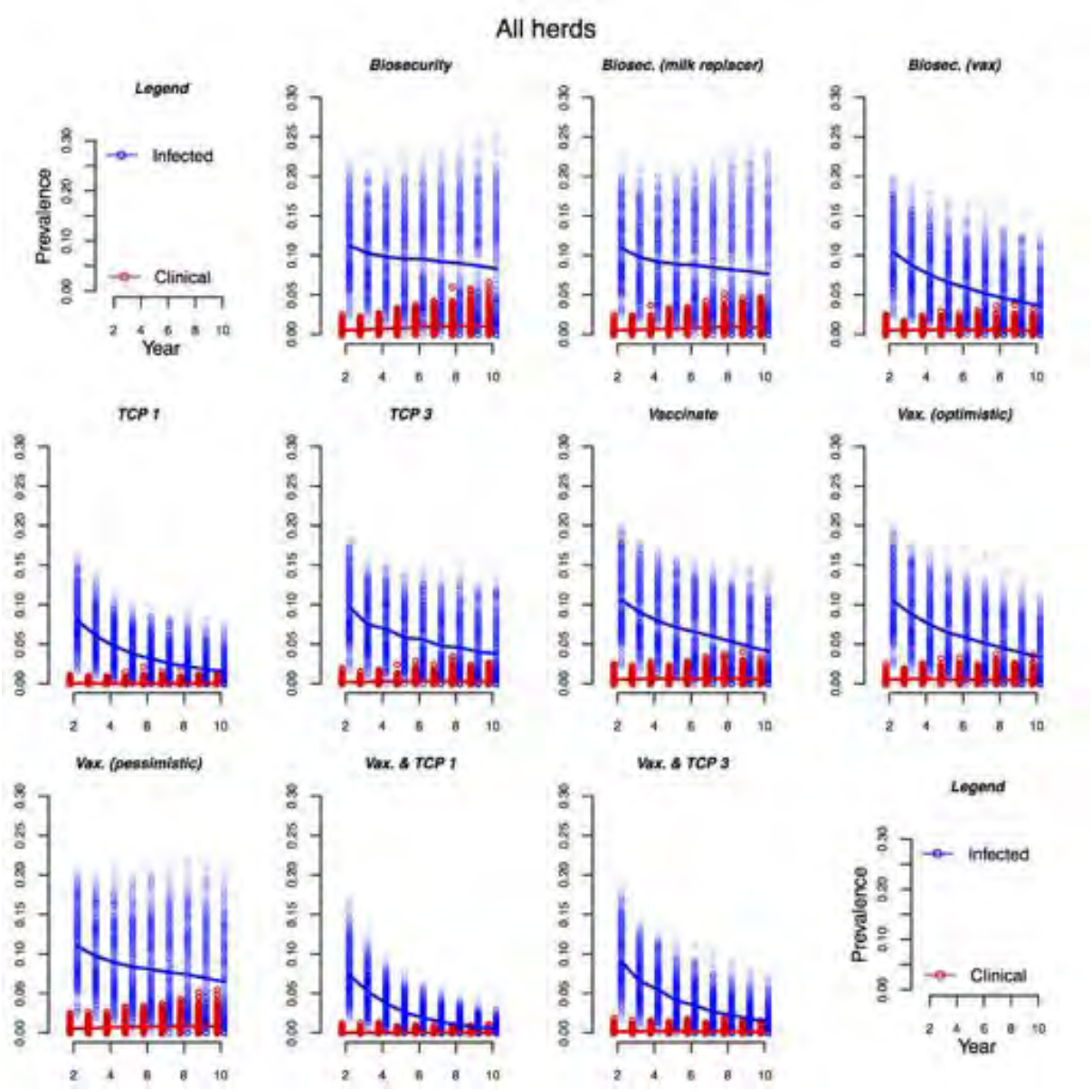


Figure 16: BJD herd prevalence (all animals) and annual clinical incidence (adult herd) and trend lines by time since initiation of control scenario

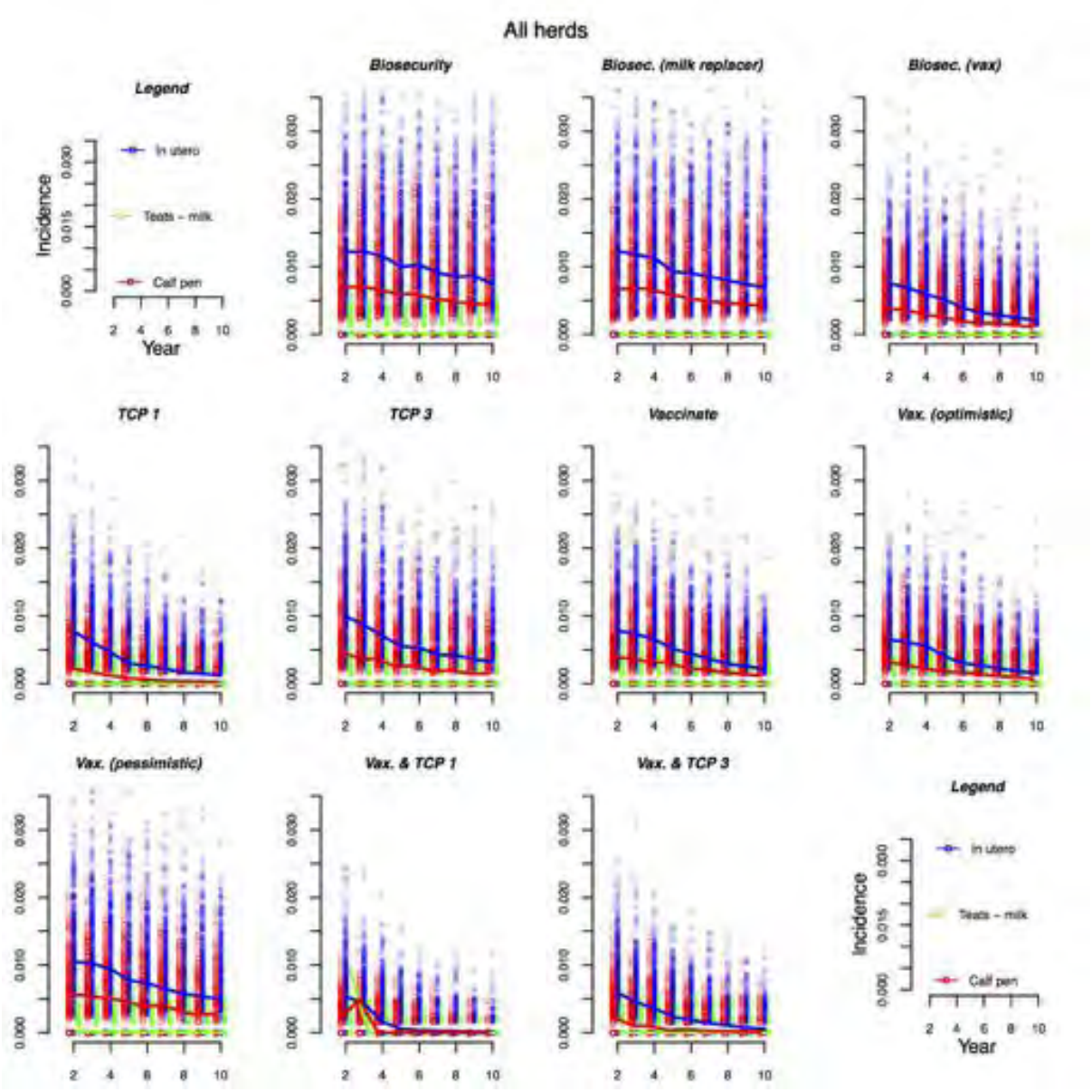


Figure 17: Annual incidence rate of new infections with trend line by infection modality by time since initiation of control scenario

8.3.1 Results from the Simulations

8.3.1.1 Summary of Main Observations

The TCP-based programs (TCP1 and TCP3) provided for the most rapid decline in within-herd prevalence and the incidence of disease. This is because these programs are based on a test-and-cull practice that identifies and removes a proportion of the infected and high-risk contact animals. This was also the only practical way of controlling the in-utero transmission cycle. Other control programs did not actively remove infection from the herd and therefore provided for a slower decline in prevalence and new infections (especially via

the in-utero route), as infected animals only leave the herd due to clinical disease or natural causes. This approach provided no practical control over the in-utero transmission pathway.

The change from TCP1 to TCP3 (moving from testing 2-year-old and older animals every year in TCP1 to testing 4-year-old and older animals every second year in TCP3) resulted in significantly reduced performance of TCP. On average, the TCP1 scenario provided for a lower prevalence, lower shedder prevalence and lower incidence of clinical disease than the TCP3 scenario. There was also a smaller range of these parameters across participating herds for TCP1 compared with TCP3 – TCP1 offered a more predictable and reliable reduction in disease than TCP3. It appeared that the restricted and delayed testing resulted in retention of infected animals in the herd for longer, and this reduced effective control of environmental contamination.

BJD-specific biosecurity controls (Three-Step Calf Plan with vat milk for calves, and Three-Step Calf Plan with milk replacer for calves) when initiated alone and without a test-and-cull or vaccination component provided only a modest reduction in the level of disease. The long-term prevalence of disease, prevalence of shedders and incidence of clinical cases was only slightly lower than the initial levels. Statistics for Year 5 and Year 10 are given in Table 28. The feeding of milk replacer instead of waste milk from cows did not provide for a marked reduction in disease levels. Examination of the source of infection from these scenarios indicated that the role of calf milk was minor when compared to faecal-oral transmission (non-milk) and the in-utero route of infection. Contaminated calf milk was more important in larger herds and in seasonally calving herds, where calf drops are larger, calves are more concentrated and calf milk was provided by more cows than for other farming systems. However, the magnitude of reduction in disease level in large seasonally calving herds comparing the basic Three-Step Calf Plan with Three-Step Calf Plan plus calf milk replacer was not great (approximately 0.5% reduction in prevalence).

Vaccination provided for a similar long-term (10-year) level of control of disease as the current program (TCP3). TCP1 offered better 10-year control of BJD than vaccination under the assumptions given in Section 8.1.4. The relative performance of vaccination compared to TCP3 appeared to be consistent across all calving patterns and all herd size combinations. It should be noted, however, that the trend line for the vaccination scenarios continued to be directed downwards at the 10-year time point, whereas the TCP3 trend line was more stable at 10 years (Figure 13 to Figure 17). TCP's test-and-cull component actively removed disease from the herd whereas the vaccination program required natural attrition or clinical disease to remove disease and provided no preferential culling of high-risk individuals. The level of disease in vaccinating herds may therefore require more than 10 years to reach a steady state. This result implies that over longer time horizons than have been modelled here (i.e. greater than 10 years) vaccination may well provide for a greater reduction in the level of BJD in infected herds when compared to TCP3. It should also be noted that effective vaccination will only provide for a gradual and incremental improvement in disease control each year of use, and that decades of annual use may be necessary to stabilise disease within a herd.

An important finding was that the impact of vaccination on disease levels was only moderately sensitive to assumptions about vaccine performance. The pessimistic scenario

appeared to be less effective than TCP3 – but this gap is likely to reduce beyond 10 years as the compounding effects of vaccination continue to accrue. The optimistic scenario provided a modestly improved performance.

Combination scenarios offer a range of synergies. Combining a test-and-cull component (TCP1 and TCP3) with vaccination provided for rapid, sustained and consistent reduction in disease levels in farms. When vaccination was combined with TCP3, disease declined markedly, but remained patent in the majority of farms after 10 years of simulation. When vaccination was combined with TCP1, however, the majority of participating farms successfully graduated from the combined program within 10 years. This was a key result for the analysis. Practically, the TCP component will need to be staged and terminated before the first crop of vaccinated animals become eligible for ELISA testing because of the likely interference by vaccination with the ELISA test. Currently the HT-J-PCR test is not an acceptable individual animal test under the current SDRGs and faecal culture is expensive and too slow to provide a practical alternative to the ELISA test. The combination of number of years of TCP test-and-cull component with sometimes delayed onset of calf vaccination was specifically examined in Appendix 2.

8.3.2 Calving Pattern and Herd Size Effects

When all calving patterns were considered, there were no clear and consistent herd size effects (Figure 18 and Figure 19). The disease appeared to be more prevalent in seasonally-calving than split calving herds (Figure 20 and Figure 23). There may be an interaction between herd size and calving pattern, with large seasonally-calving herds experiencing higher levels of disease than smaller split-calving herds (Figure 22 and Figure 23). The performance of the various control scenarios appeared to be consistent across the different herd size and calving pattern combinations.

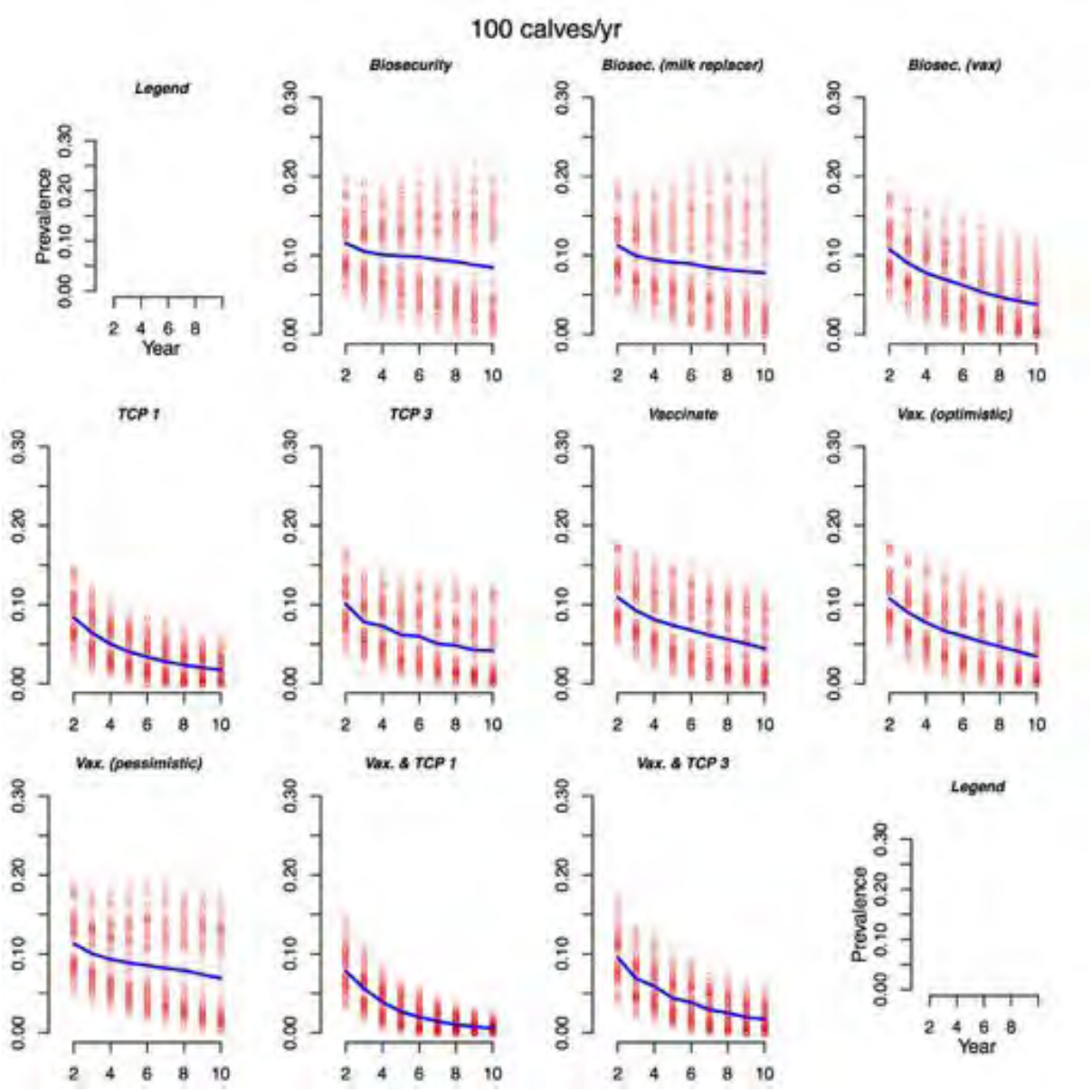


Figure 18: Distribution of BJD prevalence (all animals) and trend line by time since initiation of control scenario for large herds (averaging 100 replacement calves per year)

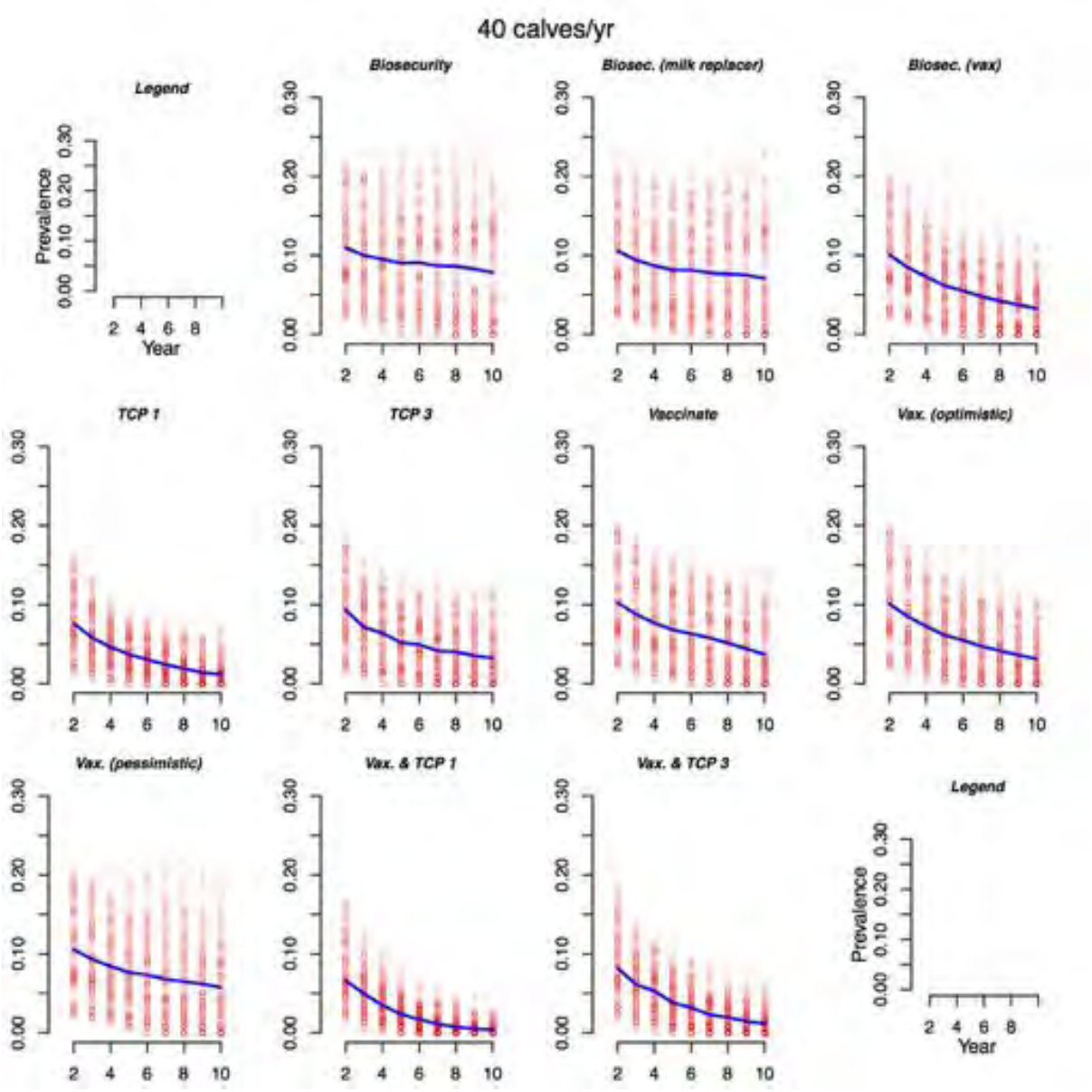


Figure 19: Distribution of BJD prevalence (all animals) and trend line by time since initiation of control scenario for small herds (averaging 40 replacement calves per year)

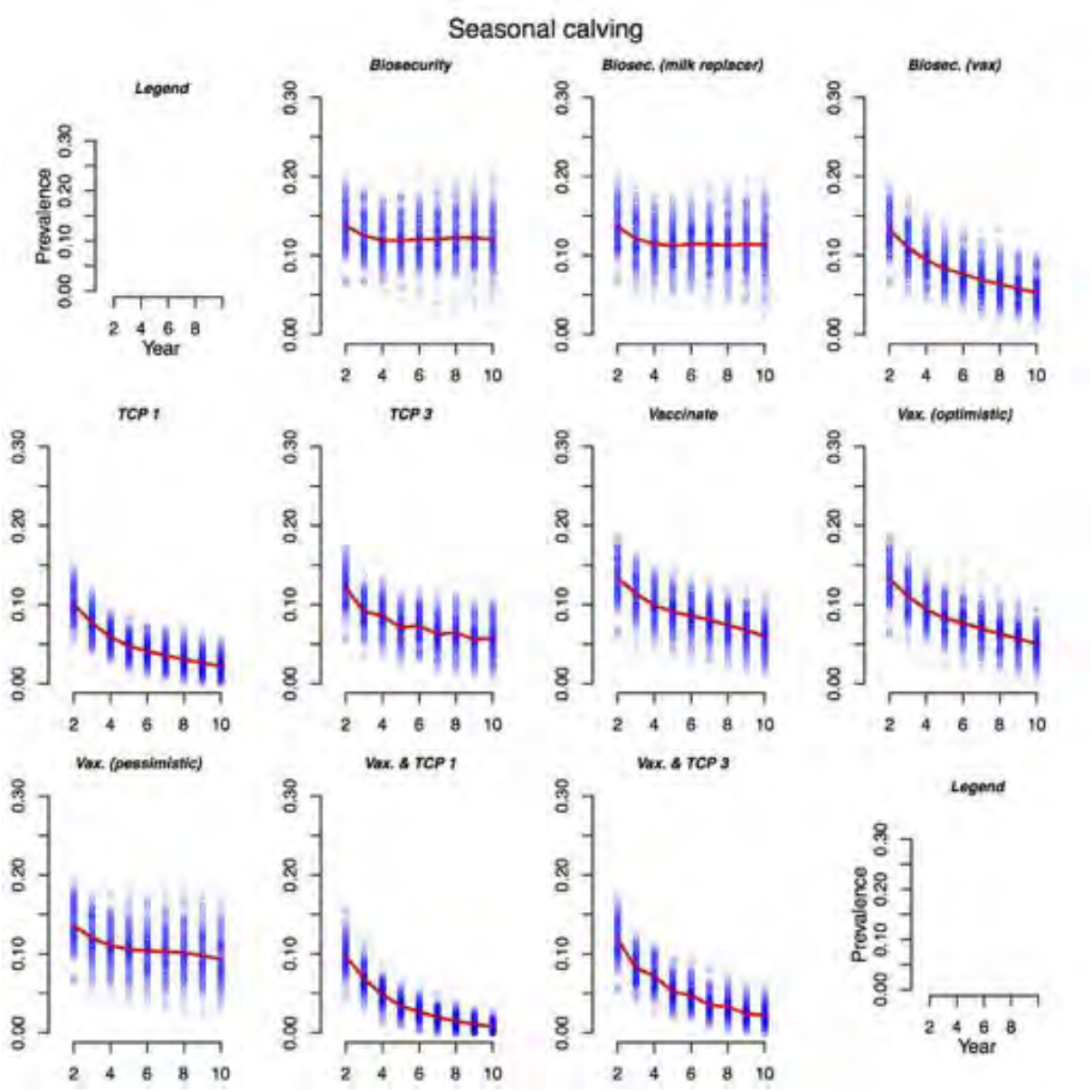


Figure 20: BJD shedder prevalence (all animals) and trend line by time since initiation of control scenario for seasonally calving herds

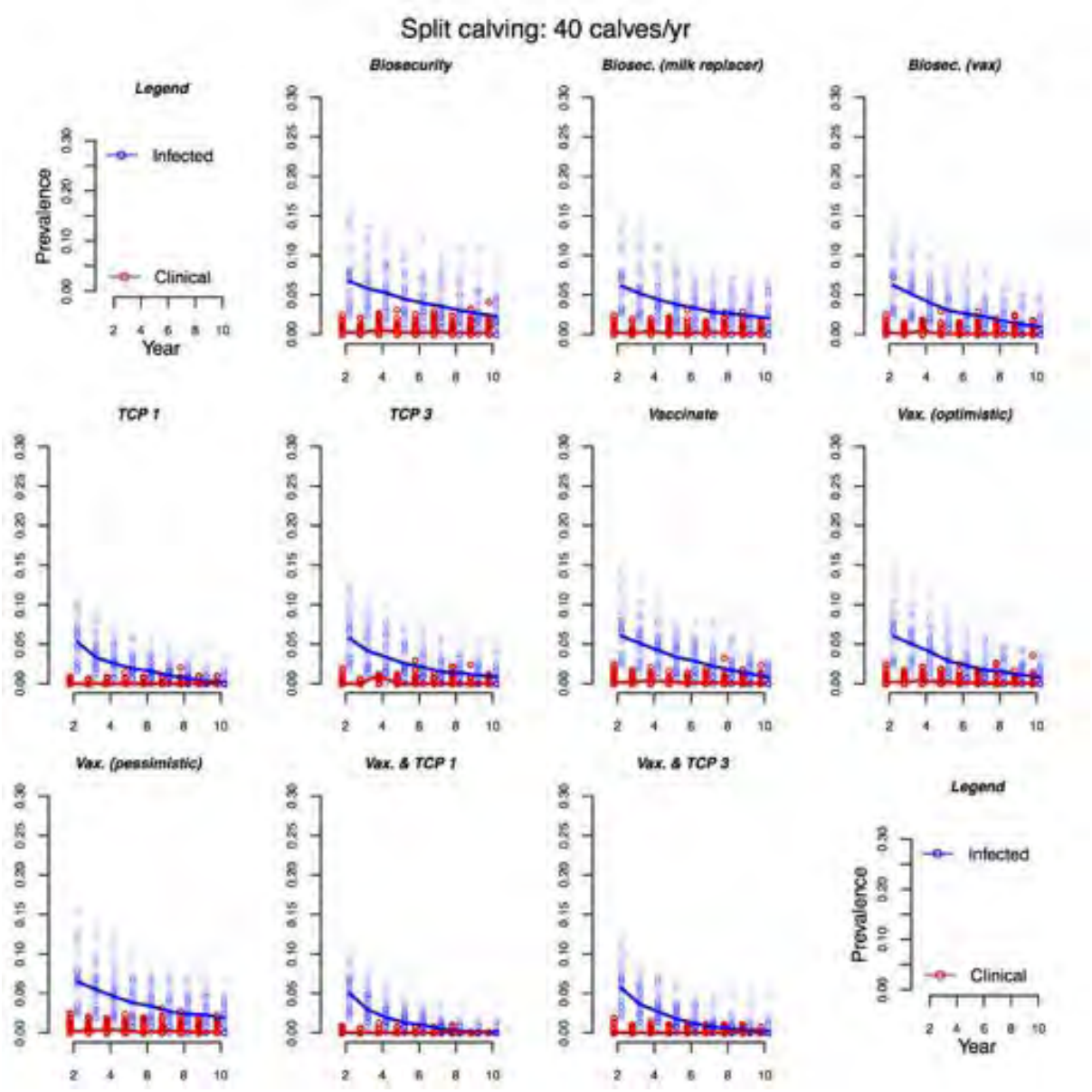


Figure 21: BJD herd prevalence (all animals) and annual clinical incidence (adult herd) and trend lines by time since initiation of control scenario for small split-calving herds

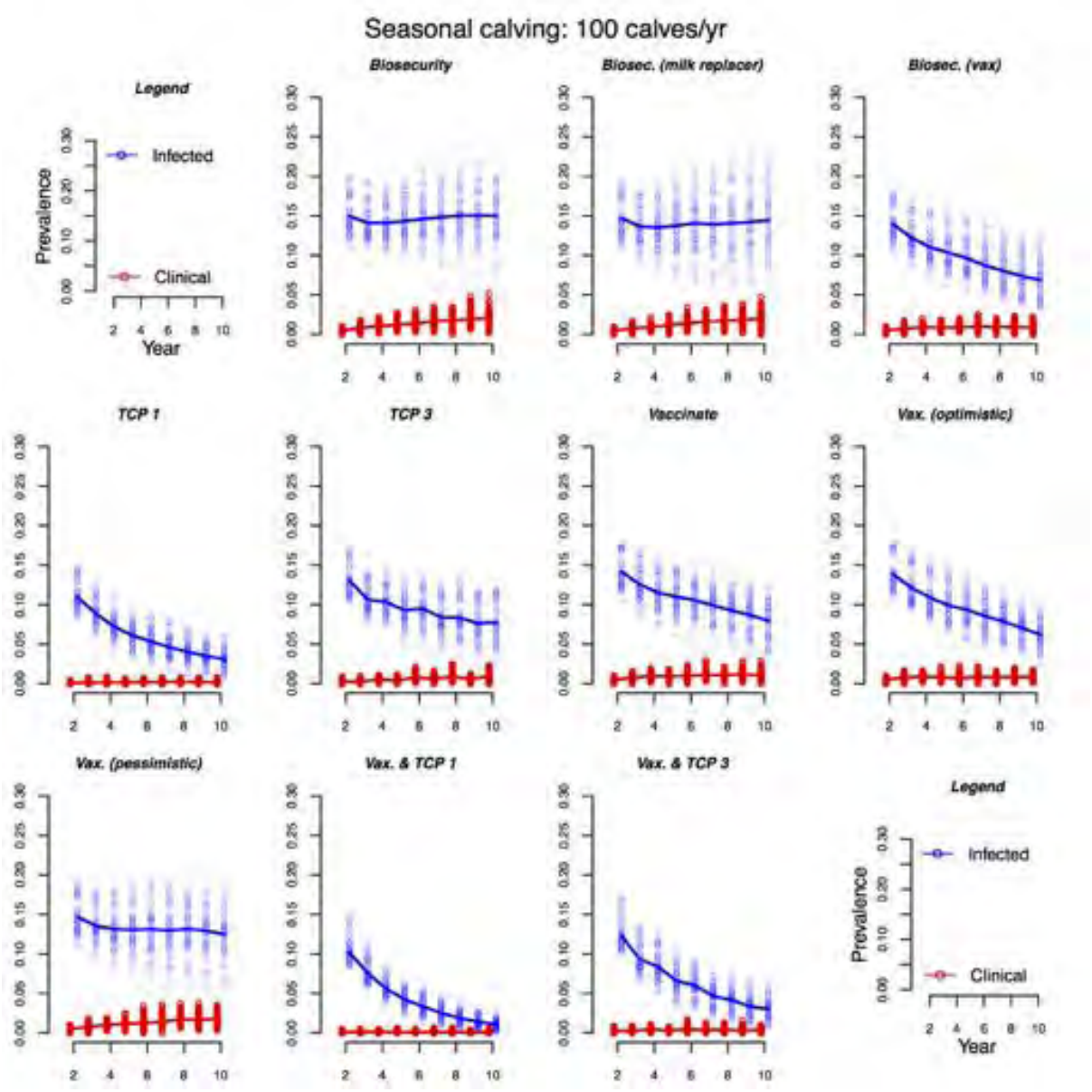


Figure 22: BJD herd prevalence (all animals) and annual clinical incidence (adult herd) and trend lines by time since initiation of control scenario for large seasonally-calving herds

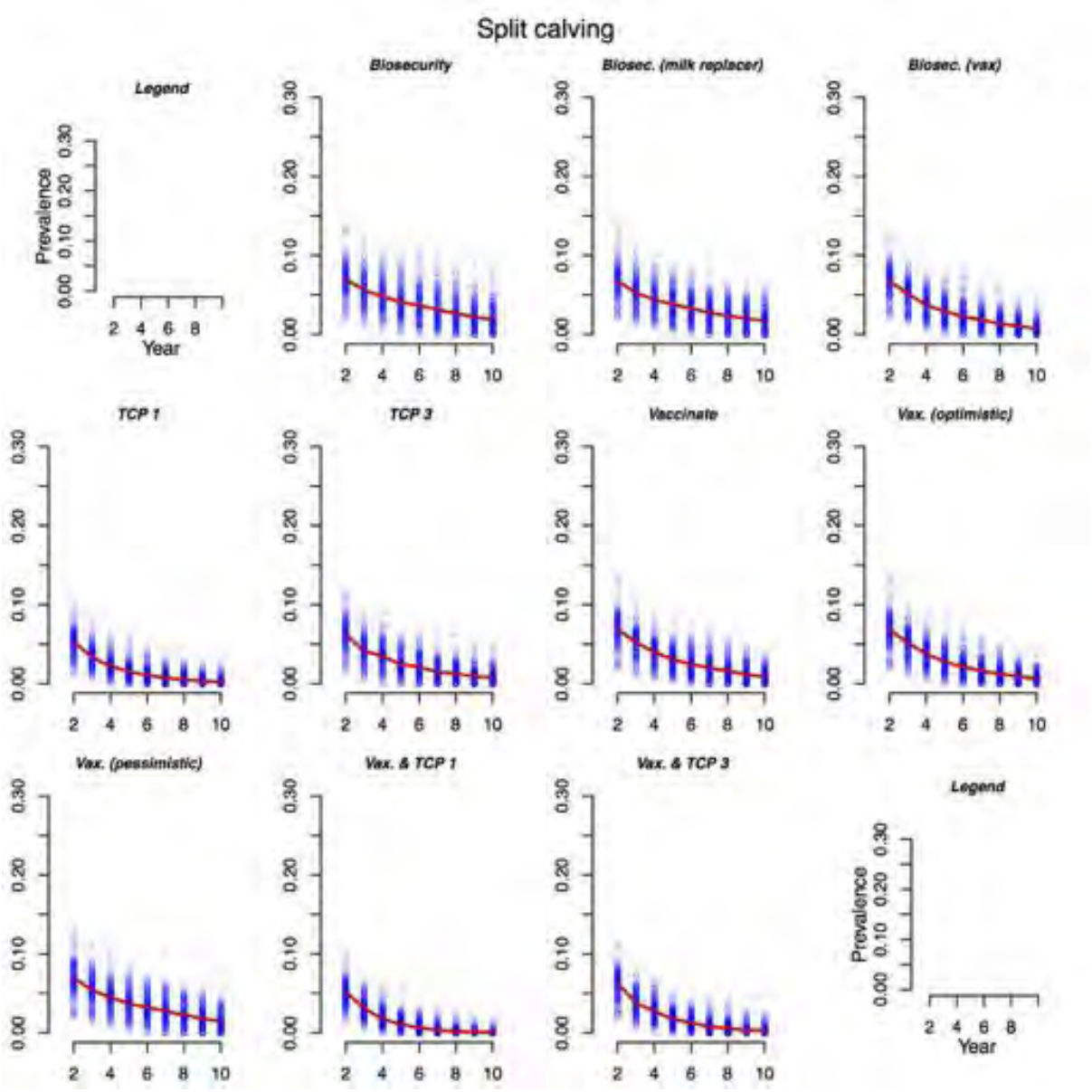


Figure 23: BJD shedder prevalence (all animals) and trend line by time since initiation of control scenario for split calving herds

The relative importance of the faecal-oral route in young stock was greater for seasonal than for split-calving herds. This is presented in Figure 24 (seasonally calving), Figure 25 (split calving), Figure 26 (large seasonally calving) and Figure 27 (small split calving)[27]. This result suggested that the role of transient shedding by infected young stock was an important mechanism for disease maintenance in dairy herds. The faecal-oral transmission from calf-to-calf becomes increasingly important as the number of calves increases. This is achieved by increasing herd size or by concentrating the calving period. The result has implications for the Three-Step Calf Plan. The likelihood of one or more transient shedders

[27] Calf pen includes unweaned calf areas and young stock paddocks (up to 12 months of age)

being present increased as the number of calves carried together increased. This reduced the effectiveness of the separation of young stock from adults, and was likely to be contributing to the persistence of disease in herds despite the long-term implementation of hygienic calf rearing practices.

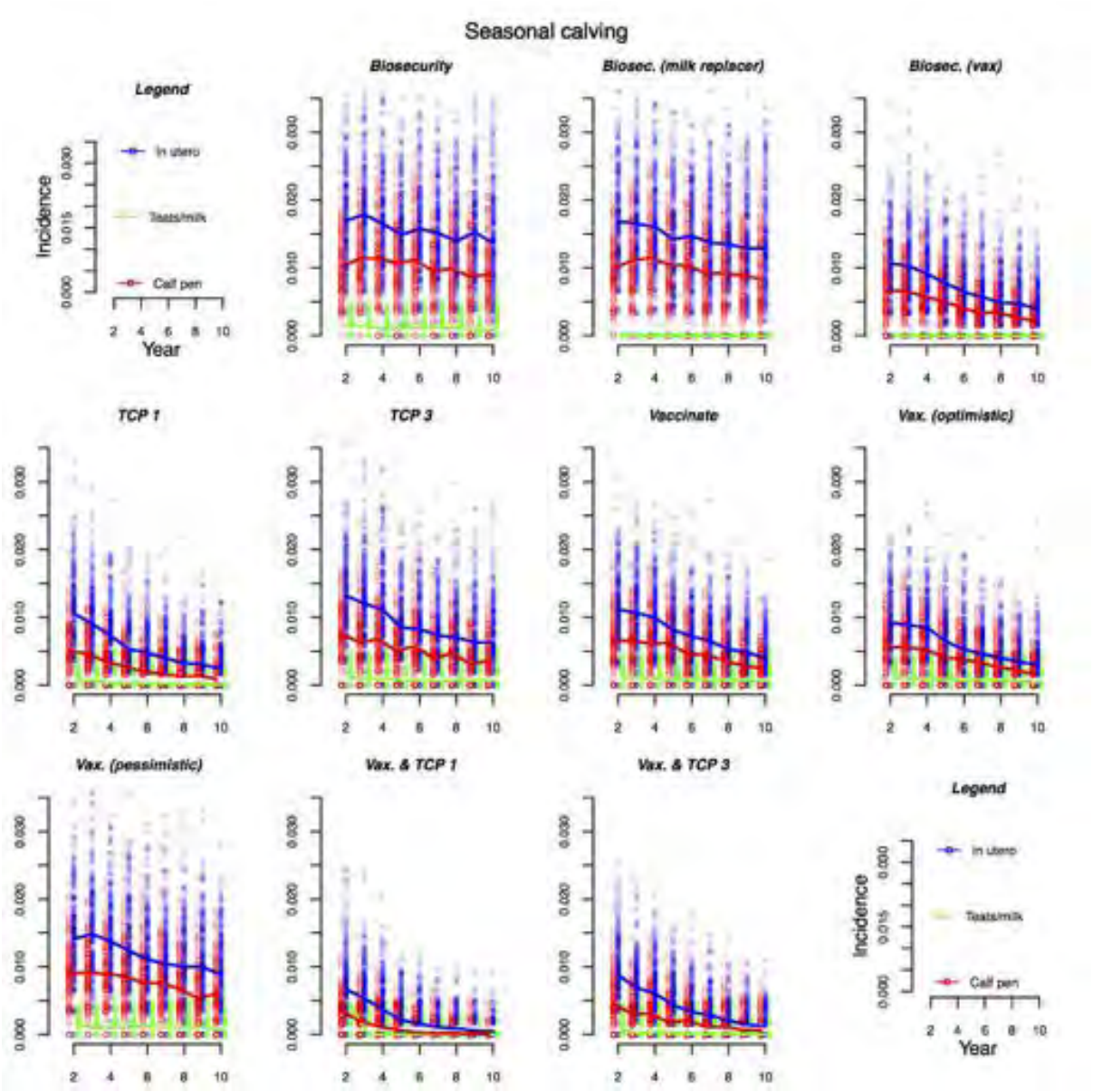


Figure 24: Annual incidence rate of new infections with trend line by infection modality by time since initiation of control scenario for seasonally calving herds

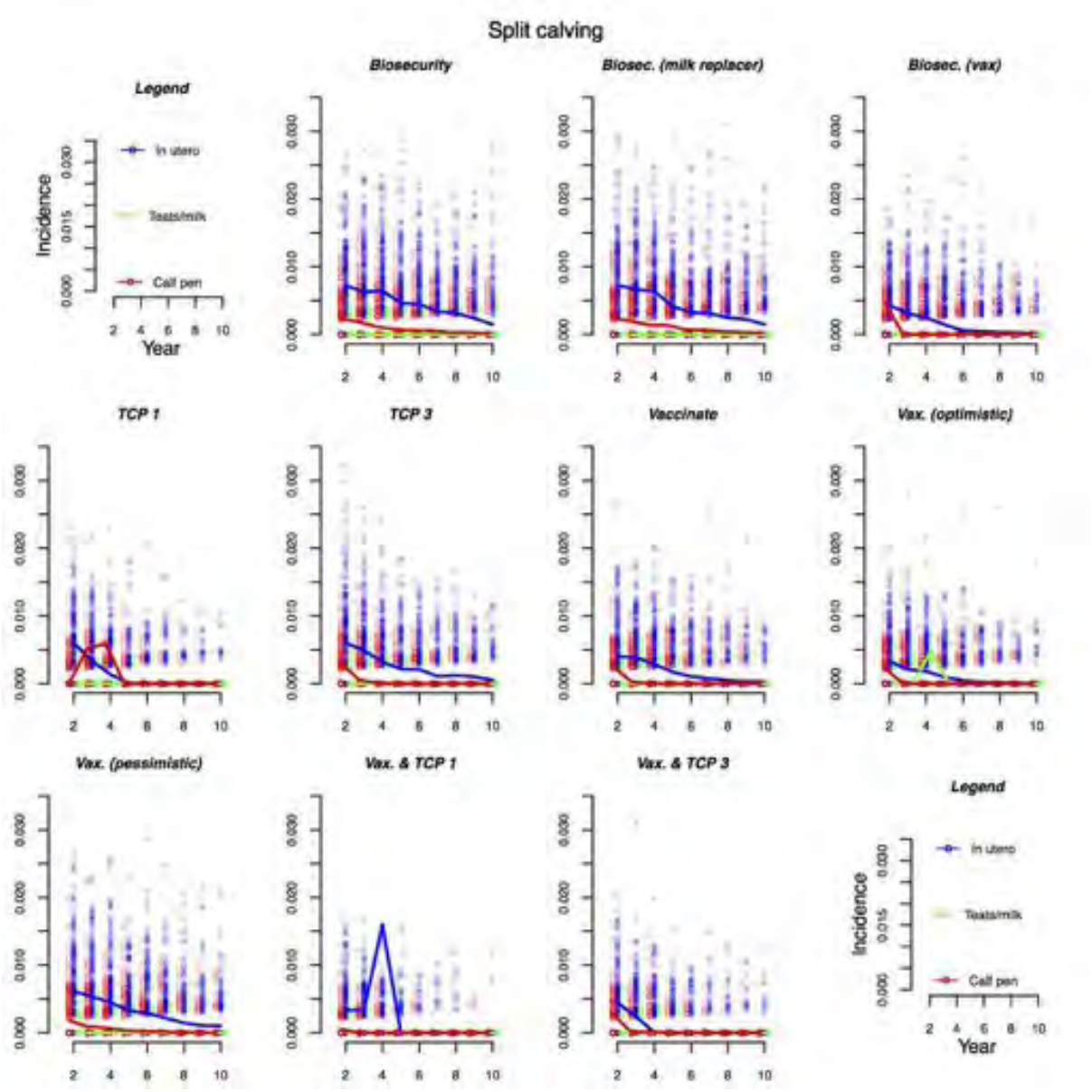


Figure 25: Annual incidence rate of new infections with trend line by infection modality by time since initiation of control scenario for split calving herds

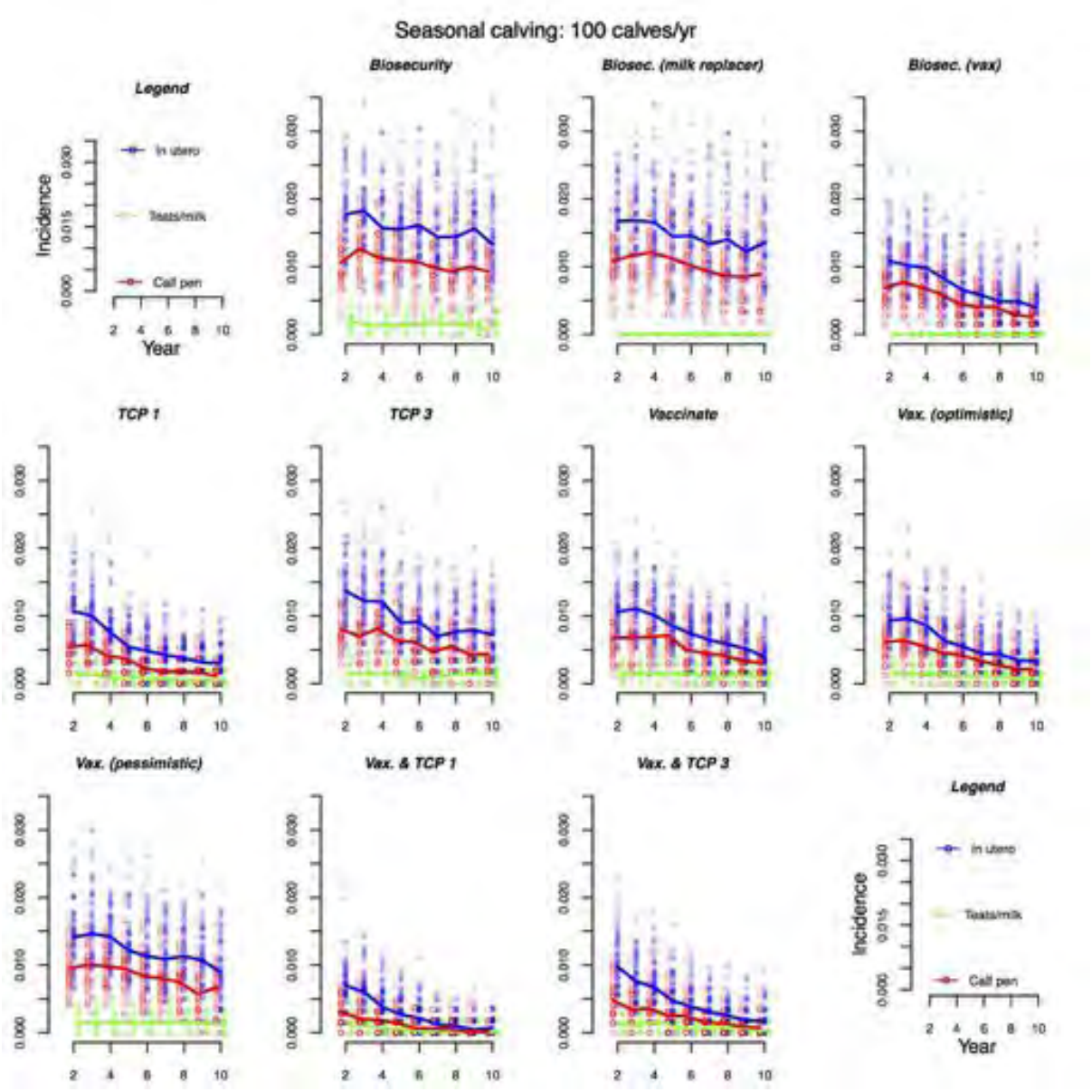


Figure 26: Annual incidence rate of new infections with trend line by infection modality by time since initiation of control scenario for large seasonally calving herds

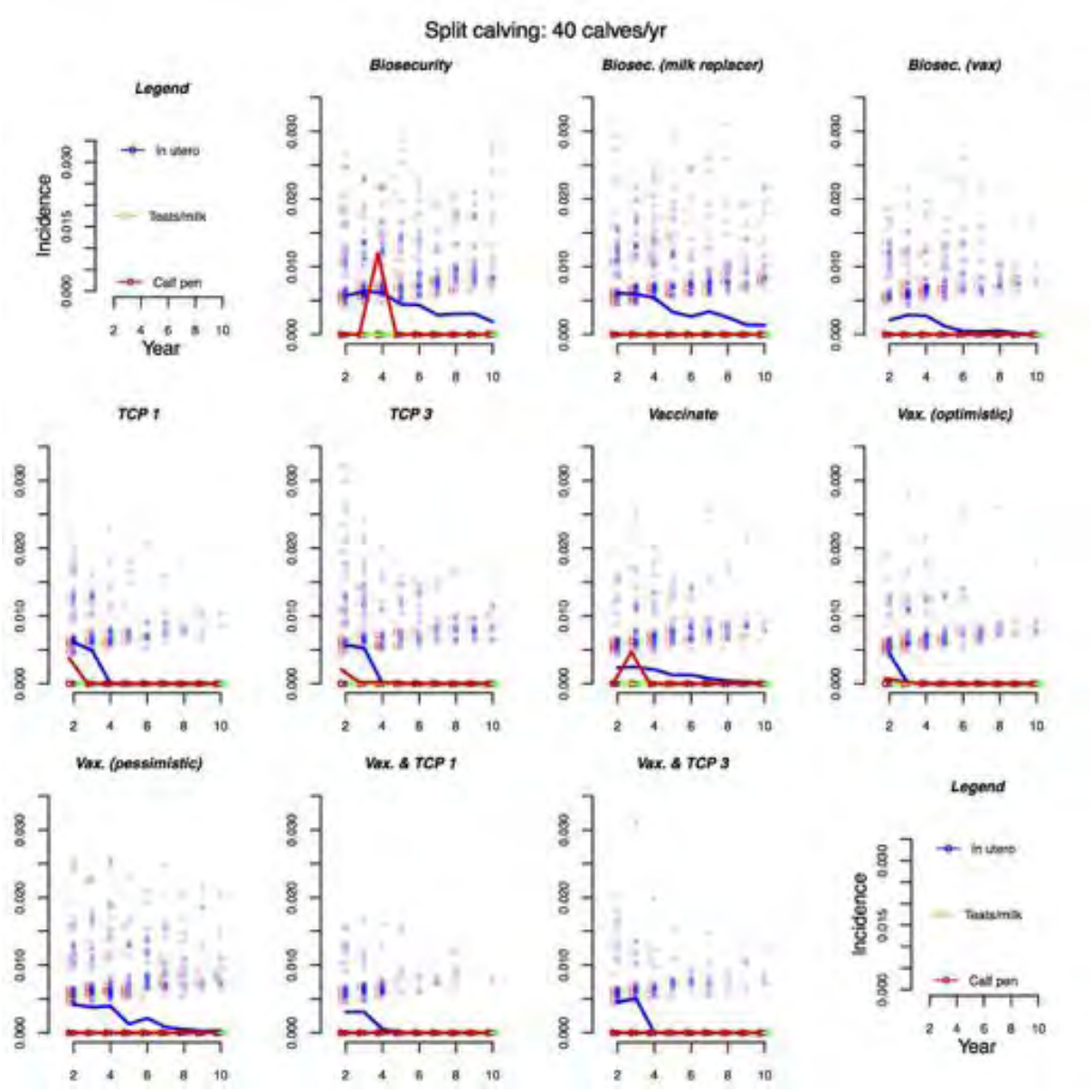


Figure 27: Annual incidence rate of new infections with trend line by infection modality by time since initiation of control scenario for small split calving herds

8.4 Economics for the Simulated BJD Control Scenarios

8.4.1 Farm-Level Economics

The template described in Section 4.3 was used to examine the economic impact of the various control scenarios at the farm level. For each scenario, the prevalence and clinical disease incidence at the 10-year time point was used to represent the scenario for the steady state. It should be noted that for some scenarios (including vaccination) the prevalence had not stabilised after 10 years and was still in decline. This is for a herd with an average of 250 milking cows.

The baseline prevalence of disease in uncontrolled herds was set at 8.8% of animals and the clinical case rate in adults was set at 2.6%. For all scenarios that involved test-and-cull, the reactor rate was set at twice the clinical case rate. The cost of a reactor cull was assumed to the same as the cost of a clinical case. TCP data indicated that both clinical cases and reactors were on average 5 years of age. Results are presented in Table 29.

The economics of subsidised vaccination (as part of a formal BJD control program) versus unsubsidised vaccination was specifically examined. Results are presented in Table 30. It has been assumed that any subsidised vaccination program would require vaccine to be administered by the program veterinarian. The cost of vaccine administration by the program veterinarian was assumed at $10.00 per vaccinated calf.

Table 29: Partial budget of annual disease and control costs for BJD under various control scenarios for a 250 cow dairy herd in Victoria

Parameter	Scenario										
	Baseline	3-step calf plan with vat milk	3-step calf plan with milk replacer	3-step calf plan with vaccination[b]	TCP1	TCP3	Vaccination[b] (median)	Vaccination[b] (optimistic)	Vaccination[b] (pessimistic)	Vaccination[b] & TCP1	Vaccination[b] & TCP3
Prevalence	8.8%	8.6%	8.0%	3.8%	1.7%	4.1%	4.2%	3.4%	6.8%	0.6%	1.6%
Reactor incidence	5.2%	4.8%	4.4%	2.2%	0.6%	2.2% (1.1%)[1]	2.4%	1.8%	4.0%	0.2%	0.8% (0.4%)[b]
Clinical incidence	2.6%	2.4%	2.2%	1.1%	0.3%	1.1%	1.2%	0.9%	2.0%	0.1%	0.4%
Farm cost	$21,656	$21,712	$23,352	$12,458	$9,378	$20,176	$13,291	$10,793	$19,955	$5,955	$8,515
Farm gain (relative to baseline)	-	-$56	-$1,696	$9,198	$12,278	$1,480	$8,365	$10,864	$1,701	$15,701	$13,141
Regulatory cost (CCF)	-	-	-	-	$1,690	$1,259	-	-	-	$1,589	$3,110
Farm gain + regulatory gain (relative to baseline)	-	-$56	-$1,696	$9,198	$10,588	$221	$8,365	$10,864	$1,701	$14,112	$10,031
ROI CCF ($ for $)	-	-	-	-	7.2:1	1.2:1	-	-	-	9.9:1	4.2:1

a – assumes vaccination is not subsidised by CCF; b – testing occurs every 2nd year in TCP3; the annual reactor detection rate in TCP3 is half the reactor prevalence estimate

Table 30: Partial budget of annual disease and control costs for BJD comparing subsidised with unsubsidised vaccination scenarios for a 250 cow dairy herd in Victoria

Parameter	Scenario								
	Baseline	Unsubsidised vaccination (median)	Subsidised vaccination (median)	3-step calf plan with unsubsidised vaccination	3-step calf plan with subsidised vaccination	Unsubsidised vaccination and TCP1	Subsidised vaccination and TCP1	Unsubsidised vaccination and TCP3	Subsidised vaccination and TCP3
Prevalence	8.8%	4.2%	4.2%	3.8%	3.8%	0.6%	0.6%	1.6%	1.6%
Reactor incidence	5.2%	2.4%	2.4%	2.2%	2.2%	0.2%	0.2%	0.8% (0.4%)[b]	0.8% (0.4%)[b]
Clinical incidence	2.6%	1.2%	1.2%	1.1%	1.1%	0.1%	0.1%	0.4%	0.4%
Farm cost	$21,656	$13,291	$11,717	$12,458	$10,884	$5,955	$4,381	$8,515	$10,719
Farm gain (relative to baseline)	-	$8,365	$9,939	$9,198	$10,772	$15,701	$17,275	$13,141	$10,937
Regulatory cost (CCF)	-	-	$2,204	-	$2,764	$1,589	$3,793	$3,110	$906
Farm gain + regulatory gain (relative to baseline)	$0	$8,365	$7,735	$9,198	$8,008	$14,112	$13,483	$10,031	$10,031
ROI CCF ($ for $)	-	-	4.5:1	-	3.9:1	9.9:1	4.6:1	4.2:1	12.1:1

a – assumes a $10 fee is payable to program veterinarian to administer vaccine – testing occurs every 2nd year in TCP3; the annual reactor detection rate in TCP3 is half the

Economic analysis confirmed that TCP3 has been a retrograde step for Victoria. The cost of compliance, combined with the cost of culling reactors and clinical cases, has resulted in reduced gain – specifically, a decrease in farmer gains from $12,300 under TCP1 to $1,500 under TCP3. When the costs of program delivery (CCF) and administration (DEPI) were included, the small farmer gain of $1,500 was almost completely offset by the cost of the program – the move from TCP1 to TCP3 has effectively eliminated any gains from the program.

Using only BJD-specific biosecurity (Three-Step Calf Plan) without a test-and-cull component was ineffective, and resulted in increased financial losses due to the increased labour cost of compliance. Using only the Three-Step Calf Plan (BJD-specific biosecurity-only) approach to disease control in infected farms is not supported by modelling.

Conversion to vaccination coupled with the cessation of testing of individual cows would result in an eventual improved farm profitability of around $10,900 (unsubsidised) or $12,400 (subsidised) per farm (optimistic scenario). It must be emphasised, however, that these returns would not be experienced until at least 10 years after the commencement of a vaccination program. It is also possible that vaccination-based control would result in a lowered prevalence of disease and incidence of clinical reactors beyond 10 years, as modelling suggested that the prevalence and incidence of disease was still trending downwards at the 10-year time point. Vaccination performance strongly determined the long-term economic performance of the program. Whilst the general trend of reduced prevalence and incidence of disease was similar between the three vaccination scenarios the final steady state disease level determines the long-term economic performance of the program. Minor differences in vaccination performance compound over time and increased vaccine efficacy results in lower prevalence and incidence and more rapid declines to the steady state level than reduced vaccine efficacy scenarios. Vaccine performance at least as high as the median modelled performance will be essential to provide the necessary economic support for a vaccination-based control program should one be considered.

8.4.2 State-Level Economics

The economics module was used to extrapolate the costs and benefits of the various control scenarios at the state level. The cost of vaccination was assumed to be covered by the accredited program and included a $25 vaccine and a fee of $10 per dose paid to the program veterinarian. Calf milk replacer was costed at $1.25 per calf per day for the first 42 days of life. Results are presented in Table 31. A comparison of subsidised and non-subsidised vaccination-based programs is presented in Table 32.

The analysis indicated that TCP3 has failed to deliver a net benefit to the Victorian dairy industry. The most physically effective control program was TCP1 combined with vaccination. This combination provided the greatest reduction in disease and disease impact to the Victorian dairy industry. It was, however, the most expensive program to deliver if subsidised vaccine is provided by the program, being between two- and three-times the cost of TCP1 alone. Interestingly, the cost of a combined (unsubsidised) vaccination and

TCP1 program is (slightly) less than the cost of a TCP1 program (without vaccination) – this is because vaccination will reduce the number of reactors and clinical cases in affected herds thereby reducing follow-up testing costs. If there was a 25% uptake rate amongst infected farms then this subsidised vaccination and TCP1 program would be conservatively estimated to cost in excess of $2.25 million per annum – but would return a benefit of $7.7 million to Victorian farmers and realise a net benefit of approximately $8.1 million after program costs to participating farmers. The equivalent figures for an unsubsidised vaccination program with TCP1 – assuming equal participation rates – are a CCF program cost of approximately $1.0 million per annum and a slightly reduced net benefit for participating farmers of $7.7 million (farmers pay for vaccine). The return on investment for the CCF expenditure is estimated at 3.4:1 for a subsidised vaccine program and 8.5:1 for an unsubsidised vaccine program.

The most effective return on limited CCF investment is therefore TCP1 and vaccination – but with non-subsidised vaccine. Return on investment ratios in excess of 8:1 can be expected. However, the acceptability of a compulsory and unsubsidised vaccine component within a TCP framework is highly questionable.

A return to TCP1 may provide greater return on investment for the CCF – if a high proportion of infected farms can be encouraged to enrol. It is estimated that a five- to six-fold return on every dollar spent on TCP1 would be returned to the Victorian dairy industry; a $1 million investment in TCP1 would be expected to return an extra $5.0 million to participating farmers (after costs). The main economic driver of this response appears to be the rapid and effective reduction in the prevalence of disease, the incidence of reactors and the incidence of clinical cases occurring under the test-and-cull component of TCP1. It is the reduction in reactor and clinical case rates to very low levels that drives economic performance. Further reductions in reactor rates and clinical case rates below the levels achieved by TCP1 suffer from reduced marginal returns. Whilst the addition of vaccination to TCP1 can drive disease to lower levels and even – and may even increase the number of farms successfully graduating from such a program – the economic cost-benefit for farmers is reduced because fewer cull cows (reactors and clinicals) are saved as a result of the addition of subsidised vaccination to the program.

Table 31: Victorian dairy BJD disease and control program costs and benefits for various control program scenarios and at varying levels of uptake by infected farms

Uptake %	Item	Baseline	Three-step and vat milk	Three-step and milk repl.	Three-step and vacc.	TCP1	TCP3	Vacc (med)	Vacc (opt.)	Vacc (pess.)	Vacc and TCP1	Vacc and TCP3
5%	Farmer cost ($ mill.)	51.3	51.6	51.8	50.5	50.2	51.5	50.6	50.4	51.4	49.8	50.1
	Program (CCF) cost ($ mill.)	0.00	0.00	0.00	0.00	0.20	0.15	0.00	0.00	0.00	0.19	0.37
	Total farm cost ($ mill.)	51.3	51.6	51.8	50.5	50.4	51.6	50.6	50.4	51.4	50.0	50.4
	CBA (c.f. Baseline $ mill.)	-	-0.34	-0.54	0.76	0.92	-0.31	0.66	0.96	-0.13	1.34	0.86
	CCF ROI ($ for $)	-	-	-	-	4.60	-2.07	-	-	-	7.11	2.32
25%	Farmer cost ($ mill.)	51.3	51.7	52.7	46.2	44.3	50.8	46.7	45.2	50.6	42.3	43.8
	Program (CCF) cost ($ mill.)	0.00	0.00	0.00	0.00	1.01	0.75	0.00	0.00	0.00	0.95	1.85
	Total farm cost ($ mill.)	51.3	51.7	52.7	46.2	45.3	51.5	46.7	45.2	50.6	43.2	45.7
	CBA (c.f. Baseline $ mill.)		-0.37	-1.34	5.14	5.96	-0.20	4.64	6.13	0.68	8.06	5.63
	CCF ROI ($ for $)	-	-	-	-	5.93	-0.27	-	-	-	8.53	3.04
50%	Farmer cost ($ mill.)	51.3	51.7	53.7	40.7	37.0	49.9	41.7	38.7	49.6	33.0	36.0
	Program (CCF) cost ($ mill.)	0.00	0.00	0.00	0.00	2.01	1.50	0.00	0.00	0.00	1.89	3.70
	Total farm cost ($ mill.)	51.3	51.7	53.7	40.7	39.0	51.4	41.7	38.7	49.6	34.9	39.7
	CBA (c.f. Baseline $ mill.)		-0.40	-2.35	10.61	12.26	-0.07	9.62	12.59	1.69	16.46	11.60
	CCF ROI ($ for $)	-	-	-	-	6.10	-0.05	-	-	-	8.70	3.13
75%	Farmer cost ($ mill.)	51.3	51.7	54.7	35.2	29.7	49.0	36.7	32.3	48.6	23.6	28.2
	Program (CCF) cost ($ mill.)	0.00	0.00	0.00	0.00	3.02	2.25	0.00	0.00	0.00	2.84	5.55
	Total farm cost ($ mill.)	51.3	51.7	54.7	35.2	32.7	51.2	36.7	32.3	48.6	26.5	33.7
	CBA (c.f. Baseline $ mill.)		-0.44	-3.36	16.08	18.56	0.06	14.59	19.05	2.70	24.85	17.57
	CCF ROI ($ for $)	-	-	-	-	6.16	0.03	-	-	-	8.76	3.16

Table 32: Victorian dairy BJD cost-benefit of subsidised and non-subsidised vaccination-based scenarios at varying uptake by infected farms

Uptake %	Item	3step & vacc.	3step & subs. vacc.	Vacc.	Subs. Vacc.	Vacc. (opt.)	Subs. Vacc. (opt.)	Vacc. (pess.)	Subs. vacc. (pess.)	Vacc. & TCP1	Subs. vacc. & TCP1	Vacc. & TCP3	Subs. Vacc & TPC3
5%	Farmer cost ($ mill.)	50.5	50.4	50.6	50.5	50.4	50.2	51.4	51.4	49.8	49.6	50.1	50.3
	Program (CCF) cost ($ mill.)	0.00	0.33	0.00	0.26	0.00	0.26	0.00	0.26	0.19	0.45	0.37	0.11
	Total farm cost ($ mill.)	50.5	50.7	50.6	50.7	50.4	50.4	51.4	51.7	50.0	50.0	50.4	50.4
	CBA (c.f. Baseline $ mill.)	0.76	0.62	0.66	0.58	0.96	0.88	-0.13	-0.40	1.34	1.27	0.86	0.86
	CCF ROI ($ for $)	-	1.88	-	2.23	-	3.36	-	-1.51	7.11	2.81	2.32	7.96
25%	Farmer cost ($ mill.)	46.2	45.2	46.7	45.7	45.2	44.2	50.6	50.6	42.3	41.4	43.8	45.1
	Program (CCF) cost ($ mill.)	0.00	1.64	0.00	1.31	0.00	1.31	0.00	1.31	0.95	2.26	1.85	0.54
	Total farm cost ($ mill.)	46.2	46.9	46.7	47.0	45.2	45.6	50.6	51.9	43.2	43.6	45.7	45.7
	CBA (c.f. Baseline $ mill.)	5.14	4.43	4.64	4.27	6.13	5.75	0.68	-0.63	8.06	7.69	5.63	5.63
	CCF ROI ($ for $)	-	2.69	-	3.25	-	4.39	-	-0.48	8.53	3.41	3.04	10.45
50%	Farmer cost ($ mill.)	40.7	38.8	41.7	39.8	38.7	36.8	49.6	49.6	33.0	31.1	36.0	38.6
	Program (CCF) cost ($ mill.)	0.00	3.29	0.00	2.62	0.00	2.62	0.00	2.62	1.89	4.51	3.70	1.08
	Total farm cost ($ mill.)	40.7	42.1	41.7	42.4	38.7	39.5	49.6	52.2	34.9	35.6	39.7	39.7
	CBA (c.f. Baseline $ mill.)	10.61	9.19	9.62	8.87	12.59	11.84	1.69	-0.93	16.46	15.71	11.60	11.60
	CCF ROI ($ for $)	-	2.80	-	3.38	-	4.52	-	-0.36	8.70	3.48	3.13	10.76
75%	Farmer cost ($ mill.)	35.2	32.4	36.7	33.9	32.3	29.4	48.6	48.6	23.6	20.8	28.2	32.1
	Program (CCF) cost ($ mill.)	0.00	4.93	0.00	3.93	0.00	3.93	0.00	3.93	2.84	6.77	5.55	1.62
	Total farm cost ($ mill.)	35.2	37.4	36.7	37.8	32.3	33.4	48.6	52.5	26.5	27.6	33.7	33.7
	CBA (c.f. Baseline $ mill.)	16.08	13.96	14.59	13.47	19.05	17.93	2.70	-1.23	24.85	23.73	17.57	17.57
	CCF ROI ($ for $)	-	2.83	-	3.42	-	4.56	-	-0.31	8.76	3.51	3.16	10.86

9 CONCLUSIONS

BJD is a complex disease with effective mechanisms for persistence in infected herds provided by:

- Limited infection of animals in the herd, leaving a reservoir of uninfected animals;
- Multiple transmission pathways, but dominated by faecal-oral spread;
- Slow progression of infection, allowing disease to spread and to evade early detection;
- Very high rates of bacterial shedding by late-stage infected animals, ensuring mass contamination of the farm environment; and
- Prolonged environmental persistence, providing a long-term reservoir of infective material.

These intrinsic features of the disease, when combined with the generally poor (insensitive) ante-mortem tests, mean that disease can persist in economically-viable and functioning herds and can effectively evade efforts to detect and eradicate disease from the herd.

TCP3 aims to disrupt the spread of infection from cow to calf by identifying a portion of the infected animals and removing them and their high-risk contacts. TCP3 also isolates calves and young stock from infective material. Whilst sound in theory, these test-and-cull and biosecurity-based programs have been ineffective at eradicating disease from infected herds. As such they were 'rebadged' as control programs whose primary objective was to reduce the level and impact of disease within and between herds. Since TCP3 commenced, only four herds have graduated to 'Tested to MAP Standard' (TMS) status with a small number of the preceding TCP2 program herds attaining TMS status between 2000 and 2010. A large number of known infected herds have subsequently withdrawn from TCP3 and numbers of participants continue to decline. The majority of participating TCP3 herds remain at low prevalence.

However, there is strong evidence that TCP3 has reduced the number of reactors and the prevalence of clinical disease in most participating herds. The long-term prevalence of clinical disease in infected Australian dairy herds undertaking no controls suggests that a prevalence of 8-9% can be expected – with up to 2.5% clinical cases per year. The prevalence in long-term TCP3 herds is approximately 4% with 1.0% clinical cases. The economics of TCP3-based disease control supports involvement in the program. The benefits from a reduction in the annual clinical incidence rate of at least 1.5% per annum that can be expected under long-term adherence to TCP3 are slightly greater than the cost to the farmer of participation in the program. Whilst the benefits of disease control are not substantial – failure to control disease is unlikely to result in many business failures – there is generally a lack of awareness of the economic advantages from better control by farmers, veterinarians and other stakeholders.

This lack of awareness of the private benefits that can be expected by owners of infected herds from participating in TCP3 was confirmed by discussions with stakeholders. Participants are realistic about the constraints of the program, but there is some frustration at not being able to graduate from the program. There are practical issues – such as failure

of the program to acknowledge false positives to the ELISA test – that contribute to general disenchantment with the program. The seemingly costly culling of apparently healthy reactor animals is a major source of frustration. The lack of understanding by all stakeholders of the long-term economic benefits of disease control causes participant farmers to view the culling of reactors as a cost without any subsequent benefit.

Stakeholders also expressed the view that the complete cessation of TCP, without replacement with another, comparable (subsidised) program, would be unsatisfactory. Simply terminating TCP3 therefore presents a substantial risk to future dairy disease control programs. The authorities (including DEPI) could lose significant credibility. Stakeholders also expressed uncertainty and caution regarding vaccination. The absence of evidence from field trials provides the greatest source of uncertainty. The potential role and economic impact of vaccination will need to be evaluated, and presented to participants and stakeholders, to allow rational decision making by farmers and their veterinary advisors.

The high prevalence of BJD in Victoria, and the zoning approach to management of BJD throughout Australia, can make BJD a significant barrier to trade for some producers who sell livestock to other farmers across borders. The performance of TCP3 when viewed in light of the national objectives implies that the program is not achieving any practical change to the level or distribution of disease within the state herd. Whilst it may be important to other jurisdictions that an 'official' control program is in operation the practical output from TCP3 is negligible.

There are a number of newer technologies that have potential to change the approach to the management of BJD – although the ideal high-sensitivity, high-specificity, real-time and low-cost individual animal test is still not on the horizon. These new technologies are the high-throughput PCR (HT-J-PCR) and herd environmental culture (HEC) tests and the Silirum® vaccine. The potential application of these new technologies needs to be explored and where relevant they should be incorporated into the overarching JD control plan and SDRGs.

We used a modelling approach to examine future control options for BJD in Victoria. Modelling has the advantage of being relatively inexpensive, fast and adaptable. For complex diseases, models provide the only meaningful way of combining (interpolating and extrapolating) the findings of multiple experiments into a form that allows prediction of outcomes given certain starting conditions. The disadvantages of modelling include the challenge of accurately quantifying the large number parameters necessary to code highly complex ecologies (disease in herds), difficulties of validating performance and, finally, the fact that simulation model outputs can be viewed with scepticism by some stakeholders.

An existing dairy herd model template was adapted to include a BJD sub-module. Output was validated against existing industry data (from Dairy Australia's InCalf program) and specifically for BJD against a detailed analysis of TCP1 by Jubb and Galvin (2004a). A structured series of control scenarios was then examined using the model.

The modelling study reinforced the evidence of actual testing data that the move from TCP1 to TCP3 has been retrograde. The long-term prevalence and clinical incidence of BJD in TCP3 herds was significantly higher and more variable for TCP3 herds than for TCP1 herds. The economic benefit for participating farmers was significantly reduced after transition from

TCP1 to TCP3, and the benefit for farmer participation was negligible over the longer term. When the costs of program administration and delivery were included, gains from participation in TCP3 were offset by the cost of the program to DEPI and CCF.

Modelling also showed mixed results from a move away from the test-and-cull approach and toward BJD-specific biosecurity (Three-Step Calf Plan) or vaccination. BJD-specific biosecurity alone (the Three-Step Calf Program) is essentially ineffective, resulting on average in a higher prevalence and incidence of disease than the current program (TCP3) and with a marked increase in variability between farms. We concluded that a move from the test-and-cull approach to self-management by industry revolving around the Three-Step Calf Plan would be ineffective at both reducing disease and reducing product contamination levels. It would also be uneconomical for participating farmers as the level of disease and clinical case rate would increase substantially and result in greater losses. Whilst costs of control are less than for other control options the increased cost of further disease overwhelms these savings. The application of the Three-Step Calf Plan alone becomes practically impossible when the impact of low-sensitivity individual animal diagnostic tests is considered as there no way of assuring freedom from disease in replacement stock such as bulls. The movement to reliance solely upon the Three-Step Calf Plan (BJD-specific biosecurity) cannot be recommended.

Vaccination may offer improved control over disease in infected herds. Caution must be applied, however, until the results of the Australian dairy Silirum® vaccine trial have been analysed and the performance of the vaccine has been confirmed. The simulations showed that switching from the test-and-cull approach to the vaccination of replacement calves is likely to at least provide for an equivalent level of disease control as the current program (TCP3) in the short-to-medium term – perhaps better control beyond the ten-year horizon of the model study. Modelling also suggested that the effects of vaccination are likely to compound over time, although without a concurrent test-and-cull component a number of generations would be required to break the in-utero transmission pathway and to reduce the prevalence of disease in the herd. Vaccination in combination with TCP1 – whereby the ELISA individual animal test is replaced with the HT-J-PCR test – was found to offer the highest level of disease control. The modelling analysis showed that a significant proportion of participating dairy farms would successfully graduate from a combined TCP1 and vaccination program within 10 years. The cost of participation in a vaccination and TCP1 combined program however would be higher than for other control options. A staged approach may also be necessary. Vaccinated and uninfected animals may react to the individual ELISA test. Currently the alternative HT-J-PCR test is not accepted for use as an individual animal test and the high cost and prolonged time for results of the faecal culture test prohibits its use as a replacement to ELISA in TCP. One or more years of TCP1 with staged introduction of vaccination (and cessation of TCP1 testing before vaccinates obtain 2 years of age) may be required. The performance of staged cessation of TCP1 ELISA-based test-and-cull with calf vaccination was examined (Appendix 2). Results suggest that two years (only) of ELISA-based test-and-cull (TCP1) with concurrent vaccination of replacement calves provides many advantages including: fast reduction in disease prevalence and clinical incidence; high economic benefit to producers; reduced program expenditure on ELISA testing; and potentially a high rate of successful graduation from the program within ten years.

The choice for the future for BJD control in Victoria therefore depends very much on the objectives of industry and the key participants and on the availability of funds. The continuation of TCP3 is not supported under any argument – effectiveness, economics or current acceptance. If the desire is to reduce the impact of BJD on the profitability of infected herds then disease control options may be employed. The effective options include a reversion to TCP1 or vaccination, or a combination of both. Neither TCP1 nor vaccination alone is likely to reliably eradicate the disease on participating farms, and these programs can therefore be viewed as options that reduce and control the prevalence of infected animals in a region. Either approach would minimise the impact of disease on participating dairy farms, prevent an increase in the level or rate of product contamination (milk and meat – reducing spill-over of disease into the Victorian beef industry), and would be seen by trading partners as a reasoned approach to the control of disease. However, this is unlikely to reduce the prevalence of infected farms. The return on investment is likely to be greater for TCP1 than for the combined TCP1 and vaccination program.

If a move towards the eradication of BJD from the Victorian cattle herd is envisaged, then a reduction in the prevalence of infected farms as well as a reduction in the prevalence of infected animals will be required. The combination of vaccination and TCP1 would be likely to in a control program would likely allow a high proportion of participating farms to successfully graduate within 10 years of deployment. For some producers (cattle studs, in particular), graduating from the program with a return to pre-BJD trading environment may be the overarching priority. The combination of vaccination and TCP1 is the strategy most likely to provide for this. It needs to be emphasised, however, that changes to the SDRGs would be required. In particular, the HT-J-PCR (or similar) would be needed to replace the individual animal ELISA test in vaccinating herds.

Our conclusions from the modelling studies and preceding reviews and evaluations are that the ongoing management of BJD in Victoria might follow one of four possible pathways:

1. Abandon the Victorian BJD control program (currently TCP3) and effectively deregulate the control of BJD, understanding that disease prevalence, incidence and economic impact will increase under this approach, and that there may be negative implications for future disease control programs as some current participants will feel abandoned;
2. Return to TCP1, understanding that a greater recruitment of infected farms will be necessary for real benefit to accrue at the state level;
3. Provide for subsidised vaccination, understanding at least 10 years will be required for farms that have not undergone a test-and-cull prelude to vaccination to accrue observable benefit; or
4. Adopt TCP1 and vaccination, understanding that this will evoke the highest standard of control, benefit to producers but also the highest program cost. This adoption may be as concurrent vaccination and testing (with an approved test for use in vaccinated animals) or as a staged conversion from TCP1 to vaccination that ensures no vaccinated animals are subject to the individual animal ELISA test.

The BJD model that was developed for this project remains as a resource for monitoring and tracking disease progress under the chosen scenario. Recording and monitoring actual performance against projected performance (model output) provides both insight into the

relative effectiveness of delivery and compliance with controls, and early warning of changes to the background levels of disease. We recommend regular assessment of field disease levels and program performance using the model.

There is another growing concern in Johne's disease in cattle that has been more difficult to deal with in this review but must be acknowledged: the increasing number of detections of ovine-strain Mptb in beef herds. The detection of ovine-strain infection in a herd of cattle, whether associated with clinical disease or not, does not cause that herd to be classified as 'Infected' with BJD (or ovine JD for that matter) under the SDRGs. This is premised upon a lack of definitive evidence showing that cattle are capable of becoming infected with ovine-strain Mptb, sustaining the infection and becoming a source of infection for other cattle following the removal of the original source population of sheep.

There is emerging evidence from Australia and New Zealand that ovine-strain Mptb may be more sustainable in cattle herds than previously thought. The national program has a key objective to protect beef herds from becoming infected with JD, largely by segregating them from dairy herds, with other beef herds generally being regarded as low risk under the 'Beef Only' classification. The definition of 'Beef Only' may need to be reconsidered and expanded under the SRDGs to recognise that cattle co-grazing with sheep may in some circumstances present a risk of JD infection to other cattle.

This review recommends that DEPI maintain a watching brief on the prevalence of ovine-strain Mptb infection in cattle herds, and make appropriate representations to the national program should Victoria determine that this presents an unacceptable risk to the cattle population.

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11 APPENDIX 1: SIMULATION MODEL PARAMETERS AND SETTINGS

The relevant parts of the simulation model describing the parameterisation of herd structure and herd dynamics and also of BJD disease within the herd are presented in Table 33.

Table 33: Herd parameters used in the model

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td>1</td><td>Seasonal calving</td><td>AI Period duration: 49 days
Total mating duration: 147 days</td><td>Mating period start date = 1 Nov</td><td>Dairy Research and Development Corporation (2000); Dairy Australia (2011)</td></tr>
<tr><td>2</td><td>Split-calving</td><td>AI Period 1 duration: 49 days
Total mating period 1 duration: 147 days
AI Period 2 duration: 21 days
Total mating period 2 duration: 42 days</td><td>Mating period 1 start date = 1 Nov, Mating period 2 start date = 1 Jul</td><td>Dairy Research and Development Corporation (2000); Dairy Australia (2011)</td></tr>
<tr><td>3</td><td>Year-round calving</td><td>Voluntary withhold period: 40 days
Maximum no AIs per cow: 3
Maximum no matings per cow: 6
Last mating post calving (before marking for culling): 200 days</td><td></td><td>Dairy Research and Development Corporation (2000); Dairy Australia (2011)</td></tr>
<tr><td>4</td><td>Submission</td><td><table><tr><th>Days calved</th><th>Submission Rate</th></tr><tr><td>95+</td><td>0.89</td></tr></table></td><td>The baseline submission risk for a cow that cycles naturally and is submitted for mating by the number</td><td>Dairy Australia (2011)</td></tr>
</table>

ID	Parameter	Value	Comment	Reference
		75-94: 0.84 53-74: 0.75 32-52: 0.62 1-31: 0.20	of days since last calving (assumes 100% of heats are detected)	
5	Conception	*Days calved* / *Conception Rate* 95+: 0.51 75-94: 0.49 53-74: 0.40 32-52: 0.32 1-31: 0.22	The baseline conception risk for a cow that cycles naturally and is submitted for mating by the number of days since last calving	Dairy Australia (2011)
6	Heat detection	Heat detection efficiency: 0.93	Baseline proportion of cows on heat that are detected by farmers	J Morton (pers. com.)
7	Infertility	Proportion of cows infertile after calving: 0.05	Infertile animals have their conception rates set to 0	J Morton (pers. com.)
8	Early embryonic loss / phantom cows	Phantom cow rate: 0.25 Delayed return to oestrus of 64 days	Percentage of matings without conception that experience delayed return to oestrus (early embryonic loss)	J Morton (pers. com.)
9	Abortion	Abortion rate: 0.03	Proportion of pregnancies	J Morton (pers. com.)

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>that do not calve. These cows slip their calves after implantation</td><td></td></tr>
<tr><td>10</td><td>Voluntary culling</td><td><table><tr><th>Parameter</th><th>Cull score points</th></tr><tr><td>Carryover cow</td><td>8</td></tr><tr><td>Age</td><td>5 for every year older than 7</td></tr><tr><td>Mastitis</td><td>10 – if chronic</td></tr><tr><td>Production</td><td>6 if in lowest quartile</td></tr><tr><td>Non-pregnancy</td><td>15</td></tr><tr><td>Stage of lactation penalty</td><td>-9 (0-149 days)
-6 (150-199 days)
-3 (200+ days)
10 (non lactating)</td></tr></table></td><td>Voluntary cull score is calculated for each cow and updated each day.
If voluntary culling is required the highest ranked cows on cull score are removed from the herd are removed until the quota is met.
Necessary to ensure there is targeted culling of cows within a herd</td><td>Estimated</td></tr>
<tr><td>11</td><td>Involuntary culling</td><td>Age: Cows: 12 years, bulls: 7 years
Mastitis: Third clinical episode mastitis per lactation</td><td></td><td>HiCo/ADHIS data
Countdown Downunder recommendations</td></tr>
<tr><td>12</td><td>Mortality</td><td><table><tr><th>Age</th><th>Annual mortality</th><th>Propn mortality in first month after calving</th></tr><tr><td>1</td><td>0.05</td><td>0.8</td></tr><tr><td>2</td><td>0.01</td><td>0.08</td></tr></table></td><td></td><td>Derived from HiCO MISTRO data</td></tr>
</table>

ID	Parameter	Value			Comment	Reference
		3	0.01	0.7		
		4	0.01	0.7		
		5	0.01	0.7		
		6	0.01	0.7		
		7	0.02	0.7		
		8	0.02	0.7		
		9	0.02	0.7		
		10	0.02	0.7		
		11	0.03	0.7		
		12	0.03	0.7		
		Bulls	0.05	0.08		
13	Litres				Litres = A * SOL^{B} * exp(-C * SOL), where SOL = stage of lactation (days) 3YO: A = 19.0 4YO: A = 21.5 5-9YO: A = 23.0 10YO+: A = 21.5 Within-herd A sd: 3.0 (95% range of A 17.0-29.0)	Derived from ADHIS data (stats1112.xls – see www.adhis.com.au)

Calendar month of calving	*A*	*B (E-02)*	*C (E-03)*
1	23.0	7.00	1.60
2	23.0	7.98	1.62
3	23.0	9.93	2.18
4	23.0	12.19	2.97
5	23.0	13.93	3.81
6	23.0	14.95	4.42
7	23.0	15.24	4.69

ID	Parameter	Value				Comment	Reference
		8	23.0	14.79	4.58		
		9	23.0	13.23	4.09		
		10	23.0	10.98	3.31		
		11	23.0	8.28	2.51		
		12	23.0	6.00	1.80		
14	Fat %	*Calendar month of calving*	A (E-02)	B (E-05)	C (E-07)	Fat (%) = A + B * min(SOL, 300) + C * min(SOL, 300)^2, where SOL = stage of lactation (days)	Derived from ADHIS data (stats1112.xls – see www.adhis.com.au)
		1	3.9	2.4	-0.8		
		2	4.2	-2.6	0.6		
		3	4.3	-4.9	1.5		
		4	4.4	-7.2	2.5		
		5	4.3	-8.1	3.1		
		6	4.2	-7.4	3.4		
		7	4.1	-4.9	3.0		
		8	3.9	-1.9	2.0		
		9	3.8	-1.0	1.0		
		10	3.7	-2.2	0.4		
		11	3.7	-3.5	-0.3		
		12	3.9	-1.1	0.2		
15	Protein %					Protein (%) = A + B * min(SOL, 300) + C *	Derived from ADHIS data (stats1112.xls – see

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><th>Calendar month of calving</th><th>A (E-02)</th><th>B (E-05)</th><th>C (E-07)</th></tr>
<tr><td>1</td><td>3.1</td><td>0.6</td><td>4.9</td></tr>
<tr><td>2</td><td>3.1</td><td>1.3</td><td>1.2</td></tr>
<tr><td>3</td><td>3.2</td><td>1.3</td><td>0.8</td></tr>
<tr><td>4</td><td>3.2</td><td>1.4</td><td>-1.1</td></tr>
<tr><td>5</td><td>3.2</td><td>1.0</td><td>-0.3</td></tr>
<tr><td>6</td><td>3.3</td><td>-0.3</td><td>4.5</td></tr>
<tr><td>7</td><td>3.4</td><td>-2.6</td><td>12.8</td></tr>
<tr><td>8</td><td>3.5</td><td>-3.6</td><td>16.4</td></tr>
<tr><td>9</td><td>3.4</td><td>-4.5</td><td>14.7</td></tr>
<tr><td>10</td><td>3.4</td><td>-2.7</td><td>21.5</td></tr>
<tr><td>11</td><td>3.2</td><td>-1.9</td><td>16.2</td></tr>
<tr><td>12</td><td>3.2</td><td>-2.8</td><td>14.6</td></tr>
</table>
</td><td>min(SOL, 300)^2, where SOL = stage of lactation (days)</td><td>www.adhis.com.au)</td></tr>
<tr><td>16</td><td>S. aureus</td><td>S. aureus new infection baseline daily risk:
P = (2* exp(-0.20 * Month_of_Lactation + 17)) / 30.4)
50% become clinical. Clinical duration set at 5 days
Clinical disease daily recurrence risk: 0.004
Cure rates: Spontaneous: = 0.25; Dry cow cure: = 0.75</td><td>Baseline risk for this contagious pathogen is scaled by the ratio of within-herd prevalence of S. aureus infection by baseline prevalence (0.15).
Recurrence risk 50% chance of 1 and 25% chance of 2 clinical breakdowns during</td><td>Shephard (2000)</td></tr>
</table>

ID	Parameter	Value	Comment	Reference
			current lactation	
17	*S. uberis*	*S. uberis* new infection baseline daily risk: P = (2* exp(-1.1 * Month_of_Lactation + 2.1)) / 30.4) 50% become clinical. Clinical duration set at 5 days Cure rates: Spontaneous: = 0.50; Dry cow cure: = 0.90	No scaling of baseline risk for this environmental pathogen No increased risk of clinical recurrence during current lactation for *S. uberis* assumed	Shephard (2000)
18	SCC	Log_{10} SCC Base = 2.22 + 4.8E-4 * SOL - 3.1E-06 * SOL^2 - 0.522 * Log_{10} SOL, where SOL = min(stage of lactation (days), 300) Log_{10} SCC = L_{10}SCCBase + 0.0354 * S.aureus - 0.2785* S.uberis + 1.50*Clinical + 1.25*Sublclinical - 3.4E-04 * DurnInf * S.aureus + 1.7E-04 * DurnInf * S.uberis Where Log_{10} SCC = Log_{10} SCC Base, S.aurues = *S. aureus* infection status (0 or 1), S.uberis = *S. uberis* infection status (0 or 1), Clinical = clinical mastitis status (0 or 1), DurnInf = duration of mastitis infection (days)	[See 16 for *S. aureus* and 17 for *S. uberis* mastitis risk function]	Shephard (2000)

Table 34: BJD parameters used in the model

ID	Parameter	Value	Comment	Reference
19	Prevalence	BJD Seropositive farm prevalence: = 0.50 BJD within-farm prevalence: = 0.10	Used to generate start-up population and to provide background risk of purchase of disease (e.g. herd bulls)	Champness (2010)
20	Infection stages	A numerical coding system for stages was used: 0 = uninfected, 1 = in-utero, 2 = transient shedder, 3 = latent, 4 = early subclinical, 5 = late subclinical, 6 = clinical	The codes allow events for a number of processes listed below to be determined by the infection status of the animal and the stage of disease	
21	Transient phase duration	Proportion of transient shedders: p = 0.45 Duration of stage: sample(180:365, 1) days	Random sample of a value in the range 180 to 365 days (equal probability) Animals move to latent phase below on completion of this phase. Phase durations are predetermined at birth or introduction of animals into the herd.	Mitchel *et al.* (2012)(page 14)
22	Latent phase duration	Duration of stage: rtriang(min = 9, mode = 12, max = 18) months	Random sample of a value from the triangular distribution. Converted to days (x 365). Latent phase	Mitchel *et al.* (2012)(page 14)

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>duration is unaffected by (previous) transient shedding phase. Phase durations are predetermined at birth or introduction of animals into the herd</td><td></td></tr>
<tr><td>23</td><td>Subclinical (early and late) phase duration</td><td>The model will generate a random number between 0 and 1 and use this value as a look-up to select the subclinical period for the animal using the table below<table><tr><th>Subclinical Period (Years)</th><th>Probability</th></tr><tr><td>1</td><td>60%</td></tr><tr><td>2</td><td>15%</td></tr><tr><td>3</td><td>10%</td></tr><tr><td>4</td><td>5%</td></tr><tr><td>5</td><td>4%</td></tr><tr><td>6</td><td>3%</td></tr><tr><td>7</td><td>2%</td></tr><tr><td>8</td><td>0.5%</td></tr><tr><td>9</td><td>0.25%</td></tr><tr><td>10</td><td>0.25%</td></tr><tr><td></td><td></td></tr></table></td><td>Duration of the subclinical phase is equally divided between early subclinical and late subclinical stages. Subclinical duration is converted to days. Phase durations are predetermined at birth or introduction of animals into the herd</td><td>Page 16</td></tr>
<tr><td>24</td><td>Clinical phase duration</td><td>Duration of stage: rtriang(min = 30, mode = 90, max = 180) days</td><td>This provides the time a clinical case can exist in the</td><td>Combination of Groenendaal et al. (2002),</td></tr>
</table>

ID	Parameter	Value	Comment	Reference
			herd before being forcibly culled. Note that clinical cases (and subclinical cases) may be unknowingly culled for other non-disease reasons (empty, low production, mastitis). Phase durations are predetermined at birth or introduction of animals into the herd	Marce *et al.* (2011) and Lu *et al.* (2008, 2010, 2013a, 2013b)(page 17)
25	In-utero (Trojan) infection probability	Trojan pregnancy probability (per pregnancy in infected dams): Early subclinical (stage = 4): P = rtriang(1, min = 0.06, mode = 0.09, max = 0.14) Late subclinical (stage = 5) or Clinical (stage = 6): P = rtriang(1, min = 0.20, mode = 0.39, max = 0.60)	Early subclinical stage pregnant cows will infect (on average) 9% of pregnancies. Late subclinical and clinical pregnant cows will infect (on average) 39% of pregnancies. [See item 20 for BJD Stage]	Whittington and Windsor (2009)(page 25)
26	Teat contamination levels	The level of teat contamination (faecal origin) in infected and shedding lactating cows (cfu/day): if subclinical, cont. = rpert (1, min = 0, mode = 40, max = $2x10^{10}$) if clinical, cont. = rpert(1, min = 700, mode = $14x10^{4}$, max =	Output is cfu ingested per day – via the teats (direct) or via calf milk. It represents total load and it is assumed the Marce *et al.* (2011) data represents the	Marce *et al.* (2011)(page 23)

ID	Parameter	Value	Comment	Reference
		$2x10^{10}$) if vaccinated, cont. = cont. * (1 - vaccine shedding efficacy)	total daily teat load (i.e. irrespective of daily milk production level)	
27	Faecal excretion levels	The amount of Mptb excreted in dung by infected and shedding animals per day: If transient shedder, excr. = 3 (yearling), 63 (heifer), 188 (adult) If early subclnical, excr. = 63 (< 3 YO), 188 (adult) If late subclinical, excr. = 313 (< 3 YO), 938 (adult) If clinical, excr: = 625 (< 3 YO), 1880 (adult) Excretion is in units of 10^4 cfu per animal per day	This is a function of stage of disease and age (i.e. size) of the animal Output is total Mptb faecal excretion per day (in units of 10^4 cfu/animal /day)	Crossley *et al.* (2005) and Marce *et al.* (2011)(Table 4, page 32)
28	Milk excretion levels	The amount of Mptb excreted in milk by infected and lactating and shedding animals per day: If early subclinical (stage = 4), excr. = 5.0 * rbinom(1,1,0.03), where prob. transient shedder = rbinom(1,1,0.03) If subclinical or clinical excr. = rpert(1, min = 2.2, mode = 5.0, max = 8.8) Where prob. subclinical/clinical shedder = 1.0 Excretion is in 10^4 cfu/l Result is cfu per L per day	The total amount of Mptb excreted is a function of the concentration of Mptb per litre obtained by these equations multiplied by the total amount of milk produced (litres) per day by the animal (item 13 above).	Marce *et al.* (2011) and Sweeney *et al.* (1992)(page 25)
29	Site Mptb contamination	The amount of live Mptb per hectare per site: Contamination/Ha = sum (total mob Mptb excretion for day / paddock size) + residual contamination/Ha The site total new faecal excretion is the sum of the amount excreted by all members. Average paddock size is	[See Item 27 for daily faecal excretion function and Item 30 for environmental Mptb decline function]	Derived (page 31)

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td>determined by the milking cow stocking rate (User input: set at 4 cows per hectare). All grazing paddocks are the same size.</td><td></td><td></td></tr>
<tr><td>30</td><td>Environmental Mptb decline</td><td><table><tr><th>Season</th><th>Daily decline (proportion)</th></tr><tr><td>Summer</td><td>0.08</td></tr><tr><td>Autumn</td><td>0.07</td></tr><tr><td>Winter</td><td>0.06</td></tr><tr><td>Spring</td><td>0.07</td></tr></table></td><td>This is the proportion of residual live environmental Mptb that die each day</td><td>Derived from Whittington et al. (2004) and Eppleston and Whittington (2014) pers. comm.</td></tr>
<tr><td>31</td><td>Vaccination</td><td>The probability that an individual vaccinate will become protected: 0.75
Immunity assumed after 15 days post vaccination and to last for life in responders
Proportional reduction in risk of new infection in vaccine responders:
Pessimistic = 0.25, most likely = 0.60, optimistic = 0.75
Proportional reduction in Mptb shedding (all modalities) by vaccine responders:
Pessimistic = 0.25, most likely = 0.60, optimistic = 0.75
Proportional prolongation of subclinical stage of disease by vaccine responders:
Pessimistic = 0, most likely = 0.1, optimistic = 0.25</td><td>This is modelled as 75% of vaccinates responding to immunisation. Those that respond have 60% reduced probability of infection as well as 60% less shedding of Mptb (if infected) and a prolongation of pre-clinical phases of disease by 10%. Non-responders have no alteration to probability of infection, rate of shedding or length of disease phases. For the pessimistic scenario, 75% of vaccinates are assumed to respond but</td><td>Assumed. Preliminary analysis of Zoetis Australian field trial data suggests a slight prolongation of pre-clinical phases (10%) and 60% fewer shedders amongst vaccinates</td></tr>
</table>

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td></td><td>there is only a 25% reduction in probability of infection, 25% reduction in shedding (if infected) and no extension of pre-clinical disease phases. Under the optimistic scenario, 75% of vaccinates respond and in these there is a 75% reduction in probability of disease and of Mptb shedding in infected. Preclinical phases of disease are also 25% longer.</td><td></td></tr>
<tr><td>32</td><td>ELISA test</td><td><table><tr><th>Stage</th><th>Sensitivity</th><th>Specificity</th></tr><tr><td>Uninfected</td><td>0.0</td><td>99.7%</td></tr><tr><td>Transient shedder</td><td>0.0</td><td>99.7%</td></tr><tr><td>Latent</td><td>1%</td><td>99.7%</td></tr><tr><td>Early subclinical</td><td>10%</td><td>99.7%</td></tr><tr><td>Late subclinical</td><td>60%</td><td>99.7%</td></tr><tr><td>Clinical</td><td>80%</td><td>99.7%</td></tr></table></td><td>The sensitivity of the ELISA test depends upon the stage of disease
See item 20 for BJD disease stages</td><td>Groenendaal (2012)(Table 10, page 49)</td></tr>
<tr><td>33</td><td>Faecal culture</td><td>Individual animal</td><td>A conservative approach was adopted for faecal</td><td>Timms et al. (2011)(page 52)</td></tr>
</table>

<table>
<tr><th>ID</th><th>Parameter</th><th>Value</th><th>Comment</th><th>Reference</th></tr>
<tr><td></td><td></td><td><table><tr><td>Stage</td><td>Sensitivity</td><td>Specificity</td></tr><tr><td>Uninfected</td><td>0%</td><td>100%</td></tr><tr><td>Transient shedder, Low shedder</td><td>45%</td><td>100%</td></tr><tr><td>High shedder, clinical</td><td>93%</td><td>100%</td></tr></table></td><td>culture sensitivity</td><td></td></tr>
<tr><td>34</td><td>Culture test (HEC-test)</td><td>Herd-level sensitivity = 45%, specificity = 100%</td><td></td><td>Timms et al. (2011)(page 52)</td></tr>
<tr><td>35</td><td>HT-J-PCR test</td><td>Individual animal
<table><tr><td>Stage</td><td>Sensitivity</td><td>Specificity</td></tr><tr><td>Uninfected</td><td>0%</td><td>100%</td></tr><tr><td>Low shedder, subclinical</td><td>4%</td><td>100%</td></tr><tr><td>High shedder, clinical</td><td>80%</td><td>100%</td></tr></table></td><td></td><td>Lu et al.(2008)(page 55)</td></tr>
<tr><td>36</td><td>Reproductive performance impact</td><td>Submission rate reduction: max(0, (Stage - 3))* 0.025
Conception rate reduction: max(0, (Stage - 3))* 0.025</td><td>The relative reduction in SR and CR for an early subclinical is 2.5%, for a late subclinical is 5.0% and for a clinical is 7.5% of expected. [See 20 for BJD Stage, 4 for submission and 5 for conception rate tables]</td><td>Assumed</td></tr>
</table>

ID	Parameter	Value	Comment	Reference
37	Mastitis impact	New infection increased risk: 0.05 (5% increase in risk) Cure rate reduction: 0.05 (5% reduction in cure rate)		Assumed
38	Production impact	Reduction = (BJD stage - 3) * 0.05	An early subclinical produces 5% less milk, a late subclinical 10% less milk and a clinical 15% less milk than uninfected or pre-clinically infected and lactating cows [See 20 for BJD Stage]	See DAV (1994).

12 APPENDIX 2: STAGED TCP1 AND VACCINATION SCENARIO ASSESSMENT

12.1 Introduction

Modelling showed that the Silirum® vaccine is likely to be an effective control for disease at both the individual animal and infected herd level. Vaccination with Silirm® in commercial dairy herds appears to: (a) reduce the risk of new infection in vaccinated individuals; (b) reduce the rate of progression and the onset (and perhaps the level) of shedding of Mptb in infected vaccinates; and (c) reduce the incidence of clinical disease in infected vaccinates. The combined effect of increased resistance and delayed progression and severity of disease appears to reduce both the prevalence of disease and the level of Mptb shedding and thereby environmental contamination on vaccinating farms. Whilst modelling of the (currently hypothetical) scenario of concurrent and combined TCP1 (testing of all animals aged 2 years and older annually with culling of positive animals and their high risk contacts) and vaccination (of all retained calves and introduced animals) indicated that a high proportion of farms would graduate from the program within 10 years, this program is currently not possible under the current SDRGs. Only the ELISA test or faecal culture test are approved for testing of individual animals – PCR tests are not. Vaccination can be expected to produce antibodies in at least a proportion of animals, and this may result in an increased risk of false positive ELISA test reactions in later years. The ELISA test cannot differentiate vaccinates from natural infections and thereby the application of the ELISA test in animals that have been vaccinated is not recommended or supported by the current SDRGs.

The TCP1 test-and-cull component was demonstrated to provide the most rapid reduction in within-herd prevalence of disease and in the annual incidence of clinical cases. This rapid reduction in the number of clinical cases that follows successful implementation of the TCP1 test-and-cull component provides for the greatest (and fastest) net benefit returned to participating farmers. It also gives a clear demonstration to participants of progress in the control of the disease, as progress can be seen within 5 years on most farms.

Vaccination appears to be effective in reducing both the prevalence and incidence of clinical cases in vaccinating herds. However, because vaccination does not control the in-utero pathway and offers limited control over contamination of calf milk (high-risk animals are not preferentially removed from the herd in solely vaccination-based controls) the rate of progression of control is likely to painfully slow for most participants. Modelling suggests that the prevalence of disease – and the incidence of clinical cases – will still be in gradual decline 10 years after initiating the program. It is highly likely that many farmers will not see evidence of progress in the control of BJD within 5 years of initiating a vaccination program. This is expected to be a major disincentive to producers to continue with the administration of an expensive and potentially hazardous vaccine that provides incomplete protection for vaccinates.

It is important that any change to TCP be both effective and acceptable to the participants. Failure to graduate and failure to appreciate progress in disease control have been cited by farmers as reasons for disenchantment with the current TCP (TCP3).

Similarly, the CCF needs to show a demonstrable benefit for their investment. The ongoing spending of industry levies demands more than the current low participation rate of approximately 15% of infected Victorian farms, if it is to ensure that benefit is returned to more cattle producers and to the state of Victoria as a whole. Simply increasing the recruitment of farms under the current TCP1 program will increase the expenditure of the CCF dramatically. Whilst this is likely to be cost-effective at the individual farm level – and therefore regional and state level – the low rates of graduation from the program essentially commit the fund to an ever increasing spiral of expenditure.

The combination of TCP1 and vaccination appears to offer a high proportion of farms the opportunity to graduate within 10 years. Therefore the combined use of vaccination with TCP1 – especially when concerted regional efforts are applied – would be expected to cap annual expenditure. This will occur when the number of newly recruited program participants matches the number of farms that graduate each year.

Because individual animal testing of vaccinated animals with PCR tests (e.g. HT-J-PCR) is not currently approved, the use of a staged transition from TCP1 (individual animal ELISA testing) to vaccination has been examined. This offers a number of potential advantages. The rapid reduction in prevalence provided by the test-and-cull component provides encouragement (and economic benefit) to the participant, reduces the challenge experienced by vaccinates and, importantly, caps the program expenditure on the testing of individual animals. It also provides assurances to the producer that the culling of seemingly healthy reactors will not be ongoing. These factors combine to make a combined and staged TCP1 and vaccination program a feasible alternative that could be implemented immediately if acceptable to the stakeholders.

We have therefore modelled the implementation of TCP1 for a number of years with staged transition to ongoing vaccination. All scenarios modelled cease the TCP1 test-and-cull component when the first vaccinates attain 2 years of age, thereby preventing any issues relating to differentiating vaccinated from natural infections in ELISA reactors.

12.2 Staged TCP1 and Vaccination Scenarios

Five staged TCP1 and vaccination scenarios were examined.

12.2.1 Test-and-Control Program 1 (TCP1) component

The common features of application of the TCP1 component within each scenario are:

- Calf rearing was undertaken according to the JDCAP/Three-Step Calf Plan rules. These include: (1) removal of calves from dams before 12 hours after birth; (2) managing of the calf rearing area to ensure calves have no contact with the effluent of susceptible species; and (3) rearing calves to 12 months of age on pastures that have not carried adult stock or known BJD-infected stock during the past 12 months.
- Each year all animals aged 2 years or older were submitted for individual ELISA testing. Positive reactors were culled immediately as was the reactor's dam and offspring. Under each scenario, test-and-cull did not continue after the first vaccination age cohort attained 2 years of age.

- Clinical cases of BJD were culled when identified, along with their dam and offspring.

12.2.2 Vaccination Scenario

The common features of the vaccination component within each scenario are:

- Calves were vaccinated with Silirum® at 3 weeks of age. Immunity following vaccination was assumed to take 15 days to develop. Only a proportion of vaccinated and uninfected calves were assumed to respond to the vaccine – i.e. not all were protected. Only those animals that responded were partially protected, once sufficient time (15 days) had passed since vaccination for the development of a competent immune response. The proportion of vaccinated calves that responded to the vaccine was set at 75%. Infected vaccinated non-responders experienced the same sequelae following infection as non-vaccinates.
- Vaccinated responders became partially immune to infection, and had reduced rates of Mptb shedding if subsequently infected. The risk reduction for both of these components was set at 60%, this being the relative reduction in risk compared to non-vaccinated animals. Infected vaccinated responders were also coded to have a 10% increase in the duration of each phase of disease up to, but excluding, the clinical phase. The magnitude of risk reduction, and the extension of pre-clinical phases of disease in vaccinates, was based on estimates obtained from interim analysis of Zoetis Silirum® clinical vaccine trial data.
- Vaccination did not start until 2 years (or less) before the last programmed test-and-cull component.

12.2.3 TCP1 and Vaccination Scenarios

Five scenarios were examined. These are presented in Table 35.

Table 35: Staged TCP1-to-vaccination scenarios modelled

Scenario	Year of first vaccination	Year of first test-and-cull	Year of last test-and-cull	Total test-and-cull years
TCP-1-Vax	1	1	1	1
TCP-2-Vax	1	1	2	2
TCP-3-Vax	2	1	3	3
TCP-4-Vax	3	1	4	4
TCP-5-Vax	4	1	5	5

12.3 Results

The performance of all scenarios described in Table 35 was similar. There was no marked improvement in performance from extending the test-and-cull component for more than 2 years. Because TCP-2-Vax represents the simplest system to implement – both ELISA testing and vaccination can begin on entry to the program – this is presented as the most suitable variant for further consideration.

12.3.1 Physical Performance

The distribution of disease parameters at 5 and 10 years after initiation of a combined test-and-cull (TCP1) component for 2 years only with onset of permanent vaccination of calves in the TCP-2-Vax scenario is presented in Table 36. The test-and-cull component is as described in the TCP1 program (ELISA testing of all animals aged 2 years and older each year with culling of positive animals and high-risk contacts of positive animals). Test-and-cull ceases when vaccinated animals first attain 2 years of age (no ELISA testing of vaccinated animals occurs). The prevalence distribution plot over time is provided in Figure 28 and the faecal shedder prevalence distribution plot over time is provided in Figure 29.

Table 36: Model output at 5 and 10 years after initiation of TCP1 test-and-cull component for 2 years only, with concurrent calf vaccination control scenario (TCP-2-Vax)

Parameter	Year 5		Year 10	
	Mean (range)	Median (IQR)	Mean (range)	Median (IQR)
Avg. no. infected	10.70 (0.00-51.00)	7.00 (3.00-17.00)	1.99 (0.00-29.00)	0.00 (0.00-3.00)
No. new infections	2.13 (0.00-14.00)	1.00 (0.00-3.00)	0.37 (0.00-8.00)	0.00 (0.00-0.00)
No clinicals (year)	0.82 (0.00-6.00)	0.00 (0.00-1.00)	0.24 (0.00-4.00)	0.00 (0.00-0.00)
Avg. no. shedders	9.23 (0.00-43.42)	5.92 (2.58-14.52)	1.68 (0.00-24.33)	0.17 (0.00-2.60)
Prevalence (%)	2.81 (0.00-10.09)	2.61 (1.30-4.01)	0.54 (0.00-5.41)	0.00 (0.00-0.91)
Incidence (%)	0.54 (0.00-3.67)	0.40 (0.00-0.87)	0.10 (0.00-2.67)	0.00 (0.00-0.00)
Clinical incid. (adults - %)	0.31 (0.00-2.40)	0.00 (0.00-0.57)	0.09 (0.00-1.41)	0.00 (0.00-0.00)
Shedder prev. (%)	2.43 (0.00-8.44)	2.28 (1.07-3.52)	0.46 (0.00-5.20)	0.09 (0.00-0.77)

Figure 28: Prevalence distribution plots and trend line over time for TCP-2-Vax scenario

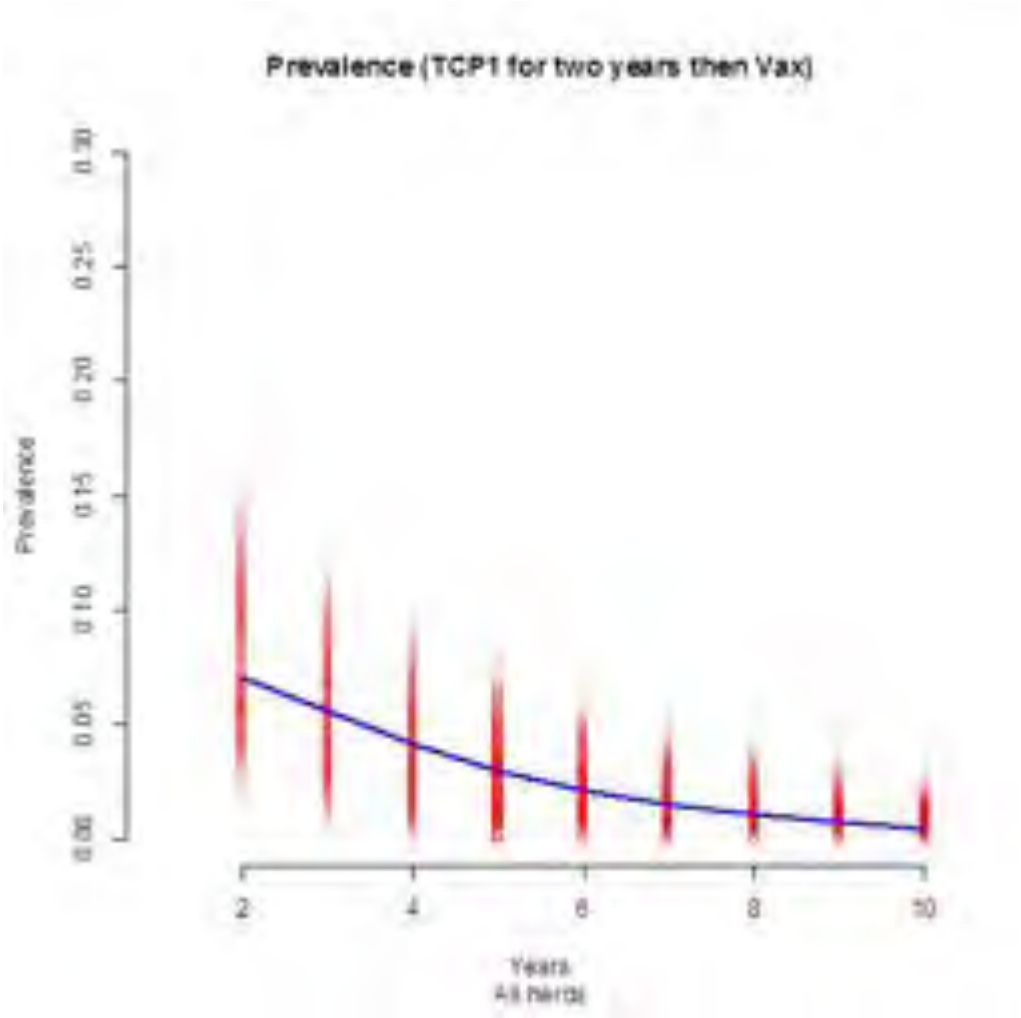
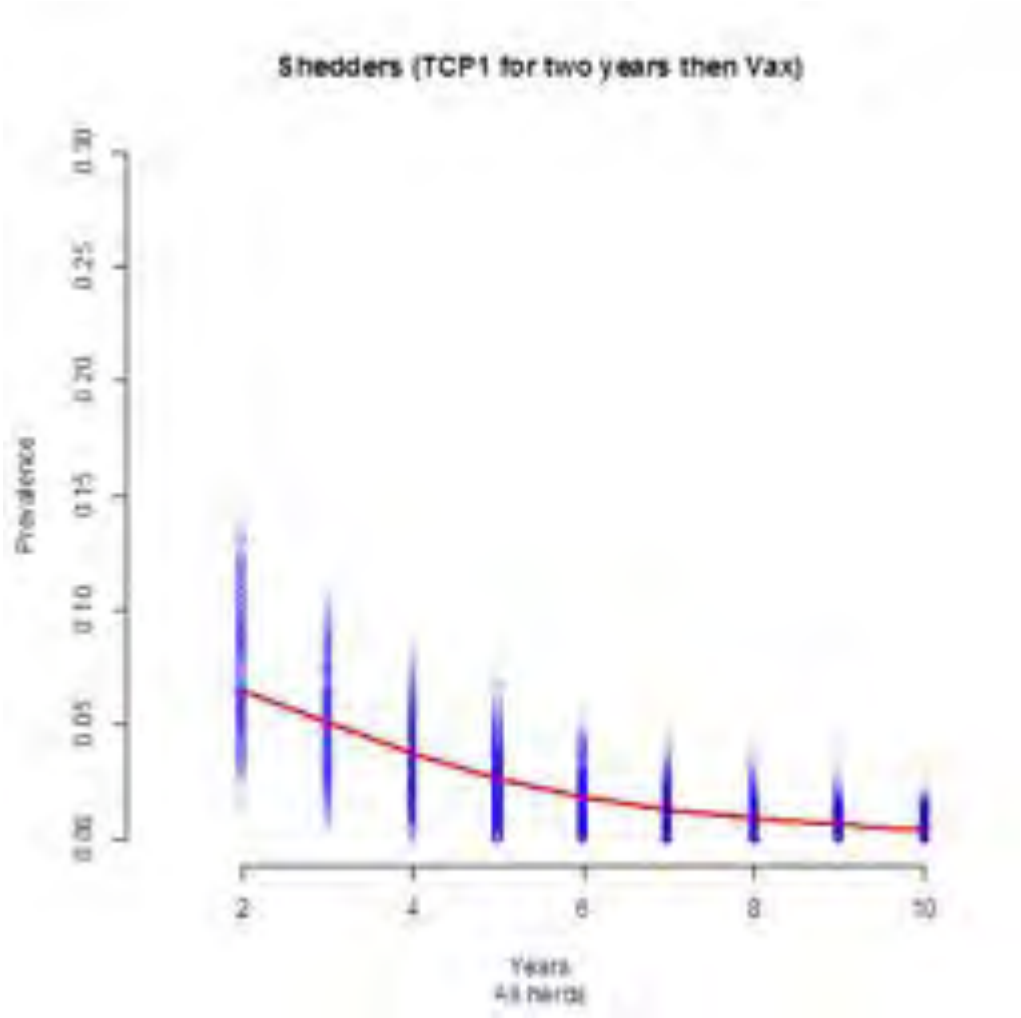


Figure 29: Shedder distribution plots and trend line over time for TCP-2-Vax scenario



Modelling suggests that a high proportion of infected farms may graduate within 10 years under the TCP-2-Vax scenario.

12.3.2 Economic performance

Farm-level: the combined TCP (2 years of test-and-cull) with calf vaccination program appears to be both physically and financially effective. The median 10-year prevalence and clinical incidence is predicted to be below 1.0% on the majority of participating farms. Besides demonstrating real progress to participants in control of disease the economic benefits arising from the reduction in clinical cases is strongly positive. Results for a typical 250 cow Victorian dairy farm under unsubsidised and subsidised vaccination programs are presented in Table 37.

Table 37: Partial budget of annual disease and control costs for BJD for TCP test-and-cull component for 2 years only, with calf vaccination control scenario for a 250 cow dairy herd in Victoria

	Scenario		
Parameter	**Baseline**	**Unsubsidised TCP1 (2 years[a]) and vaccinate (10 yr avg. cost – pa)**	**Subsidised TCP1 (2 years[a]) and vaccinate (10 yr avg. cost – pa)**
Prevalence	8.8%	0.5%	0.5%
Reactor incidence	5.2%	0.25%	0.25%
Clinical incidence	2.6%	0.1%	0.1%
Farm cost	$21,656	$8,454	$6,880
Farm gain (relative to baseline)	-	$13,202	$14,777
Regulatory cost (CCF)	-	$1,263	$3,467[b]
Farm gain + regulatory gain (relative to baseline)	$0	$11,940	$11,310
ROI CCF ($ for $)	-	10.5:1	4.3:1

a – ELISA testing of cattle aged 2 years and older occurs every year in TCP1 for 2 years only.

b – assumes a $10 fee (in addition to the $20 vaccine cost) for the program veterinarian to administer vaccine

Program-level (CCF): the costs and benefits to the Victorian industry at varying levels of recruitment and uptake by infected herds are presented in Table 38. Subsidising vaccination presents a marked increase in the CCF costs for delivery of the program. At 50% recruitment of affected farms, the CCF costs are estimated at a maximum of $1.5M for unsubsidised vaccine increasing to a maximum of $4.1M for subsidised vaccine.

Table 38: Victorian dairy BJD disease and control program costs and benefits for TCP test-and-cull component for 2 years only, with calf vaccination control scenario and at varying levels of uptake by infected farms

Uptake %	Item	Baseline	Unsubsidised TCP1 (2 years[a]) and vaccinate (10 yr avg. cost – pa)	Subsidised TCP1 (2 years[a]) and vaccinate (10 yr avg. cost – pa)
5%	Farmer cost ($ mill.)	51.3	50.1	49.9
	Program (CCF) cost ($ mill.)	0.00	0.15	0.41
	Total farm cost ($ mill.)	51.3	50.2	50.3
	CBA (c.f. Baseline $ mill.)	-	1.08	1.01
	CCF ROI ($ for $)	-	7.16	2.45
25%	Farmer cost ($ mill.)	51.3	43.8	42.9
	Program (CCF) cost ($ mill.)	0.00	0.76	2.05
	Total farm cost ($ mill.)	51.3	44.5	44.9
	CBA (c.f. Baseline $ mill.)		6.76	6.39
	CCF ROI ($ for $)	-	8.93	3.11

Uptake %	Item	Baseline	Unsubsidised TCP1 (2 years[a]) and vaccinate (10 yr avg. cost – pa)	Subsidised TCP1 (2 years[a]) and vaccinate (10 yr avg. cost – pa)
50%	Farmer cost ($ mill.)	51.3	35.9	34.1
	Program (CCF) cost ($ mill.)	0.00	1.51	4.11
	Total farm cost ($ mill.)	51.3	37.4	38.2
	CBA (c.f. Baseline $ mill.)		13.86	13.11
	CCF ROI ($ for $)	-	9.15	3.19
75%	Farmer cost ($ mill.)	51.3	28.1	25.3
	Program (CCF) cost ($ mill.)	0.00	2.27	6.16
	Total farm cost ($ mill.)	51.3	30.4	31.5
	CBA (c.f. Baseline $ mill.)		20.96	19.83
	CCF ROI ($ for $)	-	9.23	3.22

However, because a high proportion of participating farms are expected to graduate total annual expenditure on the program is likely to be less than the maximums predicted above. Farms that leave the program on graduation incur no further costs. There are approximately 4,200 dairy herds in Victoria with around 50% thought to harbour BJD (2,100 herds). Under the assumption that at most only 50% of infected farms would join a new TCP (2 year) and vaccination BJD program and at an annual herd recruitment rate of 5% of infected farms the maximum annual CCF outgoings are predicted at $1.3M for unsubsidised vaccine and $3.5M for subsidised vaccine – both occurring in year 10 of the new program. The predicted peak annual costs are slightly less than the maximums predicted assuming all recruitments occur in the first year of the program. Cash flow predictions suggest that annual costs will decline after peaking in year ten as (successful) graduations begin to occur and accrue. Results for the first twenty years of the program are presented in Table 39.

Table 39: Predicted program enrolments and CCF program costs for TCP (2 years) and vaccination (subsidised and unsubsidised) at 5% maximum new recruitments per year and 50% maximum cumulative recruitment of infected farms

Year	No. farms recruited	Cum. total recruited	No. farms graduating	Cum. Total graduated	Total farms enrolled	CCF cost (Unsubs. Vax)	CCF cost (Subs. Vax)
1	107	107	0	0	107	$414,310	$650,121
2	107	214	0	0	214	$828,620	$1,300,242
3	107	321	0	0	321	$893,930	$1,601,363
4	107	428	0	0	428	$959,240	$1,902,483
5	107	535	0	0	535	$1,024,550	$2,203,604
6	107	642	0	0	642	$1,089,860	$2,504,725
7	107	749	0	0	749	$1,155,170	$2,805,846
8	107	856	0	0	856	$1,220,480	$3,106,967
9	107	963	0	0	963	$1,285,790	$3,408,088
10	107	1070	75	75	995	$1,305,322	$3,498,142
11	0	1070	75	150	920	$910,544	$2,938,076

Year	No. farms recruited	Cum. total recruited	No. farms graduating	Cum. Total graduated	Total farms enrolled	CCF cost (Unsubs. Vax)	CCF cost (Subs. Vax)
12	0	1070	75	225	845	$515,766	$2,378,010
13	0	1070	75	300	770	$469,988	$2,166,944
14	0	1070	75	375	695	$424,210	$1,955,878
15	0	1070	75	450	620	$378,432	$1,744,812
16	0	1070	75	525	545	$332,654	$1,533,746
17	0	1070	75	600	470	$286,876	$1,322,680
18	0	1070	75	675	395	$241,098	$1,111,614
19	0	1070	75	750	320	$195,320	$900,548
20	0	1070	0	750	320	$195,320	$900,548

12.4 Discussion

Whilst a staged combination of test-and-cull and vaccination appears to be both physically and financially effective, barriers to farmer participation still remain. The program must recruit a large proportion of infected farms if it is to meet the objectives of CCF involvement. There is a widespread and long-standing dissatisfaction and mistrust of the existing TCP3 program. This is compounded by the commonly held belief that farmers with the disease are better off not declaring their status and thereby allowing them to continuing to trade in cattle, to secure and provide agistment and, most importantly, to sell surplus heifers to the live export trade. The low rates of program graduation have led many farmers to believe that a diagnosis of BJD on their property is a life sentence.

For any modified test-and-cull and vaccination program to be successful, and to ensure there are adequate (and satisfied) recruits, it is critical that the economic impacts of uncontrolled disease compared to controlled disease be strongly marketed and advertised to the farming and support community. This must be supported by provision of a herd-level test that can allow vaccinating herds to graduate – that is to demonstrate that disease cannot be detected in the herd. Given the current SDRGs, we recommend that the HEC test be used to determine shedding status of the herd after a minimum of 7 years of the program. The provision of three annual and consecutive negative whole herd HEC tests should be the criterion for graduation. The HEC test will need to be accepted for this use within the SDRGs if this is to be possible.

We also advise that all components of the test-and-cull and vaccination program be fully subsidised for 10 years. This equates to two whole-herd ELISA tests, 10 years of calf cohort vaccinations, annual inspections and audits by the program veterinarian and at least three HEC tests. This approximated to two ELISA tests and two vaccinations for each milking cow as well as three herd HEC tests and ten annual veterinary audit fees. Using the costs listed in Table 20, and with the HEC test cost estimated at $200 per test (including the veterinarian's time), this equates to approximately $26 in ELISA tests and $70 in vaccination cost per milking cow ($100 per milking cow across 10 years) plus approximately $200 per year for veterinary audit and inspections costs ($2,000 over ten years) for herd-level costs. Therefore, a 250-cow herd would be expected to cost in the order of $26,000 over 10 years or approximately $2,600 per year.

12.5 Conclusions

The application of the test-and-cull component for 2 years with concurrent introduction of vaccination provides the best compromise between program effectiveness (2 years of removal of ELISA reactors, shedders and high-risk contacts), ease of administration (both test-and-cull and vaccination begin in the first year), acceptability for farmers (limited culling of reactors, rapid prevalence knock-down) and cost-effectiveness for CCF funds.

Annual recruitment targets should be set to both maximise efficiency of physical resources and to manage current and future CCF cash flows. This approach also provides opportunity to optimise the recruitment and training of veterinarians and farmers thereby giving the best chance for high levels of commitment and compliance by participating farmers and their TCP veterinarians.