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A review of science underpinning eradication of bovine TB from New Zealand

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TB Free New Zealand

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Contents

Executive summary

Review of science underpinning proposition of TB eradication

The science underpinning the proposition that *Mycobacterium bovis* (TB) can be completely eradicated from New Zealand is on the whole sound. The scientific material put forward for this review covers off on the key components required for eradication, namely:

- effective disease management systems in livestock enabling straight forward disease eradication in the absence of a wildlife disease reservoir,
- adequate knowledge of the epidemiology of TB in New Zealand wildlife,
- effective control technologies of brushtail possum populations (the primary wildlife maintenance host for *M. bovis*) backed by robust compliance monitoring of control operations, and
- quantitative methods for making inference on the presence of TB in wildlife populations through the integration of multiple surveillance sources, and thus monitoring the success of the program in real operational time.

There are aspects of the science that could potentially be improved. The Proof of Freedom utility has some inbuilt assumptions that in some situations could lead to the probability of eradication being overestimated, although judicious use should avoid this leading to incorrect decisions. It also appears to under-predict the possibility of Tb persisting in possums in some environments. For this reason there should be consideration given to some form of validation.

Technical feasibility of biological eradication

I consider that the biological eradication of TB is feasible with current levels of funding, and can be achieved under existing timeframes. The methodology currently being deployed is adequate for the control and eradication of TB in livestock and wildlife, with efficacy measures that can be supported empirically. There remains the opportunity to optimize the allocation of resources, particularly in relation to the level of certainty of TB eradication required within Vector Control Zones before moving to surveillance only.

I consider that at this stage the known potential risks to successful eradication can be managed with current knowledge and technical capabilities. The 'Proof of Concept' areas in the Hokonui Hills and Hauhungaroa/Rangitoto Ranges are well progressed toward eradication, clearly demonstrating the technical feasibility of achieving eradication over large inaccessible areas.

Technical feasibility of eradication using alternatives to 1080

It will remain technically feasible to achieve biological eradication of TB from New Zealand without the use of compound 1080, though with increased costs, and potentially longer timeframes.

Management agencies charged with managing TB should maintain an operating environment where innovation can continue to occur, across all aspects of the eradication program, as has occurred since the implementation of the first National Pest Management Strategy for TB.

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1 Terms of reference for review

1.1 Purpose

A peer-review of the scientific research that has been carried out to date into the eradication of Bovine Tuberculosis (TB) in New Zealand.

1.2 Background

Control of TB in New Zealand is carried out under a National Pest Management Plan (Plan) under the Biosecurity Act 1993 (the Act) managed by TBFree New Zealand Ltd.

The Minister for Primary Industries is required to start a statutory review of the Plan by 1 July 2016, pursuant to s100D of the Act. The review must be on the basis of a proposal, which can be prepared by the Minister or any other party. The Plan was last reviewed following notification of an amendment proposal by the Minister of Agriculture in September 2009 (at that time pursuant to s88(6) of the Act). An Order in Council amending the Plan came into effect on 1 July 2011.

The Plan Governance Group[1] has been established to prepare the proposal, which will bring together an overall review of the TB Plan and describe how it will be funded. As part of this work, the requirement for an independent review of the science research for TB management has been identified, particularly where the science relates to the technical feasibility of eradication.

1.3 Scope

The review will look at the science underpinning the proposition that TB [bovine tuberculosis arising from *Mycobacterium bovis* infection] can be completely eradicated from New Zealand. The review will assess how robust and comprehensive that science is. Focusing on evidence gathered from the Proof of Concept project, the review will assess the level of confidence that TB can technically be eradicated in New Zealand.

1.4 Out of scope

1. Areas outside of the scope of the review include:
    - Looking at research into the control of TB vectors for biodiversity purposes[2];

1 The Plan Governance Group represents the TB Plan funding parties, with membership including the Chief Executives of Beef+Lamb, DairyNZ, DeerNZ & OSPRI, an MPI representative, an independent member and an independent Chair.

2 A need has been identified for separate scientific research into the impacts of TB plan vector control on biodiversity values, and on the interplay between possum control for TB disease management purposes and NZ biodiversity conservation objectives. The Plan Governance Group is considering this issue.

- Considering the merits of different management options for TB in New Zealand; and
- Commenting on the operational management of the TB Plan, i.e. how scientific research is incorporated into TBFree NZ's operational policies and reflected in key performance measures against which achievement of the Plan's objectives are met.

1.5 Methods of review

1. TBFree NZ will compile information on the research programme including:
   - A cover paper outlining the case that the Proof of Concept project[3] is progressing well towards TB freedom in the test areas;
   - The TB eradication research that has been completed or is in progress and the reports documenting this work; and
   - The research that has been commissioned since 2009 (noting that the review must not duplicate the 2009 review of the TB science – see Appendix One) and any other relevant research from outside the TBFree NZ research portfolio.
2. The expert reviewer will review the written material and, if necessary, interview key researchers, funding partners and the management agency as appropriate. The interviews will be facilitated by TBFree NZ and the TB Plan Review Secretariat.

1.6 Outputs

1. The expert reviewer will write a report, peer-reviewing the existing science underpinning the proposition that TB can be completely eradicated from New Zealand (noting that the Proof of Concept process, where TB eradication is being pursued in two large and inaccessible forest blocks, has not yet been completed).

2. The report should provide an expert opinion on whether biological eradication of TB is feasible, and whether the right methodology is being used. It should also comment on the proposition of reducing the probability of freedom at which an area is declared TB free from the current 95%.

[3] The Proof of Concept process: TB eradication is being pursued in two large and inaccessible forest blocks in the Hokonui, Hauhungaroa and Rangitoto Ranges. In these areas, TBFree NZ is trialling different control methodologies, followed by intensive wildlife surveillance, to prove that eradication is possible in deep bush areas and that these methods can be used on a wider scale.

2 Methods of review

2.1 Peer review of existing science underpinning eradication

Full details of key scientific papers used in preparing this review are as follows:

Paper 1: Livingstone, P. G., Hancox, N., Nugent, G., and de Lisle, G. W. (2015). Toward eradication: the effect of *Mycobacterium bovis* infection in wildlife on the evolution and future direction of bovine tuberculosis management in New Zealand. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.971082

Paper 2: Buddle, B. M., de Lisle, G. W., Griffin, J. F. T., and Hutchings, S. A. (2015). Epidemiology, diagnostics, and management of tuberculosis in domestic cattle and deer in New Zealand in the face of a wildlife reservoir. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.929518

Paper 3: Nugent, G., Buddle, B. M., and Knowles, G. (2014). Epidemiology and control of *Mycobacterium bovis* infection in brushtail possums (*Trichosurus vulpecula*), the primary wildlife host of bovine tuberculosis in New Zealand. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.963791

Paper 4: Byrom, A. E., Caley, P., Paterson, B. M., and Nugent, G. (2015). Feral ferrets (*Mustela furo*) as hosts and sentinels of tuberculosis in New Zealand. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.981314

Paper 5: Nugent, G., Gortazar, C., and Knowles, G. (2015). The epidemiology of *Mycobacterium bovis* in wild deer and feral pigs and their roles in the establishment and spread of bovine tuberculosis in New Zealand wildlife. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.963792

Paper 6: Barron, M. C., Tompkins, D. M., Ramsey, D. S. L., and Bosson, M. A. J. (2014). The role of multiple wildlife hosts in the persistence and spread of bovine tuberculosis in New Zealand. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.968229

Paper 7: Warburton, B., and Livingstone, P. (2015). Managing and eradicating wildlife tuberculosis in New Zealand. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.981315

Paper 8: Anderson, D. P., Ramsey, D. S. L., de Lisle, G. W., Bosson, M., Cross, M. L., and Nugent, G. (2015). Development of integrated surveillance systems for the management of tuberculosis in New Zealand wildlife. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2014.963830

Paper 9: Livingstone, P. G., Hancox, N., Nugent, G., Mackereth, G., and Hutchings, S. A. (2015). Development of the New Zealand strategy for local eradication of tuberculosis from wildlife and livestock. *New Zealand Veterinary Journal*, Early online. doi: 10.1080/00480169.2015.1013581

In addition, the review critiques material from the unpublished summary paper 'Evidence supporting the technical feasibility of eradicating entrenched bovine tuberculosis (TB) infection from wildlife in forested areas or difficult operational terrain' by Nugent & Livingstone (2015). This was provided as further reference material along with a summary documents detailing the process of undertaking proof of freedom analyses by the TBFree Review team during May 2014. Other literature was used where necessary, but emphasis was placed on the previously mentioned sources.

2.2 Feasibility of biological eradication

The methodology required for a successful eradication programme was reviewed, starting with the management of bovine tuberculosis (TB) in livestock, epidemiological understanding of TB in free-ranging wildlife, choice of target species for control, control methods and surveillance methods for monitoring eradication progress.

Furthermore, the author considered ways in which an attempt at eradication may fail.

The technical feasibility of eradicating TB using alternatives to 1080 was assessed using the literature and interviews with key personnel.

3 Review of underpinning science

3.1 Summary of designated papers

Table 1. Brief summary of the findings of the key research papers included in this review.

Study	Method	Key findings/comments
Livingstone *et al.* (2015a). Toward eradication ...	Review	Management of TB in possums is central to New Zealand's TB control programme. Wide-scale eradication of TB from wildlife populations is a realistic prospect.
Buddle *et al*. (2015)**.** Epidemiology, diagnostics, and management of tuberculosis in domestic cattle and deer in New Zealand ...	Review	Describes state-of-the art approaches to diagnosis and management of TB in NZ livestock. Improved testing and stakeholder engagement has resulted in major reductions in the number of TB-infected deer herds, thus solving what had been a previously challenging problem. DNA typing of *M. bovis* isolates has contributed to improved decision making through better inference on source of infection.
Nugent *et al*. **(2015a).** Epidemiology and control of *Mycobacterium bovis* infection in brushtail possums ...	Review	Existence of threshold population density for TB persistence in possums. Demonstration of eradication of TB in possums in response to population reduction. Vaccination not at a stage where it can meaningfully contribute to managing or eradicating TB from possum populations.
Byrom *et al.* (2015). Feral ferrets (*Mustela furo*) as hosts and sentinels of tuberculosis in New Zealand	Review	Transmission is density-dependent, though population densities are typically insufficient to exceed threshold densities for TB persistence. Risk of transmission of TB to possums outside VRA negligible. Failed to observe pigs scavenging on ferret carcasses, leading to ferret-to-pig transmission being considered low

		probability. Increasingly important as sentinel species as program moves into surveillance.
Nugent *et al*. (2015b). The epidemiology of *Mycobacterium bovis* in wild deer and feral pigs ...	Review	Key role of hunting (both recreational and aerial commercial) in maintaining wild deer and feral pig populations at densities below what is required for TB persistence. Hence control operations targeting deer not needed to achieve freedom. Feral pigs are the most important sentinel species in deep forested habitat where they occur.
Barron *et al.* (2015). The role of multiple wildlife hosts in the persistence and spread of bovine tuberculosis in New Zealand	Modelling. Differential equation approach with parameters derived from the literature.	Identified mechanism for potential TB control failure in 3-host system (possums-ferrets-pigs). Recommended monitoring in relevant environments (e.g. Molesworth Station) to check. Some key parameters are highly uncertain, including ferret-to-pig transmission rates through scavenging. See note previous note from Byrom *et al*. that failed to document pigs scavenging on ferret carcasses, so this finding remains hypothetical.
Warburton & Livingstone (2015). Managing and eradicating wildlife tuberculosis in New Zealand	Review	Lethal control remains the only viable option for managing *M. bovis* infection in New Zealand wildlife. Highlights the key role that possum monitoring has played in driving improvements in control methods.
Anderson *et al*. (2015). Development of integrated surveillance systems for the management of tuberculosis in New Zealand wildlife	Summarizes the work of Anderson *et al.* (2013) underpinning the Proof of Freedom utility.	Assumes the possums are the only true maintenance host for *M. bovis.* Ferrets are particularly useful as TB sentinel species in farmed areas where feral pigs and wild deer are absent.
Livingstone *et al*. (2015b). Development of the New Zealand strategy for local eradication of tuberculosis	Reviews the progressive development of NZs national strategy for control of bovine TB.	Note that progress is ahead of schedule. Documents four decades of evolution and improvement such that TB freedom has been achieved in large areas in

from wildlife and livestock	Vector Risk Areas [areas with TB in wildlife]. Continued reduction in the number of TB-infected herds and the size of VRAs. Predict that eradication of TB prior to year 2055 providing funding maintained near current levels.

3.2 Wildlife epidemiology

3.2.1 General

The key scientific papers in Table 1 reveal considerable scientific endeavour to assess the host status of free-ranging mammal species, and to a lesser extent species complexes.

3.2.2 Host status

At a species level, it is incontrovertible that the brushtail possum (*Trichosurus vulpecula*) is maintenance host for *M. bovis* in New Zealand (Livingstone *et al.* 2015a). Efforts to understand the epidemiology of *M. bovis* in possums have been extensive, and further insights into mechanisms of intra-specific transmission have been made since the last review although understanding remains incomplete (Nugent *et al.* 2015a), particularly in relation to the relative importance of the different transmission pathways. The only other species of potential concern are feral pigs (*Sus scrofa*), wild deer (*Cervus* spp.) and feral ferrets (*Mustela furo*). These are dealt with in turn.

Feral pigs

Based on the review presented in Nugent *et al.* (2015b) and ongoing surveillance data of pig populations in areas subject to intensive broad-scale possum control (Nugent and Livingstone 2015), the empirical inference that pigs are spillover hosts in New Zealand environments continues to strengthen. Furthermore, the rate of horizontal transmission between feral pigs appears low enough that their basic disease reproductive rate (R_0) is much less that one, and hence there is little doubt they are unable to act as a maintenance host for *M. bovis* in New Zealand environments. This is consistent with the host status of feral pigs in northern Australia (Corner *et al.* 1981; McInerney *et al.* 1995), but at odds with the apparent maintenance host status of wild boar in Mediterranean Europe (Boadella *et al.* 2012). Postulated reasons for the difference revolve around different wildlife management systems (e.g. provision of water and food), ecology and climate in Mediterranean Europe leading to higher density and more highly aggregated populations of boar. Nugent *et al.* (2015b) furthermore estimate that the effect of hunting of pigs in New Zealand is to reduce populations to 1-2 orders of magnitude less than *M. bovis*-infected boar populations inhabiting hunting estates in Spain with supplementary food and water.

Wild deer

At high densities found on farms, or in free-ranging conditions with supplemental feeding, it is well established that several deer species may act as maintenance hosts for *M. bovis*. Nugent *et al.* (2015b) argue that year-round hunting in New Zealand results in low-density populations living individually or in small family groups, in contrast to the larger aggregations observed overseas where the hunting season is short and densities elevated. Indeed the presence of helicopter hunting has prevented deer utilizing the tussock country above the tree line and forming large herds. In contrast, deer in New Zealand that are largely restricted (through learned behavioural avoidance) to the forest edge and deep forest tend to form much smaller herds. This is argued to result in reduced intra-specific transmission rates between deer in New Zealand, to the extent that most deer populations in New Zealand are incapable of acting as maintenance hosts for *M. bovis.* Nugent *et al.* (2015b) present empirical data to support a major reduction and downward trend in the prevalence of *M. bovis* infection in red deer (*Cervus elaphus*) to low levels (but not zero) in the central North Island in response to possum control. More recent unpublished data (Nugent and Livingstone 2015) confirms this decline to a very low prevalence of infection (0.4%) in areas to long-term high quality possum control. Note however, that strictly speaking, a low prevalence alone does not rule out maintenance host status. An overseas example of the persistence at low prevalence of *M. bovis* (albeit not as low as 0.4%) in a reasonably low density population of wapiti elk (*Cervus elaphus manitobensis*) is Riding Mountain National Park, Canada (Nishi *et al.* 2006). This elk population subjected to seasonal hunting only, but is subject to ongoing wolf (*Canis lupus*) predation. Importantly from the point of understanding factors that elevate disease transmission, the population was still subject to supplementary feeding in winter until recent times (O'Brien *et al.* 2011). In response to restricting access to supplementary feeding (fencing hay storage yards adjacent to the park boundary) it appears that TB in this elk herd is on track for eradication. Supplementary feeding is a recurring risk factor for increased transmission and persistence of TB in wildlife (Miller and Sweeney 2013).

The empirical data collected in New Zealand to date are not inconsistent with wild deer being spillover hosts for *M. bovis* in New Zealand environments. The very low level of residual TB found in deer in the Hauhungaroa Ranges 'Proof of concept" area could possibly be explained by either residual possum-to-deer infection, or by limited deer-to-deer transmission. Importantly, the latter should not be interpreted as being inconsistent with *M. bovis* infection being unable to persist in deer populations in these environments (i.e. spillover host classification).

At a Vector Control Zone (VCZ) scale, evidence to date also remains not inconsistent with the spillover host classification for deer – many of VCZs with eradication declared have resident wild deer populations. Indeed, the central forested area of the Hokonui Hills 'Proof of concept' area which increasingly appears to be free of disease (Nugent and Livingstone 2015) contains resident red deer.

Note should be made that sika (*Cervus nippon*) and fallow deer (*Dama dama*) attain locally high densities, partly as a result of not being targeted by commercial operations, which should heighten the potential rate of intra-specific TB transmission. That said, in the unlikely event that TB had entered and was persisting in these populations, remedial action would be reasonably straightforward technically, though potentially politically challenging if local resistance to control is encountered.

Feral ferrets

Ferrets have received considerable research attention as a potential host for TB, and studies revealed that intra-specific transmission, predominantly through scavenging, is density-dependent and at high densities can potentially be sufficient for disease persistence (Byrom *et al.* 2015). That said, there are very few if any locations in New Zealand where the presence of TB ferrets is stymieing eradication efforts. Nugent & Livingtone (2015) note the possibility of ongoing TB transmission in ferrets on farmland surrounding the Hokonui Hills proof of concept area. The distribution of ferrets is restricted to more accessible open environments, which lessens their ability to complicate efforts at TB eradication. As such, they can readily be controlled if need be using a variety of methods. As a result of widespread possum control activities, there is increasing empirical evidence that the inference of Caley & Hone (2005) that ferrets are spillover hosts in all but the highest density habitats is correct. For example, Scargill Valley in North Canterbury supports moderate ferret numbers, and prior to possum control instigated in the late 1990s, ferrets had a moderate TB prevalence (*c.* 11% with macroscopic lesions). During eradication surveillance during 2011—2013 none of 211 ferrets captured had evidence of TB (TBFree NZ unpublished data).

Species complexes

Quantifying the importance of species complexes as hosts for TB is particularly challenging from an experimental point of view, as typically there are too few data to empirically test the rates of intra- and inter-species transmission (Nugent 2011). For that reason, the science underpinning the knowledge of the importance of multi-host complexes has relied on modelling (e.g. Barron *et al.* 2015). Using the best available data, Barron *et al*. examined a possum-deer-pig complex in forest and a possum-pig-ferret complex in un-forested semi-arid shrub and grasslands. Within the forest habitat, the presence of pigs or deer did not jeopardise the success of possum control in eradicating Tb using best practice control methods. In contrast, for the possum-pig-ferret system possum control alone could potentially result in eradication failure, although this result is reliant on an extrapolated value for what is an unknown probability of feral pigs scavenging on ferret carcasses. Notably, Byrom *et al*. (2015) report no scavenging of feral pigs on ferret carcasses in a reasonable scale experiment in which pigs where known in the study site, so it appears the ferret-to-pig transmission rate parameter used by Barron *et al*. (2015) is likely too high. Supporting this contention is the observation that areas of North Canterbury subject to possum control that contain good sympatric populations of both feral pigs and ferrets (e.g. McDonald Downs VCZ) are progressing smoothly to eradication status (TBFree NZ unpublished data), as would be expected on the basis of the pig-ferret complex being unable to maintain infection.

3.3 Response to control

The effect of possum control operations on possum populations is well understood as a result of considerable research and development as summarised by Warburton and Livingstone (2015). It is now possible to predict with reasonable certainty the likely outcome of control operations, whether they be ground-based or aerial.

It probability cannot be overstated how important the development and application of a standardised method of monitoring possum abundance has been in driving innovation and improved performance in the possum control sector and hence TB-control outcomes. Featuring the key components of randomization, replication, and standardisation, it demonstrates best-practice applied on a scale unparalleled. Compliance levels are very high (Nugent and Livingstone 2015).

The effect of possum control operations on the TB incidence is well understood in cattle (Livingstone *et al.* 2015a), possums (Nugent *et al.* 2015a), wild deer and feral pigs (Nugent *et al.* 2015b) and ferrets (Byrom *et al.* 2015). All these studies document extensive research underpinning the current National Pest Management Strategy (NPMS) for TB.

3.4 Monitoring progress – Proof of Freedom Utility

3.4.1 General

The Proof of Freedom utility (PoF) is a critical component of eradication in quantifying freedom of disease at the operational scale. Importantly, the inference of likely eradication allows resources to be redeployed elsewhere, with such resource allocation decisions potentially subject to optimisation.

3.4.2 Robustness of inference

The underlying Bayesian approach is both logical and on the whole sound. One issue of note, however, is the assumption of spatial independence of wildlife surveillance sampling in different years. In particular, when undertaking updating (‘revision’) of the probability of TB freedom on the basis of wildlife surveys, the inferential method assumes that the proportion of units sampled within the VCZ are selected randomly in space. There may be an issue if accessibility dictates that samples are only possible from a portion of the VCZ, and this inaccessibility persists between surveys. In this case, calculations may overestimate the probability of eradication. This concern does not apply for possum control followed by a single set of surveillance data, but rather when incorporating surveillance data collected at sequential time periods when surveillance is patchy and tending to be from the same locations. Such patchiness could be due to reasons of accessibility or availability of sentinel species. Note it is possible to plug ‘holes’ in surveillance using, for example, sentinel released pigs (Nugent *et al.* 2014).

Possible approaches/solutions include:

1. Ignoring the potential biases and dealing with incorrect TB freedom declarations as they become apparent.
2. Ensuring upfront that repeated wildlife surveillance surveys are not biased in spatial location.
3. If spatial sampling of surveillance is not independent, combining sequential surveys deemed close enough together into a single surveillance event, and hence a single (rather than sequential) updating step for the probability of freedom.
4. Subdividing the VCZ into smaller units to reflect the difference in surveillance intensity.

5. Modifying the underlying calculations within the PoF to maintain the fine-grained spatial component of the inference.

All options have pros and cons that are best considered in light of their impact on operational outcomes and the overall success of the programme. A point to keep in mind is that in relation to its use as an operational management tool, increasing the complexity of the PoF to handle all possible scenarios with respect to surveillance intensity in space and time may not be warranted. A degree of professional judgement is inevitably involved, and more complex VCZ cases are possibly best dealt with as special cases. Indeed, the current application of the PoF utilizes expert opinion of vector control managers in the evaluation process. Early indications are that VCZs declared free to date are not relapsing at a rate that would suggest the PoF is anything but conservative.

3.4.3 Validation

Nugent & Livingstone (2015) argue that the inference arising from the PoF is on the conservative side for a number of reasons. This includes restricting the prior belief in eradication arising from the spatial possum TB model (SPM) (Ramsey and Efford 2010) to be no higher than 0.9, when in reality it may be higher. In addition, they argue that if the residual possum population within a VCZ is sufficiently below the threshold for disease persistence, then the probability of eradication will increase for as long as the recovering population remains under this threshold, whereas the PoF simply uses the time point immediately following possum control as it's measure of prior belief of eradication, based on the SPM. These arguments have validity. Reasons for a conservative approach typically include wanting to minimise the probability of falsely declaring eradication (a Type I error). Of course, in the current TB management scenario there is a trade-off between committing resources to increase the level of confidence in eradication and allocating the resources elsewhere. This is addressed below in Section 3.4.4.

I have examined the decision making process that utilizes the PoF (TBFree NZ unpublished data), and can find at least one example VCZ (Scargill, North Canterbury) where the conservative application of the PoF corrects what appears to be incorrect prediction of the Spatial Possum Model. To be specific, Tb failed to persist in the possum population in any of the simulations, which is at odds with the discovery of a TB possum on the slopes of Mt Alexander in the mid 1990s and the strong inference that an *M. bovis*-infected possum population was the underlying cause of the moderate incidence of infection observed in ferrets (Caley *et al.* 2001b; Caley and Hone 2004). That is, the discovered possum was not a 'one-off' event that can be ignored. Indeed, prior to possum control in the Scargill Valley area, the residual trap catch index within possum habitat was moderate 13.1% (Caley *et al.* 2001b). The reasons for this error could be errors in the habitat map (patches of suitable possum habitat not being included), or bias in the spatial possum model. I note that other VCZs in North Canterbury (e.g. Doctors Hills) also predict no persistence of *M. bovis*-infected possums despite mentioning that they have been found in the general vicinity. So there appears to be a case for undertaking some further validation of the spatial possum model in areas which contain small patches of habitat with moderate densities of possums. I note that Ramsey & Efford (2010) didn't undertake small-scale validation of their model like I have alluded to here. I strongly suspect it is under-predicting the establishment and persistence of TB possums in these environments. In this case is appears that restricting the prior probability of TB eradication to 0.9 may be correcting for bias in the PoF in these habitats – supporting the conservative approach for these habitats in particular. The predictions of the possum/Tb component of the PoF in more extensive forested areas are likely to be better calibrated, as features of possum Tb epidemiology from such environments were used by Ramsey & Efford (2010) during model development.

Such questions also highlight the issue of (1) whether empirical validation of the PoF is needed, and if so, (2) how best to achieve this. Given the eradication programme is set to run for several decades, and at considerable expense, it would seem that a degree of empirical validation of the PoF could be beneficial. A degree of validation can already occur using data arising from the current target threshold probability of P_{free}>0.95 – under this stopping rule the expectation would be for TB to re-emerge in less than 5% of VCZs declared TB free. With approximately 100 VCZs to be declared free by the end 2014/15 out of approximately 780 VCZs (Nugent and Livingstone 2015), it is clear that data on failures will be reasonably sparse in the early stages using this threshold unless the PoF is strongly biased towards optimism (in which case there will be more failures than expected). Gathering data on failures more quickly could be achieved by using a lower threshold for P_{free} for declaring eradication, although this would come with potential challenges relating to stakeholder expectations.

Nugent & Livingstone (2015) note the near 200 VCZ years of freedom with no failure, but it is clearly early days, and it may take some time to discover what eradication failure looks like, especially in terms of time to detection, and size of infected possum cluster. For those VCZs that do fail, one would expect the risk in doing so to rise from an initial low base. There is a need to scope out possible approaches to validating the PoF empirically, including consideration of the statistical model required to make reasonable inference.

Nugent & Livingstone (2015) also present other useful refinements to the approach including undertaking possum TB surveillance prior to control, incorporation of herd testing and abattoir surveillance data, early initiation of surveillance, and more flexible stopping rules (see Section 3.4.4). All are worthy of consideration.

3.4.4 Target threshold probability for declaring success

Currently TB freedom is declared in management areas (termed Vector Control Zones, VCZs) when the probability of freedom from disease, P_{Free} reaches 95%. This is recognized as an arbitrary trigger threshold. The development of a decision-support framework should assist in optimising the allocation of resources with respect to the cost and/or rapidity of disease eradication. This would likely lead to different optimal stopping rules depending on the location and situation (Anderson *et al.* 2015). Stakeholder acceptance of target thresholds is of course critical.

4 Feasibility of biological eradication of TB

4.1 Methodology

4.1.1 General

Livingstone *et al*. (2015b) document a culture of continuous improvement in evaluation of the National Pest Management Strategy for TB. They identify four key drivers of success relating to (1) Engagement with stakeholders, (2) Clear lines of responsibility and accountability, (3) Improvements in TB livestock management, and (4). A scientific and evidence-based approach to the surveillance and control of TB in wildlife. I concur with these conclusions. Furthermore, what would be described as adaptive management has been central – ideas were generated, methods were applied, outcomes were recorded and evaluated and subsequent approaches adjusted. There has been considerable innovation across all areas of the programme.

4.1.2 Target species

The current strategy correctly targets the brushtail possum as the key and probably only maintenance host for *M. bovis* in New Zealand environments (Nugent *et al.* 2015a). Wild deer and feral pigs are not currently targeted for control. Ferrets are targeted in some areas to reduce their ability to act as maintenance hosts, but largely to inform Proof of Freedom calculations. There remains the potential issue of 'spill-back' transmission, particularly in forested areas from potentially long-lived infected deer to possum populations. The risk of this remains unclear, although infected farmed deer (for which infection has often been characterized as having a more 'explosive' nature) have been identified as the source of TB possum populations on a number of occasions so it cannot easily be ruled out. Modelling by Barron *et al*. (2013) suggests that major reductions in deer would little reduce the duration of spill-back from deer to possums. The appropriate response at this stage appears to be ongoing surveillance using feral pigs in particular, as they are by far the most effective sentinel species (Anderson *et al.* 2015).

Feral pigs themselves also pose a risk of spill-back transmission, though are less long-lived. Of more concern is the movement of both live pigs and pig carcasses long distances by hunters, with subsequent release or discarding of the head, respectively. Again, the gains from targeting pigs directly are unlikely to be great (apart from informing Proof of Freedom calculations), particularly compared with the possible gains through changing hunter behaviour. As noted by Nugent *et al*. (2015b), a degree of intra-specific TB transmission for both deer and pigs, even at levels well below that needed to achieve maintenance host status, has the potential to obscure the fact that TB may have been eradicated from possum populations.

4.1.3 Livestock testing methods

In the absence of a wildlife reservoir of infection, the systems for diagnosis and management of TB in domestic cattle and deer herds would have achieved eradication of TB many years ago. The methods developed for TB testing outlined by Buddle *et al*. (2015) would be considered world's best practice.

4.1.4 Wildlife control methods

There has been extensive research and development into improving the efficacy and efficiency of possum control in New Zealand (Warburton and Livingstone 2015). The current operational targets of a mean residual trap-catch index (RTCI) of 1-2% couple with individual line maxima appear to be achievable over large scales, even in inaccessible extensive forested areas (Nugent *et al.* 2015a). There is empirical evidence for the existence of a threshold density for *M. bovis* persistence in possums (see Figure 1 in Nugent *et al.* 2015a), but some evidence this may not be consistent between habitats. In particular, TB infection in possums inhabiting the West Coast of the South Island appears to be more persistent in the face of control efforts, potentially requiring higher levels of control to achieve eradication (Nugent *et al.* 2015a). Elsewhere, such reductions in possum density are reliably achieving eradication of TB from possum populations, and other sympatric hosts.

4.1.5 Wildlife surveillance methods

Extensive development of the sentinel species approach has culminated in the Proof of Freedom utility (Anderson *et al.* 2015). Notwithstanding the possible improvements outlined in Section 3.4, I consider this provides, along with expert input, a robust approach for monitoring the success of any TB eradication programme in a timely manner.

4.1.6 Re-emergence

It is inevitable that there will be re-emergence in some vector control areas declared free, and what could be considered 'spontaneous' wildlife infection geographically removed from known Vector Risk Areas, for which the source is unclear. The one recent outbreak outside of the known VRAs, in the Rolleston Range, mid Canterbury, appears to have been effectively controlled by a localized response (Nugent and Livingstone 2015). Abattoir surveillance of livestock, despite its low sensitivity, can be an effective back-up for other surveillance methods wherever livestock occur.

4.1.7 Overseas experience

It is becoming increasingly likely that Australia has successfully eradicated bovine tuberculosis (and brucellosis) from domestic livestock and free-ranging hosts. The free-ranging hosts of particular relevance were water buffalo (*Bubalus bubalis*) and feral pigs (*Sus scrofa*) inhabiting the floodplain habitats of the 'Top end' of the Northern Territory.

Key facts of note include whilst buffalo populations on the floodplains were very nearly eradicated (e.g. the number remaining in Kakadu National Park potentially in single digits), it is probable that the disease wasn't eradicated by the end of the population reduction phase. Rather, the disease died out as the effective disease reproduction number within the residual population was too small for persistence (i.e. less than unity).

The key message is that killing every last TB-infected individual is not essential to achieve disease eradication.

4.2 Proof of Concept area findings

All the components required for eradication were brought to bear in to two so-called 'Proof of Concept' (POC) areas, the Hokonui Hills in Southland and the Haughungaroa/Rangitoto Ranges in the Central North Island.

4.2.1 Hokonui Hills

As outlined in the material provided in Nugent and Livingstone (2015), there is strong evidence (p_{free}≥99%) that Tb has been eradicated from the 160 km^2 heavily forested centre of the Hokonui Hills Vector Risk Area. This evidence takes the form of necropsies of >4,000 possum and some tens of feral pigs with no Tb found. The trial suggests that eradication was probably achieved within the core area following just two aerial poisoning operations.

4.2.2 Hauhungaroa and Rangitoto Ranges

The Hauhungaroa and Rangitoto POC areas are substantially larger (1,200 km^2) than the Hokonui Hills, and contain higher populations of wild deer and feral pigs. With a long history of Tb in wildlife, this area would be considered as logistically challenging as any VRA except perhaps the more rugged parts of the West Coast of the South Island.

The notable operational outcome was the success of the 2005 aerial possum control operation comprising intensive dual pre-feed, followed by 1080 baits. Covering 830 km^2, the operation produced an exceptionally low residual trap catch index (0.04%), much less that the pre-control index of >20%. Where monitored directly, Tb infection in possums has disappeared from areas where it was previously prevalent. Elsewhere, operational surveillance of Tb in deer and pigs has been instigated, and has demonstrated that it is feasible to obtain sufficient numbers of pigs in particular, to make robust inference on Tb freedom within a reasonable time frame. The reduction in the prevalence of Tb in the sampled feral pigs has been dramatic, and consistent with the eradication of Tb from possums. Ongoing Tb is expected to persist in pigs until it is no longer present in deer, due to their high sensitivity as a sentinel species.

The reduction in the prevalence of Tb in deer has also been large, with only one in 226 (0.4%) sampled since 2011 being infected. The sole infected individual was sampled in 2013 from a location in close proximity to a previous known cluster of possum Tb, although it's estimated age suggested infection may have occurred following the 2005 possum control operation. This should not be seen as cause for concern at this stage, as even with high levels of possum control (to below the disease threshold), it is possible that some Tb-infected possums would survive. Furthermore, Tb could persist for a period until the deterministic forcing from the population being at less than the disease threshold leads to the chains of infection becoming extinct. That said, it is important to recognise that the process of disease elimination has a stochastic (chance) component, and ongoing surveillance (in this case using sentinel species) is the best way of detecting and dealing with low probability outcomes.

The Proof of Freedom utility predicts that Tb freedom will be reached for most of the VCZs within the area following final aerial poisoning operations during the winter of 2016.

4.3 Risks

It is valuable to consider what may be considered 'left-field' risks to a successful TB eradication programme in New Zealand.

4.3.1 Unknown wildlife maintenance species and/or species complex

The restricted number of mammalian species makes it unlikely that there is an as yet unknown maintenance host species, and I consider reasonably exhaustive studies have covered off on all potential mammalian species of concern. Tb infection has been recorded in feral goats (*Capra hircus*) in New Zealand (Allen 1987), though management evidence strongly demonstrates that goats are insignificant spillover hosts in New Zealand. For example, Tb has been successfully locally eradicated from areas of the King Country where feral goats are numerous, and undoubtedly would have been exposed to Tb infection. A limited number of feral cattle (*Bos spp.*) occur in locations in both islands. In the event of these herds becoming infected with *M. bovis*, this would complicate eradication at the local level, though should be relatively straightforward with existing technologies (e.g. Judas collar method). There has been no need to assess the host status of either Himalaya tahr (*Hemitragus jemlahicus*) or chamois (*Rupicapra rupicapra*) for bovine Tb, and I see no need to include them in the eradication programme at this stage.

Both alpacas (*Lama pacos*) and llamas (*Lama* glama) are susceptible to infection by members of the *M. tuberculosis* complex. At this stage I would consider it unnecessary to consider additional surveillance (e.g. herd testing) beyond routine animal husbandry and abattoir surveillance. If epidemiological evidence suggests within-herd transmission of Tb, then clearly further action will be required.

The key issue is whether Tb will be controllable—the Tb programme continues to generate additional empirical evidence that there is no need to invoke alternative explanations (e.g. an as yet unidentified maintenance host) to explain observed TB infection in either livestock or wildlife.

4.3.2 Reintroduction of *M. bovis* strain of animal health importance

There exists a very low but non-zero probability of unassisted reintroduction of *M. bovis* into New Zealand, for example from TB strains infecting seals (Cousins *et al.* 2003). Research to date, however, suggests that horizontal transmission within cattle of such strains is near to non-existent (Loeffler *et al.* 2014). If the disease did spill into wildlife hosts such as possums, this would be detected in abattoir surveillance with follow up wildlife surveillance, population control and disease eradication. The scale of such an eradication operation would be small, even allowing for the expected delays before the disease was detected in livestock.

There is also the remote, but real possibility of reintroduction through wildlife trade of *M. bovis* infected animals, typically as part of zoo transfers (e.g. Pavlin *et al.* 2009). Effective controls are in place to eliminate this risk. Furthermore, if an outbreak occurred in a zoo environment, where possums may have access, then surveying the possum population and eradicating any disease outbreak would be considered routine. There is also a risk of Tb reintroduction arising from the importation of farm animals — there are small numbers of cattle imported into New Zealand, and a steady trade in the import of alpacas. Import health standards are available for other species so these could potentially be imported too. In the advent of an undetected introduction, again I consider that eradication would be reasonably straightforward.

4.3.3 Pathogen evolution to genotype with lowered threshold density for persistence.

The *Mycobacterium* complex clearly has the ability to evolve to persist in different mammalian hosts (e.g. seals, goats). An argument could be made that ongoing suppression of possum populations should provide selection pressure for *M. bovis* variants with a higher transmission rate within possum populations. It is highly unlikely, however, that *M. bovis* will be able to respond to this selection pressure – being a slow growing and slow acting pathogen, the rate of selection of *M. bovis* is unlikely to be able to keep up with the rapidity of the control measures imposed on its host population.

4.3.4 Reduction in hunting pressure

As noted in Section 4.1.2, recreational and commercial hunting is argued to be a factor in preventing both wild pigs and wild deer acting as maintenance hosts in New Zealand environments, including remote locations such as Fiordland. Increasing population turnover is a well known method of increasing the likelihood of eradication of many pathogens. This arises through reducing the infectious period over which and infected individual can transmit infection, and in this case also by reducing density and the extent of animal aggregations. In the short-medium term (10-20 years) there is probably little risk of a major reduction in the off-take from recreational hunting. Over the longer term, however, it would be prudent to monitor ongoing harvesting levels as generational changes in attitudes to hunting are possible. The future of helicopter-based commercial hunting of deer is harder to predict in both the short and longer term. Monitoring of hunting off-take, particularly in VCZs scheduled for later eradication, would seem wise. Any major decline could be countered with TBFree-funded aerial culling operations that could also serve to inform proof of freedom calculations.

4.3.5 Game parks

Game parks or privately run holdings that artificially inflate the densities of wild deer and/or wild pigs through the provision of artificial feedings sites appear capable of creating conditions in which both species may act as maintenance hosts for *M. bovis.* The creation of game parks within Vector Risk Areas would be considered unwise unless subject to tight surveillance measures, backed up by the ability to destock should *M. bovis* become established.

4.4 Technical feasibility of eradication using alternatives to 1080

Assuming that aircraft can still be used to broadcast toxic bait, there remains a range of toxins that could be used in place of 1080, albeit with typically lower expected kill rates and higher costs.

Options include zinc phosphide (Eason *et al.* 2013), cholecalciferol (Hix *et al.* 2012), and the anticoagulants brodifacoum and pindone (Eason *et al.* 1993).

If it is the ability to aerially broadcast toxic bait that is the issue, then VCZs currently or planned to be subject to aerially based control would need to be subject to ground control methods. It is believed that all but the steepest terrain can be controlled using ground based techniques, but at substantially increased cost (about 4-fold has been mentioned – Graham Nugent pers. comm.). That said, there is probably scope for innovation in control methods, for example using aircraft to deliver non-toxic pre-feed followed by ground-based bait delivery along pre-feed lines, and using helicopters to ferry bait and workers to areas difficult to reach by foot. It should also be noted that aerial 1080 is used in *c.* 25% of the currently managed area.

Much of the more difficult terrain is at altitudes where the possum density is low, and TB predicted to be low if present at all (see Caley *et al.* 2001a). Monitoring of both possums and sentinel species would play a important role in targeting control in such areas.

In my opinion, under either scenario it will remain technically feasible to achieve biological eradication of TB from New Zealand without compound 1080, though with increased costs, and potentially longer timeframes.

Other factors that may play into this debate include:

- Current indications are that resources should be available for reallocation as additional VCZs are declared TB free.
- From a communications perspective, it should soon be possible to forecast a decline in 1080 usage as the number of VCZs reduces, thus potentially alleviating the concerns of interest groups.

5 Summary findings

Review of science underpinning proposition of TB eradication

The science underpinning the proposition that *Mycobacterium bovis* (TB) can be completely eradicated from New Zealand is on the whole sound. The scientific material put forward for this review covers off on the key components required for eradication, namely:

- effective disease management systems in livestock enabling straight forward disease eradication in the absence of a wildlife disease reservoir,
- adequate knowledge of the epidemiology of TB in New Zealand wildlife,
- effective control technologies of brushtail possum populations (the primary wildlife maintenance host for *M. bovis*) backed by robust compliance monitoring of control operations, and
- quantitative methods for making inference on the presence of TB in wildlife populations through the integration of multiple surveillance sources, and thus monitoring the success of the program in real operational time.

There are aspects of the science that could potentially be improved. The Proof of Freedom utility has some inbuilt assumptions that in some situations could lead to the probability of eradication being overestimated, although judicious use should avoid this leading to incorrect decisions. It also appears to under-predict the possibility of Tb persisting in possums in some environments. For this reason there should be consideration given to some form of validation.

Technical feasibility of biological eradication

I consider that the biological eradication of TB is feasible with current levels of funding, and can be achieved under existing timeframes. The methodology currently being deployed is adequate for the control and eradication of TB in livestock and wildlife, with efficacy measures that can be supported empirically. There remains the opportunity to optimize the allocation of resources, particularly in relation to the level of certainty of TB eradication required within Vector Control Zones before moving to surveillance only.

I consider that at this stage the known potential risks to successful eradication can be managed with current knowledge and technical capabilities. The 'Proof of Concept' areas in the Hokonui Hills and Hauhungaroa/Rangitoto Ranges are well progressed toward eradication, clearly demonstrating the technical feasibility of achieving eradication over large inaccessible areas.

Technical feasibility of eradication using alternatives to 1080

It will remain technically feasible to achieve biological eradication of TB from New Zealand without the use of compound 1080, though with increased costs, and potentially longer timeframes.

Management agencies charged with managing TB should maintain an operating environment where innovation can continue to occur, across all aspects of the eradication program, as has occurred since the implementation of the first National Pest Management Strategy for TB.

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