Predicting prolonged bovine tuberculosis breakdowns in Great Britain as an aid to control


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ABSTRACT

Bovine tuberculosis (bTB) is an important notifiable disease in cattle in Great Britain (GB), and is subject to statutory control measures. Despite this, disease incidence has increased since the mid-1980s, and around 30% of herd breakdowns continue for more than 240 days. This is twice the shortest possible time for confirmed breakdowns to test clear from infection (≈120 days), and four times the shortest possible time for unconfirmed breakdowns (≈60 days). These “prolonged” breakdowns consume substantial resources and may act as an ongoing source of infection. It is not clear why some breakdowns become prolonged.

Existing detailed case–control data have been re-analysed to determine risk factors for breakdowns lasting longer than 240 days, the strongest of which was the confirmation status of the breakdown: OR 12.6 (95%CI: 6.7–25.4). A further model restricted to data available early on in a breakdown for all breakdowns nationally, can predict 82–84% of prolonged breakdowns with a positive predictive value of 44–49% when validated using existing national datasets over a 4-year period. Identification of prolonged breakdowns at an earlier stage could help to target bTB controls in GB.

1. Introduction

Bovine tuberculosis (bTB) is a notifiable infectious disease of cattle, caused by the bacterium Mycobacterium bovis. European Union (EU) legislation stipulates that governments of member states are obliged to develop an eradication policy for the disease (EU Council Directive 77/391/EEC, 1977). The economic impact of these measures can be substantial; in Great Britain (GB), bTB expenditure cost the GB economy approximately £108 million in 2008–2009 (Defra, 2009). Despite these strategies, the annual number of new confirmed herd breakdowns has increased by an average of 18% since the mid-1980s (Defra, 2005) and the disease has been described as GB’s “biggest endemic animal health issue” (Bovine TB Advisory Group, 2009). New control strategies are urgently required.

Current bTB controls in GB are based on a surveillance programme. This consists of a “test-and-slaughter” policy, where cattle are tested for bTB infection using a single intradermal comparative cervical tuberculin (SICCT) skin test (Monaghan et al., 1994; Defra, 2008b) and routine slaughterhouse surveillance of cattle carcasses for visible M. bovis lesions. Herds are SICCT tested at intervals of 1, 2, 3 or 4 years, depending on the local incidence of infection (Defra, 2008c). Where an animal tests positive to the SICCT test (“reactor”) or visible lesions of bTB yielding M. bovis on culture are identified in an animal in the course of meat inspection after commercial slaughter (“slaughterhouse...
case”), the herd is classified as having a “breakdown”. In addition, if an “inconclusive” reactor (incomplete response to the SICCT test) tests inconclusive again at its first retest, a breakdown will be triggered. Following post-mortem and microbiological examination of slaughtered animals, the breakdown is classified as “confirmed” where there is evidence of visible lesions or culture of M. bovis in at least one of the slaughtered reactors. By definition, bTB breakdowns initiated by slaughterhouse cases are always “confirmed” (as they do not trigger a breakdown unless M. bovis is isolated from the suspect bTB lesions).

Breakdown herds are subjected to a series of measures to control the spread of infection, including the slaughter of reactors and the imposition of movement restrictions, where non-reactor animals may only be moved off the farm to slaughter or to approved isolation units under special licence. Cattle can also be moved into the herd during the breakdown, but again, only under special licence. Herds suffering a confirmed breakdown must undergo two whole-herd SICCT tests (short-interval tests conducted at minimum intervals of 60 days) with negative results before movement restrictions are lifted. Herds with unconfirmed breakdowns only require one of these tests with negative results.

Although the shortest period that herds will remain restricted is that spanning two short-interval tests (≈120 days) where breakdowns are confirmed and one short-interval test (≈60 days) where unconfirmed, around 30% of all new breakdowns per year (2003–2006) take ≥240 days to resolve and have movement restrictions lifted (Figure S1, supplementary material). Herds that fail to clear infection through SICCT testing alone can be prescribed additional control measures (e.g. gamma interferon testing) although for chronic confirmed breakdowns in endemic areas, this is not conducted until the later stages of a breakdown. Prolonged breakdowns consume substantial financial and logistical resources compared to shorter breakdowns, with a considerable cost to Defra in terms of repeated testing and compensation (paid to the farmer for slaughtered animals). In addition, movement restrictions can be extremely disruptive to normal farming practices; for example, optimal stocking densities may not be achieved and restrictions can prevent both national and international trade (EU Council Directive 64/432/EEC, 1964), with animal movement being permitted only under special licence or if destined for slaughter. This can have a substantial financial impact on farmers, despite compensation, although it has been shown that there is a lot of variability in this effect between farms (Bennett and Cooke, 2006).

The factors associated with prolonged bTB breakdowns are not clearly understood. Various studies have attempted to identify risk factors for bTB breakdowns, but did not consider the breakdown duration (Green and Cornell, 2005; Johnston et al., 2005; Carrique-Mas et al., 2008). One exception was a study conducted in 2007 which compared risk factors for transient (≤6 months) breakdowns with those for persistent (>6 months) breakdowns, relative to control herds that had tested clear of bTB (Reilly and Courtenay, 2007) within bTB endemic areas in the UK. In addition, an older case–control study conducted in Ireland (Griffin et al., 1993) examined risk factors for herds with “chronic” breakdowns (>12 months duration or recurring within approximately 4 years). In both studies they compared long-term breakdowns with controls that had been tested to be negative for bTB.

Our study examined the impact of farm-level characteristics on persistence in terms of breakdown prolongation. We have taken a novel approach by selecting the case population (“breakdowns”) only from an existing detailed case–control dataset, and re-classifying these into prolonged or non-prolonged breakdowns. Our new case definition therefore relates to the duration of the breakdown, which is likely to be associated with, but not necessarily determined by, the infection status of the herd. We therefore model breakdowns as a function of both infection and the underlying regulatory testing regime. The ability to predict which breakdowns will go on to become prolonged using early markers was tested and validated by fitting a further model to nationally available data. Identification of prolonged breakdown herds at an earlier stage than is currently possible could allow the early implementation of additional controls and hence could improve the control of bTB.

2. Methods

2.1. Study design and data

Data were available from a previous case–control study (CCS05) designed to explore farm-level management risk factors for breakdown herds vs. “test-clear” herds. This study was conducted at the time of the Randomised Badger Culling Trial but was carried out in areas mainly outside of the trial areas (Independent Scientific Group, 2007). Herds were located in counties with different bTB incidence and the data were collected in the form of a questionnaire administered to the farmer. Data quality was monitored throughout by an independent auditor (Wahl, 2006).

The herds that were originally selected as breakdown herds in the CCS05 study were taken as the study population, re-classified into prolonged (breakdown duration ≥ 240 days; “cases”) and non-prolonged (breakdown duration < 240 days; “controls”) breakdowns (Table S1, supplementary material). This resulted in 113 cases and 288 controls. To extract further information, the CCS05 questionnaire data were linked to the national VetNet bTB breakdown data (Defra, 2008a) and cattle movement (Cattle Tracing System) data (Defra, 2007). The numbers of cattle movements onto the farm, stratified by whether they originated from higher incidence areas or from herds that had suffered recent breakdowns, or whether they came through markets, farm sales and the monthly rate of movements onto the farm during the breakdown were considered. The number of movements from the farm to markets, and to farm sales; the number of reactors at the start of the breakdown; the breakdown history of the herd and of contiguous farms were also included in the analysis. Two herds were excluded from the analysis of the full dataset as the data for the monthly rate of movements onto the farm during the breakdown could not be calculated due to there not being an end date to
the breakdown (these breakdowns were prolonged but still ongoing).

2.2. Statistical methods

A dataset was created such that categorical variables with expected counts less than 5; discrete or continuous variables with fewer than 100 non-zero values; and variables with fewer than 300 observations were excluded. In order to linearise the relationship between the non-categorical explanatory variables and the response variable, a log transformation was performed. To account for zeros in the data, and thus minimise bias in the covariates, 0.5 was added prior to the log transformation (Cox, 1955). Where multiple options existed for measuring a particular herd characteristic, a univariable analysis was conducted selecting the most statistically significant to be made available for the analysis.

The remaining variables were put into a stepwise routine using a multivariable logistic regression modelling approach. Due to the number of available variables, a manual forward stepwise routine was used. The data were truncated such that herds containing missing values for any of the remaining variables were removed (this is a condition of the stepwise routine). At each stage, the variable not yet in the model that had the lowest p-value according to a likelihood ratio test (LRT) was added (provided that p was < 0.05). Each variable remaining in the model was then dropped in turn, and removed and made available to the forward selection again, if the LRT gave a p-value of > 0.1. The process was repeated until no new variable could make a statistically significant contribution (p < 0.05 by the LRT) to the model fit. Once the final model was obtained it was re-fitted to the data including any of these removed herds that were fully observed for the variables that remained in the model.

All biologically plausible interaction terms between variables in the model were then considered for inclusion in the model. Any outlying points with high leverage and influence were removed if they had a noteworthy (Fox, 2002, pp. 197–199) Cook’s distance and a hat value greater than three times the average (Krzanowski, 1998, pp. 103–104). For model validation we used the Hosmer–Lemeshow goodness-of-fit test to assess model fit, and the predictive power of the model was assessed by calculating the area (AUC) under the Receiver Operating Characteristic curve (see e.g. Hosmer and Lemeshow, 2000, pp. 147–164), along with the sensitivity, specificity and positive/negative predictive values.

Two models were fitted using the statistical methods described (Fig. 1). The first model (Model 1) was fitted to the full dataset (combined CCS05 questionnaire, CTS and VetNet variables), the aim being to identify any important risk factors that are not currently routinely collected for all breakdowns, but that may aid in the management of prolonged breakdowns. The second model (Model 2) was fitted to a restricted dataset (only those variables in the full dataset available early on during a breakdown for all breakdowns nationally), with the aim to test this model for its ability to be used as a predictive tool to identify prolonged breakdowns in the early stages of a breakdown. In addition, Model 2 was used to produce predictive measures on national VetNet data, over four separate years (2003, 2004, 2005, 2006), as a validation of the model.

All data were stored in Microsoft Office Access and Excel (2003) and analyses were carried out using the GNU R package (R Development Core Team, 2008).

3. Results

3.1. Model 1: fitted to the full dataset

After the eligibility screening processes, 104 variables were available for the stepwise routine. The final model (Table 1) included 393 observations (110 cases and 283 controls), did not exhibit any significant lack-of-fit (Hosmer–Lemeshow goodness-of-fit test, p = 0.62) and had good discriminatory power (AUC = 0.86). Three observations were removed due to high leverage or influence values. Removal of these observations made little difference to the parameter estimates, sensitivity and positive predictive value.

As an additional check for the consistency of the variables remaining in the final model, a series of alternative models was run with differing assumptions. These included a model where certain factors thought to be important
with respect to the risk of bTB breakdowns (irrespective of breakdown duration) or the incidence of bTB (herd size, herd type and parish testing interval) were included in the model in order to adjust for their effects. Both the adjusted and unadjusted models were also fitted without log-transforming the non-categorical variables.

Five variables were present in all four fitted models: confirmation status of the breakdown, covered yard housing, cattle contacting domestic species from non-contiguous farms, use of salt licks inside farm buildings and herd size (Table S2, supplementary material). Since the predictive ability (as measured by the AUC) differed little between these models (Table S2, supplementary material), only results from the unadjusted, log-transformed model are reported here (Table 1).

The strongest effect size was associated with the confirmation status of the breakdown, where confirmed breakdowns were 12.6 times more likely to be prolonged compared to unconfirmed breakdowns (95%CI: 6.7–25.4). The percentage of breakdowns that were confirmed was 85.0% compared to non-confirmed breakdowns (95%CI: 6.7–25.4). As a result it seems that the predominant indicator of prolongation appears to be the confirmation status of the breakdown reduced the AUC dropped, in turn, and the AUC recalculated. Dropping the confirmation status of the breakdown reduced the AUC from 0.86 to 0.76. Dropping each of the other variables, month of the number of cattle moved onto the farm during the breakdown (associated with increased odds), the area of farm land tilled, use of mains water supply, the number of cattle moved onto the farm from farm sales in the 12 months prior to the breakdown and the presence of dead wildlife (other than badgers or deer) on the farm (all associated with decreased odds).

In order to check the effect of each variable on the discriminatory power of the model, each variable was dropped, in turn, and the AUC recalculated. Dropping the confirmation status of the breakdown reduced the AUC from 0.86 to 0.76. Dropping each of the other variables, in turn, did not result in the AUC dropping lower than 0.84. As a result it seems that the predominant indicator of prolongation appears to be the confirmation status of the breakdown.

### 3.2. Model 2: fitted to restricted dataset

Fourteen variables were available for the stepwise routine. The final model (Table 3) contained three variables (confirmation status, herd size and the number of cattle moved onto the farm from farm sales) and 397 observations (109 cases and 288 controls). Two observations were removed due to high leverage or influence values. Removal of these observations made little difference to the parameter estimates, sensitivity and positive predictive value. The final model did not exhibit any significant lack-of-fit (Hosmer-Lemeshow test \( p = 0.86 \)) and had good predictive power with an AUC of 0.79.

The variable with the largest effect size was again seen with confirmation status; breakdowns were 8.8 times more

### Table 1
Final logistic regression model (Model 1): Analysis based on 393 herds (110 cases and 283 controls). See Appendix (supplementary material) for definitions of the variables in the model.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>Lower 95%CI</th>
<th>Upper 95%CI</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmation status of breakdown</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cattle housed in large groups in covered yards</td>
<td>12.6</td>
<td>6.7</td>
<td>25.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Contact with domestic animals from non-contiguous farms</td>
<td>Yes</td>
<td>5.0</td>
<td>2.1</td>
<td>12.8</td>
</tr>
<tr>
<td>Mixed groups (&gt;1 class of cattle kept in the same group)</td>
<td>Yes</td>
<td>2.1</td>
<td>1.1</td>
<td>4.2</td>
</tr>
<tr>
<td>Reported dead wildlife on farm (other than badgers or deer)</td>
<td>Yes</td>
<td>0.6</td>
<td>0.2</td>
<td>2.3</td>
</tr>
<tr>
<td>Mains water supply on farm</td>
<td>Yes</td>
<td>0.4</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>No. cattle moved onto farm from farm sales</td>
<td>Yes</td>
<td>0.5</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>No. cattle moved onto farm during breakdown (rate per month)</td>
<td>log scale(a)</td>
<td>0.7</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Herd size</td>
<td>log scale(a)</td>
<td>1.9</td>
<td>1.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Area tilled (ha)</td>
<td>log scale(a)</td>
<td>2.5</td>
<td>1.6</td>
<td>4.0</td>
</tr>
<tr>
<td>Salt licks kept inside farm buildings</td>
<td>Yes</td>
<td>0.1</td>
<td>0.02</td>
<td>0.4</td>
</tr>
<tr>
<td>[Mixed groups] (\times) [salt licks kept inside farm buildings]</td>
<td>Yes</td>
<td>7.3</td>
<td>1.6</td>
<td>34.5</td>
</tr>
</tbody>
</table>

* Indicates per unit increase on the loge scale (or equivalent to a 2.7-fold increase).

### Table 2
Confirmation status of breakdowns.

<table>
<thead>
<tr>
<th>Breakdowns</th>
<th>No. breakdowns confirmed (%)</th>
<th>No. breakdowns unconfirmed (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS05 herds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>218 (54.4)</td>
<td>183 (45.6)</td>
</tr>
<tr>
<td>Cases (prolonged breakdowns)</td>
<td>96 (85.0)</td>
<td>17 (15.0)</td>
</tr>
<tr>
<td>Controls (non-prolonged breakdowns)</td>
<td>122 (42.4)</td>
<td>166 (57.6)</td>
</tr>
<tr>
<td>National data(b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>7974 (60.5)</td>
<td>5196 (39.5)</td>
</tr>
</tbody>
</table>

likely to be prolonged if they were confirmed (95% CI: 5.0–16.5). The number of cattle moved onto the farm from farm sales in the 12 months prior to the breakdown was associated with decreased odds and increased herd size was associated with increased odds, but the effect sizes were much smaller compared to that of confirmation status.

This model was then validated on larger national VetNet datasets from 2003 to 2006. Using the parameter estimates from the CCS05 fit, we calculated the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the model for each year. To examine the variation in these measures, a range of cut-off fitted probability thresholds was explored (Table S3, supplementary material). Using a fitted probability threshold of 0.2, the model performed consistently across the 4 years tested with a sensitivity of 82–84% and PPV of 44–49% (Table 4).

4. Discussion

This study took a novel approach by re-analysing existing detailed data to examine potential farm-level management characteristics that may be associated with the likelihood of bTB breakdown prolongation. By focusing on breakdown herds only, we are addressing an explicit problem relating to the impact of the current control mechanisms on farming practices.

Potential mechanisms for prolongation include suboptimal SICCT test performance, time-delays in its application to a herd and/or re-introduction of infection. The SICCT test sensitivity has been reported to be 75.0–95.5% (de la Rua-Domenech et al., 2006). Failure to detect infected animals creates potential for within-herd persistence of infection and onward transmission of infection. In addition, during the GB surveillance programme, many animals are never tested in their lifetime (Mitchell et al., 2006) although they would be included in a control programme in infected herds. Breakdowns may also have been prolonged through re-introduction of infection into the herd (between tests), from local wildlife reservoirs or contact with infected cattle.

We developed a multivariable statistical model based on factors associated with breakdowns becoming prolonged, before testing its ability to identify these herds using information available at an early stage of a breakdown. A series of models was fitted to the full dataset, using different assumptions, to determine model consistency. Of the five variables that remained in all of the models, confirmation status was by far the most important in terms of both effect size and contribution to discriminatory power. This is consistent with descriptive results from a previous study (Reilly and Courtenay, 2007), where 97% of persistent breakdowns (>6 months) were confirmed compared to 63% of transient breakdowns (≤6 months).

There are various mechanisms that could explain this strong association. Current legislation requires that confirmed breakdowns test negative at an additional short-interval test before movement restrictions are lifted, potentially increasing the likelihood of breakdown prolongation. However, our definition of 240 days is twice the minimum time that a confirmed breakdown should remain under movement restrictions under the current testing regime, and this buffer means that it is unlikely that this is the sole cause of the observed effect. (This should also cover for delays in testing – though in this study only 14 [12%] of prolonged breakdowns appear to have obvious delays. Nationally, although the time between short-interval tests is positively skewed with many tests being delayed, the distribution has a median of 70 days [unpublished data], and so is unlikely to lead to considerable miscategorization.)

A perhaps more plausible mechanism is that a more stringent (“severe”) interpretation of the SICCT test is employed on herds that have confirmed infection. At the standard test interpretation, animals must have a positive bovine reaction more than 4 mm greater than a positive or negative avian reaction to be classified as a reactor. However, at the severe interpretation, any animal showing a positive bovine reaction and negative avian reaction will be classified as a reactor, or where there is a reaction to both, only a difference of more than 2 mm is the required. The resulting increase in sensitivity and decrease in specificity (Defra, 2008b) could lead to a greater number of reactors

Table 3
Final logistic regression model (Model 2). Data restricted to variables in full dataset available nationally and analysis based on 397 herds (109 cases and 288 controls).

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmation status of breakdown (Intercept)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Confirmed</td>
<td>8.8</td>
<td>5.0</td>
<td>16.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Herd size</td>
<td>log scale #</td>
<td>2.2</td>
<td>1.6</td>
<td>3.2</td>
</tr>
<tr>
<td>No. cattle moved onto farm from farm sales</td>
<td>log scale #</td>
<td>0.8</td>
<td>0.7</td>
<td>0.9</td>
</tr>
</tbody>
</table>

* Indicates per unit increase on the loge scale (or equivalent to a 2.7-fold increase).

Table 4
Validation using national VetNet data (2003–2006): calculated using a cut-off threshold fitted probability of 0.2. AUC = Area under the Receiver Operating Characteristic (ROC) Curve; PPV = positive predictive value; NPV = negative predictive value.

<table>
<thead>
<tr>
<th>Year</th>
<th>AUC</th>
<th>Sensitivity (95%CI)</th>
<th>PPV (95%CI)</th>
<th>Specificity (95%CI)</th>
<th>NPV (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>0.78</td>
<td>84 (82–87)</td>
<td>49 (47–52)</td>
<td>63 (61–65)</td>
<td>90 (89–92)</td>
</tr>
<tr>
<td>2004</td>
<td>0.76</td>
<td>82 (80–84)</td>
<td>48 (45–50)</td>
<td>60 (58–62)</td>
<td>88 (87–90)</td>
</tr>
<tr>
<td>2005</td>
<td>0.75</td>
<td>83 (80–85)</td>
<td>45 (43–47)</td>
<td>55 (53–57)</td>
<td>88 (86–89)</td>
</tr>
<tr>
<td>2006</td>
<td>0.75</td>
<td>84 (82–86)</td>
<td>44 (42–46)</td>
<td>56 (54–58)</td>
<td>90 (88–91)</td>
</tr>
<tr>
<td>Entire period (2003–2006)</td>
<td>0.76</td>
<td>83 (81–84)</td>
<td>46 (45–48)</td>
<td>60 (59–61)</td>
<td>89 (88–90)</td>
</tr>
</tbody>
</table>
(both true and false positives) being detected. This may decrease the duration of infection through increased detection of true positives, but at the potential cost of increasing the breakdown duration through detection of more false positives (since only a single reactor is needed at each short-interval test to keep movement restrictions in place). Application of a testing regime which results in higher levels of false positive reactors (e.g. when the SICCT severe interpretation is used), suggests that breakdown duration is a function of not only infection status of the herd but also the underlying testing regime.

Confirmation of infection may be reflective of increased underlying levels of the disease within the herd. Indeed confirmed breakdowns had a larger number of reactors during the breakdown, providing more opportunities to confirm infection. Unconfirmed breakdowns had a higher percentage of singleton reactors during the breakdown (59%) compared to confirmed breakdowns (18%), providing only a single opportunity to confirm infection, by methods (detection of visible lesions/culture) that are known to lack sensitivity. Furthermore, unconfirmed breakdowns may be at a less advanced stage of disease that is not yet detectable post-mortem. The gamma interferon test can detect animals at an earlier stage of infection and has been shown to detect a substantial proportion of animals that are SICCT test-negative (Pollock et al., 2005).

A further plausible mechanism for unconfirmed breakdowns being less likely to become prolonged is that they might not actually be infected with bTB (false positive breakdowns). Although the proportion of these breakdowns that are falsely positive cannot be quantified without knowing their true infection status (by the very nature of being unconfirmed, this information is not available for these breakdowns), for any herd it is possible to calculate the probability of obtaining the observed number of reactors (given the herd size) under the assumption that all animals in the herd are uninfected. This provides a per-herd probability of that particular breakdown being a false positive for a given animal-level specificity. A study conducted in locations in GB where bTB prevalence (as judged by post-mortem examination) tended to zero, reported the animal-level specificity to be 99.99% (Goochchild and Clifton-Hadley, 2001). Given this specificity we obtain a median probability of the breakdown being a false positive of 0.011 with an inter-quartile range of 0.0004–0.023 across the unconfirmed breakdowns in the study population. This suggests that the overall proportion of unconfirmed breakdowns that are false positives is likely to be low.

The number of reactors at the start of the breakdown was associated with breakdown duration, but due to its strong association with confirmation status, it did not remain in the final model. The total number of reactors during a breakdown can be an indicator of the risk of recurrence of bTB within a herd (Olea-Popelka et al., 2004; Wolfe et al., 2010). However, this variable is directly confounded with our response variable as increasing numbers of reactors are a prerequisite for increasing breakdown duration. In addition, this information is not available for predictive purposes at the outset of a breakdown, and so was not included in the analysis.

The strong effect size of confirmation status compared to other farm management characteristics raises important questions regarding whether the current testing regime is predisposing towards prolonged breakdowns. In addition, even with the use of severe interpretation on confirmed breakdowns, 30% of herds with prolonged breakdowns suffer a further breakdown within 12 months after the lifting of movement restrictions, compared to around 20% of non-prolonged breakdowns (unpublished data). The higher rate of recurrence within prolonged breakdowns may be representative of within-herd persistence and/or a propensity to re-infection from local wildlife populations and/or contact with infected cattle.

Herd size has been identified as a risk factor for herds suffering a bTB breakdown (Griffin et al., 1996; Munroe et al., 1999; Green and Cornell, 2005) but in a study where breakdown duration was considered (Reilly and Courtaney, 2007), the increased odds associated with increased herd size was similar for both transient and prolonged breakdowns when compared to herds that had tested clear of infection. Brooks-Pollock and Keeling (2009) reported an association between herd size and persistence of bTB in the national VetNet data but this was unadjusted for any other variables. Although herd size was associated with increased odds in all four models in our study, it provided little contribution to prediction.

Many of the variables identified are plausible and biologically interesting but contributed little to predictive ability. For example, keeping cattle in covered yard housing may increase transmission of M. bovis through close contact of shared airspace and has been identified previously as a risk factor for bTB breakdowns (Johnston et al., 2005). Contact between cattle on the farm and domestic species (other than cattle) from non-contiguous farms (see Appendix, supplementary material) was also associated with increased odds of prolongation, though the mechanism behind this is less clear. Use of salt licks inside farm buildings was associated with decreased odds of prolongation of the breakdown, which could be postulated to be due to minimising shared use by wildlife, thus decreasing opportunities for transmission.

There is good evidence that bTB can be transmitted through cattle movements (Gilbert et al., 2005; Johnston et al., 2005; Gopal et al., 2006; Carrique-Mas et al., 2008). However, of movement practices examined, only two variables remained in the final model: the monthly rate of cattle movements onto the farm during the breakdown (associated with increased odds) and the number of cattle moved onto the farm from farm sales in the 12-month period prior to the breakdown (associated with decreased odds). Farmers may need to alter their farming practices while under movement restrictions in order to sustain a viable business, and can buy in animals under a special licence. This may carry a considerable risk in terms of maintaining infection (due to an influx of new susceptible animals), or re-introducing infection. Alternatively, as the breakdown increases in duration, farmers may be more likely to buy in animals to maintain their herd size. To address that it may be a cause or effect, the monthly rate of cattle movements onto the farm (instead of the total number of movements) during the breakdown was calculated. Buy-
ing in cattle from farm sales in the 12 months prior to the breakdown was associated with decreased odds of prolongation. The mechanism behind this association is unclear but one explanation could be that it is a proxy for a high turnover of cattle, assisting in the removal of infected animals, providing less opportunity for bTB to establish in the herd. As cattle movements are recorded at the holding level, and not the herd level, we cannot be certain whether the movements were related to the herd suffering the breakdown itself or to a herd kept at a different location, albeit part of the same holding.

Although identification of these factors might suggest that modifications to farming practices may lower the probability of breakdown prolongation (e.g. stopping cattle movements onto the farm during the breakdown, moving salt licks inside farm buildings), the small effect sizes and poor contribution to prediction must be taken into account. In addition, altering other farming practices such as the housing management of the cattle needs to be balanced against the effect on cattle welfare and productivity, or may be impractical for the farmer. There was a lack of consistency between variables identified in our study and those identified in previous studies that have considered breakdown duration. Griffin et al. (1993) found that herds with “chronic” breakdowns (>12 months duration or recurring within approximately 4 years) were more likely to be intensively managed, using practices such as spreading of slurry, purchase of animals and were also associated with nutritional factors and a greater presence of badgers. Reilly and Courtenay (2007) found that transient (<6 months) breakdowns were associated with purchase of cattle, whereas persistent breakdowns (>6 months) were influenced by factors relating to herd enterprise, use of a silage clamp and a relatively high density of active badger sets on the farm. However, these studies are not directly comparable to ours as they employed different selection criteria for the control groups along with the mixed case definition (Griffin et al., 1993) that included recurrent breakdowns.

In risk factor identification there will be a degree of confounding between variables, and we have attempted to be cautious in our interpretation, putting more emphasis on risk factors that have a strong effect in terms of predictive power as well as effect size. We have also focused on those factors that were identified consistently across the different models tested. Nonetheless, the inclusion of certain variables in the model may be confounded by variables that were/were not considered in this study and interpretation of risk factors as being absolute should thus be considered with care.

A further model was fitted to data available nationally (Model 2) to ascertain the predictive capacity of the model based on currently available data. This is necessary as not all of the risk factors identified from the full dataset are available at the national level. The model was fitted to the CCS05 data but performed consistently when validated independently on the national data. We report results here using a threshold of 0.2, which provides a high sensitivity (82–84%) and a reasonable PPV (44–49%) at the expense of lower specificities and NPVs but the optimal cut-off threshold fitted probability will be dependent on the situation to which it will be applied in the field. For example, in high incidence areas, it may be more important to identify most of the prolonged breakdowns (requiring a higher sensitivity), and less important that some breakdowns that are incorrectly predicted to be prolonged have additional controls applied to them. In practice, the advantages gained (financial/speed of breakdown resolution) by applying additional controls to those breakdowns correctly predicted to become prolonged would need to be offset by the cost (financial/testing personnel/stress to farmer) of applying controls to herds that are incorrectly predicted to be prolonged. Indeed, although applying additional controls to breakdowns predicted to become prolonged should reduce the duration of infection, they may in fact prolong the breakdown further through detection of more true or false positives. For this reason identifying the underlying mechanisms relating to prolongation is vital in order to have a sound epidemiological justification for the practical implementation of these control options.

5. Conclusion

Confirmation status was found to be the most important risk factor in terms of the effect size and contribution to prediction. Currently the use of additional tests, such as gamma interferon, in chronic confirmed breakdowns is considered only at a relatively late stage of the breakdown. The predictive model developed in this study can identify which breakdowns are more likely to be prolonged at an earlier stage with a higher sensitivity and reasonable PPV. A TB taskforce (DG SANCO 10200/2006, 2006), set up to make recommendations for speeding up the eradication of bTB, recognised that the current legislation (EU Council Directive 64/432/EEC, 1964) was primarily set up to manage trade regulations and is not necessarily optimal for eradication in terms of the testing regimes it dictates. While new strategies for controlling bTB in GB are urgently needed, this could be a useful tool for adapting current testing regimes, in line with current legislation, to identify the herds on which to focus controls and resources early on in a breakdown.

Conflict of interest statement

The authors declare that there are no known conflicts of interest that may have influenced this work.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.prevetmed.2010.09.007.

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