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Is There an Association between Levels of Bovine Tuberculosis in Cattle Herds and Badgers?

Christl A. Donnelly and Jim Hone

Abstract

Wildlife diseases can have undesirable effects on wildlife, on livestock and people. Bovine tuberculosis (TB) is such a disease. This study derives and then evaluates relationships between the proportion of cattle herds with newly detected TB infection in a year and data on badgers, in parts of Britain.

The relationships are examined using data from 10 sites which were randomly selected to be proactive culling sites in the UK Randomized Badger Culling Trial. The badger data are from the initial cull only and the cattle incidence data pre-date the initial badger cull.

The analysis of the proportion of cattle herds with newly detected TB infection in a year, showed strong support for the model including significant frequency-dependent transmission between cattle herds and significant badger-to-herd transmission proportional to the proportion of *M. bovis*-infected badgers. Based on the model best fitting all the data, 3.4% of herds (95% CI: 0 – 6.7%) would be expected to have TB infection newly detected (i.e. to experience a TB herd breakdown) in a year, in the absence of transmission from badgers. Thus, the null hypothesis that at equilibrium herd-to-herd transmission is not sufficient to sustain TB in the cattle population, in the absence of transmission from badgers cannot be rejected (p=0.18). Omitting data from three sites in which badger carcase storage may have affected data quality; the estimate dropped to 1.3% of herds (95% CI: 0 – 6.5%) with p=0.76.

The results demonstrate close positive relationships between bovine TB in cattle herds and badgers infectious with *M. bovis*. The results indicate that TB in cattle herds could be substantially reduced, possibly even eliminated, in the absence of transmission from badgers to cattle. The results are based on observational data and a small data set to provide weaker inference than from a large experimental study.

KEYWORDS: badger, bovine tuberculosis, host-disease model, model averaged prediction, vaccination

Author Notes: The Randomized Badger Culling Trial (RBCT) in Britain was designed, overseen and analysed by the Independent Scientific Group on Cattle TB (John Bourne, Christl Donnelly,

David Cox, George Gettinby, John McInerney, Ivan Morrison and Rosie Woodroffe). The RBCT was funded by the Department of Environment, Food and Rural Affairs (Defra) with the cooperation of the many farmers and land occupiers in the trial areas who allowed the experimental treatments to operate on their land. JH acknowledges support from the University of Canberra and CAD acknowledges the MRC for Centre funding support. D. Pedersen is thanked for statistical advice.

Introduction

Wildlife have a variety of diseases that includes rabies and bovine tuberculosis (TB) (Keeling and Rohani 2008; Hone 2007; Krebs 2009; Delahay, Smith and Hutchings 2009). Some diseases such as bovine TB, caused by *Mycobacterium bovis*, are a focus for wildlife control because of effects of the disease on livestock production (Anderson and Trewhella 1985; Barlow 1991, 2000; Donnelly *et al*. 2003, 2006, 2007; Jenkins *et al*. 2007, 2008, 2010). Simulation studies, such as those by Roberts (1999) and Smith *et al*. (2001), have suggested vaccination of wildlife may be useful for control of TB. Vaccination of foxes (*Vulpes vulpes*) has reduced rabies incidence in parts of Europe (Blancou *et al*. 2009).

Cattle and badgers (*Meles meles*) are both known hosts of, and subject to control to limit the spread of, bovine TB in cattle herds in the U.K. and Ireland. Cattle herds in the UK are regularly tested for TB in accordance with EU legislation. The testing interval is parish based and ranges from 1 year to 4 years, with lowest incidence parishes receiving 4-yearly routine herd tests and highest parishes receiving annual whole-herd tests. Additional herd tests, for example in response to TB being detected in a herd linked through geographic proximity or through trade, are also undertaken, as well as slaughterhouse checks of all cattle slaughtered for consumption. A herd is said to experience a TB ‘‘breakdown’’ if one or more members of a cattle herd fail the conventional TB skin test or show evidence of TB lesions at slaughterhouse inspection that are positive to *M. bovis* on culture.

This paper evaluates evidence for bovine TB association between cattle herds and badgers in an observational study in ten 100km^2 areas of England. Alternative hypotheses, as epidemiological models, of the association are assessed. We also estimate the proportion of herds detected with TB in the absence of transmission from badgers, such as could occur with completely effective vaccination.

Modelling

A model of bovine TB in cattle herds in a part of New Zealand (Barlow *et al*. 1998; their equation 6) assumed that the rate of change of the number of herds with TB (and hence on movement control) was related to the rate of change from uninfected to infected herd status as modified by the duration of the time being infectious. It was assumed in a second (separate, but linked) area that wildlife, for example brushtail possums (*Trichosurus vulpecula*), could transmit TB to cattle herds, at a rate *k*. Reinfection of wildlife from cattle was considered to be rare in regularly tested herds, so the model did not include such infection.

We consider the analogous model for a single area with density-dependent transmission between cattle herds subjected to wildlife transmission risk such that

$$\frac{dU}{dt} = \frac{M}{p} - U(\beta I + k) \qquad \text{eqn 1}$$

$$\frac{dI}{dt} = U(\beta I + k) - Ic \qquad \text{eqn 2}$$

$$\frac{dM}{dt} = Ic - \frac{M}{p} \qquad \text{eqn 3}$$

where cattle herds move between states U (uninfected), I (infected, and equivalently infectious, but undiagnosed) and M (under movement controls and thus not infectious to other herds). U, I and M are the numbers of herds, rather than cattle, in each of these states and N is the total number of herds (N=U+I+M). The transmission coefficient β represents the between-herd risk per annum while *k* is the rate of infection from wildlife (and is equivalent to the force of infection) per annum. The per-annum rate at which infected herds go on to movement controls is represented by *c* and *p* is the average time on movement control in years. We, like Barlow *et al.* (1998), assume no reinfection of wildlife (in our case, badgers) from cattle herds. Such an assumption is one possibility and the inferences made here are conditional on any such reinfections being negligible.

At equilibrium

$$I^* = \frac{M^*}{cp} \qquad \text{eqn 4}$$

where the superscript * denotes that I* and M* are at their equilibrium values. Similarly,

$$I^* = \frac{U^* k}{c - U^* \beta} \qquad \text{eqn 5}$$

$$\frac{M^*}{p} = U^*(\beta I^* + k) \qquad \text{eqn 6}$$

and N = U* + I* + M*.

Using substitution, it can be shown that the equilibrium value I* can be obtained from the solution of this quadratic equation:

$$I^{*2}(\beta + p\beta c) + I^*(-N\beta + k + pck + c) - Nk = 0 \qquad \text{eqn 7}$$

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In the special case of no risk from wildlife (k=0) and $\beta > 0$, the equilibrium solution is given by:

$$U^* = \frac{c}{\beta}, \qquad I^* = \left(N - \frac{c}{\beta}\right)\frac{1}{1+pc}, \text{ and } M^* = \left(N - \frac{c}{\beta}\right)\frac{pc}{1+pc}. \qquad \text{eqn 8}$$

whereas if there is no herd-to-herd transmission (β=0) and $k > 0$, the equilibrium solution is given by:

$$U^* = N\frac{\frac{c}{k}}{1+pc+\frac{c}{k}}, \qquad I^* = N\frac{1}{1+pc+\frac{c}{k}}, \text{ and } M^* = N\frac{pc}{1+pc+\frac{c}{k}} \qquad \text{eqn 9}$$

We also consider the analogous model with frequency-dependent transmission:

$$\frac{dU}{dt} = \frac{M}{p} - U\left(\beta\frac{I}{N} + k\right) \qquad \text{eqn 10}$$

$$\frac{dI}{dt} = U\left(\beta\frac{I}{N} + k\right) - Ic \qquad \text{eqn 11}$$

$$\frac{dM}{dt} = Ic - \frac{M}{p} \qquad \text{eqn 12}$$

At equilibrium

$$I^* = \frac{M^*}{cp} \qquad \text{eqn 13}$$

(as before) where the superscript * denotes that I* and M* are at their equilibrium values, whereas

$$I^* = \frac{U^*k}{c - U^*\frac{\beta}{N}} \qquad \text{eqn 14}$$

$$\frac{M^*}{p} = U^*\left(\beta\frac{I^*}{N} + k\right) \qquad \text{eqn 15}$$

Using substitution, it can be shown that the equilibrium value I* can be obtained from the solution of this quadratic equation:

$$I^{*2}\left(\frac{\beta}{N} + p\frac{\beta}{N}c\right) + I^*(-\beta + k + pck + c) - Nk = 0 \qquad \text{eqn 16}$$

In the special case of no risk from wildlife (k=0) and $\beta > 0$, the equilibrium solution is given by:

$$U^* = N\frac{c}{\beta}, \qquad I^* = N\left(1-\frac{c}{\beta}\right)\frac{1}{1+pc},$$
$$\text{and } M^* = N\left(1-\frac{c}{\beta}\right)\frac{pc}{1+pc}. \qquad \text{eqn 17}$$

We consider four alternatives for k, that it equals 0 (i.e. no transmission from wildlife), that, it is proportional to the total number of badgers culled in the area in question (N_w), that it is proportional to the number of infected badgers culled in the area in question (I_w), and it is proportional to the ratio of infected culled badgers to all culled badgers (I_w/N_w). Thus, when k is related to badgers, $k=\alpha N_w$, $k=\alpha I_w$ or $k=\alpha(I_w/N_w)$ where α is the proportionality constant assumed to be non-negative. We recognize that there may be other sources of infection of British cattle herds, for example deer. However, studies of farmland wildlife found very little evidence of infectiousness from wildlife other than badgers (Mathews *et al.* 2006).

A herd scale has been used previously to model disease dynamics, such as the farm being the unit of study and transmission in models of foot-and-mouth disease dynamics in the U.K. (Ferguson, Donnelly and Anderson 2001; Keeling *et al.* 2001). The additive nature of transmission between cattle and between an external agent (wildlife or environment) reflects the additive assumptions in two-host disease models such as described by Barlow *et al.* (1998) and Hone and Donnelly (2008). The models considered (Table 1) represent alternative hypotheses, in the sense of Chamberlin (1965), of the determinants of the proportion of cattle herds with TB.

Methods

Data on bovine TB in cattle herds and badgers at 10 sites in Britain are from the Randomized Badger Culling Trial (RBCT), which has been described in detail previously (Bourne *et al.* 2007; Donnelly *et al.* 2003, 2006; Hone and Donnelly 2008). The data on cattle herds and TB in cattle herds are from Donnelly *et al.* (2006). The badger data are from the initial cull of badgers in the proactive badger culling treatment sites as used by Hone and Donnelly (2008). TB diagnosis was based on skin test for cattle and culture tests for badgers as used by Hone and Donnelly (2008). The number of cattle herds varied between sites from 63 to 245; data are presented in the Appendix.

The data from three sites (triplets A, C and E) may have been influenced by the freezing of badger carcases (Hone and Donnelly 2008) so the analyses

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were repeated after deleting data from those three sites. For disease modelling and management it was assumed that cattle infection as shown by reaction on skin test was equivalent to the animal being infectious, and that there is no carrier state in cattle or badgers.

For both the density-dependent and the frequency-dependent models, the number of herd breakdowns in a one-year period, B, among N herds, is on average, at equilibrium, equal to I**c* where *c* is the rate at which infected herds are detected and put under movement controls. In other words, 1/*c* is the average time in years that a herd is infected before it is detected. In a single year the proportion of herds in which infection is newly detected (i.e. which experience TB herd breakdowns) is thus:

$$\frac{I^{*}c}{N} \qquad \text{eqn 18}$$

The binomial log likelihood is therefore given by:

$$l = Bln\left(\frac{I^{*}c}{N}\right) + (N-B)ln\left(1-\frac{I^{*}c}{N}\right) \qquad \text{eqn 19}$$

ignoring an additive constant.

The rate at which infected herds are detected and put onto movement controls, *c*, is derived to incorporate detection of infected herds at routine herd testing (following Cox *et al*., 2005) as well as slaughterhouse detection. With routine testing every *b* years and the assumption that repeated tests on the same herd are independent with the same herd test sensitivity, *s*, each time, the average time between infection and detection is given by:

$$\mu_R = b\left(\frac{1}{2}+\frac{(1-s)}{s}\right) \qquad \text{eqn 20}$$

assuming that infection of herds starts at a random time between tests. The *b*(1-*s*)/*s* term arises from the geometric distributions of retests needed when a test with imperfect sensitivity is used (i.e. *s*<1) (Cox *et al*. 2005). Of course, herd test sensitivity is greater than the test sensitivity for a single infected animal whenever there is more than one infected animal to be tested within the herd. (The formulation given by Barlow *et al*. (1998, equation 8), $\mu_R=b/s$, is not correct.)

The average time to detection at slaughterhouse, in the absence of routine herd testing, would depend not just on the age distribution of routinely slaughtered cattle, but also on the number of infected cattle within the herd. We make the simplifying approximation that *c*, the overall rate at which infected herds are detected and put onto movement controls includes a component due to slaughterhouse detection, *a*, such that:

$$c = a + \frac{1}{\mu_R} = a + \frac{2s}{b(s+2(1-s))} \qquad \text{eqn 21}$$

Estimates for β and α were obtained using maximum likelihood, with confidence intervals obtained from profile likelihoods. We assume values for the remaining parameters: *p* (the average time on movement control in years); *a*/*c* (the proportion of infected herds detected and put onto movement controls which are detected through slaughterhouse surveillance); *b* (the interval between routine herd tests) and *s* (the herd test sensitivity, that is the proportion of infected herds that are successfully detected by a routine herd test).

The average time that a herd remains under movement controls due to a confirmed TB breakdown rose from 215 days to 292 days between 1997 and 2002 (the period in which the initial proactive culls of the RBCT were undertaken) (Defra, 2004). We approximate and assume that *p* equals 0.7 years (255 days) for all areas analysed.

In 2005, 14% of confirmed TB herd breakdowns were detected through slaughterhouse surveillance (Bourne *et al*., 2007), so we approximate *c* by setting *a*/*c*=0.14 and solving we obtain

$$c = 1.16\frac{2s}{b(s+2(1-s))}. \qquad \text{eqn 22}$$

Because RBCT areas were selected to be in areas of highest cattle TB risk, we assume that all herds under analysis were subjected to annual routine herd testing; thus, *b* equals 1 year.

We consider herd test sensitivity (*s*) values between 0.9 and 1.

Akaike weights based on the Akaike information criterion, corrected for sample size (AICc), (Anderson, 2008) were used to assess the relative support of the data for a particular model across the range of models considered.

Results

The analysis of the proportion of cattle herds with newly detected TB infection in a year, including data from all ten areas, showed that the best fitting model included frequency-dependent transmission between cattle herds (β=1.98, 95% CI: 1.84 – 2.07) and badger-to-herd transmission proportional to the proportion of badgers infectious for *M. bovis* (α=0.047, 95% CI: 0.013 – 0.119) (Figure 1). This model achieved an Akaike weight of 0.966 (Table 1). Based on this model, 3.4% of herds (95% CI: 0 – 6.7%) would be expected to have TB infection newly detected (i.e. to experience a TB herd breakdown) in a year, in the absence of transmission from badgers (calculated assuming from the maximum likelihood estimate of β, 1.98, and its 95% confidence interval, and setting *k*=0). Thus, the

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null hypothesis that at equilibrium herd-to-herd transmission is not sufficient to sustain TB in the cattle population, in the absence of transmission from badgers cannot be rejected (p=0.18). Other models received very little support from the data analysed with Akaike weights being close to 0 (Table 1).

Similar results were obtained when data from triplets A, C and E were omitted due to concern about their data quality. The analysis of the proportion of cattle herds with newly detected TB in a year showed that the best fitting model included frequency-dependent transmission between cattle herds (β=1.93, 95% CI: 1.59 – 2.06) and badger-to-herd transmission proportional to the proportion of badgers infectious for *M. bovis* (α=0.065, 95% CI: 0.015 – 0.203) (Figure 1). This model achieved an Akaike weight of 0.923 (Table 2). Based on this model, 1.3% of herds (95% CI: 0 – 6.5%) would be expected to have TB infection newly detected (i.e. to experience a TB herd breakdown) in a year, in the absence of transmission from badgers (calculated assuming from the maximum likelihood estimate of β, 1.93, and its 95% confidence interval, and setting k=0). Thus, the null hypothesis that at equilibrium herd-to-herd transmission is not sufficient to sustain TB in the cattle population, in the absence of transmission from badgers cannot be rejected (p=0.76). Other models received very little support from the data analysed (Table 2).

These results were obtained assuming a herd test sensitivity of 0.9. However, similar results were obtained assuming a herd test sensitivity of 1.

The best model fits imply that a completely infected (100% prevalence) badger population would be associated with roughly 20% of the cattle herds being newly detected with TB each year (Figure 1). While incomplete identification of *M. bovis* infection in badgers at necropsy (i.e. diagnostic sensitivity less than 100%) does not affect the model fits obtained, it does affect the interpretation of the x-axis in Figure 1 (the observed prevalence of *M. bovis* infection in badgers). Crawshaw *et al.* (2008) estimated, on the basis of a study comparing standard and detailed necropsy protocols for badgers, that the overall sensitivity of the standard protocol, to which RBCT badgers were subjected, was only 54·6 per cent (95% CI: 44·9 – 69·8%), relative to the more detailed protocol. The observed prevalence in badgers could then be corrected by this parameter, denoted s_B, and used to plot the observed data with the best-fitting models now interpreted as having k proportional to the true *M. bovis* infection prevalence in badgers with slope αs_B (Figure 2). With the correction for incomplete sensitivity of the badger testing, the best model fits imply that a completely infected badger population would be associated with roughly 15% of the cattle herds being newly detected with TB each year (Figure 2). The correction has no effect on the estimated proportion of herds with TB infection newly detected (i.e. to experience a TB herd breakdown) in a year, in the absence of transmission from badgers.

Table 1. Estimates and log likelihood values associated with density-dependent (DD) and frequency-dependent (FD) transmission models fitted to the data on TB in cattle and badgers **including data from all ten triplets**. β is a measure of herd-to-herd transmission while *k*, such that $k=\alpha N_w$, $k=\alpha I_w$ or $k=\alpha(I_w/N_w)$, where N_w equals the number of badgers culled in the area and I_w equals the number of infectious badgers culled in the area, represents the transmission risk from badgers to cattle. Each of the models has one (α or β) or two fitted parameters, β and α. Throughout herd test sensitivity is assumed to equal 0.9. The model with most support (highest Akaike weight) is shown in bold.

Between-herd transmission	Transmission from wildlife[1]	Num. of param	β	p-value H_0: β=0	α	p-value H_0: α=0	Log likelihood	AICc	Akaike weight
None	pt N_w	1	--[2]	--[2]	0.00025	N/A[3]	-353.79	710	0.000
None	pt I_w	1	--[2]	--[2]	0.0026	N/A[3]	-349.77	702	0.000
None	pt I_w/N_w	1	--[2]	--[2]	0.80	N/A[3]	-329.18	661	0.000
DD	None	1	0.031	N/A[3]	--[2]	--[2]	-739.78	1482	0.000
DD	pt N_w	2	0	1	0.00025	<0.001	-353.79	713	0.000
DD	pt I_w	2	0	1	0.0026	<0.001	-349.77	705	0.000
DD	pt I_w/N_w	2	0	1	0.80	<0.001	-329.18	664	0.000
FD	None	1	2.09	N/A[3]	--[2]	--[2]	-322.25	647	0.019
FD	pt N_w	2	2.09	<0.001	0	1	-322.25	650	0.004
FD	pt I_w	2	2.06	<0.001	0.000040	0.16	-321.24	648	0.011
FD	**pt I_w/N_w**	**2**	**1.98**	**<0.001**	**0.047**	**<0.001**	**-316.74**	**639**	**0.966**

[1] pt =proportional to; [2] When α or β is assumed to be zero, the parameter estimate is omitted from the table and no p-value is calculable. [3] When only one parameter (α or β) is fitted and the other is assumed to equal zero, the calculation of a p-value for the null hypothesis that the single fitted parameter is also equal to zero is not applicable (N/A), as that null model would have no disease transmission and thus at equilibrium no disease. Alternatively, one could think of such p-values as equalling zero, because the model with no disease has a log likelihood of negative infinity.

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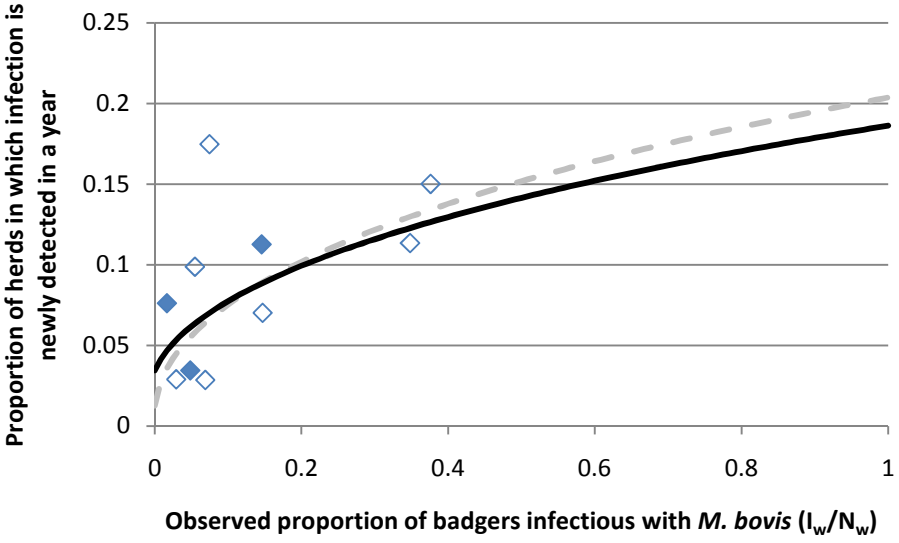
Table 2. Estimates and log likelihood values associated with density-dependent (DD) and frequency-dependent (FD) transmission models fitted to the data on TB in cattle and badgers **excluding triplets A, C and E**. β is a measure of herd-to-herd transmission while *k*, such that $k=\alpha N_w$, $k=\alpha I_w$ or $k=\alpha(I_w/N_w)$, where N_w equals the number of badgers culled in the area and I_w equals the number of infectious badgers culled in the area, represents the transmission risk from badgers to cattle. Each of the models has one (α or β) or two fitted parameters, β and α. Throughout herd test sensitivity is assumed to equal 0.9. The model with most support (highest Akaike weight) is shown in bold.

Between-herd transmission	Transmission from wildlife[1]	Num. of param	β	p-value H_0: β=0	α	p-value H_0: α=0	Log likelihood	AICc	Akaike weight
None	pt N_w	1	--[2]	--[2]	0.00026	N/A[3]	-266.39	536	0.000
None	pt I_w	1	--[2]	--[2]	0.0023	N/A[3]	-260.37	524	0.000
None	pt I_w/N_w	1	--[2]	--[2]	0.71	N/A[3]	-250.25	503	0.013
DD	None	1	0.031	N/A[3]	--[2]	--[2]	-608.71	1220	0.000
DD	pt N_w	2	0	1	0.00026	<0.001	-266.39	540	0.000
DD	pt I_w	2	0	1	0.0023	<0.001	-260.37	528	0.000
DD	pt I_w/N_w	2	0	1	0.71	<0.001	-250.25	508	0.002
FD	None	1	2.10	N/A[3]	--[2]	--[2]	-249.18	501	0.038
FD	pt N_w	2	2.10	<0.001	0	1	-249.18	505	0.005
FD	pt I_w	2	2.04	<0.001	0.000064	0.084	-247.69	502	0.020
FD	**pt I_w/N_w**	**2**	**1.92**	**<0.001**	**0.065**	**0.001**	**-243.88**	**495**	**0.923**

[1] pt =proportional to; [2] When α or β is assumed to be zero, the parameter estimate is omitted from the table and no p-value is calculable. [3] When only one parameter (α or β) is fitted and the other is assumed to equal zero, the calculation of a p-value for the null hypothesis that the single fitted parameter is also equal to zero is not applicable (N/A), as that null model would have no disease transmission and thus at equilibrium no disease.

Figure 1. The observed proportions of herds in which infection is newly detected (i.e. which experience TB herd breakdowns) in a year (filled symbols represent triplets A, C and E) and fitted models (solid line fit includes all data and dotted line fit omits triplets A, C and E) of the proportion of herds in which infection is newly detected (i.e. which experience TB herd breakdowns), (I**c*/N, equation 18) as a function of the observed proportion (I_w/N_w) of badgers infectious with *M. bovis* in parts of Britain. The parameter estimates used are from the models with the lowest AICc. (The graph is plotted over the entire possible range of I_w/N_w (i.e. from 0 to 1) to demonstrate the fit of the model to the observed data as well as the implications of the model for cattle in the presence of badger populations with high observed *M. bovis* prevalence levels.)



Discussion

The evaluation of the association between TB in cattle herds and badgers showed evidence of a strong positive relationship, similar to the results of Hone and Donnelly (2008), although in this study the important badger variable was the proportion of badgers infectious with *M. bovis* implying much stronger support for frequency-dependent badger-to-cattle transmission than density-dependent badger-to-cattle transmission. The analyses were based on epidemiological models derived from the TB model of Barlow *et al*. (1998) which examined transmission between cattle herds and from brushtail possums to cattle herds in New Zealand.

If the reported associations between bovine TB in cattle herds and badgers in parts of Britain reflect causal relationships, then the results imply that reducing the prevalence of *M. bovis* infection in badgers, such as by effective vaccination of badgers, may be important in reducing TB incidence in cattle herds. However,

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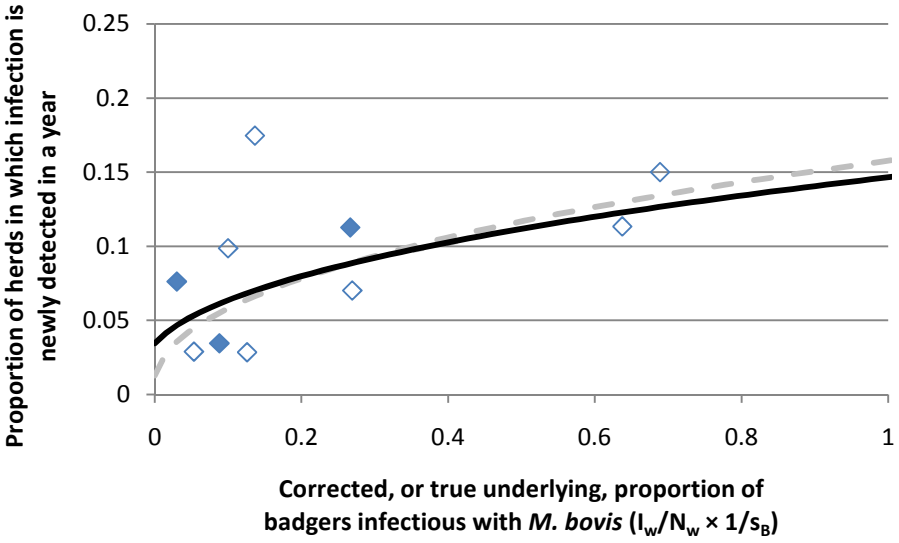
Figure 2. The observed proportions of herds in which infection is newly detected (i.e. which experience TB herd breakdowns) in a year (filled symbols represent triplets A, C and E) and fitted models (solid line fit includes all data and dotted line fit omits triplets A, C and E) of the proportion of herds in which infection is newly detected (i.e. which experience TB herd breakdowns), (I^*c/N, equation 18) as a function of the corrected, or true underlying, proportion ($I_w/N_w \times 1/s_B$) of badgers infectious with *M. bovis* in parts of Britain. The parameter estimates used are from the models with the lowest AICc. (The graph is plotted over the entire possible range of badger infection prevalence (i.e. from 0 to 1) to demonstrate the fit of the model to the observed data as well as the implications of the model for cattle in the presence of badger populations with high observed *M. bovis* prevalence levels.)



stronger inference (Platt 1964; McArdle 1996) would be possible from an experimental study. Such an experiment might take the form of monitoring TB incidence among cattle herds in areas randomised to receiving and not receiving badger vaccination, where the magnitude would need to be similar to that of the RBCT (i.e. ten 100km^2 areas per randomised 'treatment' monitored for 5 years) in order to achieve comparably precise estimates of the effects of badger vaccination on TB incidence in cattle herds. Vaccination experiments would help interpretation and application of previous simulation studies, such as by Smith *et al*. (2001), of vaccination. Vaccination has been successful for rabies control (Blancou *et al*. 2009) and is an area of active research for TB control.

Experimental evidence suggests reduction in badger density can have positive and negative effects on the incidence of TB in cattle herds (Donnelly *et*

al. 2006). The present study makes no inferences about any effects on TB in cattle herds in surrounding areas, and hence about whether negative effects may occur.

The analysis of the proportion of cattle herds with newly detected TB in a year showed that the Akaike weights of the best models were close to 1.0 (Tables 1, 2). While the estimation of the equilibrium disease state in the absence of transmission from badgers (k=0) involved some extrapolation beyond the range of the observed data, examination of Figure 1 shows the extrapolation was quite limited as the lowest value of the linear predictor of k, prevalence of *M. bovis* infection in badgers, was 1.6%. The conclusions may have been influenced by the small sample sizes of the data sets studied. For example, a small data set may generate wider 95%CI than a much larger data set, and so a 95%CI may include a particular value, 0 for example, due to the sample being limited in size. However, it is difficult to foresee a larger dataset becoming available while accurate diagnosis of *M. bovis* infection still requires badgers to be killed and subjected to a detailed necropsy.

Mathematical models have a long history of effective use in infectious disease epidemiology. Models such as those presented here are, of course, highly idealized while aiming to describe the key features of an epidemic. Those utilising the results of this and similar modelling studies need to understand the limitations of any model of interest, its structure and the details of the data used to estimate model parameters. In this case the data were observational, despite being collected as baseline data for the experimental study known as the Randomised Badger Culling Trial.

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Appendix. Data used in the analysis of association of bovine TB in cattle herds and badgers.

Triplet	Herd breakdowns detected in 12 months preceding initial proactive cull[1]	Total herds[1] (N)	Badgers culled[2] (N_w)	Infectious badgers culled[3] (I_w)
A	8	71	55	8
B	15	152	238	13
C	8	105	243	4
D	11	97	293	102
E	4	116	602	29
F	4	138	446	13
G	7	245	422	29
H	11	63	161	12
I	15	100	218	82
J	8	114	442	65

[1] Based on the numbers of total herds and TB-affected herds in the 12-month periods preceding the initial proactive badger culls, as published by Donnelly *et al*. (2006) in the form of Supplementary Data based on location data as recorded in the VetNet database. [2] Based on the numbers of badgers culled in initial proactive culls (excluding 19 with incomplete data), as published by Woodroffe *et al*. (2005). [3] Based on the numbers of badgers culled in initial proactive culls found to be *M. bovis* infected, as published by Woodroffe *et al*. (2005).

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