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Estimating disease transmission in wildlife, with emphasis on leptospirosis and bovine tuberculosis in possums, and effects of fertility control

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Summary

1. We present methods for estimating disease transmission coefficients in wildlife, using *Leptospira interrogans* infection (a bacterial disease transmitted predominantly during social contacts) in brushtail possums *Trichosurus vulpecula* as a model system.
2. Using data from a field experiment conducted on a naturally infected possum population, we estimated disease transmission coefficients assuming either 'density-dependent' or 'frequency-dependent' transmission.
3. A model-selection approach determined that density-dependent transmission was the most appropriate form of the transmission of *L. interrogans* infection in brushtail possums.
4. We used the chosen model of transmission to examine experimentally the effect of tubally ligating female brushtail possums on the epidemiology of *L. interrogans*. The estimated transmission coefficient was 28% higher ($P = 0{\cdot}16$) in populations subject to tubal ligation, raising the possibility that fertility control of this type may increase disease transmission rates.
5. Altering mating behaviour through fertility control may have the potential to control diseases such as bovine tuberculosis in brushtail possums, although the potential of fertility control techniques to change disease transmission coefficients and disease epidemiology requires further investigation. This would require models that examine the combined effects of fertility control on population dynamics, social behaviour and disease transmission coefficients simultaneously.

Key-words: epidemiology, *Leptospira interrogans*, modelling, *Mycobacterium bovis*, *Trichosurus vulpecula*.

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Introduction

Based on the projections of host–pathogen models, reducing susceptible host abundance is often proposed as a strategy for eradicating diseases from wildlife populations, such as *Mycobacterium bovis* (Karlson & Lessel) infection (bovine tuberculosis) in brushtail possums *Trichosurus vulpecula* (Kerr) (Barlow 1991b, 1996; Roberts 1996) and badgers *Meles meles* (L.) (White & Harris 1995), and *Brucella abortus* infection (brucellosis) in bison *Bison bison* (L.) (Dobson & Meagher 1996). Indeed, reducing the population density of animals is one of the most frequently attempted management strategies for controlling disease in wild animals (Wobeser 1994). This logically follows from the paradigm of threshold density for the establishment and persistence of disease (Kermack & McKendrick 1927; Anderson & May 1979; May & Anderson 1979) and the implicit assumption underlying this paradigm that disease transmission scales positively with abundance. However, the projections of these host–pathogen models are greatly affected by the way in which transmission between infected and susceptible hosts is modelled (McCallum, Barlow & Hone 2001). Estimating disease transmission coefficients is considered to be a very difficult parameter estimation problem (Anderson & May 1991) and remains a great challenge in field ecology today (McCallum, Barlow & Hone 2001). Disease transmission coefficients are model-dependent, and an important issue is the form of the model for the scaling between host population density and parasite transmission rate (McCallum,

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Barlow & Hone 2001; Grenfell & Bolker 1998 and references therein). Resolving this issue can be considered a model-selection problem for which Akaike's information criterion (AIC) provides an approach for choosing between competing models of transmission (Burnham & Anderson 1998), providing data sets exist. Studies that estimate transmission coefficients for diseases of free-living vertebrates, let alone estimate the effect of management on disease transmission, are uncommon in both the laboratory (Bouma, De Jong & Kimman 1995) and the field (Hone, Pech & Yip 1992; Swinton *et al*. 1997; Begon *et al*. 1999). A result of this is a general paucity of data on transmission rates (De Leo & Dobson 1996).

Reducing susceptible host abundance and/or population density may be achieved by a variety of means, such as lethal control, vaccination or reducing fertility (fertility control). Fertility control has been proposed as an alternative non-lethal tactic for reducing the abundance of species such as brushtail possums (Barlow 1996; Cowan 1996; Barlow, Kean & Briggs 1997) and badgers (Swinton *et al*. 1997; Tuyttens & Macdonald 1998) below the threshold for disease (*M. bovis*) persistence. Here, fertility control is broadly defined as a reduction in the birth rate that should decrease the rate of population increase, assuming no compensatory change occurs in the death rate (Hone 1992). The possibility that population control may cause a change in transmission coefficients through effects on social behaviour is receiving increasing theoretical interest. For example, social perturbation arising from lethal control of badgers may act to promote transmission of *M. bovis* (Swinton *et al*. 1997). In contrast, Tuyttens & Macdonald (1998) considered that fertility control (sterilization) of badgers could reduce vertical transmission of *M. bovis*, and transmission of *M. bovis* during mating through changed behaviour.

Endemic *M. bovis* infection in New Zealand possum populations is the single biggest threat to the nation's livestock industry, with *M. bovis*-infected possums occurring over about 24% of the land mass (Coleman & Caley 2000). The presence of this wildlife reservoir of *M. bovis* infection has hampered efforts at controlling the disease in livestock (O'Neil & Pharo 1995; Coleman & Caley 2000), similar to the problem encountered in England (Zuckerman 1981) and Ireland (OMairtin *et al*. 1998a,b) arising from *M. bovis*-infected badgers. While reducing abundance by non-selective culling is presently the primary strategy for controlling *M. bovis* infection in brushtail possum populations in New Zealand (Barlow 1991b; Caley *et al*. 1999), fertility control is being pursued as an alternative method of reducing abundance (Cowan 1996, 2000). Methods of fertility control that block fertilization, such as immunocontraception, may leave the endocrine system intact. Thus sterile but hormonally competent females may have an increased frequency of mating contacts due to an increased frequency of oestrus, as observed in white-tailed deer *Odoicoileus virginianus* (Miller) (McShea *et al*. 1997) and elk *Cervus elaphus* (Bailey) (Heilmann *et al*. 1998) subjected to this type of contraception. This prediction is supported for brushtail possums by a field trial by Ji, Clout & Sarre (2000). Whilst increased frequency of mating could enhance the transmission of a hypothetical transmissible biocontrol vector in brushtail possums (Barlow 1994), it could possibly also increase the transmission coefficient of *M. bovis*, thus negating some of the benefits of reduced abundance resulting from fertility control. Alternatively, methods of fertility control that target endocrine control of reproduction may result in behavioural changes, including inhibition of mating behaviour. For brushtail possums this could mean reduced sexual contacts and possibly also reduced agonistic contacts, which would be associated with a reduction in disease transmission. Clearly, altered behaviour arising from fertility control techniques potentially may help or hinder disease management in wildlife, although little attention has been given to altering high risk behaviour of wildlife to reduce disease transmission. This is in contrast to the management of disease in humans, where behaviour modification (e.g. changing sexual habits in the case of sexually transmitted diseases) is one of the most commonly used methods of management of public health (Anderson & May 1991; Morris 1996).

In this paper, we present methods for estimating disease transmission coefficients in wildlife, using *Leptospira interrogans* serovar *balcanica* (Kmety & Dikken 1993) (hereafter *L. balcanica*) infection in brushtail possums as a model system. We compared two models of transmission (density-dependent and frequency-dependent) and used the selected best model to estimate from a field experiment the effect of behavioural changes induced by fertility control (here tubally ligating female possums) on the transmission of disease. We then examined the theoretical implications of attempting to use fertility control to manage *M. bovis* infection in brushtail possums.

Materials and methods

FRAMEWORK FOR EVALUATING DISEASE CONTROL STRATEGIES

The ability of a pathogen to establish and persist in animal populations is largely determined by the basic reproductive rate of the disease (R_o). This is defined as the expected number of secondary infections caused in an entirely susceptible population by a typical infected host. By definition, if R_o is greater than or equal to unity the disease will establish and, conversely, if R_o is less than unity the disease will fail to establish (Anderson & May 1991). We use a simplified version of the compartment model for a directly transmitted disease, as presented by Anderson & May (1979), to illustrate the possible effects of fertility control relative to that of culling and vaccination. We choose a model with horizontal transmission, a negligible latent period and no

life-long immunity. Host population dynamics assume exponential population growth, with the exponential rate of increase $r = a - b$, where a and b are the instantaneous per capita birth and death rates, respectively. Note that this is an illustrative example, rather than an exact description of the dynamics of infection. Under this model, mixing is assumed to be homogenous and hence transmission is 'density-dependent', occurring at a rate βSI, where β is the disease transmission coefficient and S and I are the abundance of susceptibles and infectives, respectively. R_o is estimated as:

$$R_o = \frac{\beta N}{\alpha + b + v} \qquad \text{eqn 1}$$

where α is the per capita disease-induced death rate, b is the per capita natural death rate, v is recovery rate from disease, and N is the initial size of the susceptible population. Equation 1 can be interpreted as an infected animal making β infectious contacts per unit time with N susceptibles for its life expectancy. Life expectancy is the reciprocal of the combined mortality rate due to natural causes and disease. By setting R_o equal to unity in equation 1, the threshold density (K_T) for disease establishment is found:

$$K_T = \frac{\alpha + b + v}{\beta} \qquad \text{eqn 2}$$

The approximation of density-dependent transmission is reasonable for many directly transmitted diseases, but may not be adequate for sexually transmitted diseases, for example, where the number of sexual partners (η) is independent of the absolute population size and hence no threshold abundance exists (May & Anderson 1979). In this situation, the transmission rate may be approximated by $\beta\eta SI/N$ (May & Anderson 1979), or here by $\beta' SI/N$ (replacing $\beta\eta$ with β'). This model of transmission (commonly termed 'frequency-dependent' transmission; Begon *et al*. 1999; McCallum, Barlow & Hone 2001) is most appropriate for diseases transmitted through contacts that are largely density-independent (e.g. mating). However, De Jong, Diekmann & Heesterbeek (1995) and Bouma, De Jong & Kimman (1995) suggest that frequency-dependent transmission may have wider application to host–pathogen systems where disease contact rates are not necessarily density-independent. For frequency-dependent approximation of the transmission process, the maintenance of disease is independent of the population size, and occurs when $\beta' > (b + \alpha + v)$ (May & Anderson 1979). It follows that the basic reproductive rate may be calculated (Roberts & Heesterbeek 1993; Heesterbeek & Roberts 1995) as:

$$R_o = \frac{\beta'}{\alpha + b + v} \qquad \text{eqn 3}$$

which is independent of population size or density.

We use equations 1, 2 and 3 to investigate qualitatively the possible effects of fertility control-induced behaviour change on disease. Under density-dependent transmission, R_o is decreased by either reducing the numerator (βS), increasing the denominator ($\alpha + b + v$) or reducing βS by proportionally more than ($\alpha + b + v$) is reduced. For example, culling of possums aims to increase the mortality rate (b) and reduce the abundance of susceptible possums (S), both of which act to lower R_o. Vaccination also acts to reduce the abundance of susceptible possums; in effect, vaccinated possums are removed from the susceptible population, thus reducing S. Equation 3 makes the important prediction that for frequency-dependent transmission, disease may only be controlled by increasing the mortality rate (assuming β', α and v are constants).

Equations 1, 2 and 3 clearly illustrate that wildlife management could target the actual mechanisms of disease transmission that make up β as an alternative to targeting hosts *per se*. Historically, β is considered difficult to measure, as it subsumes many processes involved in initiating infection (Anderson & May 1991). Additionally, β is model-specific. So, given a model, how do we estimate the transmission coefficient from field data? For simplicity, we consider our simple disease–host model where the transmission of disease is either frequency-dependent or density-dependent. Under density-dependent transmission, susceptibles are infected at rate βSI, hence the per capita instantaneous incidence of disease (λ), termed the force of infection (Muench 1959), equals βI, and β can be simply expressed in terms of the abundance of infectives and the force of infection:

$$\beta = \frac{\lambda}{I} \qquad \text{eqn 4}$$

A similar argument gains an expression for β' in terms of prevalence (p):

$$\beta' = \frac{\lambda N}{I} = \frac{\lambda}{p} \qquad \text{eqn 5}$$

Importantly, equations 4 and 5 show that under the simple models chosen, β and β' may be calculated from the force of infection and the abundance of infectives. This is done below for *L. balcanica* infection in brushtail possums.

CASE STUDY: *L. BALCANICA* INFECTION IN BRUSHTAIL POSSUMS

To determine if methods of fertility control that block fertilization (e.g. immunocontraception) could result in behavioural changes affecting the transmission coefficient β, we undertook an experiment to estimate the transmission rate of *L. balcanica* in wild populations of the brushtail possum subject to fertility control (tubal ligation of females). *Leptospira balcanica* is a commonly occurring disease in possums thought to be transmitted predominantly by sexual contact (Durfee & Presidente 1979; Day *et al*. 1997, 1998). Clinical disease due to *L. interrogans* infection in most wild animals is rare (Bender & Hall 1996) and no clinical

symptoms were observed in possums infected with *L. balcanica* in a study by Hathaway (1981). The hypothesis tested in the present study was that immunocontraception as modelled by tubal ligation increased frequency of oestrus in sterilized females, leading to increased mating contacts with males, resulting in a higher transmission coefficient for *L. balcanica*. Increased frequency of oestrus in tubally ligated captive female possums has been demonstrated experimentally in both captive (Rekha 1997) and free-ranging (Ji, Clout & Sarre 2000) possums.

The experiment formed part of a larger study to determine the effects of various levels of fertility control on the population dynamics of brushtail possums (Ramsey 2000). Four live-trapping grids were established in podocarp/broadleaf forest in the lower North Island of New Zealand, two in the Orongorongo Valley (separated by *c.* 500 m), east of Wellington (174°58′ E, 41°21′ S), and two in the Turitea catchment (separated by *c*. 1 km), east of Palmerston North (175°41′ E, 40°26′ S). Each grid consisted of 150 cage traps set at 30 m spacing. Sites were established in October 1995 and trapped three times yearly in January, June and September. Experimental treatments, consisting of either 0% (although with 80% of females subject to sham operations) or 80% of mature females surgically sterilized by tubal ligation, were applied randomly to the two blocks in the Orongorongo Valley and the two blocks in the Turitea catchment between January–April 1996. Each year the number of sterilized females was adjusted to maintain the 80% sterility level. Movement of animals between grids at each location was negligible.

On first capture, possums were anaesthetized with ether and given a unique tattoo and ear tag for identification. During the June trapping sessions from years 1996–99, *c*. 5 ml of blood was collected from 60–100 possums on each of the experimental control (0% sterilized) and 80% treatment grids. The June trapping period was selected for sampling as it occurs directly after the main autumn breeding period of March–June (Fletcher & Selwood 2000). The serum was separated by centrifugation and submitted to the Central Animal Health laboratory, Wallaceville, New Zealand, for serology. The serological micro-agglutination test (MAT), using doubling dilutions of serum beginning at 1 : 50, was used to detect the presence of leptospiral antigens (Horner, Heath & Cowan 1996). If no reaction was seen in the 1 : 50 dilution, the result was scored as negative. A positive result indicated the presence of active leptospiral infection (Cowan, Blackmore & Marshall 1991).

ANALYSIS

For testing the effect of sterilization treatment on the transmission coefficient for *L. balcanica* infection of possums, we assume that the force of infection is constant within years (although not necessarily between years) with no disease-induced mortality ($\alpha = 0$). This allows us to use the very tractable exponential distribution (Lee 1992) to model the force of infection observed in the experiments. Over n intervals of length t_i, each having a force of infection λ_i and abundance of infectives I_i, the probability of an individual acquiring infection (p) is given by:

$$p = 1 - e^{-\sum_{i=1}^{n} \lambda_i t_i} \qquad \text{eqn 6}$$

The force of infection is the parameter of interest in many studies of disease (McCallum 2000); however, here it is the transmission coefficient that is of intrinsic interest. Substituting for λ from equation 4 into equation 6 and rearranging equation 6 yields an expression for the observed probability of infection (p) under density-dependent transmission in terms of the transmission coefficient (β) and the abundance of infectives (I_i) in each time interval (t_i):

$$\ln(-\ln(1-p)) = \ln\beta + \ln\left(\sum_{i=1}^{n} I_i t_i\right) \qquad \text{eqn 7}$$

Likewise, for frequency-dependent transmission, substituting for λ from equation 5 into equation 6 gives an expression for the observed individual disease prevalence in terms of transmission coefficient (β') and the prevalence of infectives (Z_i) in the population during each time interval (t_i):

$$\ln(-\ln(1-p)) = \ln\beta' + \ln\left(\sum_{i=1}^{n} Z_i t_i\right) \qquad \text{eqn 8}$$

Equations 7 and 8 are generalized linear models (GLM) that enable direct estimation of the transmission coefficients, and testing of the effect of sterility control treatment on them. They are somewhat similar in structure to the GLM presented by Becker (1989) for estimating β from an outbreak with complete observability (i.e. a notifiable disease with all cases reported and total population known). The key difference is that, rather than having a known absolute number of cases during the experiment, in our experiment we have a sampled proportion of new-case individuals, hence our data are binomially rather than normally distributed.

Equations 7 and 8 were fitted to the incident cases of *L. balcanica* that occurred during the experiment using a GLM utilizing a complementary log–log link, and the logarithmic term on the right-hand side of each equation fitted as an offset (equivalent to fixing the slope of the regression to 1; Collett 1991). The response variable was the number of incident cases of disease during the experiment with the binomial denominator equal to the number of individuals tested. Individuals who were seropositive on their first sample were discarded from the analysis, except when calculating the overall prevalence of disease (Z_i). The exceptions were animals that showed a greater than twofold increase in antibody titre between serum samples. In studies on captive animals, *L. balcanica* infection in possums was

followed by a peak in antibody titres within a month of infection (Hathaway 1981). Antibody titres then slowly decreased over the following 13 months. The most likely explanation for a large (> 2 doubling dilutions) increase in antibody titres between annual serum samples, therefore, is that the individual had been recently re-exposed to infection. The treatment 0% or 80% sterility was fitted as a factor. The abundance of infectives on each grid in each year (I) was estimated from the sampled prevalence of disease, and the abundance of possums estimated using the jack-knife estimator (Burnham & Overton 1978). Time at risk (t) for an individual was defined as the period from the date of first capture or the date of application of treatments for possums resident before the start of the study to the date of last serum sampling. Locality (Orongorongo Valley or Turitea) was fitted as a fixed block effect in all models. The competing hypotheses of density-dependent vs. frequency-dependent transmission, as represented by equations 7 and 8, were compared by calculating AIC scores for each, with the best model selected being that with the lowest AIC score (Burnham & Anderson 1998). All statistical analysis was performed in S-plus version 2000 (Mathsoft, Seattle, WA).

Results

CASE STUDY: *L. BALCANICA* INFECTION IN BRUSHTAIL POSSUMS

A summarized form of the data used to estimate disease transmission coefficients is shown in Table 1. The point prevalence of *L. balcanica* infection was high although variable (mean = 55·2%, range 38·8–70%), as was the abundance of possums on each trapping grid (mean = 148, range 63–257). The incidence of *L. balcanica* was estimated from 213 possums with more than one serum sample. Of these 213 possums, 30 of 103 possums in experimental control sites, and 39 of 110 possums in the sterility sites, sero-converted during the course of the study (Table 1).

The model assuming density-dependent transmission was most strongly supported by the data, based on having the lowest AIC (Table 2). However, we present the results of both models as, based on a ΔAIC of 3, the model assuming frequency-dependent transmission is bordering on having substantial support in comparison (Burnham & Anderson 1998). There was little evidence from either model that the transmission coefficient differed between geographical locality (density-dependent $P = 0{\cdot}77$, frequency-dependent $P = 0{\cdot}22$), so this variable was removed from the models. Assuming density-dependent transmission, β was estimated to be 1·3 times higher in the 80% sterility sites than the experimental control sites, although there remained doubt as to the probability that this was a true treatment effect ($P = 0{\cdot}16$; Table 2). Estimates of β′ under the frequency-dependent transmission model were 1·24 times higher for possums in the 80% sterility sites than for possums in the experimental control sites (Table 2).

With negligible disease-induced mortality ($\alpha = 0$), no disease recovery ($v = 0$) and natural instantaneous mortality rate (b) for adult possums of 0·24 year^{-1} (Efford 1998), the threshold abundance for the establishment for *L. balcanica* infection in brushtail possums is estimated to be 96 possums for unmanipulated populations, and 75 possums with 80% tubal ligation of females, a reduction of 16%. For the grid size used in our study with an effective trapping area of *c*. 22 ha (D. Ramsey, unpublished data), the corresponding population densities for disease establishment are 4·4 possum ha^{-1} for unmanipulated populations and 3·4 possum ha^{-1} for populations subject to 80% tubal ligation of females.

Table 1. Prevalence of *Leptospira balcanica* ($\hat{Z}$), estimated possum abundance ($\hat{N}$), number of possums at risk of infection that were sampled (S), and the number of incident cases of *Leptospira balcanica* (I) for different levels of sterility treatment

Treatment	Site	Year	$\hat{Z}$ (%)	$\hat{N}$	S	I
0% sterility	Turitea	1996	53·4	257	19	5
	Turitea	1997	51·6	226	13	1
	Turitea	1998	63·2	142	23	4
	Orongorongo	1996	56·1	136	30	11
	Orongorongo	1997	59·6	110	22	5
	Orongorongo	1998	54·1	123	17	4
80% sterility	Turitea	1996	59	63	24	10
	Turitea	1997	43·9	106	24	7
	Turitea	1998	38·8	90	17	3
	Orongorongo	1996	70	190	27	12
	Orongorongo	1997	54·7	171	17	4
	Orongorongo	1998	57·9	163	16	3

Table 2. Parameter estimates from generalized linear models fitted to incident cases of *Leptospira balcanica* in possums subject to 0% or 80% sterilization of females, assuming density-dependent (transmission type βSI) or frequency-dependent (transmission type $\beta' SI/N$) disease transmission. The parameter estimate for '+ Sterility' is the contribution of the 80% sterility treatment to ln(β). P-values are for one-tailed tests. ΔAIC gives the comparative AIC scores for the two models

Transmission type	Model parameters	Parameter estimate	SE	Z*	P	ΔAIC
βSI	ln(β)	−8·49	0·19	–	–	–
	+ Sterility	0·25	0·26	1	0·16	0
$\beta' SI/N$	ln(β′)	−3·45	0·19	–	–	–
	+ Sterility	0·21	0·26	0·8	0·21	3

*Standard normal deviate.

Using the mean abundance on our grids of 148 possums, the R_o of *L. balcanica* infection in brushtail possums, assuming density-dependent disease transmission, is estimated to be 1·5 for unmanipulated populations and 2·0 with 80% tubal ligation of females. Assuming frequency-dependent transmission, R_o is estimated to be 1·6 for unmanipulated populations and 2·0 for populations subject to 80% tubal ligation of females.

CASE STUDY: *M. BOVIS* INFECTION IN BRUSHTAIL POSSUMS

We now briefly explore the implications of various hypothetical fertility control agents for managing *M. bovis* (bovine tuberculosis) in brushtail possums. *Mycobacterium bovis* infection in brushtail possums is considered to be a respiratory disease, with transmission occurring principally by infectious aerosol (Morris, Pfeiffer & Jackson 1994). As *M. bovis* does not survive long in the environment (Jackson, de Lisle & Morris 1995), direct possum-to-possum transmission by aerosol is the most important route of transmission (L.A. Corner, unpublished data). The prevalence of disease appears to be largely density-independent (Barlow 1991a), which appears to rule out density-dependent mechanisms of disease transmission such as simultaneous den sharing as significant routes of infection (Caley *et al*. 1998). As brushtail possums live a solitary existence, with most close interactions occurring around the time of mating (Winter 1976), it appears that mating behaviour presents the most significant opportunities for disease transmission (Morris & Pfeiffer 1995). Not mentioned so far, although potentially important, is pseudovertical transmission from mother to offspring (Morris & Pfeiffer 1995), a direct consequence of mating.

The potential effects on *M. bovis* infection in possums of a fertility control agent that blocks fertilization but leaves the individual hormonally intact can be investigated qualitatively using equation 1. The R_o of *M. bovis* infection in brushtail possums has been estimated at 1·8–2·0 (Barlow 1991a). Increasing the transmission coefficient for *M. bovis* infection by *c*. 30% (a similar amount to that potentially observed here for *L. balcanica* infection) would increase R_o by the same magnitude, and reduce K_T by *c*. 23%.

Conversely, if fertility control suppresses hormonal regulation of breeding, resulting in a reduction in the frequency of mating contacts, then we may significantly reduce the disease transmission coefficient, and hence R_o, without having to reduce density (N). The amount by which R_o is reduced will depend on what proportion of the potentially sexually active population no longer participates in mating, and what contribution mating makes to disease transmission. This is illustrated graphically in Fig. 1. If, for example, mating makes up 75% of disease transmission, maintaining 60% or greater of potentially sexually active possums sterile (and not participating in mating behaviour) will theoretically eliminate *M. bovis* infection by reducing R_o below unity. As the contribution of mating to disease transmission decreases, the reductions that can be achieved through fertility control diminish, to the point where if only 50% of transmission is due to mating, it is nearly impossible to eliminate disease by targeting mating contacts alone (Fig. 1).

Discussion

There is a growing debate on the general form of mixing between susceptible and infected hosts, especially for non-sexually transmitted diseases (Begon *et al*. 1999 and references therein; McCallum, Barlow & Hone 2001). Our study is one of the few that has estimated disease transmission coefficients and compared models of transmission from field studies of free living

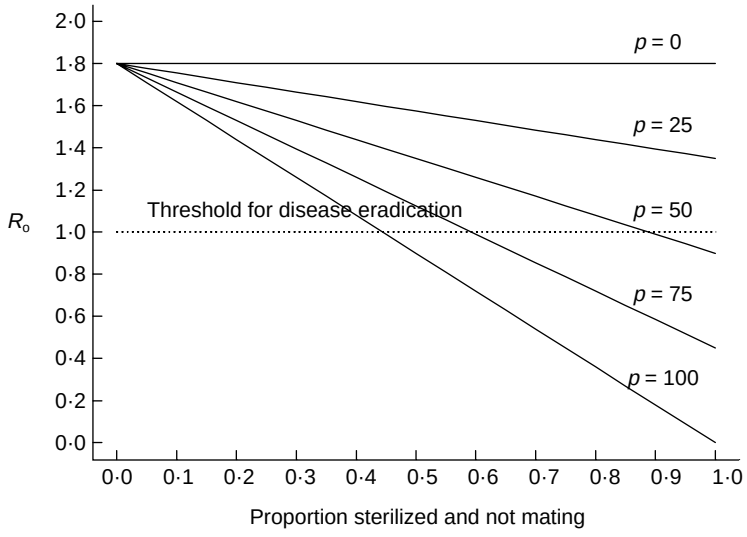

Fig. 1. Relationship between the basic reproductive rate of *Mycobacterium bovis* infection in possums (R_o) and the proportion of possums sterilized, for varying levels of p, where p is the percentage contribution of mating to disease transmission.

mammals. Given the proposed importance of mating as a route of transmission of *L. balcanica* between possums, we were surprised that the density-dependent model of transmission fitted our data better than the frequency-dependent model. In contrast, Begon *et al.* (1999) reported frequency-dependent transmission to be a superior descriptor over density-dependent transmission for the transmission rate of cowpox virus in mixed populations of free-living rodents, and called into question the general assumption that transmission rate for non-sexually transmitted diseases is density-dependent. Clearly more work is needed on understanding the mechanisms of mixing and hence disease transmission between infected and susceptible wildlife hosts, as the results of the few studies undertaken to date are somewhat contradictory. An obvious factor to consider when comparing models of transmission is the influence of scale on the results of field studies. The size and areas of populations under study need to be appropriate to the models of transmission being postulated and compared. McCallum, Barlow & Hone (2001) recommend that densities rather than numbers be used when modelling transmission. Future field studies should avoid restricting their group of candidate models for disease transmission to density-dependent or frequency-dependent, and consider alternative models (Knell, Begon & Thompson 1998; Barlow 2000; Diekmann & Heesterbeek 2000).

Our experimental study of *L. balcanica* infection in brushtail possums suggests that fertility control by tubal ligation of females possibly increases the disease transmission parameter (regardless of the type of transmission), resulting in an increase in R_o. When interpreting the results of hypothesis testing in ecology, Krebs (2000) recommends concentrating on the ecological significance of effect size. In our study the implications for management (in terms of having to sterilize a higher proportion of individuals to control disease) may be only slight, as the relationship between population sterility levels and population suppression is highly non-linear for high sterility levels (Barlow 1997). Indeed, the level of sterility (80%) eliciting the observed response in our study is projected to cause 100% suppression of possum density (Barlow 1997). Alternatively, increases in disease transmission arising from fertility control may not be such a problem if the aim is to suppress the population recovery rate following conventional control, as abundance may already be well below any disease threshold. Perversely, however, the most promising aspect of fertility control technologies for disease management could well be the ability to modify behaviour. Using methods of fertility control that inhibit normal sexual behaviour eliminates disease transmission associated with this behaviour. Methods of fertility control that interfere with hormonal regulation of breeding, such as inhibiting GnRH binding in the pituitary (Eckery *et al.* 1998), are candidate methods that will most probably result in the cessation of normal mating behaviour as a side-effect of sterility. We have shown that a reduction in density arising from fertility control theoretically may not be necessary for eradication of *M. bovis* infection in possums. The potential of fertility control techniques to change disease transmission coefficients and disease epidemiology through altered possum social behaviour requires further investigation. This would require models that examine the combined effects of fertility control on population dynamics, social behaviour and disease transmission coefficients simultaneously.

The pioneering modelling work of Kermack & McKendrick (1927) introduced the concept of threshold density for disease establishment. One unintended outcome of this is that disease thresholds have been viewed by many to be fixed for a given species and disease in a given locality. This view has arisen largely from the assumption of the transmission coefficient being a constant. However, recognizing that β is a function of host behaviour, and that behaviour may be modified, means that K_T can be viewed as a variable able to be manipulated. It is theoretically possible to manipulate wildlife behaviour and hence change transmission coefficients, although we recognize there are many criteria that must be fulfilled for the safe use of fertility control agents of this type in wildlife (Nettles 1997). Management techniques for disease should consider tactics that increase the threshold density for disease establishment, along with the more conventional tactics (e.g. culling and vaccination) aimed at reducing the abundance of susceptible hosts. Little attention has been given to measuring the disease transmission coefficient, let alone testing whether it is significantly influenced by management. We recommend an experimental approach (as carried out here for leptospirosis infection in possums) over the predictive approach (as performed for tuberculosis infection in possums).

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