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Enhanced early detection of Tb through use and integration of wildlife data into the national surveillance model

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Summary

Project and Client

Landcare Research, New Zealand, and Peter Caley, ANU, Australia, developed a conceptual framework for wildlife surveillance for bovine tuberculosis (Tb), management in New Zealand, for the Animal Health Board (AHB), to aid the AHB in making objective and justifiable decisions about when to stop Tb surveillance. The project was conducted between July 2004 and July 2006.

Objectives

To design a new approach to Tb surveillance based on increased use of wildlife data in conjunction with livestock testing, by:
- developing a theoretical framework for objectively assessing the adequacy of livestock-based surveillance, and assessing how much wildlife surveillance is needed to complement livestock testing;
- modelling the likely costs and benefits of ongoing wildlife surveillance in relation to the intensity of livestock testing ; and
- developing an analytical framework for assessing overall likelihood of Tb persistence by integrating information on disease surveillance from multiple sources.

Results and Conclusions

We developed a new spatially explicit approach to determining the sensitivity and coverage of wildlife surveillance. We first defined P_d as a measure of surveillance sensitivity that represents the probability that a specified minimum number of Tb-infected animals would have been detected, if present, given the amount of sampling undertaken during a particular surveillance episode. We then represented the distribution in space of the contribution to P_d by each individual sentinel as "detection kernels", based on the available data on home range size. An overall or 'whole survey' estimate of surveillance sensitivity that automatically takes in account the adequacy of survey coverage, P_{dc}, is determined simply by summing individual detection kernel contributions from each sampled individual to produce a probability surface over the area of interest. This spatial approach to defining the sensitivity of wildlife surveillance also provides the flexibility to combine data from different wildlife species into a single estimate of P_{dc} for the area of interest.

Illustrative first-approximation estimates of detection kernels were derived for each of the main wildlife sentinel species (wild pigs, deer and ferrets) using distances between consecutive radiotelemetry locations. In addition, initial ball-park estimates of the annual risk of an individual sentinel being infected, given exposure to a single focus of infection within its home range, were derived from field data. Only 0.4% of deer exposed to a single infected possum within their home range appear likely to become infected. Ferrets appear to be approximately 21 times more likely than deer to detect a single infected possum within their range, and pigs appear to be at least 60 times more sensitive than deer as sentinels. Livestock testing was estimated to have an approximate sensitivity of 0.20–0.25 (i.e. less than a quarter of infected possums on farms resulted in new cases of Tb in livestock).

We conclude that decisions about whether to stop vector control, and livestock wildlife surveillance can all be based on estimates of the probability that Tb has persisted undetected (P_{utb}). The belief that Tb has persisted undetected can be easily updated using Bayes theorem, which can also incorporate uncertainties in the sensitivity of surveillance and diagnostic testing. Hypothetical examples show that annually repeated moderate-sensitivity wildlife surveillance, coupled with herd testing data, would rapidly increase confidence that Tb was absent. Where Tb management is applied to small areas, Tb may be reintroduced and/or be present as a latent infection in residual wildlife. The estimate of P_{utb} can be adjusted to reflect this additional risk by using the technique of temporal discounting in a modification of Bayes theorem to incorporate the probability of Tb introduction.

Recommendations

We recommend that the AHB adopt the core principles of the framework outlined in this report, and determine the practicality and utility of the proposed surveillance framework through trial implementation in 2–3 contrasting areas. The core principles are that:

- decisions about whether to start or stop vector control, wildlife surveillance, and livestock testing all be based on quantitative estimates of managers' belief that Tb has persisted undetected;
- first (prior) estimates of the probability of Tb absence be based on predictions of a spatial simulation model of Tb in possums using empirical data from possum population monitoring;
- a Bayesian updating framework be used to integrate this prior belief with surveillance data from herd-testing and/or wildlife surveillance;
- a spatially explicit approach to wildlife surveillance be used. This approach is based on the characteristics of each species as a sensor for detecting Tb.

Unless vectors such as deer (which can sometimes survive for over a decade while infected) are rare or absent, the minimum duration of possum control be set at 5–7 years to reduce the chance that Tb could persist as a latent infection in residual deer populations.

Decisions about when to stop Tb management and/or surveillance should be based either (i) on finding the optimal number of clear surveillance episodes that minimises the net expected costs associated with Tb management, or (ii) on using a conservative 'get it right first time' stopping rule based on combining consecutive clear surveillance episodes until $P_{utb} < 0.01$.

Decisions about when to stop vector control or surveillance should be applied to Vector Risk Areas (VRAs) as a whole, or to large management units within them of about 100 000 ha or greater, to minimise the likelihood of Tb being reintroduced. When applying stopping rules to smaller management sub-areas, temporal discounting should be used in the calculation of P_{utb} to allow for the possibility that disease may be introduced from neighbouring VRAs.

Further research and development is required to (i) improve and/or verify our preliminary estimates of the key parameters of the detection kernels (and whether they vary greatly between habitats and between the sexes), and the relative sensitivity of each species as sentinels; (ii) further develop the new theoretical basis for use of sentinels; (iii) provide end users with the tools needed to apply the proposed surveillance framework.

1.   Introduction

Landcare Research, New Zealand, and Peter Caley, ANU, Australia, developed a conceptual framework for wildlife surveillance for bovine tuberculosis (Tb), management in New Zealand, for the Animal Health Board (AHB), to help the AHB make objective and justifiable decisions about when to start or stop Tb management. The project was conducted between July 2004 and July 2006.

2.   Background

Possums, and in some places ferrets, are now the only true maintenance hosts of Tb in New Zealand. Livestock, wild deer, feral pigs and most ferrets are spillover hosts, either because of their low density or their intrinsic nature as hosts, or because regular testing and removal of infected individuals (in the case of livestock) continually breaks the potential reinfection cycle. In that sense then, Tb in New Zealand is now primarily a wildlife disease.

Although until recently the Tb surveillance programme relied very largely on the national livestock-testing scheme, wildlife are increasingly being surveyed, with $1.82 million spent on wildlife surveys in the 2003/04 year (Animal Health Board 2005).

Recent research has identified that spillover hosts such as pigs, ferrets, and deer are potentially useful as Tb sentinels, with clear indications that the scavenger species (pigs and ferrets) are likely to provide the best indicators of Tb presence (Nugent et al. 2002; Caley 2003). Research on wildlife surveillance in New Zealand has so far focussed mainly on improving the tools available, either by assessing which host species are the best sentinels (Nugent et al. 2001), or by using bioeconomic analyses to identify optimal designs for surveys of Tb in wildlife (Ramsey 2003). This research has not been well coordinated, partly reflecting the lack of an overarching theoretical framework for the use of sentinels, and, indeed, for surveillance generally. This report endeavours to overcome that lack.

It does that first by considering the goals of Tb management, and then by developing a system for interpreting data from surveys that do not detect Tb. Such outcomes can reflect either genuine Tb absence or a failure to detect Tb that is present. It will rarely, if ever, be possible to have complete certainty that all wild animals are free of Tb. The primary focus is therefore on quantifying the probability that Tb would have been detected if it were present, and then on integrating such data across a variety of different information sources.

The concepts presented here were initially developed in the form of a discussion document in July 2005. That document was then evaluated at a workshop involving the researchers and senior AHB staff in October 2005. The purpose of the workshop was to guide subsequent refinement and further development of the initial ideas deemed likely to be most useful and practical. This report summarises the outcome of that work.

3. Objectives

To design a new approach to Tb surveillance based on increased use of wildlife data in conjunction with livestock testing, by:

- developing a theoretical framework for objectively assessing the adequacy of livestock-based surveillance, and assessing how much wildlife surveillance is needed to complement livestock testing;
- modelling the likely costs and benefits of ongoing wildlife surveillance in relation to the intensity of livestock testing ; and
- developing an analytical framework for assessing overall likelihood of Tb persistence by integrating information on disease surveillance from multiple sources.

4. Results

4.1 The problem

Tb has continued to spread, at least until very recently, and the AHB currently lacks the resources to simultaneously tackle the disease everywhere it exists. The priorities are therefore (i) to prevent or minimise the effect of new outbreaks in expanding the infected area by quickly detecting Tb whenever it occurs in new areas, and (ii) to redirect resources at the earliest sensible time from areas where Tb has been successfully eradicated.

These decisions can be made objectively by estimating values for two probabilities: the probability that Tb has persisted undetected (P_{utb}); and the probability Tb would have been detected by a given surveillance effort (P_d) if Tb was present in the area surveyed. The central objective of Tb surveillance will usually be to minimise P_{utb}. Once an estimate of P_{utb} is available, Tb managers can decide whether the risk of Tb still being present is low enough to declare eradication, or, if not, they can use the data to determine the optimum amount of additional surveillance needed to be able to make that declaration. Both scenarios are explored in this report.

4.2 Key concepts and definitions

We begin by outlining some core concepts, and defining key terms as used specifically in this report. Where possible, we illustrate those concepts with estimates of key parameter values.

Surveillance
To avoid confusion with monitoring of animal presence (e.g., trap-catch monitoring for possums), the term surveillance is used here specifically to mean the carrying out of wildlife surveys and livestock testing to identify the likelihood of Tb presence in the sample population.

Maintenance hosts

Maintenance hosts are capable of independently sustaining Tb. In New Zealand they are untested livestock (cattle and deer), and possum and ferret populations that in at least part of the area of interest exceed the density threshold for disease persistence in that species.

Spillover hosts

These are not capable of independently sustaining Tb. In New Zealand they include regularly tested livestock, low-density possum and ferret populations, and pigs and deer at any density. The minor hosts such as cats, stoats, and hedgehogs are also spillover hosts. Although spillover hosts cannot independently sustain Tb, they can carry disease through time and space and then pass it on to a maintenance host. The duration of this risk of transmission between resident animals is longest (about 10–12 years) for wild deer (Nugent 2005) and probably much the same for regularly tested but anergic livestock. For pigs, it is usually shorter, simply because the longevity of feral pigs is shorter than for deer. Most pigs are killed by hunters at a young age, with Dzieciolowski and Clarke (1989) reporting the average age at death of pigs in the northern South Island of < 1 year.

Sentinel

A sentinel species is one that is surveyed to determine Tb prevalence in another species that is a true maintenance host. Sentinels are usually spillover hosts, but possums, cattle, and deer can also be used as sentinels when their densities are too low, or when they are tested too frequently, to able to sustain Tb.

Probability of Tb persisting undetected (P_{utb})

This is the probability that Tb persists in the maintenance host population of interest (usually possums) despite not being detected by surveillance. The central goal of Tb management is to minimise P_{utb} directly or to minimise net expected costs associated with attaining a specified P_{utb}. P_{utb} can be reduced by (i) reducing the likelihood of Tb persisting in an area through culling of infected livestock and reduction in density of susceptible wildlife maintenance hosts to below the level at which they are able to sustain continued Tb transmission, and/or (ii) reducing the likelihood of non detection through surveillance of livestock and/or wildlife.

Probability of Tb detection (P_d)

This is the probability that a specified number of Tb-infected animals would have been detected, if present, given the amount of sampling undertaken during a particular surveillance episode. We will also refer to P_d as surveillance sensitivity. P_d will usually relate to Tb presence in the host that is ultimately responsible for sustaining infection when Tb has been reduced to low levels. In New Zealand that will usually be the possum. In setting the specified number of Tb-infected animals that forms the target for detection, we are interested in the most difficult case for detection. That occurs when Tb is persisting in only a single focus of infection in which there is just enough ongoing transmission to stop prevalence declining to zero. In this report, we set the target for possums as a single focus of infection that produces a minimum of one infected animal per year.

For a survey of a management area of size A, P_d will refer to the probability of detecting a single focus of infection residing somewhere within A. Hence, P_d is dependent not just on the number of animals sampled, but also on the coverage (C) as a proportion of A. The estimate of P_d that incorporates C is designated as P_{dc}.

Coverage

Coverage (C) is the proportion of the area of interest that has been surveyed. This is a crucial parameter, especially in relation to P_d, as by definition P_d is zero in areas not subject to surveillance and thus, such areas could have a disproportionate effect on the estimate of P_{utb} for the area as a whole.

For surveillance based on livestock testing, coverage is simplistically defined as the proportion of the area that is within the boundaries of the farms on which livestock are tested. For surveillance based on surveys of free-ranging wildlife, coverage is determined by the 'detection kernel' of the sex and age class of the sentinel species used for surveillance (*see below).*

Detection kernel

The detection kernel is a 2-dimensional probability distribution that defines the area around the location where the sentinel was killed (or tested) within which it has a specified probability of having acquired Tb. The area under the kernel is determined by home range size, but is larger than the home range because the sentinels will seldom be sampled at their home range centre. Thus, the detection kernel incorporates uncertainty about where the true home range was located and, hence, where the sentinel could potentially have acquired Tb. We estimate detection kernels for the main sentinel species in the next section.

Relative sensitivity

This parameter reflects the different likelihood each species of sentinel has of becoming infected when they are exposed to similar levels of infection in the possums or ferrets that from the primary reservoir of Tb. We define this as the net annual force of infection per sentinel (λ_y) given continuous exposure, on average, to an average of one infected possum within their home range. This takes into account the differences between species in rate of transmission per encounter with infected possums. It also subsumes the rate at which infection is 'lost' through either Tb-induced mortality or recovery from infection. Estimates of this parameter are outlined in detail in the next section.

Exposure per sentinel

Each sentinel species has a different life span, and is, on average, potentially exposed to infected possums for differing lengths of time, so the relative sensitivity as sentinels must be adjusted for age (in years). For livestock it is the average time since the last test, while for wildlife it is the age when killed at necropsy minus the so-called guarantee periods of 1.75 months for ferrets (Caley 2001) and 9 months for deer (Nugent 2005) when newborn young are not susceptible to becoming infected. The net force of infection in deer also declines to low levels beyond about 5 years of age (p. 47 in Nugent 2005), so we arbitrarily recommend all deer older than this should be classed as being 5 years old when calculating total exposure. This will slightly underestimate the true value of old deer as detectors, so P_d will be conservative.

4.3 Estimates of parameters

To illustrate quantitatively how herd testing and the movement and epidemiological characteristics of wildlife hosts could be incorporated with wildlife surveillance data to estimate the probability of Tb absence in wildlife, we derived ball-park estimates for key parameters using currently available data. These should not be treated as definitive estimates,

but as first approximations that will require verification and refinement before they can be used operationally.

Detection kernel

The spatial extent of the detection kernel can be estimated from the type of location data often used to estimate home range size. To illustrate, each location for 15 radio-collared feral pigs released into Hochstetter Forest was assumed to be equally likely to be the location where it nominally acquired Tb, and every subsequent location as the site where it was nominally killed and sampled (Figure 1). The frequency distribution of all possible pairs of these nominal Tb acquisition-to-sampling distances (r) was calculated for each individual. Comparisons of these frequency distributions suggested no differences between the sexes so data for each individual were combined. A half-normal density distribution (Appendix 1) was fitted to the combined frequency distribution using maximum likelihood to estimate the spatial scale of the detection kernel (σ) (Figure 2, Table 1). All the pigs were infected when they were killed and necropsied. The analysis indicated that 95% of the previous locations of these pigs were within 7.8 km of where they were nominally killed (i.e. radius of 2.45σ). Thus, it follows that the detection kernel for pigs in this type of forest can be modelled using a circular bivariate-normal probability density ($g(r)$) with spatial scale σ.

A similar analysis for six young female deer and two young male deer radio-tracked in Hochstetter Forest (Figure 2) showed the male deer had similar detection distributions to the released pigs ($\sigma = 3.6$ km), whereas those of females were approximately two-thirds smaller ($\sigma = 1.1$ km), resulting in only one-ninth the coverage (Table 1). An analysis undertaken for nine radio-collared ferrets in the Featherston area of the North Island showed that ferrets in this area had a smaller average detection kernel than did the examples for pigs and deer (Table 1).

It is likely that the estimates of r and σ will vary with sentinel density and habitat as well as species and sex. The estimates in Table 1 are indicative 'ball-park' figures that may not be accurate in areas in which the habitat and densities differ greatly from those in which the data were collected. Nonetheless, they suffice to illustrate the concepts involved.
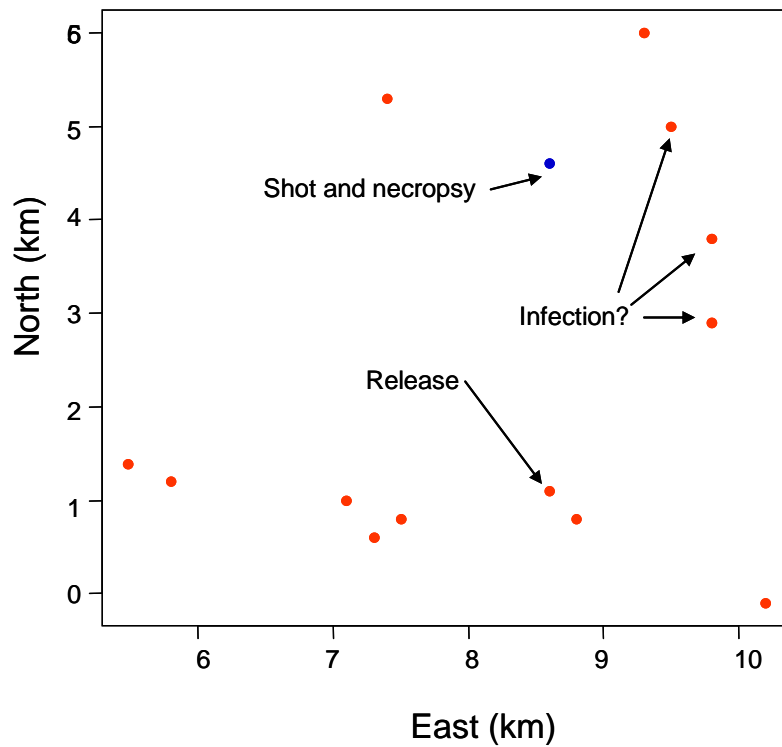
Fig. 1 Locations of one radio-collared Tb-free feral pig released into the Hochstetter forest, which was subsequently found to be infected when shot and necropsied. Any of the 12 intervening locations may have been the location where it acquired Tb. The distribution of distances between all nominal 'infection' locations and subsequent locations where it was nominally 'sampled' was used to estimate the spatial scale of the detection kernel.

Table 1 Estimates of σ, the spatial scale of the half-normal probability density (Appendix 1) fitted to the frequency distribution of distances between nominal infection locations and nominal sampling locations.

Species	σ (km)	s.e.	number of animals
Pigs	3.2	0.384	15
Red deer (male)	3.6	0.188	2
Red deer (female)	1.1	0.052	6
Ferrets	0.6	0.080	9
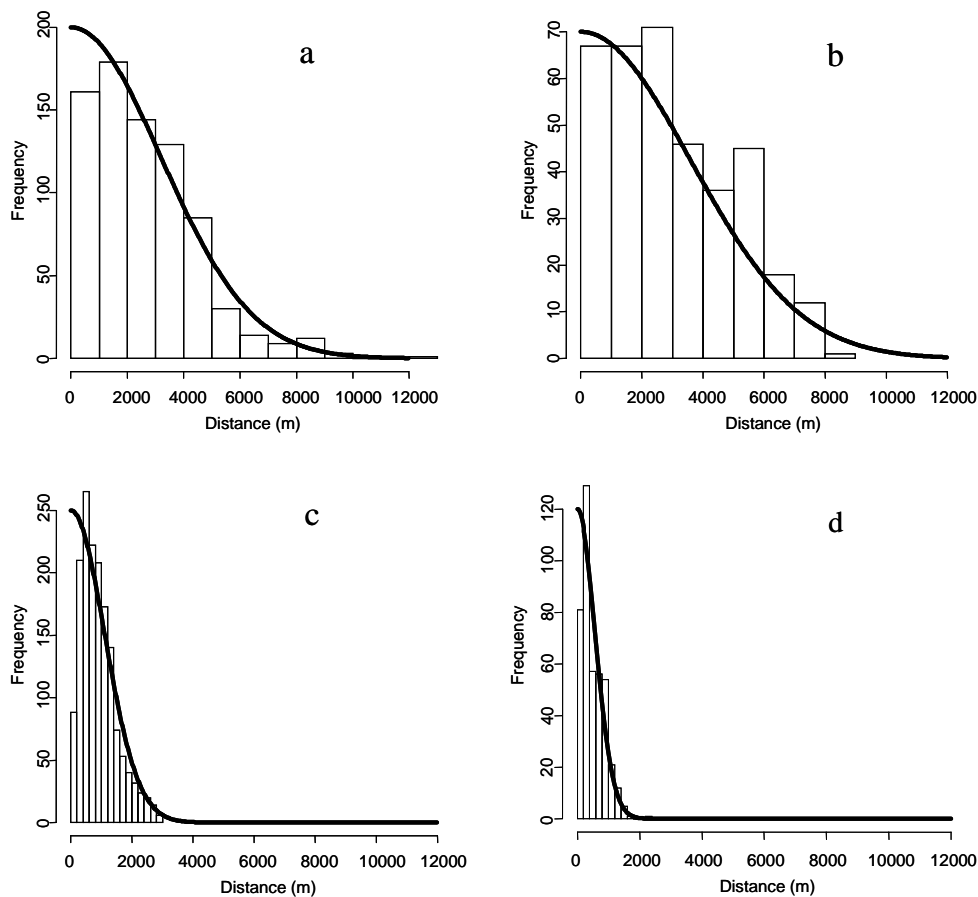
Fig. 2 Frequency distributions of relevant distances for radio-collared (a) feral pigs, (b) male red deer, (c) female red deer, and (d) ferrets. A distance was calculated for each pair of observations that potentially represented a site at which the animal could have acquired Tb and another site at which it could have been killed and necropsied. The solid line represents the best fit for a half-normal probability density with spatial scale (σ) as given in Table 1.

Relative sensitivity of sentinel species

The annual risk or hazard to each sentinel when exposed to a single focus of infection within its home range that contained on average just one infected host over the period of a year year (λ_y) was estimated from field data. The process is outlined in detail in Nugent (2005).

Using deer to illustrate the process, we used a deer density estimate from part of the Hauhungaroa Range, central North Island, to calibrate an index of deer abundance based on faecal pellet group density (Nugent et al. 1997). Based on this, pellet group density data were converted to deer density estimates for three areas (Eastern Hauhungaroa 1993/94; western Hauhungaroa 1997–2000; Hochstetter Forest 1997–2000; sources: Fraser et al. 1995; Coleman et al. 2000; Nugent 2005). Likewise, possum density estimates for these areas were estimated from either published data (Nugent et al. 1997, Nugent 2005), or by converting available trap catch data using a modelled calibration between trap catch rate and density (Ramsey et al. 2005).

We then obtained an estimate of the annual Tb incidence rate in deer. The estimate was derived from age-specific prevalence data obtained from cross sectional surveys of Tb infection in deer in these three areas (Nugent 2005). We restricted the analysis to deer less than 5 years old to remove the effect of loss of infection due to mortality or resolution. This indicated that about 17% of susceptible deer in the eastern Hauhungaroa Range in 1993/94, for example, were becoming infected each year

Simplistically combining data for both sexes, we assumed an average home range size for red deer of 3.7 km^2. Assuming possum densities of 400/ km^2 in the eastern Hauhungaroa Range in 1993/94, deer shared their ranges with about 1400 possums, of which we assumed 2% (~30) were infected. We then calculated the mean annual incidence of Tb in possums per deer home range by assuming the possum prevalence estimate was steady-state using the formula

$$I = \frac{P}{D}$$

where I is the annual incidence rate of Tb in possums, P is the steady-state prevalence estimate, and D is the duration of disease in possums, which we assumed was about eight months (Ramsey & Cowan 2003). Based on these calculations and parameter estimates, each deer was exposed to roughly 40 new cases of infection in possums each year, but only about one in six of the deer became infected each year. Despite uncertainty about the accuracy of the underlying assumptions, it is clear that the probability of an infected possum transferring infection to a sympatric deer is very low. We calculate that the average annual risk per deer with a single infected possum within its range (λ_y) in only about 0.004/year (Table 2). Estimates for pigs, and ferrets were also calculated (Table 2). Although these calculations are fairly crude, they leave little doubt that there are very large differences in the likely relative sensitivity of different wildlife hosts as sentinels of Tb in possums. Pigs are by far the most sensitive sentinel. They appear to be at least 2–3 times more sensitive than ferrets, which in turn appear to be at least 20 times more sensitive than red deer when exposed to similar levels of infection in possums.

Table 2 Estimates of the annual risk of infection for different wildlife sentinels when exposed to a single infected possum within their home range (λ_y).

| Species	λ_y	[1]Relative Risk
Red deer	0.004	1
Ferrets	0.085	21
Pigs	0.229	64

[1] Relative risks are relative to Red deer

If we assume that at low-moderate densities, infected possums share their ranges with two other possums on average and pass on Tb to one of those, it is likely that λ_y for possums would be of the order of 0.5, higher than for pigs. However, this high sensitivity in detecting infection in sympatric possums is greatly overshadowed by the smallness of the detection kernel. Although not calculated here, the detection kernel for possums will inevitably be very small because possum home range size is typically 2–3 orders of magnitude smaller than the sizes for pigs, deer, and ferrets. The home range of each individual possum therefore has a much lower probability of including the one surviving focus of infection we assume is still present. Thus, the utility of possums as sentinels is therefore much reduced because each individual covers a much smaller fraction of the survey area than do individual pigs, deer, and ferrets. This makes the point that overall utility of a species as a sentinel is determined by the combination of detection kernel size and the relative sensitivity to infection.

Sensitivity of herd testing

It is believed that >90% of infection detected in livestock nowadays is acquired from wildlife (Ryan et al. 2006). Unfortunately there has been no direct measurement of the sensitivity of livestock as sentinels. To obtain an illustrative estimate, the national livestock testing records for the 1995–2003 period were used to identify temporally isolated outbreaks. We made the assumption that such isolated breakdowns would be caused mainly by the presence of a single infected possum or ferret on the property. Isolated breakdowns were defined as short-lived outbreaks of infection in herds that had not had infection detected in the previous two years, and which subsequently returned to clear tests within one year. Deleting records for farms in which infection was possibly or known to be bought in or residual, a total of 890 herds were identified for which no other source than wildlife was suspected. The frequency distribution for the numbers of infected animals was broadly similar for all farming types (Figure 3).Overall 78% of these herds had a single Tb cases, 95% had 3 or fewer, and 99% had eight or fewer. This frequency distribution was used to estimate the proportion of herds presumed to have had an infected possum present but which had no resulting cases of infection.

This figure was estimated by transforming the percentages of herds in each case-number class to achieve linearity, and then simulating the number in the zero-cases class to obtain the best possible fit (Figure 4). The best fit was obtained when the number of zero-case herds was assumed to be about 2900, roughly three times the number of herds observed with one or more cases of Tb. This crude data model therefore suggests that only a quarter of the infected possums that are sympatric with livestock actually pass on Tb that is subsequently detectable by livestock testing. That suggests the P_d for livestock is about 0.25 when the whole herd is used as the sampling unit. Caley (2003) derived a broadly similar estimate (~0.20) for ferrets

by analysing the effect of varying levels of infection in ferrets on the reactor rates in sympatric cattle herds.
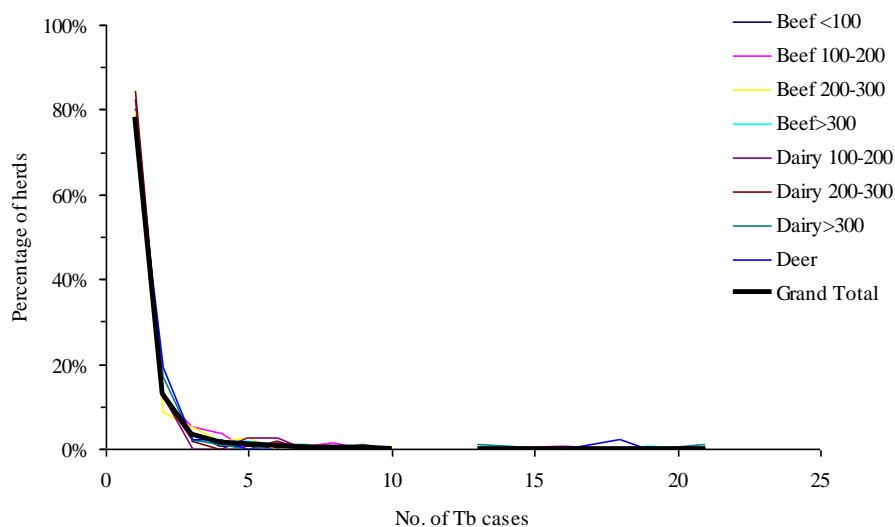
Fig. 3 Standardised frequency distribution of the numbers of herds per "No. of Tb cases" class, by herd type and size and overall
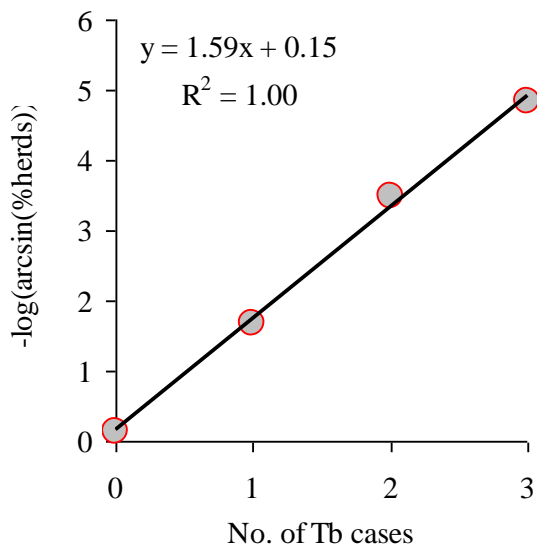
Fig. 4 Regression line predicting the $-\log_e$ (arcsine) transform of the percentage of presumed transmission-risk events that were not detected by livestock. Only data from herds with 1–3 cases actually observed were in used the simulation. These include 95% of the actual observations. Using the herds with greater numbers of Tb cases produced regression models that were less sensitive to variation in the simulated zero cases class.

4.4 Estimating probabilities of detection (P$_d$) from large-scale surveys of sentinels

Non-spatial approximation

Given the relative sensitivities of sentinels estimated in the preceding section, what is the probability of detecting Tb given a particular number of sentinels surveyed? The probability of detection (P_d) can be estimated very simply if the whole area is sampled evenly and the proportion of the sentinel population surveyed can be estimated. Unfortunately, the density of deer and pigs, and, to a lesser degree, that of ferrets and possums is difficult (and expensive) to measure accurately and precisely.

Consider the problem posed by the spread of Tb into the southern Urewera Ranges, central North Island, and assume a 900-km^2 (30 x 30 km) area of mixed broadleaved forest native forest with an average of 10–11 possums per ha, with just 1 possum infected. Each possum has about one chance in a million of being infected. Randomly surveying 10% of the population (100 000 possums) would probably cost in excess of $2 million yet provide just 10% confidence that no possum was infected and only 7% confidence if the field necropsy procedures routinely detected infection in only 70% of infected possums. Even the presence of 5 infected possums each year within our single hypothetical focus within the 900-km^2 surveillance area would represent a 0.000005% (5/1 000 000) period prevalence, a daunting target to try to detect if surveillance was confined to sampling possums.

Would more wide-ranging sentinels be more useful? We assume that the area occupied by our hypothetical focus of infected possums is just 5–10 ha. This effectively forms a point source of infection within the home range of species such as pigs and deer.

For any sample of n sentinel species sampled randomly within the survey, the estimate of P_d is given as

$$P_d = 1 - \prod_{i}^{n} (1 - P_i) \qquad\qquad \text{Eqn 1}$$

where P_i is the probability that the sentinel would be infected, given that its home range contains an infected possum. P_i is estimated as

$$P_i = 1 - e^{-\lambda_y (a_i - g)} \qquad\qquad \text{Eqn 2}$$

where a_i is the age of the ith individual sentinel when sampled minus the guarantee time g (the period during which a new born sentinel is not exposed to infection) and λ_y is the estimate of relative sensitivity (λ home range^{-1} year^{-1}) calculated in the previous section. Equation 1 is based on binomial sampling theory, and assumes that animals are sampled randomly throughout the area. It will overestimate P_d if some of parts of the area are not sampled because sentinels are absent or for some reason are difficult to obtain there. Unfortunately, the size of this bias cannot be accurately determined without information on the spatial location of sampled animals. Assuming a survey area of size A, and a sentinel home range size of H, a rough approximation of the coverage can be calculated by assuming animals have been uniformly sampled across the survey area using

$$C = \frac{nH / A}{1 + nH / A} \qquad\qquad \text{Eqn 3}$$

Using this to adjust for uncovered areas, the estimate of P_d for the whole survey is now

$$P_{dc} = P_d C \qquad \qquad \text{Eqn 4}$$

where P_{dc} is the probability of detecting a single cluster of infection, given it is located somewhere within area. Using estimates of the spatial scale of the detection kernel (σ) from Table 1 and estimates of λ_y from Table 2, the estimates of P_{dc} from a 90 000-ha management area for each of pigs, male and female red deer and ferrets are given in Figure 5.

Because Eqn 3 provides an approximation of coverage based on an assumption of uniform sampling that will usually be unrealistic, Equation 4 should be used to estimate P_{dc} only where the spatial information on the locations of sampled animals is not known or is believed to be uniformly distributed. However, its advantages are that it is easy to compute and should perform fairly well if the locations of sampling are indeed uniform. A comparison of this non-spatial approximation with the spatially explicit estimate of P_{dc} outlined in the next section is given in Appendix 2.
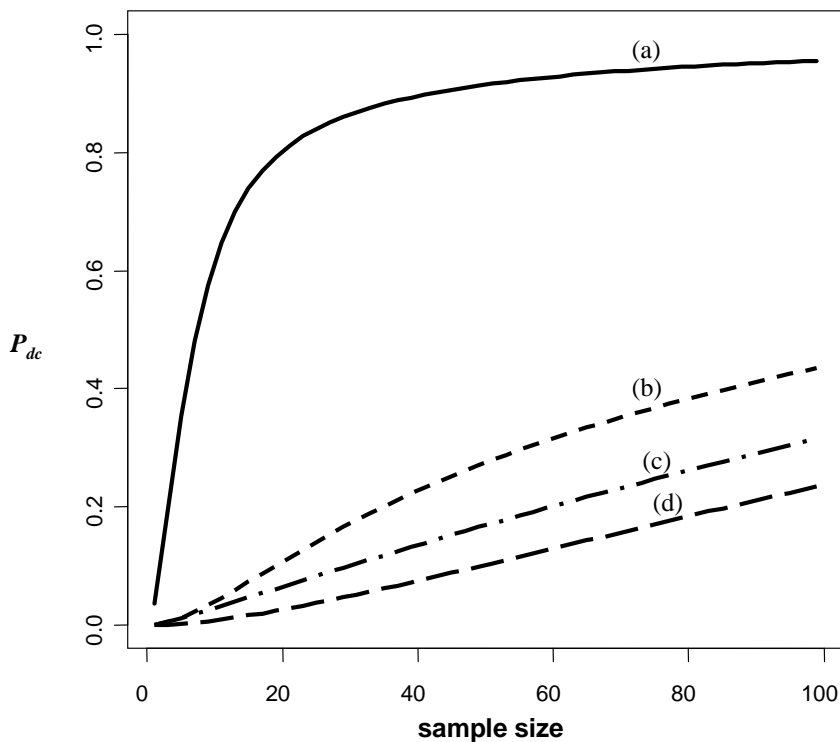
Fig. 5 Estimates of P_{dc} with sample size for (a) pigs, (b) ferrets, (c) male deer and (d) female deer sampled at random locations within a 90 000-ha management area.

Spatially explicit estimate of P$_{dc}$
If the locations of sampled wildlife are known, we can more accurately estimate coverage and hence provide a less biased estimate of P_{dc}. Given estimates for the relative sensitivity of different sentinel species, the level of exposure to infected possums within their home range (λ_y), and the size and shape of the assumed detection kernel for each species $g(r)$, the procedure is as follows:

For an individual sentinel aged *a* years and its estimate of λ_y, the risk of it being infected when sampled, given exposure to infection is given by

$$\lambda_a = \lambda_y(a - g)$$ Eqn 5

The two-dimensional detection kernel g(*r*), represents the distribution of the most likely locations that the sampled sentinel acquired infection, given where it finally killed or sampled. This can be thought of as the average search area of each sentinel. The area under each kernel can be adjusted using numerical integration to represent the risk of a sentinel (λ_a) acquiring infection given exposure to infection, as outlined in detail in Appendix 1. Where a number of sentinels are sampled within a defined area, the total risk they have been exposed to can be obtained by summing the kernel contributions from each individual. Estimation resembles the sum of individual risks spatially smoothed by bivariate density estimation to produce a risk surface map ($\lambda_{x,y}$). This allows a convenient interrogation of the risk at any point on the landscape.

The estimate of P_d for the area of interest can now be calculated by integration over the spatial extent of the area.

$$P_d = 1 - e^{\left(-\int \lambda_{(x,y)}\delta x \delta y\right)}$$ Eqn 6

Nominally, $\lambda_{(x,y)}$ is defined for the entire area of interest. However, locations greater than about 4σ from the nearest sentinel have approximately zero risk. An estimate of coverage can be calculated by finding the value of $\lambda_{(x,y)}$ that encompasses some arbitrary percentage (e.g., 95%) of the total surface volume. This can be undertaken by normalising the surface (so it integrates to 1) and then finding the value of $\lambda_{(x,y)}$ that gives the required volume. Once found, this value of $\lambda_{(x,y)}$ can be used to build a contour map of coverage at the stated volume. The proportion of the area encompassed by these contours is the estimate of coverage (*C*).

Having found an estimate of coverage, the overall estimate of P_d incorporating the coverage estimate (P_{dc}) is given by Equation 4. A worked example based on surveillance of deer and pigs follows to illustrate the methods.

Example: Pig and deer surveillance – 90 000-ha management area
This example uses the illustrative values estimated for the annual per capita force of infection λ_y given in Table 2 for pigs and female red deer of 0.229/year, and 0.004/year respectively. If, as a simple example, we assume for convenience that all sampled pigs are 1 y old and sampled deer are 4 y old, then applying equation 5 gives estimates of λ_a of 0.229 and 0.013 for pigs and female deer respectively (assuming a guarantee time of 0.75 years for deer). Thus, the *minimum* probability that an individual 1 year old pig or 4 year old deer would be infected, given *any* exposure to a *persistently* infected possum population, is estimated, from equation 2, to be 0.20 and 0.01 respectively.

Using Table 1, the magnitude (height) of the detection kernel that gave an overall volume equal to λ_a was found using numerical integration (Appendix 1). The resulting kernels are shown in Figure 6, providing a visual depiction of the marked difference in utility between the two sentinel species because of their differences both in sensitivity to infection (shown by kernel height) and in home range size (kernel area).
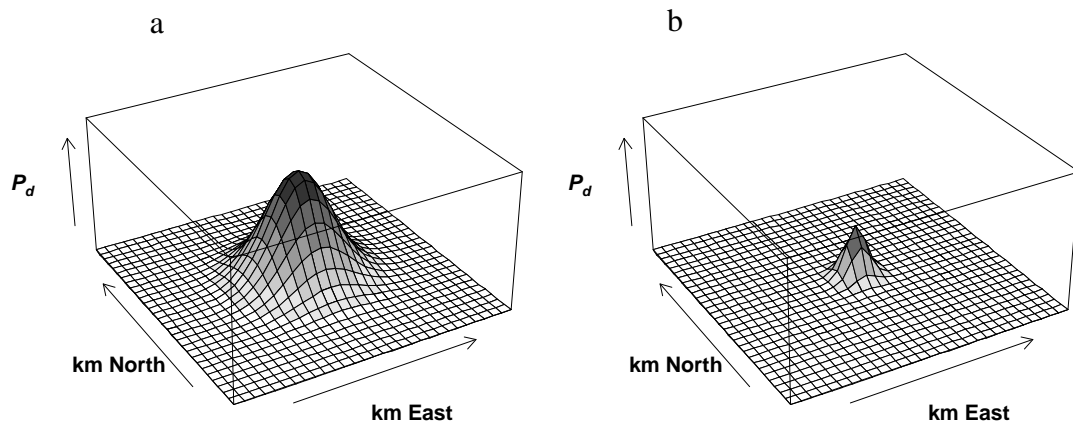
Fig. 6 Depiction of bivariate Gaussian detection kernels for (a) a 1-year-old pig, and (b) a 4-year-old female deer. The dimensions of the area are 30 x 30 km. The area under each surface is equal to a probability of 0.2 and 0.01 respectively.

Extending the example, the combined surveillance coverage and overall detection probability (P_{dc}) of 10 female deer and 10 pigs sampled within a 90 000-ha area were estimated by adding 10 kernels with randomly located centres (nominal sampled location) onto the area. For 10 female deer, the estimated probability of detection (P_d) using equation 6 was 0.12, with an estimated coverage (C) of 0.12 giving an estimate of P_{dc} using Equation 4 of 0.02 (Figure 7). The same number of 1-year-old pigs had a P_d of 0.89, with coverage of 0.66, giving an estimate of P_{dc} of 0.59 (Figure 8).

A major advantage of adopting this individually based and spatially explicit approach to estimating the P_d and coverage from sentinels is the ability to directly estimate these parameters from any arbitrary sample of sentinels, regardless of the mix of species, sex, and age within the sample. This becomes straightforward because the detection kernel for each individual provides an independently calculated estimate of P_{dc} at each point in the area, and these independent contributions can then be mathematically summed to derive an overall P_{dc} that can be represented as "detection surface" as in Figure 8.
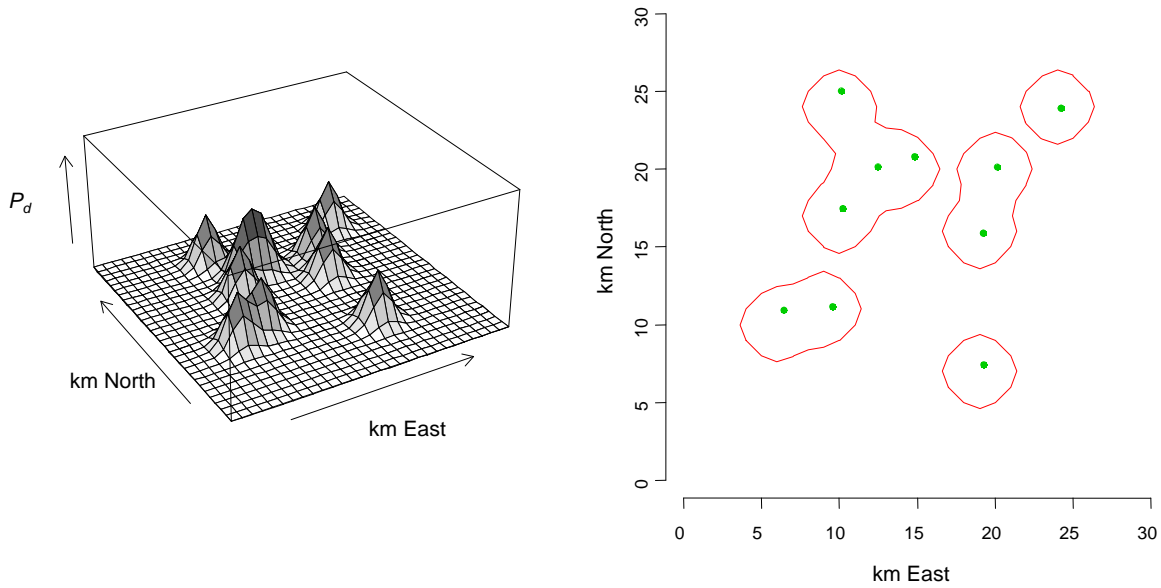
Fig. 7 Illustrative estimate of the probability of detection (P_d) and coverage provided by 10 4-y-old female deer sampled within a 30 x 30-km area.
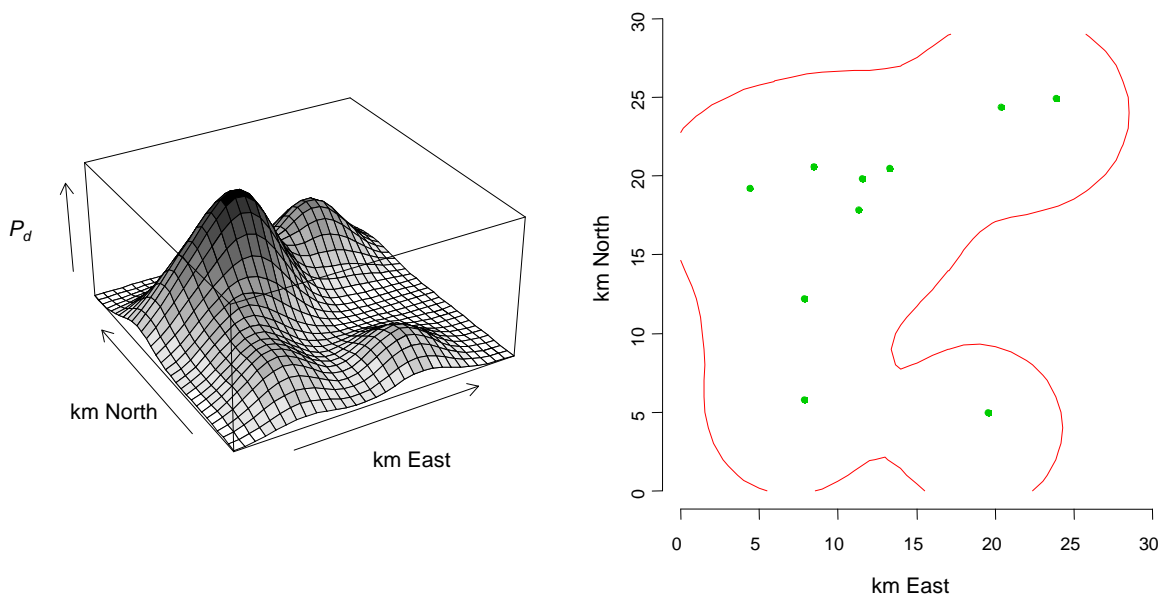
Fig. 8 Illustrative estimate of the probability of detection (P_d) and coverage provided by 10 1-year-old pigs sampled within a 30 x 30-km area.

Graphical depiction of this surface allows managers to determine 'gaps' in survey coverage easily, and target these in future surveys. Except for areas in which possum densities are naturally too low to sustain Tb, the greatest gains in detection efficiency will come from sentinels taken from locations not previously sampled. This simply reflects the law of diminishing returns – as the data from each extra sentinel taken from a particular location are added to that from previous sentinels taken from the same place, the proportional improvement in the estimate of P_{dc} progressively reduces. The first Tb-free pig killed at a site

provides a P_{dc} estimate of 0.23, whereas for two pigs the estimate is 0.41, an increase of only 0.18.

4.5 A framework for integrating multiple sources of surveillance information

Bayesian principles

Thus far, estimates of P_{dc} have assumed all information is from a single discrete survey at some point in time that may contain information from one or more sentinel species. However, surveillance data are routinely available from ongoing livestock testing, and surveillance information will need to be updated as new data become available. Ultimately all surveillance information will need to be combined to estimate P_{utb}, the probability that Tb persists in the region undetected. In addition, there will be uncertainties associated with the estimation of P_d, which will need to be accounted for in the estimate of P_{utb}. Here we develop a Bayesian statistical framework for estimating P_{utb} that combines multiple sources of survey information, incorporates uncertainties in estimates of P_d, and updates estimates of P_{utb} as new information becomes available. This framework can also be used to cope with uncertainties about the sensitivity and specificity of diagnostic tests and uncertainties associated with the degree of belief that control has eradicated Tb.

Under this approach the focus is on estimating P_{utb}. Under the Bayesian framework, this is defined as the probability that Tb persists in a maintenance host, *given that surveillance has failed to detect Tb*. This condition is important: we are only concerned with combining surveillance information from surveys that have not detected Tb. Hence we are necessarily assuming that surveys of wildlife have perfect or near perfect specificity, with every case of Tb detection in such surveys assumed to reflect continued presence of Tb in the presumed maintenance host unless it can be acceptably explained some other way.

Following or during a vector control programme, there will be some belief or level of confidence prediction based on model predictions and/or experience that Tb has been eradicated from the maintenance host. In Bayesian terminology, this is our prior probability of disease persistence, which we will call P_{tb}, and is the starting point for updating P_{utb} with new information, based on surveillance. The aim is to estimate the posterior (revised) probability that Tb persists based on surveillance information that has failed to detect evidence of Tb using Bayes theorem.

$$P(tb \mid u) = \frac{P(tb)\, P(u \mid tb)}{P(u)} \qquad\qquad \text{Eqn. 7}$$

where $P(tb/u)$ is the probability that Tb persists, given that Tb remains undetected (u) and is the Bayesian notation for P_{utb}. $P(tb)$ is our prior probability or belief that Tb persists (P_{tb}) and $P(u/tb)$ is the likelihood of obtaining a negative survey given that Tb is present (1-P_{dc}), obtained from wildlife surveillance and/or herd testing. $P(u)$ is the probability of obtaining a negative survey under all permissible hypotheses and is essentially a normalising constant.

Uncertainty in the estimates of the prior probability and/or survey information can be used to calculate a posterior probability distribution using a continuous version of Bayes theorem.

$$f(\theta \mid u) = \frac{f(\theta)\, f(u \mid \theta)}{\displaystyle\int_{\theta} f(\tau)\, f(u \mid \tau)\, d\tau} \qquad\qquad \text{Eqn. 8}$$

where $f(\theta)$ now refers to a probability density distribution.

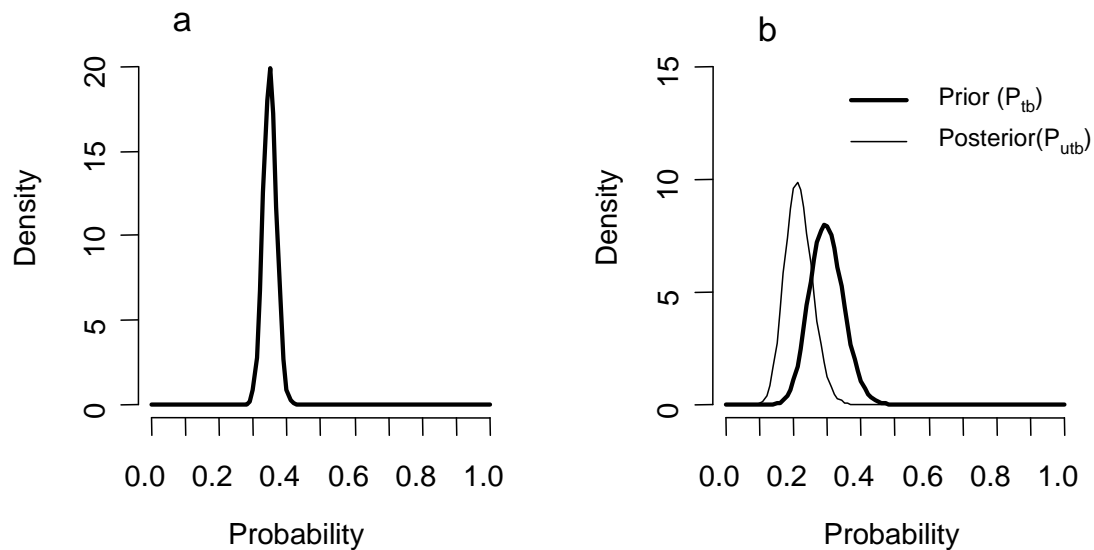### Estimating the prior probability of Tb persistence (P_{tb})

During or following Tb vector control programmes there will be some likelihood that Tb has been eradicated from the maintenance host due to control efforts. Ramsey and Efford (2005) used modelling to estimate the probability of Tb being eradicated from possum populations under various residual trap catch index (RTCI) targets. Their model predicted that where possum populations had been reduced and held at a 2% RTCI target, there was a 95% probability Tb would have been eradicated within 3-6 years, with a mean of 5 years. Their model did not account for the likely persistence of Tb in other wildlife hosts, such as deer or for the potential immigration of Tb from outside the region that could lead to persistence despite control efforts.

Hence, we propose that a minimum of 5 years of vector control be imposed in all regions where deer are present in moderate to high numbers and Tb is or was initially widespread in possums, deer, and other vectors (see next section). We also argue that the initial estimate of the prior probability for P_{tb} be conservative, to account for the uncertainty of the presence of Tb in other vectors, as well as the uncertainty about whether vector control had been uniformly applied over the area (see next section). We therefore propose, as an example but based on the model predictions referred to above, that the initial prior estimate of P_{tb}, following 5 years of vector control, be set between 0.2 and 0.5, depending on how closely the actual level of control matches the "maintained at 2% RTCI for 5 years" scenario. Because the assumptions on which these model-derived predictions have not been fully validated, it will be sensible to routinely determine the sensitivity of the posterior estimates of P_{utb} to changes in the estimated prior probability. We also advocate (in the next section) a technique that temporally discounts the posterior estimate of P_{utb} where there is a belief that Tb could be reintroduced from other wildlife hosts or other sources.

Estimating the posterior probability of Tb persistence (P_{utb})

The following examples demonstrate how a Bayesian framework can be used to update the probability that Tb has persisted undetected.

Example 1. Single surveillance following 5 years of vector control: This example assumes vector control has been undertaken for 5 years. Hence, the prior probability that Tb persists (P_{tb}) was believed to be between 0.2 and 0.5, with a mean of 0.3 (Figure 9b). Surveillance was undertaken by sampling 6 pigs aged 1 year, which had a P_{dc} of 0.35 judged 95% likely to be between 0.3 and 0.4 (Figure 9a). The survey was undertaken and no Tb was detected.

Fig. 9 The (a) probability of detecting Tb from a sample of 6 1-year-old pigs sampled randomly from within a 90 000-ha area and (b) the estimated probability of Tb persisting undetected (P_{utb}) (faint line) given the prior probability of Tb persistence (P_{tb}) (heavy line).

Following the application of Bayesian updating, the posterior estimate of P_{utb} was 0.22 with a 95% credible interval of 0.14–0.30. Thus illustrates how use of surveillance of just a few highly sensitive sentinels could substantially decrease P_{utb} relative to cost and effort involved in the 5 years of control needed to reduce the prior estimate to 0.3.

Example 2. Incorporating herd testing: This example extends the previous one to include the additional information on herd testing. From the approximation in, the P_d for herd testing was set between 0.1 and 0.5 with a mean of 0.25 (Figure 10a). The prior estimate of P_{tb} and the estimate of P_{dc} for pig surveillance was as for example 1. Where combining surveys of wildlife sentinels and herd testing, the combined P_{dc} is calculated as:

$$P_{dc} = 1 - \prod_i (1 - P_{dc_i}) \qquad\qquad \text{Eqn. 9}$$

Following the Bayesian updating, the posterior estimate of P_{utb} including the herd testing data was 0.17 with a 95% credible interval of 0.09–0.25 (Figure 10b). This example illustrates how readily, for any 1 year of surveillance, data from multiple and dissimilar can be integrated, provided each source of data can be converted to an estimate of $P_{dc.}$
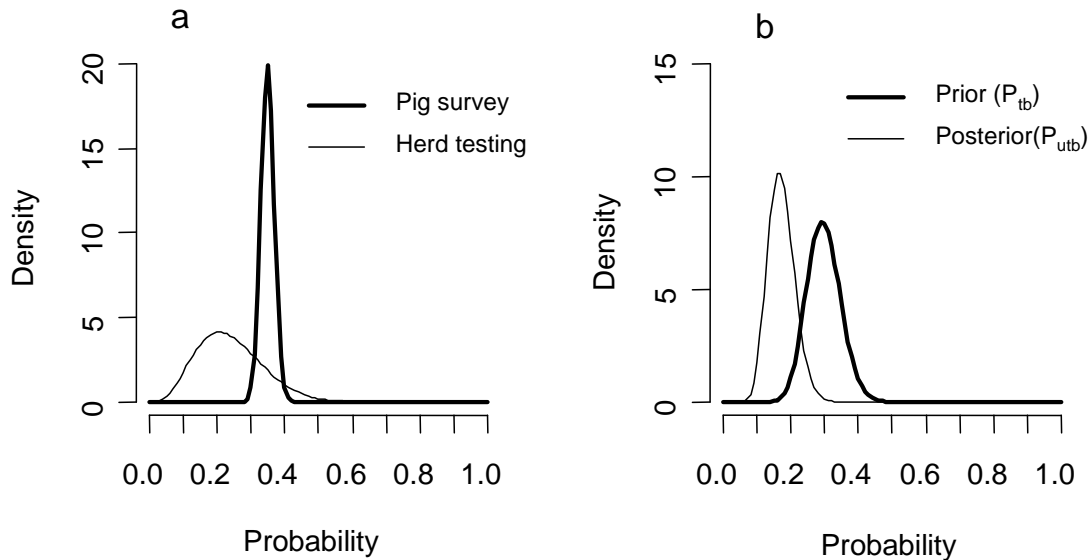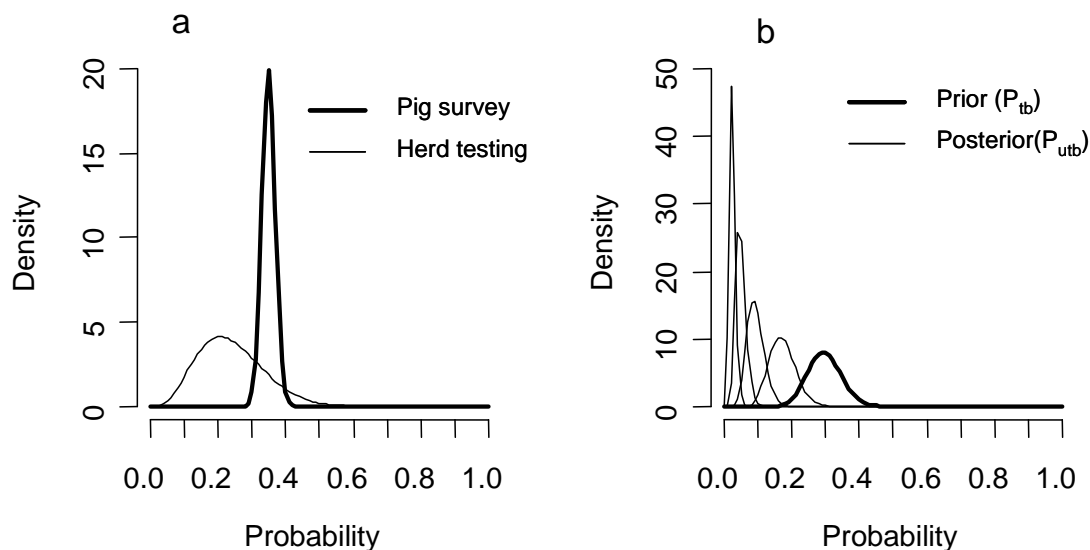
Fig. 10 The (a) probability of detecting Tb from either a sample of 6 1-year-old pigs (heavy line) or herd testing (faint line) sampled within a 90 000-ha area and (b) the estimated probability of Tb persisting undetected (P_{utb}) (faint line) given the prior probability of Tb persistence (P_{tb}) (heavy line).

Example 3. Temporal updating using multiple surveillance episodes: This example assumes that surveillance is ongoing, with new data collected annually (for example) from both wildlife surveys and herd testing. Temporal updating involves initially setting the prior probability for P_{tb}, perhaps conservatively, at some sensible but arbitrary time after the implementation of vector control. We then take the annual surveillance information for that year and adjust our estimate of P_{utb} as in Example 1. For the following year, the updated estimate of P_{utb} can be used as a new estimate of the prior probability for P_{tb} that is then updated with the new surveillance data from that year. This iterative updating of the prior probability at time *t* with the posterior probability of P_{utb} at time *t-1* continues as new surveillance information becomes available.

In this example we assume that surveillance information similar to that in Example 2 is available for each of 4 years of annual herd testing and pig survey, and the same prior probability that Tb persists, performing Bayesian updating each year produces a posterior estimate of P_{utb} after the 4th year of surveillance was just 0.02 with a 95% credible interval of 0.007–0.04 (Figure 11). Note that where vector control has continued to maintain low possum numbers, this approach will be conservative because the probability that Tb has been eradicated will have increased regardless of whether or not any surveillance has been undertaken.
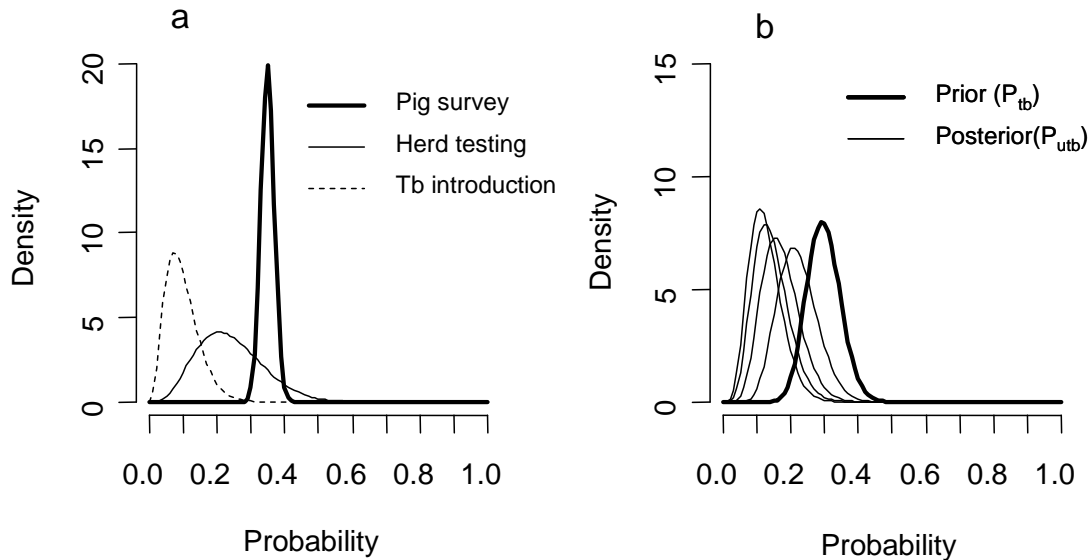
Fig. 11 The (a) probability of detecting Tb from either a sample of 6 1-year-old pigs (heavy line) or herd testing (faint line) sampled within a 90 000-ha area and (b) the estimated probability of Tb persisting undetected (P_{utb}) each year for 4 years (faint lines) given the prior probability of Tb persistence (P_{tb}) (heavy line).

Example 4.   Temporal updating using multiple surveillance episodes with temporal discounting: This example repeats example 3, except that we now assume there is some possibility (probability) of Tb being reintroduced into the area during the 4-year surveillance period. Reintroduction could perhaps result from Tb-infected possums or by occasional reestablishment of infection in possums, the long-term maintenance hosts, from resident deer or pigs that although not maintenance hosts can remain alive for up to a decade after becoming infected.

To estimate the prior probability Tb perists (P_{tb}) at time period t based on the posterior estimate of P_{utb} derived for the previous period, time $t-1$, we need to account for the probability that disease was introduced between $t-1$ and t. This can be achieved by discounting the estimate of the prior probability of P_{tb} at time t by the estimate of the probability of disease introduction (P_{int}), as follows

$$P_{tb(t)} = P_{utb(t-1)} + P_{int} - P_{utb(t-1)}P_{int} \qquad\qquad \text{Eqn 10}$$

In this example we assume that the probability of Tb being introduced between annual surveys is constant each year and, at a guess, that it lies between 0.05 and 0.2, with a mean of 0.1. Following the Bayesian updating performed each year, the posterior estimate of P_{utb} after the 4th year of surveillance, using temporal discounting was 0.13 with a 95% credible interval of 0.03–0.23 (Figure 12). Note that exactly the same logic could be used to adjust P_{tb} (in the opposite direction) for the additional likelihood of Tb being eradicated in each successive year as a result of ongoing control efforts.

Fig. 12 The (a) probability of detecting Tb from either a sample of 6 1-year-old pigs (heavy line) or herd testing (faint line) sampled within a 90 000-ha area, and (b) the estimated probability of Tb persisting undetected (P_{utb}) each year for 4 years (faint lines) given the prior probability of Tb persistence (P_{tb}) (heavy line) and including the probability that Tb is reintroduced between surveys (dashed line).

4.6 Setting stopping rules

The current AHB strategy for Tb control is to impose a culling programme wherever there is evidence Tb is present in livestock or wildlife, to include all contiguous areas into which there is some prospect of Tb spreading, and to then continue Tb-management until it is satisfied that the risk of Tb re-emergence in future is too low to warrant further management.

Stopping too soon will allow persistent Tb to re-emerge at some later date. Stopping too late will waste resources that would be better deployed elsewhere. The most economically sensible stopping point is one that minimises the net expected costs (NEC) associated with (i) the ongoing cost of undertaking surveillance, and (ii) the cost of stopping too soon and wrongly declaring eradication (e.g., Regan et al. 2006). The costs associated with (i) are readily calculated directly from the cost of undertaking a single Tb survey, i.e. either herd testing or wildlife surveys. However, the costs of wrongly declaring eradication are less easily quantified, being largely dependent on the cost of 'eradicating' Tb a second time if (when) it re-emerges many years into the future. A large component of these costs centres on the contingent risk that funding for future Tb management could be difficult or impossible to obtain as well as on uncertainty about the future availability of current control tools, which will render control costs much more expensive relative to the present.

### A potential bioeconomic approach

Given that the cost of wrongly declaring eradication can be quantified, the optimal stopping time is the number of consecutive, clear surveillance episodes that minimise NEC. Hence for i (annual) surveillance episodes, NEC can be calculated as

$$NEC_i = (i-1) \times C_s \times C_e P_{utb(i)}$$

Eqn 11

Where NEC_i is the net expected cost following the ith surveillance episode, C_s is the cost of each surveillance episode, C_e is the cost of wrongly declaring eradication, and $P_{utb(i)}$ is the probability that Tb persists undetected after the ith surveillance episode (modified from Regan et al. 2006).

To illustrate, we can estimate what the optimal stopping time for surveillance is based on the scenario given in Example 4 above. For this, we assume that the ratio of the unit surveillance costs (e.g., the cost of 1 year of herd testing and wild pig surveys) to the cost of wrongly declaring eradication is either 1:25, 1:50, 1:100, or 1:200 (i.e. the cost of wrongly declaring eradication is 25, 50, 100 or 200 times the cost of annual surveillance). Using these cost estimates and the values for P_{utb} estimated from 20 consecutive episodes of herd testing and pig surveillance and applying equation 9 gave optimal stopping times of 2, 3, 4 and 6 consecutive clear surveillance episodes for cost ratios of 1:25, 1:50, 1:100, 1:200 respectively (Figure 13). These estimates of optimal stopping times to declare eradication therefore find the optimal balance between the accumulated cost of ongoing surveillance with the cost of getting it wrong (Regan et al. 2006).

Although this cost-minimisation example is perhaps overly simplified, it illustrates that, with further development, simple bioeconomic principles could allow managers to determine in broad terms how much additional wildlife surveillance is needed to optimally supplement herd testing.
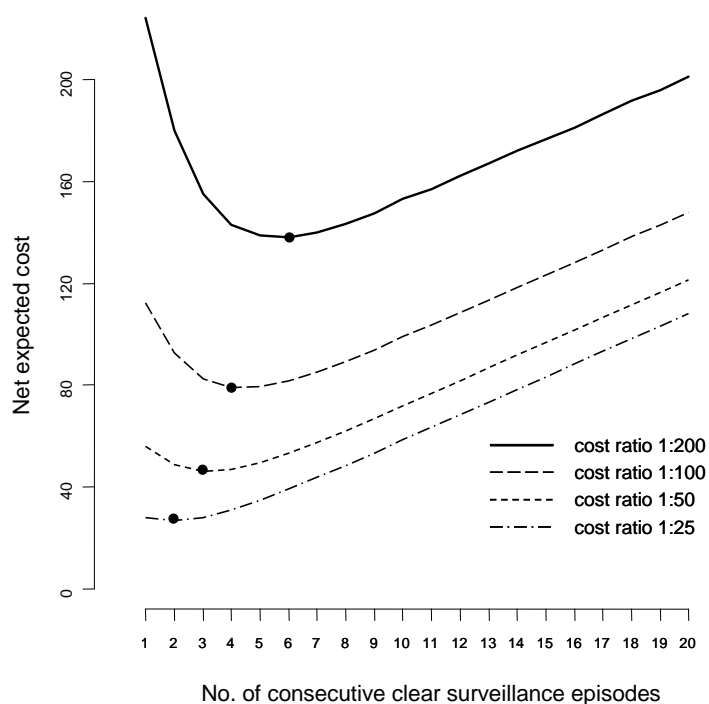
Fig. 13 The net expected cost (NEC) as a function of the number of consecutive clear surveillance episodes for four different cost ratios. The optimal time to stop surveillance and declare eradication is given by the black dots. Surveillance was assumed to use the same scenario as given in example 4 above.

Precautionary non-economic approach

As an alternative, a stopping rule could be based entirely on setting a threshold for P_{utb}. We suggest that until credible bioeconomic rules have been developed, the stopping rule be that TB management (other than the livestock testing needed to demonstrate to our trading partners the Tb status of farmed livestock) cease when $P_{utb} < 0.01$. We further propose that this be applied at to management units of about 100 000 ha.

This is not an arbitrary level or scale. Rather, the paradigm is to 'get it right the first time' and avoid the unknowable but potentially catastrophic risk of future unwillingness (after 2020, for example) to deal with re-emergence of Tb in remote unfarmed areas. It aims to enable the AHB to eliminate Tb everywhere in a single first attempt. This rule would reduce the risk of future Tb re-emergence to less than 1% across all such 100 000-ha operational areas. As the area within VRAs is currently around 10 million ha, there are only 100 such areas, so a <1% risk is less than one area (i.e. close to zero). Using this logic, splitting the total national infected area into 200 management units of c. 50 000 ha each would require a rule of $P_{utb} < 0.005$, and so on for even smaller management areas.

Obviously P_{utb} can be reduced even more quickly with greater surveillance or control effort, but a key epidemiological constraint on shortening the duration of control is the persistence of infection in long-lived spill over hosts such as deer. Tb persisted in already infected female deer for about a decade after control in the Hauhungaroa and Umukarikari Ranges in the central North Island, having initially been at prevalences of about 50% in adult females. Unless deer numbers are also reduced to, or are already at, very low levels, stopping possum control in less than 5 years risks the possum population exceeding the disease maintenance threshold before Tb has disappeared completely from deer.

Under these assumptions, annual surveillance with a sensitivity of about 45% (taking coverage into account) is required to reduce the belief that Tb is present to less than 1% after five years. Given that herd testing appears to provide about 20–25 % sensitivity to single transmission events (which we presume includes possums), it is likely that herd testing alone will provide adequate surveillance in farmed areas, where the livestock coverage is 100%. This will be an even safer assumption if possum numbers have been held to below 1% for the entire period.

4.7 Choosing a sentinel

Minimising net expected costs (as in Equation 11) should help guide managers in deciding how much should be spent on surveillance, and also what P_d they desire from a particular survey. However, it will not indicate which sentinels should be used in a particular area, because the same probability of detection could be obtained by using different sample sizes of each species. Although, all else being equal, pigs seem to be by far the most sensitive sentinel, their overall utility or cost effectiveness will also depend on the cost of obtaining each sentinel; if pigs are rare then the desired sample size may simply not be attainable at any cost.

Assume the total cost of a survey C_s is the sum of the design, implementation, and analysis costs (C_{admin}), the cost of obtaining sentinels ($C_{sentinel}$), the cost of testing or necropsying ($C_{necropsy}$), and the cost of histology and/or culture for diagnostic confirmation per sentinel ($C_{culture}$), as follows:

$$C_s = C_{admin} + N\,(c_{sentinel} + c_{necropsy} + c_{culture}) \qquad\qquad \text{Eqn 12}$$

where the lower-case c represents per sentinel cost.

However, differing testing sensitivities and specificities must first be taken into account. In this presence-absence surveillance context we assume a specificity of 1.0 (i.e. there are no false positives because any field diagnosis not confirmed by culture is not accepted), although this presumes there is no contamination of culture samples with Tb from other areas. On the other hand, sensitivity will be less than 1.0 because skin testing and necropsy are imperfect surveillance tools. This reduces confidence in survey outcomes proportionately, but we assume it can easily be compensated for by adjusting sample size, as follows;

$$N_{adj} = N\,/\,s \qquad\qquad \text{Eqn 13}$$

where s = the combined sensitivity of field and laboratory testing, necropsy and/or culture laboratory confirmation.

One subset of the cost-effectiveness question is whether mycobacterial culture of Tb samples from all sentinels is warranted, and we use this to demonstrate the basic principles. Substituting for N in Eqn 13, and expressing the costs with and without culture as a ratio that equals 1 when the cost-effectiveness of the two approaches is the same, suggests the following logic:

$$[N\,(c_{sentinel} + c_{necropsy} + c_{culture})\,/\,s_{nc}]\,/\,[N\,(c_{sentinel} + c_{necropsy})\,/\,s_n] = 1$$

$$s_{nc}/s_n = (c_{sentinel} + c_{necropsy} + c_{culture})\,/\,(c_{sentinel} + c_{necropsy})$$

$$s_{nc}/s_n = 1 + [c_{culture}\,/\,(c_{sentinel} + c_{necropsy})] \qquad\qquad \text{Eqn 14}$$

where s_{nc} = sensitivity of field necropsy and culture and s_n = sensitivity of field necropsy alone.

Put in words, this says culture is warranted where the proportional improvement in overall sensitivity is greater than the cost of culture relative to the cost of obtaining and necropsying additional sentinels. To illustrate first for possums, assume one quarter of infected possums are missed by necropsy ($s_n = 0.75$), but that 80% of these NVLs (no [macroscopically] visible lesions) are detected by culture ($s_{nc} = 0.95$), that $c_{culture} = \$50$, $c_{sentinel} = \$10$, and $c_{necropsy} = \$15$, the sensitivity ratio s_{nc}/s_n (1.27) is less than the cost ratio $c_{culture}/(c_{sentinel} + c_{necropsy})$ (2.0), so culture of each possum is *less* efficient than obtaining and necropsying further samples. Pooling nodes across three or more possums as recommended for ferrets (de Lisle et al. 2005a) but not for deer (de Lisle et al. 2005b) will, however, be more cost effective than additional survey as it reduces culture cost to $17/ sentinel or less, provided any loss of sensitivity due to pooling is minor.

For central North Island deer, assume $s_{nc} = 0.95$, $s_n = 0.70$ (i.e. about 25% NVLs; Nugent & Whitford 1993), culture will always be warranted when the cost of obtaining and necropsying additional deer is greater than $67. Culture is even more strongly cost-effective for Hochstter/Omoto deer where two-thirds of deer are NVL (Nugent & Whitford 2003).

Returning to the comparison of cost-effectiveness between sentinels, and assuming for simplicity that C_{admin} would be the same regardless of sentinel species, the usefulness of two samples of sentinels as surveillance tools is the same when they produce the same P_D the same cost, as follows;

$$N_1 (c_1) = N_2 (c_2) = N_3 (c_3) \qquad\qquad \text{Eqn 15}$$

where N_1 and c_1 = numbers and total cost per sentinel for sentinel 1, etc. Sentinel 1 will be more cost effective where $c1 < N_2 (c_2) / N_1$.

Where P_d is low (<0.30), an simple extension of Equation 14 will provide an approximation of the relative utility of sentinels;

$$N_1 (c_1)/P_{d1} = N_2 (c_2)/P_{d2} \qquad\qquad \text{Eqn 16}$$

Sentinel 1 will be more cost effective where $c_1 < N_2 (c_2) P_{d1} / N_1 P_{d2}$

Although possums appear poor sentinels (primarily because their home ranges are much smaller than for pigs, ferrets, and deer), necropsy surveys of the possums killed during annual ground-based maintenance control may be cost effective. If, for example, about one third of the possum population is killed annually, and *if* these can be necropsied at little extra cost (i.e. c_1 in Eqn 14 of close to zero), then such a survey would have P_d approaching 0.33, making it unlikely that any other sentinel could be more cost-effectively surveyed.

5. Conclusions

We developed a new spatially explicit approach to determining the sensitivity and coverage of wildlife surveillance, based on the concept of a "detection kernel". This kernel defines the area around a sampled individual that has a specified probability of having acquired Tb, given it was present as a single discrete focus of infection that produces a minimum of one infected animal per year. An overall estimate of wildlife surveillance sensitivity P_{dc}, is determined by summing individual detection kernel contributions from each sampled individual to produce a probability surface over the area of interest. In addition, the spatial approach to defining the sensitivity of wildlife surveillance allows the flexibility of combining surveys of multiple wildlife species into a single estimate of P_{dc} for the area of interest.

Preliminary first-approximation estimates of detection kernels were made for each of the main wildlife sentinel species, feral pigs, deer and ferrets using distances between consecutive radio-telemetry locations. In addition, first-approximation estimates of the annual risk of an individual sentinel being infected, given exposure to a single focus of infection within its home range, were estimated from field data. These analyses suggest that only about 0.4% of deer with an infected possum within their home range become infected during a year of exposure. They also suggest that ferrets are approximately 21 times more sensitive than deer at detecting a single infected possum within their range, and that pigs are approximately

60 times more sensitive than deer as sentinels. Livestock testing was estimated to detect about a quarter of the infected possums present on farm, an approximate sensitivity of 0.25.

The large home ranges and high sensitivity of pigs and ferrets as sentinels will generally make them the most cost-effective sentinels, at least when surveys are conducted specifically and solely for surveillance. However, possums killed during maintenance control may sometimes provide a cheaper alternative.

In summary we conclude that decisions about whether to stop vector control, wildlife surveillance, and livestock testing can all be based on quantitative estimates of the probability that Tb has persisted undetected (P_{utb}). The belief that Tb has persisted undetected can be easily updated using Bayes theorem, which can also incorporate uncertainties in the sensitivity of surveillance and diagnostic testing. The hypothetical examples presented show that moderate-sensitivity wildlife surveillance, coupled with herd-testing data would rapidly increase the belief that Tb was absent. Where Tb management is applied to small areas, consideration should be given to the possibility that Tb is reintroduced from a distant source and/or be present as a latent infection in residual wildlife. In such cases, the estimate of P_{utb} can be adjusted to reflect this additional risk, by using temporal discounting.

6.   Recommendations

We recommend that the AHB adopt the core principles of the framework outlined in this report, and determine the practicality and utility of the proposed surveillance framework through trial implementation in 2–3 contrasting areas. The Featherston and southern Urewera areas are suggested as potential candidates. The core principles are that:

- decisions about whether to start or stop vector control, wildlife surveillance, and livestock testing all be based on quantitative estimates of managers' belief that Tb has persisted undetected;
- first (prior) estimates of Tb absence be based on predictions of a spatial simulation model of Tb in possum using empirical data from possum population monitoring;
- a Bayesian updating framework be used to integrate this prior belief with surveillance data from herd-testing and/or wildlife surveillance;
- a spatially explicit approach to wildlife surveillance be used. This approach is based on the characteristics of each species as a Tb 'sensor'.

Unless 'temporal vectors' such as deer are rare or absent, the minimum duration of possum control be set at about 5 years to reduce the chance that Tb could persist as a latent infection in residual deer populations.

Decisions about when to stop Tb management and/or surveillance should be based either (i) on finding the optimal number of clear surveillance episodes that minimises the net expected costs associated with Tb management, or (ii) on using a conservative 'get it right first time' stopping rule based on combining consecutive clear surveillance episodes until $P_{utb} < 0.01$.

Decisions about when to stop vector control or surveillance should be applied to VRAs as a whole when they are small, or to management units of about 100 000 ha or greater, to try to maximise epidemiological independence. When applying stopping rules to smaller

management areas, we advise that the technique of temporal discounting be used in the calculation of P_{utb} to allow for the possibility that disease may be introduced from neighbouring vector-risk areas.

Further research is required to
- improve the robustness and applicability of the estimates of the habitat-species-sex specific parameters of the detection kernels. Estimates of the relative sensitivity for each species will be refined as an integral part of a current research project;
- further develop and formally publish in an overseas journal the new theoretical basis for use of sentinels, both in the spatially explicit form presented here, and, if valid, in the more deterministic form in which it was initially developed. This will ensure the approach is scientifically developed and internationally acceptable;
- develop an end-user accessible form of the spatial model of tuberculosis in possums, to enable ready prediction of the probability Tb has persisted undetected given the unique history of control for each management area.

7. Acknowledgements

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Appendix 1

Estimating 'per sentinel' detection kernels and coverage

Given estimates of the relative sensitivity of different sentinel species expressed as the *per capita* annual force of infection – (λ sentinel^{-1} infected possum^{-1} year^{-1}) and the distribution of detection distances estimated in Tables 1 & 2, a spatially explicit estimate of P_d (probability of detection | exposure) can be derived that includes an estimate of coverage for the area of interest (C).

The procedure is as follows: For an individual sentinel aged a with an annual risk of infection (λ_y), the total risk of infection (λ_a), given an infected possum occurs within its range, is simply

$$\lambda_a = \lambda_y (a - g) \qquad\qquad\qquad \text{Eqn 1}$$

where age is given in years. Hence, the probability than an individual sentinel is infected upon sampling, given exposure to infection is

$$P_a = 1 - e^{(-\lambda_a)} \qquad\qquad\qquad \text{Eqn 2}$$

The distribution of detection distances or detection radii (r) represents the distribution of the most likely locations in which a sampled sentinel acquired infection, given where it finally killed or sampled (the search area of a sentinel). These distances were used to define a probability distribution g(r), representing the likely distribution of search effort of the sentinel within this area (detection function). This area is larger than a home range area, reflecting uncertainty in actual location of the range given where the sentinel was eventually sampled. The distribution of detection distances can be conveniently represented in two dimensions using a bivariate kernel surface. Candidates are the circular bivariate Gaussian or uniform distributions. Each kernel thus represents the radial distribution of likely search effort by the sentinel. Hence, the area under each kernel represents the total risk (λ_a) of a sentinel aged a acquiring infection given exposure to infection.

Assuming a bivariate Gaussian kernel to describe the detection area, we found estimates of the parameter σ, representing the spatial scale of the kernel by fitting the distribution of detection distances to a half-normal probability by maximising the likelihood given in equation 3.

$$L(\sigma) = \prod_i \frac{2}{\sigma\sqrt{2\pi}} e^{\left(\frac{-r_i^2}{2\sigma^2}\right)} \qquad\qquad\qquad \text{Eqn 3}$$

Having found an estimate of the spatial scale of the kernel function (σ), we found an estimate of the magnitude of the bivariate normal kernel (height) that gave an overall area under the kernel equal to the total risk (λ_a) using integration.

$$k \int_{-kw}^{kw} \int_{-kw}^{kw} e^{\left(-0.5\left(\left(\frac{(x-x_0)^2}{\sigma^2}\right)+\left(\frac{(y-y_0)^2}{\sigma^2}\right)\right)\right)} \delta x \delta y = \lambda_a \qquad\qquad \text{Eqn 4}$$

where *kw* was the maximum span of the kernel in both the *x* and *y* dimensions for a kernel centred at (x_0, y_0). Typically, *kw* is set to $>4\sigma$, above which the risk is close to zero. The value of *k*, representing overall magnitude (height) of the bivariate kernel was found using Newton's algorithm.

Where a number of sentinels are sampled within a defined area, the total risk for the area is given by summing the individual contributions. Estimation resembles the sum of individual risks spatially smoothed by bivariate density estimation to produce a risk surface map $(\lambda_{x,y})$. This allows a convenient interrogation of the risk at any point on the landscape.

The overall estimate of P_d for the area of interest can now be calculated by integration over the spatial extent of the area.

$$P_d = 1 - e^{\left(-\int \lambda_{(x,y)} \delta x \delta y\right)}$$ Eqn 5

Nominally, $\lambda_{(x,y)}$ is defined for the entire area of interest. However, locations greater than about 4σ from the nearest sentinel have close to zero risk. An estimate of coverage can be calculated by finding the value of $\lambda_{(x,y)}$ that encompasses some arbitrary percentage (e.g., 95%) of the total surface volume. This can be undertaken by normalising the surface (so it integrates to 1) and then finding the value of $\lambda_{(x,y)}$ that gives the required volume. Once found, the value of $\lambda_{(x,y)}$ that corresponds to this volume can be used as the basis for a contour map of the coverage at the stated volume. The area encompassed by these contours divided by the total area is the estimate of proportional coverage (*C*).

Having found an estimate of coverage, the overall estimate of Pd incorporating the coverage estimate (P_{dc}) is given by

$$P_{dc} = P_d C$$ Eqn. 6

Appendix 2

Comparison of the non-spatial approximation with the spatially-explicit estimate of P_{dc}.

The estimates of P_{dc} derived using the non-spatial approximation estimator (equations 1–4) were compared with the spatially explicit estimates (Appendix 1) for each of the main sentinels considered (feral pig, female deer and ferrets) for a range of sample sizes (1–100). For the non-spatial estimator, home range size H was taken as the area of the 95% contour of the respective detection kernel with spatial scale taken from Table 1 (i.e. area of a circle with radius = 2.45σ). The estimates of λ_y were taken from Table 2 and we assumed all animals were aged 1 year old. For the spatially-explicit estimator, we assumed that all locations of sampled individuals were placed randomly on the area. Results are given in Figure 14. In general, the non-spatial estimator was unbiased compared with the spatially explicit estimator with the exception of large (>20) samples of feral pigs, where the non-spatial estimate exceeded the spatial one. This is most likely due to small areas of the sampled area failing to get coverage from a randomly placed location. Hence, the spatially explicit estimate of coverage did not converge to 100% as sample size increased.
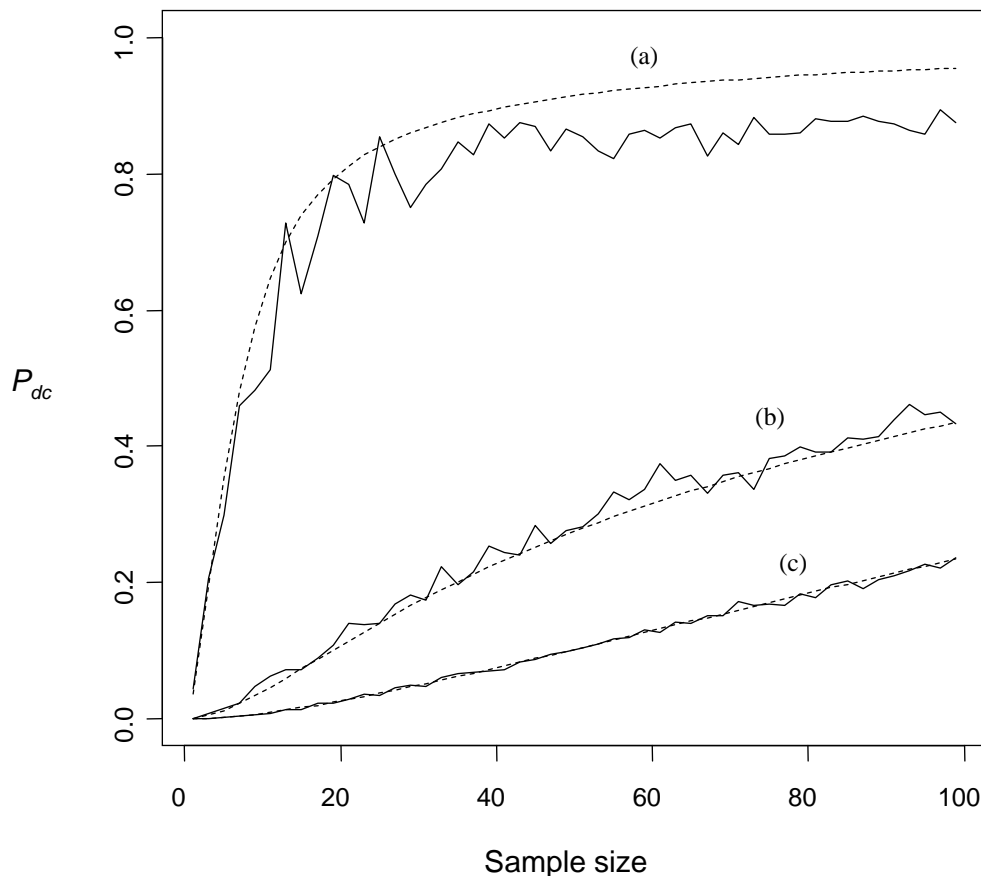
Fig. 14 Comparison of P_{dc} for the non-spatial estimator using equations 1–4 (dashed line) with the spatially explicit estimator (Appendix 1) (Solid line) for sample sizes of (a) feral pigs, (b) ferrets and (c) female deer between 1 and 100 individuals. The spatially explicit estimate is from a single realisation of that sample size.