Strathprints Institutional Repository

Johnston, W Thomas and Vial, F. and Gettinby, George and Bourne, F John and Clifton-Hadley, R.S. and Cox, D.R. and Crea, P. and Donnelly, Christl A. and McInerney, J.P. and Mitchell, A.P and Morrison, W.I. and Woodroffe, R. (2011) *Herd-level risk factors of bovine tuberculosis in England and Wales after the 2001 foot-and-mouth disease epidemic.* International Journal of Infectious Diseases, 15 (12). e833–e840.

AUTHOR QUERY FORM

ELSEVIER	**Journal:** IJID **Article Number:** 1332	**Please e-mail or fax your responses and any corrections to:** **E-mail:** corrections.eseo@elsevier.thomsondigital.com **Fax:** +353 6170 9272

Dear Author,

Please check your proof carefully and mark all corrections at the appropriate place in the proof (e.g., by using on-screen annotation in the PDF file) or compile them in a separate list. To ensure fast publication of your paper please return your corrections within 48 hours.

For correction or revision of any artwork, please consult http://www.elsevier.com/artworkinstructions.

Any queries or remarks that have arisen during the processing of your manuscript are listed below and highlighted by flags in the proof. Click on the 'Q' link to go to the location in the proof.

Location in article	**Query / Remark: click on the Q link to go** **Please insert your reply or correction at the corresponding line in the proof**
Q1	Please confirm that given names and surnames have been identified correctly.
Q2	Please check first author name in Ref. [7] for correctness.
Q3	Reference 38. I cannot access the document at the URL provided – has the page moved? (http://randd.defra.gov.uk/Document.aspx?Document=SE3029_4086_FRP.doc?) Also, please provide the 'accessed' date.

Thank you for your assistance.

International Journal of Infectious Diseases xxx (2011) xxx.e1–xxx.8

Contents lists available at SciVerse ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Herd-level risk factors of bovine tuberculosis in England and Wales after the 2001 foot-and-mouth disease epidemic

W.T. Johnston [a,*], F. Vial [a], G. Gettinby [b,c], F.J. Bourne [b], R.S. Clifton-Hadley [d], D.R. Cox [b,e], P. Crea [f], C.A. Donnelly [a,b], J.P. McInerney [b], A.P. Mitchell [d], W.I. Morrison [b,g], R. Woodroffe [b,h]

[a] Department of Infectious Disease Epidemiology, MRC Centre for Outbreak Analysis and Modelling, School of Public Health, Imperial College London, London, UK
[b] Independent Scientific Group for Cattle TB c/o Department for Environment, Food and Rural Affairs, London, UK
[c] Department of Mathematics and Statistics, University of Strathclyde, Glasgow, Scotland, UK
[d] Veterinary Laboratories Agency, New Haw, Addlestone, Surrey, UK
[e] Nuffield College, University of Oxford, Oxford, UK
[f] Animal Health, Worcester, UK
[g] Centre for Tropical Veterinary Medicine, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Roslin, Midlothian, Scotland, UK
[h] Institute of Zoology, Regent's Park, London, UK

ARTICLE INFO

Article history:
Received 13 June 2011
Received in revised form 8 August 2011
Accepted 26 August 2011

Corresponding Editor: William Cameron, Ottawa, Canada

Keywords:
Bovine TB
Mycobacterium bovis
Case–control study
Cattle movement

SUMMARY

Objectives: We present the results of a 2005 case–control study of bovine tuberculosis (bTB) breakdowns in English and Welsh herds. The herd management, farming practices, and environmental factors of 401 matched pairs of case and control herds were investigated to provide a picture of herd-level risk factors in areas of varying bTB incidence.
Methods: A global conditional logistic regression model, with region-specific variants, was used to compare case herds that had experienced a confirmed bTB breakdown to contemporaneous control herds matched on region, herd type, herd size, and parish testing interval.
Results: Contacts with cattle from contiguous herds and sourcing cattle from herds with a recent history of bTB were associated with an increased risk in both the global and regional analyses. Operating a farm over several premises, providing cattle feed inside the housing, and the presence of badgers were also identified as significantly associated with an increased bTB risk.
Conclusions: Steps taken to minimize cattle contacts with neighboring herds and altering trading practices could have the potential to reduce the size of the bTB epidemic. In principle, limiting the interactions between cattle and wildlife may also be useful; however this study did not highlight any specific measures to implement.

1. Introduction

Bovine tuberculosis (bTB) is an infectious bacterial disease of cattle and other mammals (including humans) caused by *Mycobacterium bovis*, and is a significant burden to the cattle industry in Great Britain. Despite the nationwide implementation of a cattle testing and slaughter program in 1950 by the Ministry of Agriculture and Fisheries (now the Department for Environment, Food and Rural Affairs (Defra)), which initially dramatically reduced the incidence of bTB, incidence has increased over the last 25 years, particularly in the wake of the 2001 foot-and-mouth disease (FMD) epidemic. Within Great Britain, the number of infected cattle slaughtered and the financial burden of bTB have been greatest in England and Wales. In England, bTB cost the taxpayer £63m in 2009, excluding research and development, and over 25 000 cattle were slaughtered as a result of routine bTB controls;[1] in Wales, over 11 500 cattle were slaughtered in 2009 and almost £120m has been spent on compensating farmers for bTB-related loss of cattle since 2000.[2]

The role of the Eurasian badger (*Meles meles*) population as a potential reservoir of infection has been established[3,4] and the effectiveness of badger culling in bTB control has been assessed during the Randomised Badger Culling Trial (RBCT) in England[5,6] and during the East Offaly Project[7] and the Four Area Project[8] in the Republic of Ireland. The TB99 case–control study associated with the RBCT[9] and other independent studies in Great Britain,[10–17] the Republic of Ireland,[18–22] mainland Europe,[23] the Americas,[24–27] and Eastern Africa,[28–30] have also highlighted the role of livestock husbandry and management practices in wildlife-to-cattle and cattle-to-cattle transmission of *M. bovis*.

* Corresponding author. Current address: Epidemiology and Genetics Unit, Department of Health Sciences Area 3, Seebohm Rowntree Building, University of York, Heslington, York YO10 5DD, UK.
E-mail address: tom.johnston@egu.york.ac.uk (W.T. Johnston).

1201-9712/$36.00 – see front matter © 2011 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.
doi:10.1016/j.ijid.2011.08.004

Stocking regimes (set-stocking, rotational grazing, or strip grazing), stocking densities, habitat types on the farm, and the intensification of livestock production systems influence the potential of direct and indirect (through feces and urine) exposure of cattle to the wildlife reservoir on pastures.[14,17,23,31–33] The sharing of feeds or water between cattle and wildlife inside cattle housing or on pastures,[26,29] the storing of manure indoors,[15] and the type of housing[9] are also associated with the differential risk of bTB transmission between the reservoir and the cattle populations. The most frequently reported parameters affecting risk of herd-to-herd transmission of bTB relate to herd movements and trading. General trading of cattle,[27,30] or purchase of cattle from markets,[15,29] from herds inside high bTB risk areas[10] or from infected herds,[12,20,23,25] have all been linked to increased risk of bTB outbreaks for the recipient herd.

To identify the herd-level predictors of bTB breakdowns on cattle farms enrolled in the RBCT, a case–control study (known as the TB99 study) was initiated in 1999 in three RBCT regions (known as 'triplets'), with the aim of identifying potential recommendations on farm management and husbandry practices expected to reduce bTB risk in southwest England.[9] The 2001 FMD epidemic interrupted data collection and a second case–control study (known as the CCS2005) was initiated in 2005. In this paper, we report the results of the CCS2005 case–control study, comparing herds in two areas of England and one area in Wales that experienced a confirmed bTB breakdown in 2005/2006 to matched control herds that did not experience a breakdown during the same period. A range of herd management, health, and biosecurity measures were examined in an attempt to provide a post-FMD picture of the herd-level risk factors in areas of medium and high bTB incidence that might be integrated into a package of measures to tackle bTB, contributing to "a balanced programme" as recently announced by the UK Government in its latest public consultation on bTB.[1]

2. Methods

2.1. Study sites and case and control herd selection

Data were collected from regions administered by four Animal Health Divisional Offices (AHDOs) in England and Wales that included areas with a range of bTB incidence: Stafford (including Staffordshire, Cheshire, and Derbyshire), Taunton (including Somerset and part of Dorset), Carmarthen (covering west Wales), and Carlisle (covering Cumbria). We targeted a total of 125 case herds randomly selected from all the bTB breakdowns occurring in each region in 2005/2006, except in Carlisle where all breakdowns were targeted. Monthly target numbers were then set to reflect the typical temporal distribution of breakdowns and to ensure collection of data throughout the year. On a weekly basis, staff from the AHDOs contacted managers of breakdown herds from a list sorted in a random order, proceeding down the list until the allocation for the week had been obtained. The target numbers of case herds included both confirmed breakdowns (i.e., had either a positive culture of *M. bovis* or gross lesions consistent with bTB visible at necropsy in at least one test reactor, or lesions typical of bTB identified at the slaughterhouse and subsequently confirmed by bacteriological culture[34]) and unconfirmed breakdowns (i.e., no cattle reactor with bTB-like lesions or a positive *M. bovis* culture).

Two controls were selected for each case from the same AHDO region and parish testing interval (defined as annual, two-, three- or four-yearly), which is set according to the parish bTB herd breakdown incidence (higher incidence translates to more frequent testing) – 'partially matched controls'. One of the controls was also matched to the case on herd size class, defined as small ($\leq$50 animals), medium (>50 to $\leq$100 animals), large (>100 to $\leq$150 animals), or very large (>150 animals) and herd type, defined as beef, dairy, or other (usually mixed herds) – 'fully matched controls'. Both control herds must have had at least one clear herd bTB test in the 12 months prior to the date of the disclosing test of the case herd; have not been under any bTB-related restrictions over that period and not have been overdue a herd test. Using Defra's Animal Health Information System (VetNet), two lists of potential controls (one for partially matched and one for fully matched) for each week's cases were generated as random selections from all herds fitting the inclusion criteria. Staff from the AHDOs recruited controls in the randomized sequence from these lists until all required controls for that week were obtained. More detailed information on the recruitment of herds is available in the Supplementary Information (Supplementary Information 1).

2.2. Data collection

Data collection was carried out during face-to-face interviews, conducted by staff from the AHDOs between February 2005 and March 2006, with a mean time between herd breakdown and interview of 79 days (range 16–290 days). Data were collected using a questionnaire (see Supplementary Information 2) investigating herd management practices (including numbers of animals of various ages and types, housing, feeds and water sources for cattle), potential contacts with neighboring cattle herds, and observed wildlife activity on the farm.

A map of each farm was generated from Defra's Integrated Administration and Control System (IACS) Rural Payments Agency database; the extent of the land depicted in the maps was verified with the participant during the interview and modified if required. Land cover and soil type data for each farm was determined by linking the maps to the CORINE land cover dataset (http://dataservice.eea.europa.eu/dataservice/metadetails.asp?id=1011). Information on the movement of cattle between farms was extracted from the Cattle Tracing System (CTS) database. The bTB-testing history of case herds, control herds, all the herds that cases and controls reported contacts with, and all of the herds that cases and controls sourced animals from, were determined using the VetNet system.

2.3. Data analysis

A conditional logistic regression analysis of cases and their fully-matched control (matched on AHDO, testing interval, herd type, and herd size), and an unconditional logistic regression analysis using the partially-matched controls (matched only on AHDO and testing interval) were performed. Two sets of analyses for each logistic regression were undertaken using (1) confirmed bTB breakdowns and (2) total breakdowns (both confirmed and unconfirmed) as cases. All analyses were performed using the data pooled across all AHDOs in the first instance, before building region-specific models. The results of the conditional regression analyses based on confirmed bTB outbreaks are presented in the main text. The results of all other analyses, which were broadly consistent with those presented below, are included in the Supplementary Information (Supplementary Information 1).

Construction of the conditional logistic regression models (Proc Logistic, The SAS System) was undertaken using a forward stepwise approach. All non-categorical variables were log-transformed before inclusion in these analyses. Initial screening of the variables was based on the ratio between the log odds ratio for each variable in a univariable model and its standard error. Variables with ratios greater than 1.28 (equivalent to a *Z*-test with $p = 0.2$) were considered for the first round of model construction. Before model construction began, continuous variables were eliminated if more than 25% of the observations had missing data.

Table 1
Attributes of cases and their fully-matched controls as identified from the questionnaire. Data from confirmed bTB breakdowns for 2005/2006 are presented for all four AHDOs

	Carlisle		Carmarthen		Stafford		Taunton	
Confirmed breakdowns								
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
n	7	7	61	61	90	90	60	60
Herd type: number of herds in each category (% of total number of herds)								
Beef	5 (71%)	3 (43%)	19 (31%)	15 (25%)	25 (28%)	28 (31%)	25 (42%)	21 (35%)
Dairy	1 (14%)	1 (14%)	40 (66%)	38 (62%)	59 (66%)	55 (61%)	30 (50%)	27 (45%)
Other	1 (14%)	3 (43%)	2 (3%)	8 (13%)	6 (7%)	7 (8%)	5 (8%)	12 (20%)
Herd size:								
Mean	298.00	194.14	196.90	182.61	214.56	197.43	245.28	240.88
SE	145.44	62.96	21.70	17.29	18.04	18.28	23.68	25.91
Parish testing interval: number of herds in each category (% of total number of herds)								
Annual	5 (71%)	5 (71%)	58 (95%)	58 (95%)	68 (76%)	68 (76%)	39 (65%)	39 (65%)
Not annual	2 (29%)	2 (29%)	3 (5%)	3 (5%)	22 (24%)	22 (24%)	21 (35%)	21 (35%)

bTB, bovine tuberculosis; AHDO, Animal Health Divisional Office; SE, standard error of the mean.

Categorical variables were eliminated if there were few (less than five) observations in one or more of the categories and meaningful aggregations of categories could not be created. Correlations between variables were identified and only those variables under consideration with the strongest effects (as estimated in the screening logistic regression models) were retained. For construction of the regression model, the variable with a significant parameter estimate ($p < 0.05$) that minimized the ratio of the model deviance to the number of observations was added to the model, the remaining candidate variables were screened against this new model and another variable added. Variables were added until no further variables were significant in the constructed model. Using this preliminary model, all of the variables in the dataset were re-screened and a second round of model construction undertaken using any identified variables. When this second round was complete, all two-way interactions between the variables included in the final model were tested for significance, one at a time.

3. Results

3.1. Cases and controls

The target numbers of 125 cases and two controls per case were attained in the Carmarthen, Stafford, and Taunton offices, and 27 cases with matched controls were obtained from the Carlisle office (Supplementary Information 1, Table S2). Overall, 56% of the cases were confirmed breakdowns and data collected from the questionnaire broadly agreed with the herd size and herd type matching based on VetNet data (Table 1).

3.2. Conditional logistic regression – pooled analysis of confirmed bTB breakdowns across the four AHDOs

A total of 218 confirmed case–control pairs were available for analysis (Table 1). The final conditional logistic regression model retained 13 variables (Table 2).

3.2.1. Environmental factors

Case herds were less likely than control herds to have deep clay soil (odds ratio (OR) 0.21, 95% confidence interval (CI) 0.07–0.62) or seasonally wet soil on the farm (OR 0.49, 95% CI 0.26–0.91), but were more likely to report the finding of dead badgers on the farm (OR 3.10, 95% CI 1.40–6.84).

3.2.2. Farming practices

Case herds were less likely than control herds to keep different types of cattle (i.e., replacement heifers, cows) together in groups (OR 0.32, 95% CI 0.16–0.62) and not provide housing for cattle at grazing (OR 0.36, 95% CI 0.14–0.95). Case herds were operated over more premises ($OR_{doubling\ No.\ premises}$ 2.41, 95% CI 1.46–4.01) and added fewer calves to the herd in a typical year ($OR_{doubling\ No.\ calves}$ 0.85, 95% CI 0.76–0.96) than control herds. Providing feed outside of the housing had a protective effect (OR 0.41, 95% CI 0.22–0.76), while providing feed inside the housing (OR 4.89, 95% CI 1.19–20.12) increased the risk of a confirmed bTB breakdown.

Table 2
Factors identified in the conditional logistic regression of the probability of a herd experiencing a confirmed bTB breakdown in 2005/2006 using the data pooled from all four AHDOs. Odds ratios for covariates correspond to a doubling in the value of the variable, and for proportions to an additional 10% of the value of the variable

Factor	OR	95% CI
Any deep clay soil on the farm	0.21	0.07–0.62
Keeping different types of cattle together in groups	0.32	0.16–0.62
Providing no housing at grazing (type 4)	0.36	0.14–0.95
Providing feed outside of the housing	0.41	0.22–0.76
Having seasonally wet soils on the farm	0.49	0.26–0.91
Number of calves added to the herd in a typical year	0.85	0.76–0.96
Proportion of cattle sourced from herds in four-yearly testing parishes	0.93	0.86–0.99
Number of confirmed breakdowns experienced by contacted herds in previous 24 months	2.00	1.54–2.62
Number of premises over which the farm is operated	2.41	1.46–4.01
Sourcing any cattle from a herd that had a breakdown in the previous 2 years	1.90	1.00–3.62
Any direct contacts with cattle from contiguous farms	2.24	1.24–4.05
Finding dead badgers on farm	3.10	1.40–6.84
Providing feed inside the housing	4.89	1.19–20.12

bTB, bovine tuberculosis; AHDO, Animal Health Divisional Office; OR, odds ratio; CI, confidence interval.

Please cite this article in press as: Johnston WT, et al. Herd-level risk factors of bovine tuberculosis in England and Wales after the 2001 foot-and-mouth disease epidemic. Int J Infect Dis (2011), doi:10.1016/j.ijid.2011.08.004

3.2.3. Contact and trading

Case herds were less likely to source cattle from herds in four-yearly tested parishes ($OR_{per\ additional\ 10\%\ of\ sourced\ cattle}$ 0.93, 95% CI 0.86–0.99), but more likely to source cattle from a herd that had experienced a breakdown in the previous 2 years (OR 1.90, 95% CI 1.00–3.62) than control herds. Conversely, case herds had more direct contacts with cattle from contiguous herds (OR 2.24, 95% CI 1.24–4.05) and had more confirmed breakdowns in the previous 2 years among the herds they reported having had contact with ($OR_{doubling\ No.\ breakdowns}$ 2.00, 95% CI 1.54–2.62).

3.3. Conditional logistic regression – region-specific analyses of confirmed bTB breakdowns for the three main AHDOs

Too few breakdowns were recorded inside the Carlisle AHDO (Table 1) to support meaningful region-based analysis and those

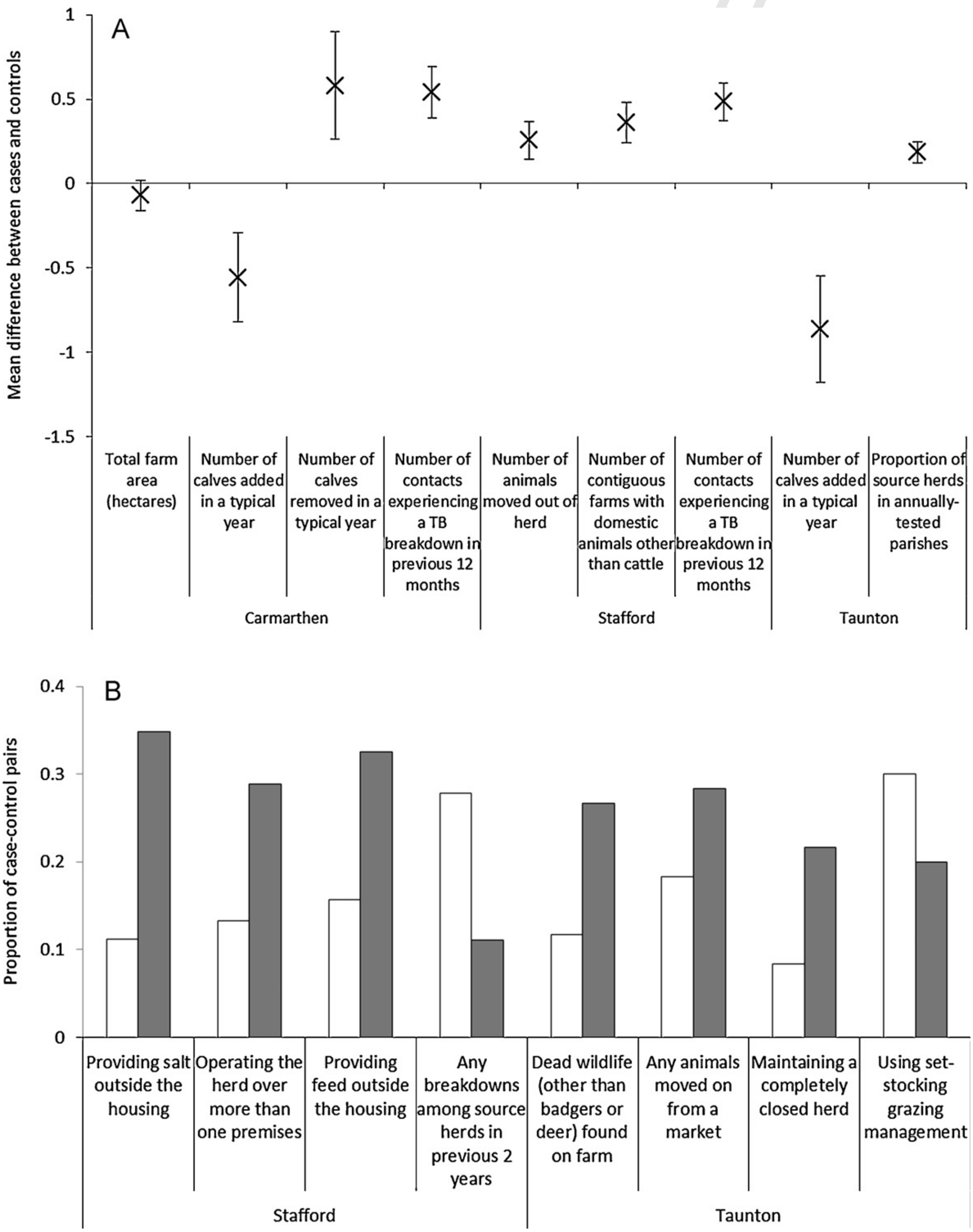

Figure 1. Description of the variables included in the final conditional logistic regression models of confirmed case–control pairs: (A) mean difference (± standard error) between case and control pairs for non-categorical variables and (B) for categorical variables, the proportions of pairs where only the case (open bars) or control (solid bars) was positive for the factor; the proportions of pairs where the exposure of the case and control was the same are not shown. There were no categorical variables included in the final Carmarthen model.

Table 3
Factors identified in the conditional logistic regression of the probability of a herd experiencing a confirmed bTB breakdown in 2005/2006 analyzing the data for the three main AHDOs separately. Odds ratios for covariates correspond to a doubling in the value of the variable, and for proportions to an additional 10% of the value of the variable

Factor	OR	95% CI
Carmarthen		
Number of hectares of farm land on all premises	0.24	0.07–0.84
Number of calves added to the herd in a typical year	0.46	0.28–0.78
Number of calves typically taken from the herd in a year	1.78	1.18–2.68
Number of confirmed breakdowns experienced by contacted herds in the previous 24 months	2.76	1.48–5.16
Stafford		
Providing salt outside the housing	0.08	0.02–0.30
Providing feed outside the housing	0.24	0.08–0.72
Number of animals moved out of the herd per year	1.80	1.10–2.94
Number of contiguous farms with domestic stock other than cattle	1.88	1.10–3.20
Number of breakdowns experienced by contacted herds in the previous 24 months	2.13	1.20–3.78
Operating the farm over more than one premises	7.53	1.87–30.25
Sourcing any cattle from a herd that had a breakdown in the previous 2 years	8.48	2.23–32.20
Taunton		
Dead 'other' wildlife found on the farm	0.09	0.02–0.51
Moving any animals into the herd from a market	0.18	0.03–0.91
Maintaining a completely closed herd	0.18	0.04–0.77
Number of calves added to the herd in a typical year	0.64	0.48–0.87
Proportion of source herds in an annually tested parish	1.41	1.11–1.81
Using set-stocking grazing management	4.78	1.32–17.32

bTB, bovine tuberculosis; AHDO, Animal Health Divisional Office; OR, odds ratio; CI, confidence interval.

herds were only included in the pooled analysis. The final conditional logistic regression models based on confirmed breakdowns from the Carmarthen, Stafford, and Taunton AHDOs included four, seven, and six variables, respectively (Table 3 and Figure 1).

3.3.1. Environmental factors

The environmental factors explored by the questionnaire seemed to be poor indicators of the risk of a confirmed bTB breakdown at the region-level, with the exception of the Taunton AHDO where dead 'other' wildlife on farms had a reduced risk of a confirmed bTB breakdown (OR 0.09, 95% CI 0.02–0.51).

3.3.2. Farming practices

Most of the farming practices identified as having an impact on a herd's risk of a confirmed bTB breakdown in the regional analyses are in accordance with the results from the pooled conditional logistic regression. For example, operating a farm over several premises resulted in an increased risk of a bTB breakdown in the Stafford AHDO (OR 7.53, 95% CI 1.87–30.25), while case herds added fewer calves to the herd in a typical year than control herds in both the Carmarthen ($OR_{\text{doubling No. calves}}$ 0.46, 95% CI 0.28–0.78) and Taunton ($OR_{\text{doubling No. calves}}$ 0.64, 95% CI 0.48–0.87) AHDOs. Similarly, providing feed outside of the housing was associated with a decreased risk (OR 0.24, 95% CI 0.08–0.72). The region-based analyses also highlight the localized impact of other farming practices. Case herds tended to be associated with smaller land areas in the Carmarthen AHDO ($OR_{\text{doubling No. hectares}}$ 0.24, 95% CI 0.07–0.84) and with a set-stocking grazing regime in the Taunton AHDO (OR 4.78, 95% CI 1.32–17.32), while providing salt outside the housing offered some protection against bTB in the Stafford AHDO (OR 0.08, 95% CI 0.02–0.30). Case herds tended to have more calves taken from the herd in a typical year ($OR_{\text{doubling No. calves}}$ 1.78, 95% CI 1.18–2.68) than control herds in the Carmarthen AHDO.

3.3.3. Contact and trading

In accordance with the results from the pooled conditional logistic regression, there were more breakdowns in the previous 2 years among herds reported as contacts of case herds in both the Carmarthen ($OR_{\text{doubling No. confirmed breakdowns}}$ 2.76, 95% CI 1.48–5.16) and Stafford AHDOs ($OR_{\text{doubling No. total breakdowns}}$ 2.13, 95% CI 1.20–3.78). Similarly, case herds in the Stafford AHDO were more likely to source cattle from a herd that had experienced a breakdown in the previous 2 years (OR 8.48, 95% CI 2.23–32.20) than control herds. Common to all three region-specific models (Table 3) was an increased risk of a confirmed bTB breakdown associated with either contacting (i.e., over shared boundaries or mixing of cattle) or trading with a herd with a recent history of bTB or at higher risk (annually tested herds). More specific to the Taunton AHDO, maintaining a completely closed herd (OR 0.18, 95% CI 0.04–0.77) and moving animals into the herd from a market (OR 0.18, 95% CI 0.03–0.91) were both associated with a decreased risk of a confirmed bTB breakdown, whereas sourcing cattle from herds in annual-tested parishes increased the risk of a breakdown ($OR_{\text{per additional 10\% of source herds}}$ 1.41, 95% CI 1.11–1.81).

4. Discussion

The net reproduction number (R_e) for bTB among cattle herds in Great Britain under the current test and remove control scheme has been estimated to be 1.1,[35] suggesting that relatively modest improvements either in diagnostic testing (test performance or frequency) or in reducing the transmission to cattle could be sufficient to bring the bTB epidemic under control. While other studies have investigated risk factors of bTB herd breakdowns post-FMD,[10,15] they have mainly focused on the bTB risk associated with UK herds that had been restocked after the FMD epidemic[10] or compared the bTB risk of herds that had been restocked with herds that remained continuously stocked throughout the 2001 FMD epidemic.[15] Our study is the first case–control study post-FMD to explicitly investigate the contribution of farming practices, herd management and husbandry, trading, and wildlife activity to the herd-level bTB risk in the wider population of cattle herds across a range of bTB risk areas.

The principal finding of this study indicates that there is an increased localized risk of a breakdown related to the occurrence of breakdowns among neighboring and/or contacted herds and possibly a shared external exposure (i.e., wildlife). This study also provides some evidence that the provision of close-quarters opportunities and further evidence that the sourcing of animals from high-risk herds and/or areas, increases the risk of experiencing a breakdown. Many risk factors tended to vary between regions, a pattern probably indicative of the complexity of the bTB problem and the possible need for disease control recommendations to reflect localized risk. These findings are discussed more extensively below.

Please cite this article in press as: Johnston WT, et al. Herd-level risk factors of bovine tuberculosis in England and Wales after the 2001 foot-and-mouth disease epidemic. Int J Infect Dis (2011), doi:10.1016/j.ijid.2011.08.004

It should be noted at this point that causal interpretations of the factors identified in this type of analysis must be treated with caution as a result of potential biases, unobserved confounders, and correlations between the large numbers of explanatory variables investigated in this study. In addition, spurious associations cannot be ruled out due to the large number of factors assessed. There was a lack of independence between some factors that we have attempted to address by identifying correlations and retaining only those factors with the strongest associations with the risk of being a case herd. This, alongside our approach to model construction that assessed the impact on the parameter estimates and standard errors of factors already in the model as further factors were added, might be expected to yield regression models with mostly independent effects. General conclusions may be drawn, as those factors ultimately included in the regression models will be representative of a group of related factors.

Evidence of a localized risk of bTB was found in the pooled model where new confirmed bTB breakdowns were associated with breakdowns among contiguous herds and/or contacts with cattle from contiguous herds. This risk associated with contacted herds may be a reflection of a common local exposure to infected cattle or an external source of infection such as a wildlife reservoir. Environmental factors may also play a role here. Increasing the number of farm premises, a risk factor identified in a case–control study of English herds before FMD,[9] and the resulting fragmentation of the herd across many land parcels, increases the number of contiguous herds. Wildlife may be involved as the source of the infection for the group of contiguous herds, since the number of dead badgers on a farm was associated with a higher risk of a confirmed bTB breakdown. Soil types, identified as significant environmental variables, may influence the behavior or abundance of wildlife: seasonally wet or deep clay soils may be less favorable to badgers.[36] Likewise, the presence of other wildlife on the farm (as identified in the Taunton model) may deter badgers from entering the premises. To counter these effects, a large farm area was found to be protective in the Carmarthen AHDO, possibly indicating a greater ability for isolating the cattle herd from contacts with neighboring herds by concentrating grazing areas in the centre of the farm. However, no data on this type of land use were available to test this hypothesis.

A number of factors were identified that may be indicative of opportunities for close-quarters contacts either between cattle or between cattle and badgers; these factors appear to be correlated with the risk of a bTB breakdown. For example, providing feeding inside the housing may promote closer associations by bringing cattle and/or badgers together, whereas not providing housing for cattle at grazing, possibly encouraging fewer close contacts, was associated with a lower risk. Cattle in housing tend to be in closer proximity than when at pasture, potentially providing a greater opportunity for cattle-to-cattle bTB transmission and for interactions with wildlife visiting the buildings. A counter point to this, and a demonstration of the potential regional variation, is that set-stocking grazing, where grazing herds have constant access to all the pasture, was found to increase the risk of a confirmed bTB breakdown in the Taunton AHDO. Such practice may promote dispersal among cattle[33] and interactions between badgers and cattle at pastures.[31]

Sourcing of cattle from herds with a recent history of bTB was associated with an increased risk of a confirmed bTB breakdown, whereas sourcing more cattle from herds in four-yearly tested parishes (low bTB risk areas) was associated with a lower risk of a breakdown in the pooled conditional logistic regression. Similarly, contacts with or sourcing cattle from herds that may be infected with *M. bovis* was recognized as the only consistent risk factor across the three AHDOs modeled individually. Concurring with these results, Gilbert and colleagues[11] found that the most important predictor of future bTB occurrence was the proportion of animals moved into the area from infected areas; whereas Carrique-Mas et al.[10] found that trading with 'highly tested' herds (equivalent to annually-tested herds or herds undergoing repeated contiguous herds tests) or herds with a history of bTB, increased the risk of a breakdown for UK herds restocked after the 2001 FMD epidemic. Trading is clearly identified as a risk-prone activity in terms of bTB. As a result of the limitations of the current bTB testing regime, undisclosed infection may remain in a source herd with a recent history of bTB even after the lifting of trading restrictions.[34] It is therefore not surprising to find that completely closed herds, as observed in the Taunton AHDO, are at significantly lower risk of a confirmed bTB breakdown.[9,11,13,16]

The simple beef/dairy/other herd type classification used in the study may not have fully accounted for variation between herd types. For example, keeping different types of cattle together and retaining calves inside the herd were both found to reduce the risk of a confirmed bTB breakdown in both the pooled and region-specific models. Both of these practices are most commonly associated with beef herds (calves are more likely to be removed from dairy herds) and possibly reflect differences in bTB risk between dairy and non-dairy herds[15,20,37] rather than differences in bTB risk linked to farming practices. In future, closer matching of herd types may be advisable.

As one of the consequences of a bTB breakdown is the imposition of movement restrictions, this can make interpretation of effects of the movement of animals on the risk of a bTB breakdown difficult when case herds have a recent history of a breakdown. For example, the number of movements out of the herd was generally correlated with the number of movements into the herd, a recognized risk factor,[9,11,13,16] but the number of outward movements was more strongly associated with bTB confirmed breakdowns. This association may be a consequence of the bTB history of the case herds: while control herds were required to have been free of bTB-related movement restrictions in the previous year, case herds could have been subjected to such restrictions and may have had excess stock on the farm that were subsequently moved out in the period between breakdowns. When the case–control pairs where the case had been under bTB-related movement restrictions for at least part of the 12 months before the breakdown considered in this study were excluded (19% of all pairs), the movement of animals out of the herd failed to enter the regression models. Likewise, movement of any animals to or from a market, which were all associated with a lower risk of bTB in the Taunton models, were not included in models excluding case–control pairs where the case had been under restriction in the previous 12 months. Thus care should be taken when setting inclusion criteria and developing measures of the numbers of cattle movements.

In conclusion, it was evident from the case–control data that coming into contact with herds with a history of bTB (either through local contacts or as sources of bought-in cattle) increased the risk of a bTB breakdown. Steps taken to limit these contacts by minimizing opportunities for contacts with neighboring herds and by altering trading patterns would have the potential to reduce the size of the bTB epidemic. Based on our findings, we would recommend that information such as bTB history of the individual source herd, as well as the area in which the source herd is located, should be considered as part of standard trading practice. In principle, limiting the interactions between cattle and wildlife may be useful given the observed increased localized risk; however this study did not highlight any specific measures to implement. The ideal means to assess the effectiveness of control measures would be some sort of prospective trial of specific measures or a package of measures. However, the required scale of this type of trial (numbers of farms and time of observation), coupled with the wide range of potential measures, makes meaningful experimental studies difficult and expensive to implement. This leaves observational studies as the more practical alternative.[38] The current study utilized a broad-brush approach; a wide ranging questionnaire with relatively simple questions designed to identify trends in the data, but which has already proved useful in predicting the occurrence of 'prolonged' (>240 days)[39] and 'recurrent'[40] bTB breakdowns. Building on the results reported here, a better targeted approach, i.e., more detailed questioning on a smaller range of potentially region-specific topics, may provide more specific guidance for farmers.

Acknowledgements

The authors would like to thank all of the staff in the Animal Health Divisional Offices and the consultancy firm ADAS for collecting the data, the team members at the Veterinary Laboratories Agency for constructing the database, entering and quality-checking the data, and providing GIS support, and the Environmental Research Group Oxford for assistance in GIS data processing. We are also very grateful to all the farmers who gave of their time to participate in this study. Thanks also to Dr Martine Wahl (the study auditor) and Dr Simon Rolfe (Welsh Assembly Government) for numerous suggestions and constructive criticisms throughout the design and implementation of this study. Finally, thanks to Mr Stephen Coleman (Defra) whose efforts were instrumental to the completion of this project. This project was funded by Defra and the Welsh Assembly Government.

Conflict of interest: FJB, DRC, CAD, GG, JPM, WIM and RW were formerly members of the Independent Scientific Group on Cattle TB (ISG) for which they received fees for time spent on ISG work and reimbursement of expenses from Defra. WTJ was formerly employed as a research assistant working with the ISG at Imperial College London. FV was employed as a research assistant working with CAD at Imperial College London. RSC-H, PC and APM are employed by the Animal Health Veterinary Laboratories Agency, an executive agency of the UK Government. Ethical approval was not required.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2011.08.004.

References

1. Defra. Bovine Tuberculosis: The Government's approach to tackling the disease and consultation on a badger control policy. London, UK: Department for Environment, Food and Rural Affairs; 2010.
2. Welsh Assembly Government. Bovine TB eradication programme: consultation on badger control in the intensive action area. London, UK: Department for Environment, Food and Rural Affairs; 2010.
3. Krebs JR, Anderson R, Clutton-Brock T, Morrison I, Young D. Bovine tuberculosis in cattle and badgers. London, UK: Ministry of Agriculture, Fisheries and Food; 1997.
4. Woodroffe R, Donnelly CA, Johnston WT, Bourne FJ, Cheeseman CL, Clifton-Hadley RS, et al. Spatial association of *Mycobacterium bovis* infection in cattle and badgers *Meles meles*. *J Appl Ecol* 2005;**42**:852–62.
5. Donnelly CA, Woodroffe R, Cox DR, Bourne FJ, Cheeseman CL, Clifton-Hadley RS, et al. Positive and negative effects of widespread badger culling on tuberculosis in cattle. *Nature* 2006;**439**:843–6.
6. Jenkins HE, Woodroffe R, Donnelly CA. The duration of the effects of repeated widespread badger culling on cattle tuberculosis following the cessation of culling. *PLoS One* 2010;**5**:e9090.
7. Máirtín DÓ, Williams DH, Dolan L, Eves JA, Collins JD. The influence of selected herd factors and a badger-intervention tuberculosis-control programme on the risk of a herd-level trade restriction to a bovine population in Ireland. *Prev Vet Med* 1998;**35**:79–90.
8. Griffin JM, Williams DH, Kelly GE, Clegg TA, O'Boyle I, Collins JD, et al. The impact of badger removal on the control of tuberculosis in cattle herds in Ireland. *Prev Vet Med* 2005;**67**:237–66.
9. Johnston WT, Gettinby G, Cox DR, Donnelly CA, Bourne J, Clifton-Hadley R, et al. Herd-level risk factors associated with tuberculosis breakdowns among cattle herds in England before the 2001 foot-and-mouth disease epidemic. *Biol Lett* 2005;**1**:53–6.
10. Carrique-Mas JJ, Medley GF, Green LE. Risks for bovine tuberculosis in British cattle farms restocked after the foot and mouth disease epidemic of 2001. *Prev Vet Med* 2008;**84**:85–93.
11. Gilbert M, Mitchell A, Bourn D, Mawdsley J, Clifton-Hadley R, Wint W. Cattle movements and bovine tuberculosis in Great Britain. *Nature* 2005;**435**:491–6.
12. Gopal R, Goodchild A, Hewinson G, de la Rua Domenech R, Clifton-Hadley R. Introduction of bovine tuberculosis to north-east England by bought-in cattle. *Vet Rec* 2006;**159**:265–71.
13. Green LE, Cornell SJ. Investigations of cattle herd breakdowns with bovine tuberculosis in four counties of England and Wales using VETNET data. *Prev Vet Med* 2005;**70**:293–311.
14. Mathews F, Lovett L, Rushton S, Macdonald DW. Bovine tuberculosis in cattle: reduced risk on wildlife-friendly farms. *Biol Lett* 2006;**2**:271–4.
15. Ramírez-Villaescusa AM, Medley GF, Mason S, Green LE. Risk factors for herd breakdown with bovine tuberculosis in 148 cattle herds in the south west of England. *Prev Vet Med* 2010;**95**:224–30.
16. Reilly LA, Courtenay O. Husbandry practices, badger sett density and habitat composition as risk factors for transient and persistent bovine tuberculosis on UK cattle farms. *Prev Vet Med* 2007;**80**:129–42.
17. White PC, Benhin JK. Factors influencing the incidence and scale of bovine tuberculosis in cattle in southwest England. *Prev Vet Med* 2004;**63**:1–7.
18. Griffin JM, Hahesy T, Lynch K, Salman MD, McCarthy J, Hurley T. The association of cattle husbandry practices, environmental factors and farmer characteristics with the occurence of chronic bovine tuberculosis in dairy herds in the Republic of Ireland. *Prev Vet Med* 1993;**17**:145–60.
19. Griffin JM, Martin SW, Thorburn MA, Eves JA, Hammond RF. A case–control study on the association of selected risk factors with the occurrence of bovine tuberculosis in the Republic of Ireland. *Prev Vet Med* 1996;**27**:217–29.
20. Olea-Popelka FJ, Costello E, White P, McGrath G, Collins JD, O'Keeffe J, et al. Risk factors for disclosure of additional tuberculous cattle in attested-clear herds that had one animal with a confirmed lesion of tuberculosis at slaughter during 2003 in Ireland. *Prev Vet Med* 2008;**85**:81–91.
21. Wolfe DM, Berke O, Kelton DF, White PW, More SJ, O'Keeffe J, Martin SW. From explanation to prediction: a model for recurrent bovine tuberculosis in Irish cattle herds. *Prev Vet Med* 2010;**94**:170–7.
22. Wolfe DM, Berke O, More SJ, Kelton DF, White PW, O'Keeffe JJ, et al. The risk of a positive test for bovine tuberculosis in cattle purchased from herds with and without a recent history of bovine tuberculosis in Ireland. *Prev Vet Med* 2009;**92**:99–105.
23. Humblet MF, Gilbert M, Govaerts M, Fauville-Dufaux M, Walravens K, Saegerman C. New assessment of bovine tuberculosis risk factors in Belgium based on nationwide molecular epidemiology. *J Clin Microbiol* 2010;**48**:2802–8.
24. Kaneene JB, Bruning-Fann CS, Granger LM, Miller R, Porter-Spalding BA. Environmental and farm management factors associated with tuberculosis on cattle farms in northeastern Michigan. *J Am Vet Med Assoc* 2002;**221**:837–42.
25. Munroe FA, Dohoo IR, McNab WB, Spangler L. Risk factors for the between-herd spread of Mycobacterium bovis in Canadian cattle and cervids between 1985 and 1994. *Prev Vet Med* 1999;**41**:119–33.
26. Palmer MV, Waters WR, Whipple DL. Investigation of the transmission of *Mycobacterium bovis* from deer to cattle through indirect contact. *Am J Vet Res* 2004;**65**:1483–9.
27. Proano-Perez F, Benitez-Ortiz W, Celi-Erazo M, Ron-Garrido L, Benitez-Capistros R, Portaels F, et al. Comparative intradermal tuberculin test in dairy cattle in the north of Ecuador and risk factors associated with bovine tuberculosis. *Am J Trop Med Hyg* 2009;**81**:1103–9.
28. Cleaveland S, Shaw DJ, Mfinanga SG, Shirima G, Kazwala RR, Eblate E, et al. *Mycobacterium bovis* in rural Tanzania: risk factors for infection in human and cattle populations. *Tuberculosis* 2007;**87**:30–43.
29. Oloya J, Muma JB, Opuda-Asibo J, Djønne B, Kazwala R, Skjerve E. Risk factors for herd-level bovine-tuberculosis seropositivity in transhumant cattle in Uganda. *Prev Vet Med* 2007;**80**:318–29.
30. Tschopp R, Schelling E, Hattendorf J, Aseffa A, Zinsstag J. Risk factors of bovine tuberculosis in cattle in rural livestock production systems of Ethiopia. *Prev Vet Med* 2009;**89**:205–11.
31. Benham PF, Broom DM. Interactions between cattle and badgers at pasture with reference to bovine tuberculosis transmission. *Br Vet J* 1989;**145**:226–41.
32. Phillips CJ, Foster CR, Morris PA, Teverson R. The transmission of *Mycobacterium bovis* infection to cattle. *Res Vet Sci* 2003;**74**:1–15.
33. Ward AI, Tolhurst BA, Delahay RJ. Farm husbandry and the risks of disease transmission between wild and domestic mammals: a brief review focusing on bovine tuberculosis in badgers and cattle. *Anim Sci* 2006;**82**:767–73.
34. de la Rua-Domenech R, Goodchild AT, Vordermeier HM, Hewinson RG, Christiansen KH, Clifton-Hadley RS. Ante mortem diagnosis of tuberculosis in cattle: A review of the tuberculin tests, gamma-interferon assay and other ancillary diagnostic techniques. *Res Vet Sci* 2006;**81**:190–210.
35. Cox DR, Donnelly CA, Bourne FJ, Gettinby G, McInerney JP, Morrison WI, et al. Simple model for tuberculosis in cattle and badgers. *Proc Natl Acad Sci U S A* 2005;**102**:17588–93.
36. Neal E, Cheeseman C. Badgers. London, UK: Poyser; 1996.
37. Porphyre T, Stevenson MA, McKenzie J. Risk factors for bovine tuberculosis in New Zealand cattle farms and their relationship with possum control strategies. *Prev Vet Med* 2008;**86**:93–106.

38. Central Science Laboratory. An investigation of potential badger/cattle interactions including the extent of badger visitations to farm buildings and food stores, and how cattle husbandry methods may limit these. London, UK: Department for Environment, Food and Rural Affairs; 2006. Available at: http://www.defra.gov.uk/science/project_data/DocumentLibrary/SE3029/SE3029_4086_FRP.doc (accessed).
39. Karolemeas K, Mckinley TJ, Clifton-Hadley RS, Goodchild AV, Mitchell A, Johnston WT, et al. Predicting prolonged bovine tuberculosis breakdowns in Great Britain as an aid to control. *Prev Vet Med* 2010;**97**:183–90.
40. Karolemeas K, Mckinley TJ, Clifton-Hadley RS, Goodchild AV, Mitchell A, Johnston WT, et al. Recurrence of bovine tuberculosis breakdowns in Great Britain: risk factors and prediction. *Prev Vet Med* 2011;**102**:22–9.

Please cite this article in press as: Johnston WT, et al. Herd-level risk factors of bovine tuberculosis in England and Wales after the 2001 foot-and-mouth disease epidemic. Int J Infect Dis (2011), doi:10.1016/j.ijid.2011.08.004