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A comparison of fertility control and lethal control of bovine tuberculosis in badgers: the impact of perturbation induced transmission

J. SWINTON[1,2], F. TUYTTENS[3], D. MACDONALD[3], D. J. NOKES[4], C. L. CHEESEMAN[5] AND R. CLIFTON-HADLEY[6]

[1] *Department of Plant Sciences, University of Cambridge, Downing Street, Cambridge CB2 3EA, UK* (js229@cam.ac.uk)
[2] *Wellcome Centre for the Epidemiology of Infectious Disease, Department of Zoology, University of Oxford, Oxford OX1 3PS, UK*
[3] *Wildlife Conservation Research Unit, Department of Zoology, University of Oxford, Oxford OX1 3PS, UK*
[4] *Department of Biological Sciences, University of Warwick, Coventry CV4 2AL, UK*
[5] *Central Science Laboratory, Sand Hutton, York YO4 1LZ, UK*
[6] *Central Veterinary Laboratory, New Haw, Addlestone, Surrey KT15 3NB, UK*

CONTENTS

SUMMARY

In this paper we use mathematical modelling to consider the broad advantages and disadvantages of fertility control over lethal control for bovine tuberculosis in badger populations.

We use a deliberately simple model, attempting to capture only the key transmission processes. The model is parametrized with reference to the long-term Woodchester Park study. Estimates of mortality rate from this study suggest no significant extra mortality risk for animals with evidence of infection as indicated by the presence of anti-*Mycobacterium bovis* antibodies or *M. bovis* isolation.

We find that large reductions in prevalence are sometimes the consequence of only moderate reductions in population numbers. If we assume that the act of control does not in itself affect transmission rates, then as far as eradication is concerned, both fertility control and mortality control operate through the same epidemiological mechanism, the removal of susceptibles: if one is in principle capable of keeping a population low enough to be infection free then so is the other. It is necessary to continue either form of control at regular intervals to maintain a constant level of infection in the long term. If control were to be stopped, return to precontrol levels of badger population and infection prevalence would be expected within a few years. Fertility control is less effective in reducing population density than lethal control since it can only act, at maximum, to remove one age cohort per year. It is also less effective in reducing transmission as it can only ever remove susceptibles, while lethal control also removes infectious badgers.

However, if the social disturbance caused by lethal control does in fact increase contact rates for the remaining infectious badgers, the relative efficacies of the two strategies become a great deal less clear. While we have no quantitative data on the extent to which social perturbation does act to promote transmission, model simulations show that it is possible to develop plausible scenarios in which the lethal control may actually act to increase the absolute numbers of animals infected, while reducing the number of uninfected animals to very low numbers.

1. INTRODUCTION

The control of bovine tuberculosis, *Mycobacterium bovis* (Tb), in badger (*Meles meles*) populations remains controversial. In the quarter century since badgers were identified as a potential reservoir for bovine tuberculosis (Muirhead *et al.* 1974), several different strategies for decreasing the risk of transmission to cattle have been instigated which have been aimed at reducing the levels of infection within badger popu-

lations. The choice of, and indeed the necessity for, such control strategies has at times been hotly debated but it is clear from the number of herd breakdowns considered to have a badger origin (MAFF 1995) that none has completely succeeded in eliminating the risk of transmission from badgers to cattle over large areas. This failure has had significant economic, ethical and conservation implications which make the continuing search for an effective and humane control strategy an urgent one (Dunnet *et al.* 1986; Tuyttens *et al.* 1995; White & Harris 1995*a*). This paper is restricted to examining the epidemiological consequences in badger populations of two alternative strategies; we do not discuss the impact, if any, on the frequency of herd breakdowns in cattle and neither do we comment on the ethical factors which also need to be taken into account in the choice of strategy (Tuyttens *et al.* 1995). The natural history of bovine tuberculosis in badgers and other mammals has been recently reviewed by O'Reilly & Daborn (1995).

There are three broad classes of control strategies currently being considered: those based on killing animals; those based on vaccinating animals; and those based on manipulating their fertility. All current and previous strategies have centred on killing badgers; a concise summary of how they differ has been given by White & Harris (1995*a*). Vaccination strategies remain theoretical at present since no vaccine candidate has yet been shown to be protective (although a field trial is currently underway in Ireland (McCarthy 1993)) and is considered no further here. Finally, fertility control has been mooted as an approach to population control (Bomford 1990). Its potential advantages are both ethical and biological; we consider here the latter in particular, in the light of the social perturbation and possible enhanced transmission caused by lethal control.

2. DATA

Until the development of an ELISA for *M. bovis*, assessments of infection or infectivity status in live animals were based only on the ability to culture the pathogen from urine, faeces or clinical samples. Based on these mycobacterial culture results, animals are known to switch from positive to negative results over time, even when subsequently found to have Tb lesions at post mortem (Clifton-Hadley *et al.* 1993). The relationship of results using ELISA to infectivity remains untested; but the possibility of switching suggests that shedding of bacillus may be an intermittent event (Clifton-Hadley *et al.* 1993). The ELISA test is diagnostic for the presence of antibody against the *M. bovis* organism (Goodger *et al.* 1994). It has a high specificity (94.3%) but a low sensitivity (40.7%) (Clifton-Hadley *et al.* 1995), so that population surveys based on this test alone are likely to underestimate the number of animals who have ever been infected with *M. bovis*.

We assume in this paper that there is no relationship between infectivity and time since infection; at any given time an infected animal may, with a certain probability, be infectious. If this is so, the number of infectious animals in the population is proportional to the number of animals in the population ever infected. Then we could take the number of infectious animals in the population to be the number who have ever been ELISA positive, multiplied by a constant factor of approximately 1/0.4 to correct for the low sensitivity of the test, multiplied by a constant but completely unknown factor to correct for the intermittency of infectiousness in an infected animal. In modelling terms this makes no difference, for these unknown factors are further multiplied by the equally unknown contact rate between susceptible and infected animals, and the product is then estimated directly from the data. In this paper, we count as infected any animal which has ever been either ELISA or culture positive. We refer to this state as positivity and we take prevalence to be the prevalence of positive animals.

For the past 20 years, MAFF has funded a study of a badger population in and around Woodchester Park, part of the Cotswold escarpment in Gloucestershire, south-west England, which has produced an invaluable and unique dataset for the epidemiological study of tuberculosis in badgers. Details of the study site and of badger population dynamics have been given elsewhere (Cheeseman *et al.* 1985, 1993) and much of our understanding of the transmission processes involved has emerged from this study (Cheeseman *et al.* 1985, 1988; Clifton-Hadley *et al.* 1993). One area of the study (referred to here as area 1), had one social group removed in 1977, but has otherwise not been the subject of any badger control operations in the lifetime of the study. Two other areas (area 2 and area 3) were the subject of badger control operations in 1978 and 1979, respectively. For more details of these areas, see Cheeseman *et al.* (1993). For the estimation of epidemiological parameters we restrict ourselves to the data from area 1, assumed to be closer to an equilibrium level than the other areas. For estimation of birth rates in populations of different sizes, we pool the data from all three areas.

The data used to parametrize our model are given in tables 1–4, taken from the Woodchester Park study. We have combined males and females and restrict attention to known-age animals within the undisturbed study area. Animals are assumed to be infectious, with some low transmission rate reflecting the intermittency of infectivity, from the time at which they are first found to be either ELISA or culture positive until death. While this has the advantages of consistency, it also has the effect of smoothing over short-term changes in infection dynamics. In particular, it will not reflect any short-term periodic dynamics over periods of less than about the mean lifespan.

3. MODELLING APPROACH

In this paper we address the question of fertility control with the aid of a mathematical model. It is

Table 1. *Total number of known-age animals present in area 1 of the Woodchester Park study area described in the text, at the start of each year by age and year of birth*

(Each horizontal row represents the number of animals surviving from a single yearly cohort.)

	age in years												
birth year	0	1	2	3	4	5	6	7	8	9	10	11	12
1977	27	10	4	2	2	0	0	0	0	0	0	0	0
1978	29	14	8	6	4	4	3	2	1	1	1	1	0
1979	51	27	19	16	13	12	9	6	4	4	3	2	1
1980	35	29	23	19	14	9	8	7	4	4	3	0	0
1981	32	26	20	15	12	9	5	3	3	2	2	0	0
1982	17	15	7	7	6	6	4	4	3	2	2	0	0
1983	31	29	22	20	16	10	11	10	9	7	5	3	
1984	52	34	27	23	17	13	10	6	2	2	2		
1985	74	64	41	31	20	17	14	13	10	2			
1986	42	36	30	22	18	17	16	13	9				
1987	56	45	33	28	21	18	13	8					
1988	56	46	36	33	26	19	12						
1989	53	25	19	14	9	7							
1990	56	41	29	19	9								
1991	85	59	44	28									
1992	58	43	30										
1993	77	50											
1994	65												

Table 2. *Number of new cases of infection each year, as diagnosed by ELISA or culture, by age and year of birth as table 1*

	age in years												
birth year	0	1	2	3	4	5	6	7	8	9	10	11	12
1977	0	0	1	0	0	0	0	0	0	0	0	0	0
1978	0	0	1	1	0	0	1	0	0	0	1	0	0
1979	0	1	1	1	0	1	0	0	0	0	0	1	0
1980	1	3	0	0	0	0	0	0	0	0	0	0	0
1981	1	4	2	0	0	0	1	0	0	0	0	0	0
1982	2	0	0	1	0	0	1	0	0	0	0	0	0
1983	2	2	1	1	0	1	0	0	0	0	0	0	
1984	2	1	0	0	4	1	0	0	0	0	0		
1985	7	1	0	1	0	0	0	1	1	0			
1986	1	3	3	0	0	1	1	0	0				
1987	5	3	1	0	0	0	0	0					
1988	5	2	1	1	0	1	1						
1989	7	0	0	0	0	0							
1990	5	3	0	0	0								
1991	12	2	0	0									
1992	5	1	1										
1993	6	0											
1994	7												

perhaps worth commenting on our choice of model structure, since there are now a number of other different models (Anderson & Trewhella 1985; Bentil & Murray 1993; White & Harris 1995*b*; Smith *et al.* 1995; Ruxton 1996) in the literature for the spread of Tb in badgers, and a further set of papers (e.g. Barlow 1994; Roberts 1996) attempting to model the superficially similar problem of bovine Tb in possums in New Zealand and Australia (compared by Barlow (1995)). We follow the approach of the most strategic of these models (Anderson & Trewhella 1985); that is to say we deliberately do not seek to include all

Table 3. *Number of never infected animals present at the start of each year by age and year of birth as table 1*

	age in years												
birth year	0	1	2	3	4	5	6	7	8	9	10	11	12
1977	27	10	4	1	1	0	0	0	0	0	0	0	0
1978	29	14	8	5	3	3	2	1	1	1	1	0	0
1979	51	27	18	14	10	9	5	3	2	2	2	1	0
1980	35	28	21	18	14	9	8	7	4	4	3	0	0
1981	32	25	15	9	7	4	3	1	1	1	1	0	0
1982	17	14	6	6	4	4	2	1	1	0	0	0	0
1983	31	27	19	16	12	8	8	8	7	6	4	2	
1984	52	32	25	22	17	11	7	5	2	2	2		
1985	74	57	35	27	18	16	13	12	8	2			
1986	42	35	27	19	15	15	13	10	7				
1987	56	41	27	21	16	15	11	6					
1988	56	42	33	30	23	17	10						
1989	53	19	15	11	6	5							
1990	56	37	23	16	8								
1991	85	48	34	19									
1992	58	39	26										
1993	77	45											
1994	65												

Table 4. *Number of infected animals present during year by age and year of birth as table 1*

	age in years												
birth year	0	1	2	3	4	5	6	7	8	9	10	11	12
1977	0	0	1	1	1	0	0	0	0	0	0	0	0
1978	0	0	1	2	1	1	2	1	0	0	1	1	0
1979	0	1	2	3	3	4	4	3	2	2	1	2	1
1980	1	4	2	1	0	0	0	0	0	0	0	0	0
1981	1	5	7	6	5	5	3	2	2	1	1	0	0
1982	2	1	1	2	2	2	3	3	2	2	2	0	0
1983	2	4	4	5	4	3	3	2	2	1	1	1	
1984	2	3	2	1	4	3	3	1	0	0	0		
1985	7	8	6	5	2	1	1	2	3	0			
1986	1	4	6	3	3	3	4	3	2				
1987	5	7	7	7	5	3	2	2					
1988	5	6	4	4	3	3	3						
1989	7	6	4	3	3	2							
1990	5	7	6	3	1								
1991	12	13	10	9									
1992	5	5	5										
1993	6	5											
1994	7												

potentially relevant factors into our model. Rather, we seek to elucidate broad principles, not precise numerical predictions, even if the latter were possible. By contrast, White & Harris (1995*a*, *b*), for example, use a large-scale multiple-parameter model. Such a model is essential when comparing detailed implementation plans, but less useful for the development of understanding about how the key epidemiological factors interact. We use a model for the spread of Tb which is deliberately simple; we are able to see clearly the way in which our assumptions affect our results and we are able to estimate the simple, aggregated transmission parameter directly from the data.

In particular, the model we adopt is deterministic

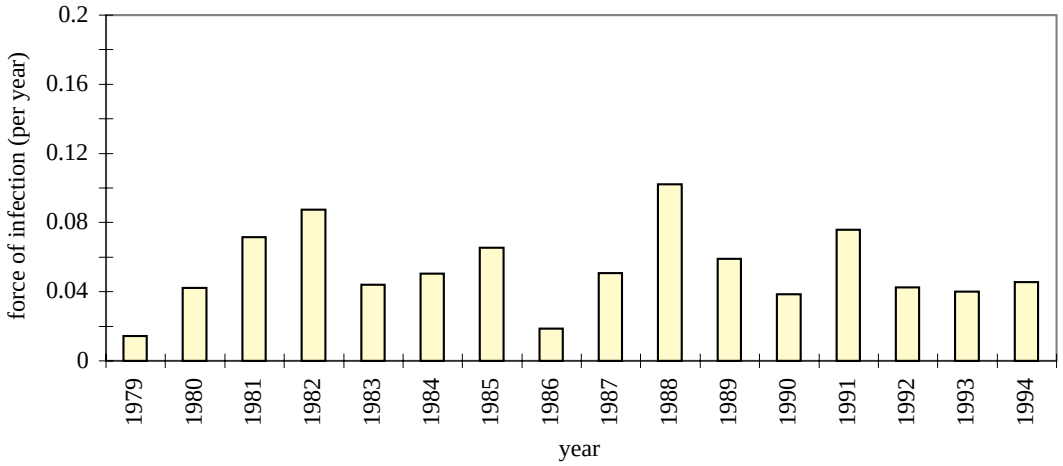

Figure 1. Force of infection as a function of time in the Woodchester Park data. Number of new conversions per year per negative animal. Mean force of infection $\lambda = 0.0444\ \mathrm{yr}^{-1}$ with likelihood-based approximate 95% confidence interval $\lambda \in [0.016, 0.076]$; slope not significantly different from zero (95% confidence interval $[-0.0021, 0.0034]$).

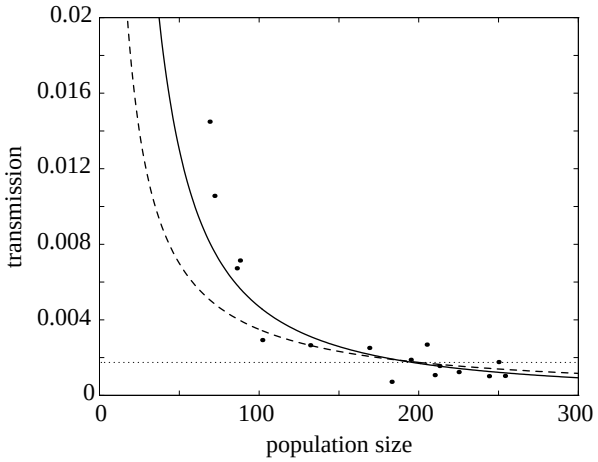

Figure 2. Possible representations of the transmission parameter β as a function of N. Data points give number of new cases of infection per susceptible per infected for each year from 1980 to 1994 within the known-age population described in tables 1–4. ——, best fit for mass action, $\beta(N) = 0.001\,747 \times (N/200)^{-1}$; – – –, best fit of the form $\beta_\alpha N^{-\alpha} = 0.001\,695 \times (N/200)^{-1.478}$; · · ·, best fit for pseudo mass action, $\beta(N) = 0.001\,745$. Fits for $\beta(N)$ were obtained by maximizing the log-likelihood summed over all years, with the log-likelihood for a year with i new cases in a population of n, including y infectious, given by $[i \log(y\beta(n)) + (n - i) \log(1 - y\beta(n))]$.

and not spatially explicit; we discuss the implications of these assumptions below. It is specified by a handful of key parameters which we choose with reference to the Woodchester Park data. We use a fit of our model to provide a parsimonious description of these data and to parametrize our analysis of control options.

Before we describe the particular model used, we discuss some general questions about the relationship between transmission intensity, the idea of a threshold density and control strategies.

(*a*) *Threshold densities and transmission functions*

The simplest infection control strategy is one which eradicates infections in badgers by eradicating badgers. At the other extreme, removal of a small number of infected animals reduces the prevalence of infection by a correspondingly small amount. In practice, we are more concerned with the third situation, intermediate between these two extremes: relatively large-scale removals which are sufficient to reduce the force of infection substantially and thus partially protect the remaining badgers from infection. Some of the simplest epidemiological models predict that this 'herd immunity' effect produces a threshold density of animals below which infection cannot persist. This relies on assuming that the force of infection, the per capita rate at which susceptible animals become infected, is proportional to the absolute number of infectious animals present (known as the pseudo-mass action approximation (De Jong *et al.* 1995) and similar to assuming that animals come into potential infectious contact with most other animals in the population). Another common assumption, that the force of infection is proportional to the fraction of all animals which are infected, is known as the (genuine) mass action approximation and is applicable when animals only mix with a small number of possible contacts. In this second case, there is no threshold population size. While there are many other possible choices for the structure of transmission, we will use these two points as a convenient way of investigating two points on a spectrum of possibilities (De Jong *et al.* 1995). In their large-scale simulation work, White & Harris (1995*b*) use an explicit representation of transmission events; since every animal within a social group is assumed to contact every other animal within that group, but only a smaller number of animals to contact a restricted number of neighbouring groups, we could interpret their model in the light of this classification as one which is pseudo-mass action within groups but mass action between groups, thus

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Table 5. *Table of symbols used*

symbol	meaning
λ	force of infection: incidence rate per susceptible
$\beta(N)$	transmission coefficient as a function of population size
N	population size
K	carrying capacity of region
X	number of susceptible animals
Y	number of infected animals
D_X, D_Y	immigration rate of susceptible and infected animals
b	per capita mortality rate
$r(N)$	discrete per capita birth rate
α	additional per capita mortality due to disease

their results lead to a threshold size for the number of animals within a group but not one for the number of groups.

(*b*) *Estimation of transmission intensity*

Figure 1 shows the incidence of tuberculosis in badgers, as a function of year, based on the Woodchester Park data. There is no significant linear trend in these data.

Thus the force of infection, λ (see table 5 for a list of model symbols and their meanings), has remained roughly constant for the last 15 years. On the other hand, the known-age population size and the number of known-age positive animals has roughly doubled (figure 3). This is at first sight more consistent with assuming that λ is controlled by mass action than assuming it is controlled by pseudo-mass action. Some further evidence for this can be found in figure 2 which shows the relationship between $\beta(N)$ (defined as λ/Y) and N; pseudo-mass action corresponds to $\beta(N)$ being a constant, while mass action assumes $\beta(N) \sim 1/N$. This plot suggests an even more rapid decrease than $1/N$ as N increases.

There are, however, a number of difficulties with such a conclusion from these data. In particular, it is sensitive to the assumption that individuals remain permanently infectious once they have appeared positive. This has the effect of inflating the number of infectious animals later in the dataset, when population sizes are also larger, and hence reducing β for large N. The higher estimates for β at small N could also be due to the effect of infection from other hosts or from immigrating badgers. A constant but small background level of such infections would also generate the pattern seen here. Thus we cannot rule out pseudo-mass action as the transmission process generating these data. Further studies into the form of the transmission process, particularly taking into account the spatial structure of the population, would be useful both theoretically and practically.

If the assumption of a threshold density were to be made (i.e. that transmission is pseudo-mass action), and its value estimated from observed prevalence data, the fundamental control question would be: how do we keep the population below this density? It doesn't particularly matter what control mechanism is used; from this viewpoint the question to ask about a strategy is how we keep the population below x animals per hectare, rather than what percentage y should be culled every year, say.

This fundamental question is complicated by a number of factors; as discussed below, some interventions may act to promote transmission among surviving animals and so threshold densities may be different for different strategies. Even if the simple theory does not predict the existence of a threshold number (i.e. if we assume mass action) then control strategies may well reduce the number of infected animals to a level at which they may all be removed by stochastic events.

(*c*) *Model structure*

The basic model is strongly reminiscent of that of Anderson & Trewhella (1985). The major differences from that model are the assumption of an annual birth cohort rather than a continuous birth process, and a choice of transmission function which allows us to pick from a variety of assumptions including mass action transmission, pseudo-mass action transmission and perturbation induced intensity of transmission. To ease parameter estimation and model interpretation, we take the Woodchester Park non-removal group survey region as the site of our model population and count the number of susceptible (X) and infected (Y) animals within this region, rather than the formally equivalent density of animals per hectare. We write

$$\frac{\mathrm{d}X}{\mathrm{d}t} = D_X - \beta(N)XY - bX, \tag{1}$$

$$\frac{\mathrm{d}Y}{\mathrm{d}t} = D_Y + \beta(N)XY - bY - \alpha Y, \tag{2}$$

with $N = X + Y$. Birth is modelled discretely: at one instant each year the population of susceptibles is increased by an amount $r(N)N$. The terms in this equation can be separated into the demographic and the epidemiological. Demographically, D_X and D_Y represent the net immigration of susceptible and infected animals into the area. In the absence of infection, animals are assumed to die at a constant per capita death rate b. We assume that infection (i.e. being in the Y compartment) is equivalent to any past positivity and to infectiousness: there is no class of latent animals, nor of recovered ones. The major epidemiological parameter is the transmission rate $\beta(N)$; the dependence on population size allows us to represent different assumptions about transmission functions and in § 3*e* we further modify this term to include effects due to population perturbation. We assume that infected animals suffer an additional risk of mortality due to infection, α; our estimates below show that this is not significantly different from zero

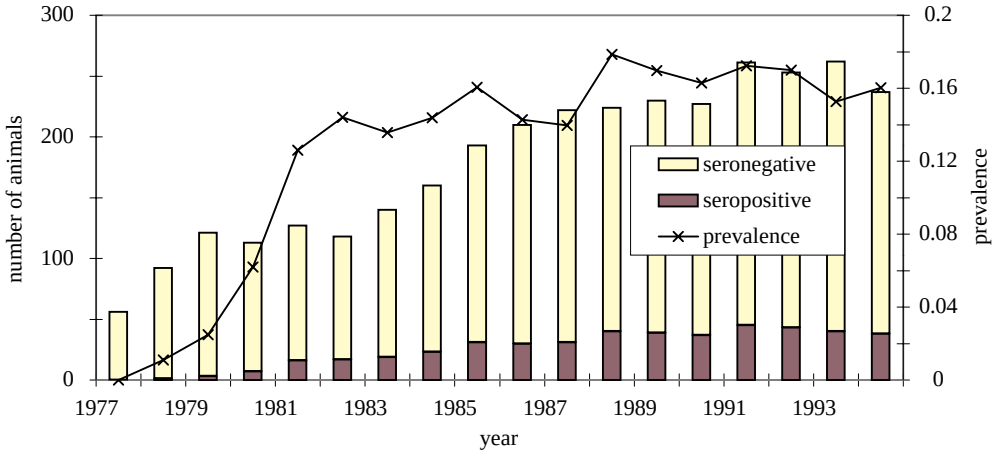

Figure 3. Total known-age population size, number of negative and positive animals and prevalence of infection over time, for the Woodchester Park data in tables 1–4.

in the dataset used, so that in some simulations α is set to zero, but it is included in others to show its potential significance for epidemiological dynamics.

(*d*) *Parameter estimation*

(i) *Birth rate*

Figure 4 plots the number of cubs in each year's data against the total population size in the previous year's data. This is the process which we seek to capture by a birth rate of the form $r(N)N$. To get an idea of the form of the function $r(N)$ we plot in figure 5 the number of cubs per head of total population against total population.

Previous work (Anderson & Trewhalla 1985), on data for population numbers alone in Europe, assumed a density dependence of the form $r(1-(N/K)^c)$ and obtained a good fit with $c = 7$, corresponding to little effect of density dependence until the population is near the carrying capacity, K. This was based on population size alone; effectively only the difference between birth and death rates can be deduced in this manner. A least squares fit of the three parameters r, K and c to the data in figure 5 yielded a best fit c of over 25, implying that if there is any density dependence it acts very severely but only at the very highest population levels, so that by its nature evidence of it cannot be found in the data. Indeed there appears to be no visual evidence of any outward convexity at all. Fortunately, we are interested here in control programmes which will always act to reduce the population numbers and so what happens at the very highest population densities is not crucial to the model; we take $c = 1$ in the simulations.

Since K is measured per unit area, it cannot be directly compared between the three groups; indeed one might expect the K estimate for all three groups taken together to be the sum of those for each group individually, and the data are not inconsistent with this (table 6). On the other hand, it is reasonable in this framework to expect a common value of r between groups.

Table 6. *Maximum-likelihood estimates of density dependent birth rate* $r(N) = r(1 - N/K)$
(Areas as described in § 2.)

areas	r	K
1, undisturbed area	0.42	640
2, control area	0.39	160
3, control area	0.47	140
1,2,3	0.35	1050
2,3	0.42	160

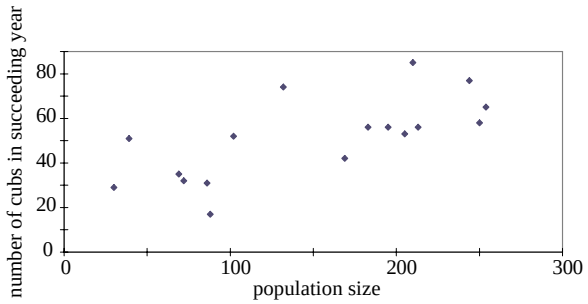

Figure 4. Estimation of effective birth rate. The number of cubs in each year is plotted against the total population in the previous year.

(ii) *Rates of migration and cross-species transmission*

We took D_X and D_Y to be 1 yr^{-1} in some simulations, corresponding to the conservative assumption of a steady trickle of infectious and susceptible animals into the area, so that eradication of infection is inevitably impossible.

This prudent assumption, that infection will always be present, means that it is not enough for a

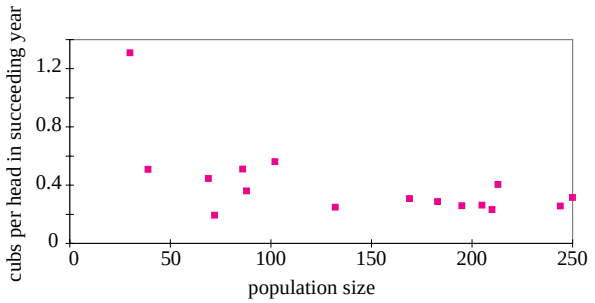

Figure 5. Estimation of effective per capita birth rate. The number of cubs in each year, divided by the total population the previous year, is plotted against the total population in the previous year.

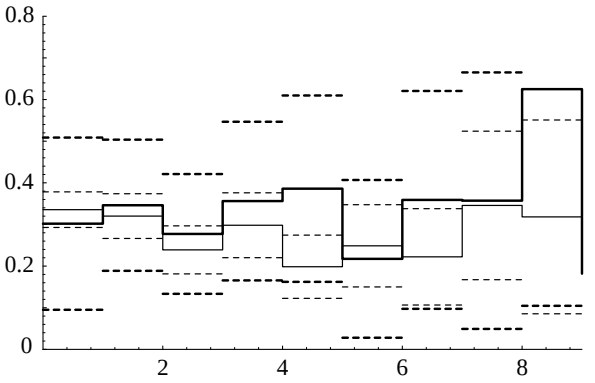

Figure 6. Mortality hazard by year. Horizontal axis: age (yr). Vertical axis: mortality hazard (yr^{-1}). Data from all years are pooled into age cohorts. For each cohort aged i, the number of susceptibles at risk of mortality, n_i is taken to be $X_i - \frac{1}{2}I_i$, where X_i is the number of negative animals known to be alive at the beginning of cohort year i and I_i is the incidence of new cases during the year. Given the number of deaths d_i, the hazard h_i is then calculated as $d_i/(n_i - \frac{1}{2}d_i)$. Hazard for positive animals is calculated similarly but using $n_i = Y_i + \frac{1}{2}I_i$, where Y_i is the number of positives alive at the beginning of the cohort year. Thin lines, negative animals; thick lines, positive animals; dashed lines, 95% confidence intervals calculated as $h_i \pm 1.96h_i\sqrt{((1 - \frac{1}{4}h_i^2)/d_i)}$ (Collett 1994).

control strategy to eradicate infection just once in a badger population: it must also maintain susceptible numbers below the level at which an epidemic might occur.

(iii) *Mortality rates*

Mortality rates for animals with and without infection can be estimated from the Woodchester Park survey data. Figure 6 shows the annual mortality hazard for infected and uninfected animals by age. The assumption of age-independent mortality in the model is equivalent to the assumption that the annual hazard is constant. The figure also shows a maximum-likelihood estimate for this hazard for infected and non-infected animals. These hazards are shown in table 7.

Table 7. *Age-independent mortality estimates calculated from data shown in figure 6*

(Annual discrete rates calculated as pooled estimates $\sum_i d_i / \sum_i (n_i - \frac{1}{2}d_i)$.)

parameter	discrete estimate	s.e.
disease free mortality, b	0.299	0.012
disease mortality, $b + \alpha$	0.344	0.036
relative risk	1.151	0.111

(iv) *Transmission parameter*

We have estimated the force of infection λ (figure 3). To use this in our model we need to convert this into a transmission rate $\beta(N)Y$ using an assumption about the form of the transmission function $\beta(N)$. The mass action (MA) assumption gives $\beta(N) = \beta_{\mathrm{MA}}\lambda/Y$, while pseudo-mass action (PMA) says that $\beta(N) = \beta_{\mathrm{PMA}}\lambda N/Y$. Figure 2 shows the force of infection divided by the number of infecteds as a function of population size. Note that in 1979 there was a case of infection despite the fact that none were recorded in the previous years; this corresponds to an infinitely large value of β for that year, since we are seeking to estimate the transmission parameter without taking into account the effect of migration or other causes of background infection. This problem is also a factor for the other estimates for smaller population sizes, but the maximum-likelihood estimate, because it is weighted to the years with larger sample sizes, does not differ greatly when only the later years are used to estimate β. This approach means that our representation of transmission is more reliable at larger population sizes and prevalence levels.

(e) *Modelling intervention strategies*

This model framework now allows us to model the effect of different intervention strategies, and specifically of fertility control and lethal control.

We model fertility control by a temporary reduction in the birth rate by a certain factor, ρ, assumed to act once only until fertility control is reapplied. Thus the number of births in a year after fertility control is not $r(N)N$ but $(1 - \rho)r(N)N$.

Lethal control is modelled by an instantaneous removal of a certain fraction, σ, of the entire population. This is assumed in the simulations to take place annually just before the point at which births occur, thus reflecting the impact of the year's losses on birth rates.

We also wish to consider the possibility that lethal control may act to promote transmission among surviving animals. There is as yet no quantitative data to guide us in the construction or calibration of any functional form to represent this effect. The best that we can do is to construct a reasonable functional form

and to examine the effect of a range of parametrizations of this form.

We choose to assume that the transmission term β depends on the number of 'recent removals'. We assume a sigmoid form for this dependency and, if the number of recent removals is V, we set

$$\beta(V) = \beta_0 \left[1 + \frac{V^2}{V^2 + (X+Y)^2}\beta_1\right]. \quad (3)$$

This functional form has been chosen so that as disturbance increases, transmission initially increases slowly from the base value, β_0 estimated from the raw data, then more quickly, and then saturates at relatively high levels of disturbance. There is no data at present which we can use to parametrize this functional form. Roughly speaking, the model is designed so that transmission is doubled when the number of recently killed animals reaches a fraction $1/\sqrt{\beta_1}$ of the recent population.

The number of 'recent removals' is modelled by placing each animal removed into the class V and then allowing the size of the class to decay in time with a 'memory' rate parameter m. Thus

$$\frac{\mathrm{d}V}{\mathrm{d}t} = -mV. \quad (4)$$

One further interaction between stress and transmission which has been mooted is that it may be that females are more prone to transmit infection when they have recently given birth. Thus fertility control could have an additional indirect effect by relieving females of the stress of giving birth and thus reducing transmission even further. As with the effect of perturbation, there is no hope at present of capturing the qualitative impact of this effect but it is possible to gain some insight by incorporating a caricature of this effect into the model.

4. RESULTS

Comparison with the Woodchester Park data suggests that precontrol prevalences should be of the order of 15% of the population. Since the birth, death and transmission parameters are derived from this dataset, it is not surprising that the model predicts approximately these prevalence levels (e.g. precontrol levels in graphs (*b*) and (*c*) of figure 7). Nevertheless, prevalence levels are extremely sensitive to the choice of transmission parameters and we assumed a range of different transmission parametrizations.

We investigated a number of simulations exploring the effects of different assumptions and control strategies. We assumed pseudo-mass action or mass action, different β values and the alternative strategies of lethal and fertility control. We varied the intensities of the control, which was applied annually or triennially. In addition, we explored the effects of applying a more intense initial control effort for either a single or five successive years prior to relaxing the maintenance control operations. We used the results of these simulations to draw general conclusions about the relative effects of fertility and lethal control which we describe below, illustrated where relevant by sets of simulation runs such as in figure 7.

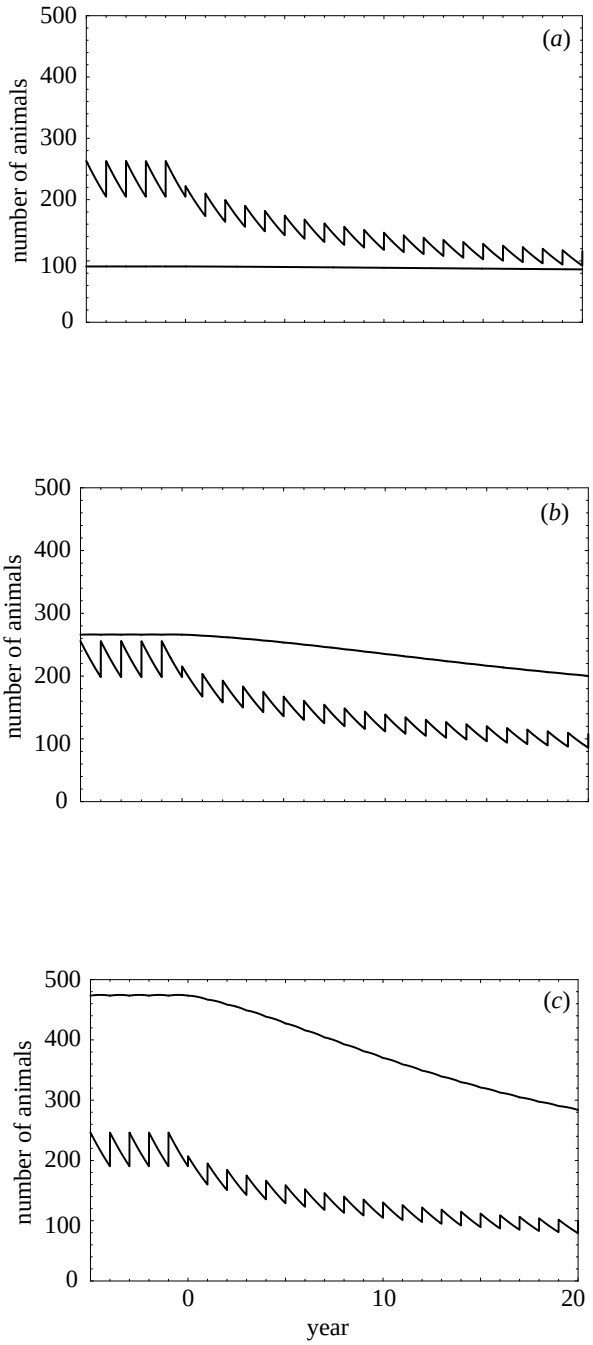

Figure 7. Result of model simulation for the effect of fertility control as a function of transmission intensity. Total population size is jagged line (due to annual birth season); smooth line gives number of infectious badgers multiplied by 10. Thus if the two lines are at the same level, prevalence of infection is 10%. At the onset of control, in year 0, fertility is reduced by 70%, followed by an annual maintenance control of 30%. The transmission structure is assumed to be mass action and the parameter values are (all rates expressed per year): $D_X = D_Y = 1$; $r = 0.42$; $K = 642$; $b = 0.26$; $\alpha = 0.044$; $\beta_1 = 0$ (no perturbation). Infection transmission coefficient, β_{MA} is 0.001×200, 0.0015×200 and 0.0018×200 in graphs (*a*), (*b*) and (*c*), respectively.

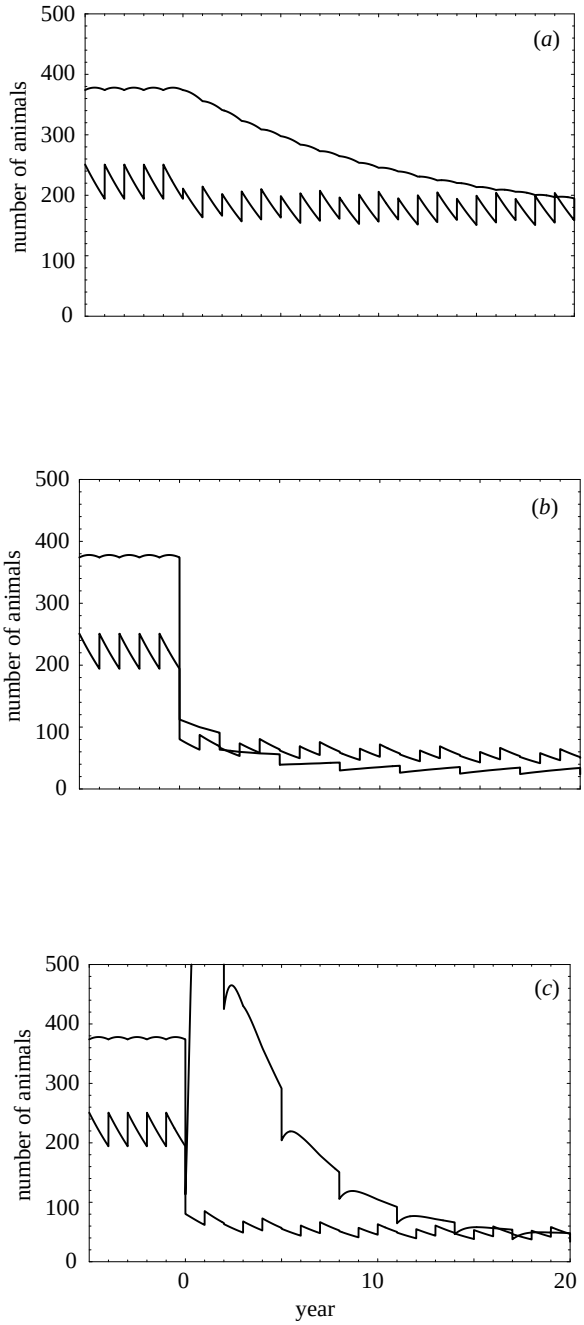

Figure 8. Graph (*a*) as figure 7*b* but with pseudo-mass action with transmission coefficient $\beta_{\mathrm{PMA}} = 0.0015$ and maintenance fertility control of 30% applied every three years only. Graph (*b*) as graph (*a*) but with lethal control applied instead of fertility control at the same schedule. Graph (*c*) as graph (*b*) but with perturbation-induced promotion of transmission following lethal control.

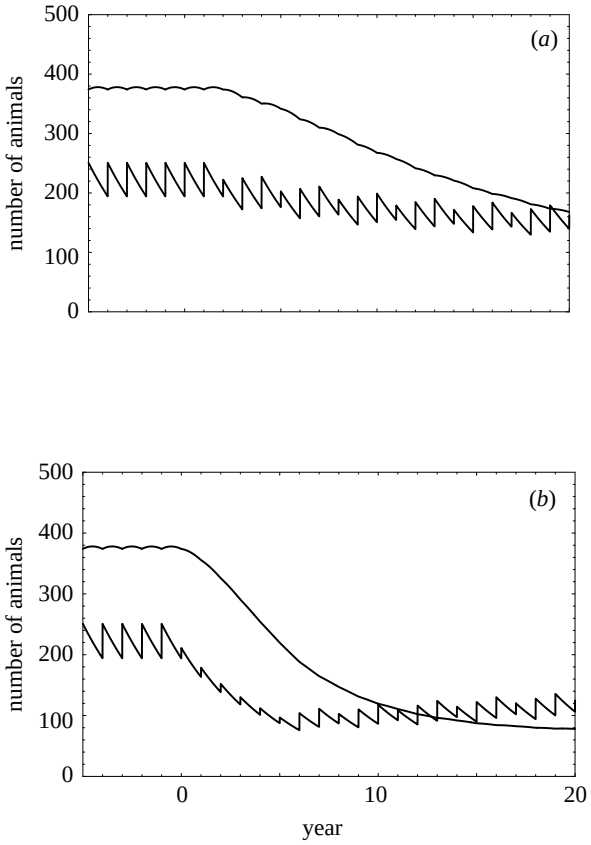

Figure 9. Effects of a fertility control schedule (*a*) of 70% in the first year and 50% every third year thereafter, contrasted with those caused by a schedule (*b*) of 70% for the first 5 years, followed by 50% every three years thereafter; other parameters as figure 8.

Each shows a range of values of simulations for different β values and with different intensities of control strategy. For each particular combination, the total population size and the number of infected animals are shown. Population size appears as a jagged line because of the annual birth process. The number of infected animals is scaled by a factor of 10; thus, if the two lines are at the same level, the prevalence of infection is 10%. Simulations were run for 100 years to allow equilibrium to be obtained before control was applied and implemented with STELLA (High Performance Systems, Inc.) and MATHEMATICA (Wolfram Research, Inc.).

5. SENSITIVITY TO OTHER ASSUMPTIONS

The model was explored under a number of different structural assumptions: comparing mass action and pseudo-mass action transmission, for example. However, the number of possible variants is unlimited; we discuss here the effects we would expect to see in the presence of some particular complications.

Other workers have included a class of animals incubating infection in their models, typically with a latent period of a few months, although the empirical evidence for such a value is scanty (Little *et al.* 1982); we chose not to include such a class in our model for the sake of simplicity. For an infection at an endemic equilibrium, this is not likely to alter our results very much, since the estimation procedure to determine β relies on all those animals known to be infectious at the beginning of the year, of which the number of incubating animals is likely to be rather low. However, this assumption would cause problems if we were to consider modelling strategies based on selecting animals on the basis of their infection status, since this latent class of animals might remain a

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significant reservoir of infection even if all infectious animals were removed. Similar considerations would apply to other modifications, such as the inclusion of a class of animals which become immune to infection.

We have ignored the dynamical effects of seasonality and stochasticity in transmission; Ruxton (1996) explores the implications of this neglect for the model of Bentil & Murray (1993) and shows that the most significant effect of this is to change the stability of transient cycles, but further work is clearly needed in this area.

We have assumed disease-induced mortality to be small or non-existent. Experience in other pathosystems suggests that even rather low levels of disease related mortality can have significant effects on host population levels in some circumstances and more sophisticated analyses need to be carried out on these and similar datasets to investigate the role, if any, of tuberculosis in controlling badger populations.

The most important simplification we have made, however, is in our representation of a homogenous mixing structure. As we have seen, the data are consistent with a mass action mixing process at all but the lowest densities. However, the known social grouping of badger populations means that we need to consider how well the consequent transmission structure can be captured in more general situations and, in particular, following a control operation. If pockets of infection are isolated then the degree to which infection persists globally is determined by a complex interaction between the chronicity of the infection within a particular group, the rate of transmission between neighbouring groups and the rate at which populations of susceptible badgers are allowed to recover. Our understanding of the dynamics of infection in such situations is at best partial. Much insight can be gained from large-scale numerical simulations (White & Harris 1995*b*), but we also need to extend these simple models (perhaps along the lines of Barlow (1991)) to encompass these factors without losing the clarity which is their chief virtue.

6. CONCLUSIONS

Both fertility control and lethal control are capable of eradicating infection, or in the face of constant re-exposure risk, at least controlling it at small levels. This must be so since both are in principle capable of eradicating the host population. This paper has confirmed the results of more general studies (Barlow 1996) showing that there is a nonlinear relationship between the intensity of control, the reduction in population size and the number of cases of infection. In some situations, particularly where external sources of infection are small and initial prevalences are high (figure 7*c*), large reductions in the numbers infected can be achieved with only moderate reductions in population numbers (figure 8*a*). This is much more marked in the model assuming pseudo-mass action, in other words in those settings where disease transmission is being driven by between group rather than within group interactions. The mechanism for this long-term reduction is the same for both fertility control and lethal control: the removal of susceptibles; if one is in principle capable of keeping a population low enough to be infection free then, in the absence of perturbative effects on transmission, so is the other.

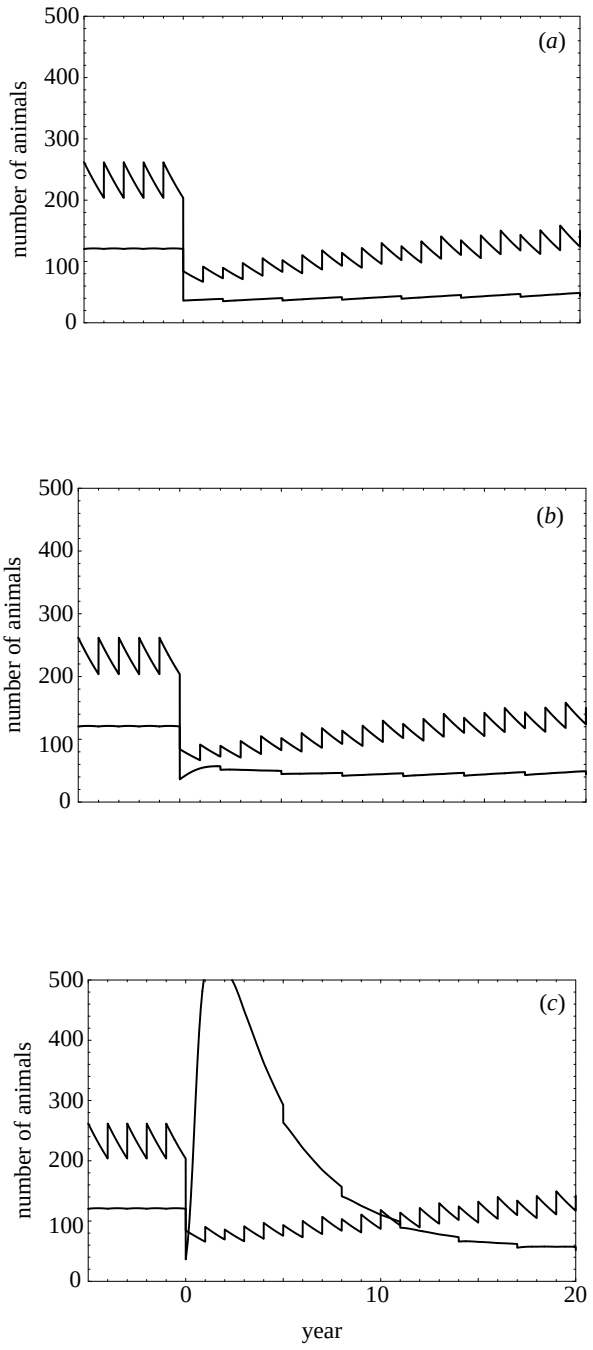

Figure 10. Effects of perturbation. Graphs (*a*) and (*b*) show the results of a lethal control strategy of 70% in the first year, followed by 10% every three years thereafter, without ((*a*) $\beta_1 = 0$) and with small and large ((*b*) small effect $\beta_1 = 10$, (*c*) large effect $\beta_1 = 100$) perturbation-induced transmission effects; other parameters as figure 8, except that $\beta_{MA} = 0.001 \times 200$.

It is necessary to continue either form of control at regular intervals to maintain a constantly depressed level of infection in the long term. If control were

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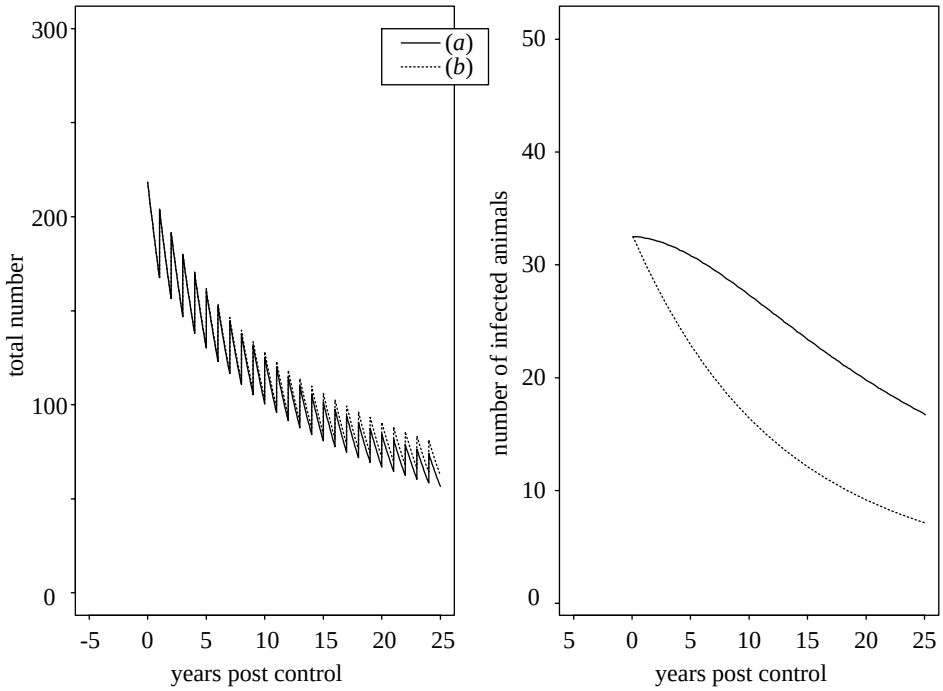

Figure 11. The relationship between fertility induced stress and transmission. Number of all and infected animals in a population subject to annual fertility reductions of 30%. Curve (a) assumes no relationship between fertility and transmissions ($D_X = 0$, $D_Y = 0.1$, $K = 642$, $r = 0.42$, $\beta_0 = 0.36$ (mass action), $b = 0.26$, $\alpha = 0.044$). Curve (b) uses the same parameter values, except that in the year following a control which reduces fertility to a fraction ρ of its normal value, transmission is modified by a factor $(1 - \beta_1(1 - \rho))$. This run took $\beta_1 = 0.2$, which is equivalent to mean transmission (by both males and females) increasing by a factor of five, when fertility is at its maximum, compared to its intensity when no breeding occurs.

to be stopped, return to precontrol levels of badger population and prevalence would be expected over a period of 5–10 yr. Even if infection has been eradicated during the control period, the recovered population would continue to be vulnerable to reinfection. The intensity of initial control does affect the speed at which the population is reduced to a minimum infectiousness but not the rate at which it recovers thereafter (figure 10).

In the short term, and in the unlikely case that there is no perturbation effect of lethal control, fertility control is less effective in reducing population density than lethal control since it can only act to remove one age cohort per year. It is also less effective in reducing transmission as it can only ever remove susceptibles, while lethal control also removes infectious badgers (figure 8). If lethal control does exert a perturbation effect, these differences are reduced and might be reversed.

A further perturbative effect might arise from the reduction in reproductive stress and other behavioural changes which could be hypothesized to act to reduce transmission as the intensity of fertility control increases. As for the perturbation effects of lethality control, we have little idea of how to model this effect. One attempt at such a model is described in figure 11; it demonstrates a substantial effect at high transmission levels and frequent interventions modelled, but of course this depends crucially on the form and magnitude of the model structure chosen. Further field work, to give such a structure a more robust footing, is essential if the likely perturbative effects are to be judged in this way.

It is against the magnitude of these short-term disadvantages of fertility control that the potential problems of lethal control in promoting transmission need to be judged (figure 10). Much more data are needed to improve the reliability of the epidemiological and demographic parameters and, in particular, on how they may be affected by population reductions caused by control operations. Since the proportion of the population that needs to be controlled to achieve an acceptable and maintained reduction in the numbers that are infectious is sometimes close to a level that endangers the viability of the badger population, any control strategy that also sought to avoid local badger extinction must be combined with close monitoring of badger numbers and prevalence levels in both badgers and cattle. Intensive monitoring may be extremely difficult in practice, but some continuous reassessment of badger population control seems essential as long as major gaps in our understanding of the dynamics of the Tb pathogen persist.

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