

**Epidemiology and Infection**

**Risk-based strategies for surveillance of tuberculosis infection in cattle for low  
risk areas in England and Scotland**

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**Supplementary Material**

1    **Supplementary text**

2

3    **S1. Cattle movements from high-risk areas (HRAs) as a predictor of bovine**

4    **Tuberculosis (bTB) breakdowns**

5

6    *S1.1. Source data*

7    The data used in this study were derived from the Cattle Tracing System (CTS)

8    movement data (RADAR), and the SAM's records of bTB tests and incidents (Defra).

9    The CTS database contains records of all inwards and outward cattle movements in

10   Great Britain. As the risk of transmission of bTB at markets is expected to be low, we

11   used a version of the dataset with markets stripped from movements: a movement

12   from  $farm_1$  to a market to  $farm_2$  is recorded as a movement from  $farm_1$  to  $farm_2$ . With

13   these data a variety of risk ratings were generated for each cattle movement from

14   2007 to 2010 and a risk rating for each farm based on the ratings of their inward

15   movements for each year of the study period.

16

17   *S1.2. Risk ratings*

18   *S1.2.1. Movement risk ratings*

19   Let  $m_{ijt} = 1$  be a movement if farm  $i$  to farm  $j$  on data  $t$ . Let  $N(m_{ijt})$  be the number

20   of animals moved on that day between those farms. For each movement, four

21   different risk ratings were calculated:

- 22   •    $R_{county}(m_{ijt}) = 1$  if farm  $i$  is in 1-year testing county, 0 otherwise.
- 23   •    $R_{num}(m_{ijt}) = k$  where  $k$  is the number of animals moved if  $i$  has had a bTB
- 24   breakdown within ten years previous to  $t$ , 0 otherwise.
- 25   •    $R_{num,time}(m_{ijt}) = k \ln(t - t_B)$  where  $k$  is the number of animals moved and  $t_B$  is
- 26   the date of the most recent breakdown at  $i$  if  $i$  has had a bTB breakdown
- 27   within ten years previous to  $t$ , 0 otherwise.
- 28   •    $R_{time}(m_{ijt}) = \ln(t - t_B)$  where  $t_B$  is the date of the most recent breakdown at  $i$  if

29            $i$  has had a bTB breakdown within ten years previous to  $t$ , 0 otherwise.

30

31           *S1.1.2. Farm risk ratings*

32           For farm  $j$  in year  $y$ :

33           •      $R_{county}(i) = R_{county}(m_{ijt})$ , where  $t$  is within two years previous to  $y$ .

34           •      $R_{num}(i) = R_{num}(m_{ijt})$ , where  $t$  is within two years previous to  $y$ .

35           •      $R_{num,time}(i) = R_{num,time}(m_{ijt})$ , where  $t$  is within two years previous to  $y$ .

36           •      $R_{time}(i) = R_{time}(m_{ijt})$ , where  $t$  is within two years previous to  $y$ .

37

38           *S1.3. Stump classifiers*

39           A stump classifier is a simple threshold classifier. Given a threshold and a set of  
40           rated examples (in this case, farms with risk ratings), all examples were classified  
41           with ratings above the threshold as positive, and below the threshold as negative. For  
42           a given rating measure, a threshold was chosen, and everything below the threshold  
43           was classified as non-risky and everything above as risky. At each threshold, the  
44           results were compared with bTB breakdowns and the number of true positives and  
45           false positives were recorded. The curve joining these points is a Receiver Operator  
46           Characteristic (ROC) curve and each curve represents the analysis of one risk rating  
47           for one given year. ROC curves are commonly used in machine learning and  
48           radiology [1] to assess the performance of a classifier or diagnostic test. A perfect  
49           classifier would be in the upper left hand corner of the plot, whereas a non-  
50           informative random classifier would be on the diagonal line from bottom left to top  
51           right corner. In order to understand if movements from high incidence areas are good  
52           predictors of bTB breakdowns, different risk ratings for all eligible herds were  
53           calculated as stump classifiers in three geographical areas: low risk areas (LRAs),  
54           Scotland and all United Kingdom. A set of distinct stump classifiers thresholds was  
55           used and compared with the actual bTB breakdowns where the number of true and  
56           false positives in each one of the three areas was recorded.

57  
58 In Figure S5, the curves of the low incidence areas in England are more  
59 concentrated on the upper left side of the graph, therefore the prediction of  
60 breakdowns in these areas using movements as risk factors is better than in  
61 Scotland or in the rest of the UK. The prediction of breakdowns in the rest of the UK  
62 is also better than in Scotland, since the ROC curves are more concentrated in the  
63 upper left corner. The variation between risk ratings values for Scotland is large,  
64 which indicates that some risk ratings predict breakdowns, while others (that are very  
65 close to the diagonal line) do not predict more than a random guess. In summary,  
66 stump classifiers evaluated the role of different movement types as risk factors for  
67 spread, and broadly speaking showed that movements from high incidence areas to  
68 low incidence areas in England were a good (better than random) predictor of risk  
69 (Figure S5).

70

## 71 **S2. Underlying risk factors for bTB incidents**

### 72 *S2.1. Data extraction from SAM and CTS databases*

73 The 'Herd table' from SAM includes data on herd type (which was separated in the  
74 categories according to Table S1). The 'Test table' from SAM includes data on all  
75 herd test types and their results, while the 'Incidents table' has data on herds that  
76 recorded new confirmed breakdowns. Holdings that are registered but do not have  
77 animals, that are not active for the entire study period, or that hold herds of different  
78 types are not considered in this analysis.

79

80 Data on births, deaths, imports and movements of individual cattle to each holding  
81 were extracted from the British Cattle Movement System (BCMS) Cattle Tracing  
82 System Database (CTS). Only herds that have animals (through birth or movement)  
83 were considered in the analysis resulting in 13327 retained herds from 15570 low risk  
84 animal holdings or land keepers registered during that period. Since Scotland has  
85 been considered a low risk area since well before the study period, and considered

86 officially bTB-free since 2012, all eligible and active herds in Scotland that follow the  
87 characteristics above have been retained (a total of 10145 herds from 11145 animal  
88 holdings or land keepers registered).

89

90 *S2.2. Multivariate logistic mixed models*

91 Multivariate logistic mixed models were formulated to assess candidate risk factors in  
92 which the outcome was 1 if holding  $i$  in county  $j$  recorded at least one confirmed  
93 incident of bTB in year  $k$ , and 0 otherwise. Data from the year 2007 was used to  
94 determine the number of movements and Irish imports for the following year, but  
95 models were constructed using data for LRAs only between 2008 and 2013. Both  
96 year and county were evaluated as random effects in order to estimate the mean  
97 distribution of the outcome in every permutation of year and county, as well as to  
98 control for any influence that these values may have on estimating holding level  
99 prevalence of infection. The following fixed effects were considered:

100 1. The mean herd size for each year. The yearly mean was computed by  
101 averaging the monthly size per holding (provided by APHA), as calculated  
102 from the number of births, deaths and recorded cattle movements off/onto  
103 individual holdings. Herd sizes were categorized to reflect population  
104 distributions in England (1-50, 51-100, 101-200, 201-350, 351-500 and >500  
105 animals for LRAs) corresponding to the categories used in the RADAR 2008  
106 Cattle Book [2]), and in Scotland (1-100, 101-350, 351-500 and >500).

107 2. The consolidated herd types found in the SAM database. These types were  
108 reduced to beef, dairy, finishing (beef animals that are ready for slaughter),  
109 suckler (a herd of cattle composed of dams and their young calves up to the  
110 point of weaning) and store (beef animals brought for finishing, normally well-  
111 grown animals of up to two years of age, which have been reared on one or  
112 more farms, and then are sold, either to dealers or other farmers) as in Table  
113 S1. An additional group including herds that did not fall into the  
114 aforementioned categories ("Other:") was excluded due to the poor

115 representation of these holdings in the bTB incidence database.

116 3. Irish imports expressed as a binary response indicating whether a holding imported

117 any Irish cattle in the previous year.

118 4. High-risk movements expressed as the number of batches (a batch being identified

119 as animals moving between the same pair of holdings in the same direction in the

120 same day) of cattle (categorised as 0, 1-10, and >10) arriving from HRAs to LRAs

121 in the previous year for LRAs or as a binary response indicating whether a holding

122 had received batches of cattle from HRAs in the previous year for Scotland.

123

124 **S2.3. Model evaluation**

125 Models were evaluated using the AIC model score. To account for possible temporal

126 and spatial clustering, year and parish were fit as random effects. The best fit models

127 were chosen by back-fitting the listed fixed effects, forward-fitting the random effects

128 and finally back-fitting the fixed effects once more to recheck the selected variables.

129 This rechecking is done because the inclusion of random effects could render certain

130 fixed effects insignificant [3]. The model was reduced and just the predictors that

131 were significant at  $p<0.05$  were included in the final model. Interactions and

132 associations between variables were also explored. The significant fixed effects are

133 presented as odds ratios (Odds) with 95% confidence intervals. The fitted values

134 extracted from the most significant model correspond to the probability of the herd

135 becoming infected in each year of the study ( $p_{intro}$ ).

136

137 **S3. Risk-based surveillance model**

138 **S3.1. Elements of risk and detection**

139 The risk-based surveillance scenarios were modelled considering the following

140 elements of infection risk and detection:

- 141 a) The size of herds, with larger herds are at a greater risk of infection;
- 142 b) The proportion of the herd's total stock that is sent to slaughterhouse, with
- 143 holdings that send fewer stock to the slaughterhouse requiring more surveillance.

144 This proportion is calculated based on the total number of cattle slaughtered in  
145 the previous year divided by the herd size. Only animals that are moved directly  
146 from the farm to slaughterhouse, or from farm to market and then direct to  
147 slaughterhouse are considered;  
148 c) Whether the herd receives animals from HRAs in GB or Ireland. It is assumed  
149 that herds that receive animals from these areas have higher chances of getting  
150 infected.

151

### 152 *S3.2. Model assumptions*

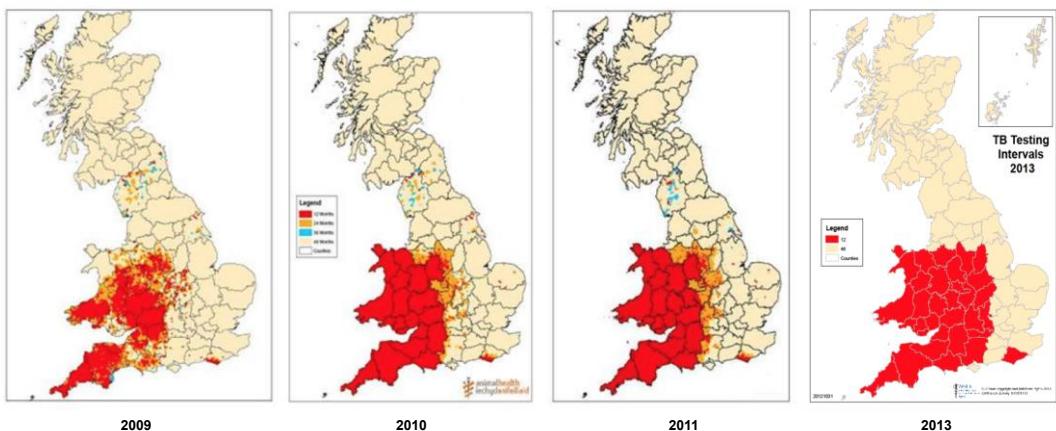
153 The risk-based surveillance scenarios were modelled considering the following  
154 assumptions:  
155 1) All herds that were consistently low risk during the entire study period and that  
156 only had one herd type could be included in the analysis;  
157 2) All animals of a herd are tested, even if some animals are not tested under RHT;  
158 3) All the other testing schemes (such as slaughterhouse, pre- and post-movement,  
159 tracings, contiguous herd, etc.) would continue; and that the sensitivity and specificity  
160 of the SICCT does not vary from herd to herd.

161

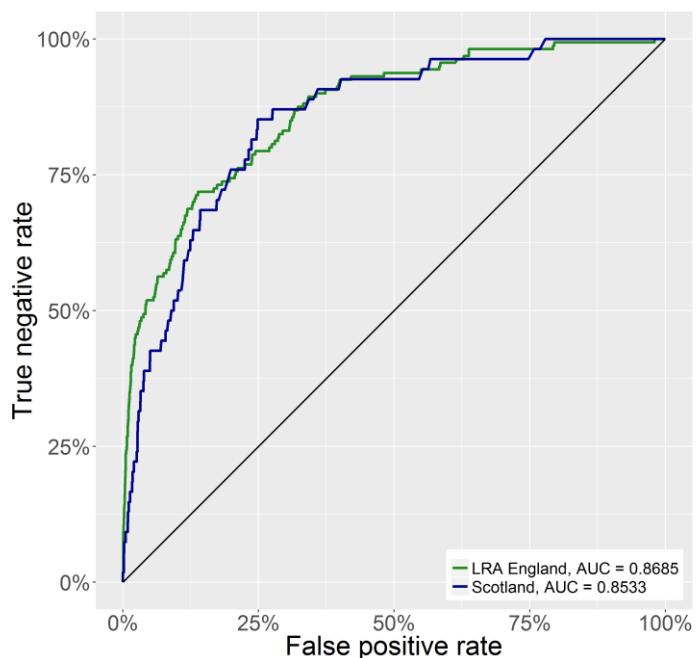
### 162 *S3.3. Point score system for risk-based scenarios*

163 During the risk-based simulations, the level of risk of each herd determines the  
164 testing interval of each herd, which is based on a point system (0 points=no testing, 1  
165 point=4 year testing, 2 points=2 year testing, 3 points=annual testing). All risk-based  
166 scenarios allow for exemption from testing for herds with very low risk, except  
167 scenarios 7-8, which are more conservative and require the testing of all herds. In  
168 these scenarios, herd size was accounted as the most important risk factor and all  
169 the herds below a certain threshold value (scenario 7: herd size  $\leq$  350, scenario 8:  
170 herd size  $\leq$  500) are tested every four years, while the ones above the threshold are  
171 tested every year.

## Supplementary Figures



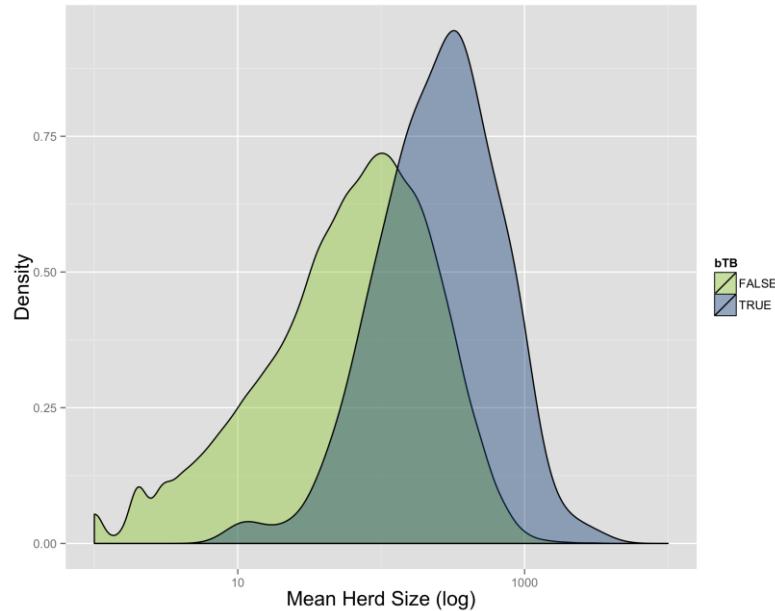
**Figure S1. Change of national bTB testing regimes between 2009 and 2013 according to Defra/AHVLA.** High-risk areas have expanded over time reducing the areas of low risk, and a two-early testing buffer (edge area) was created between 2009 and 2011. In 2013, the edge areas were expanded and the testing regime changed to only two time windows (1-year testing for high risk and edge areas, and 4-year testing for areas of low risk).



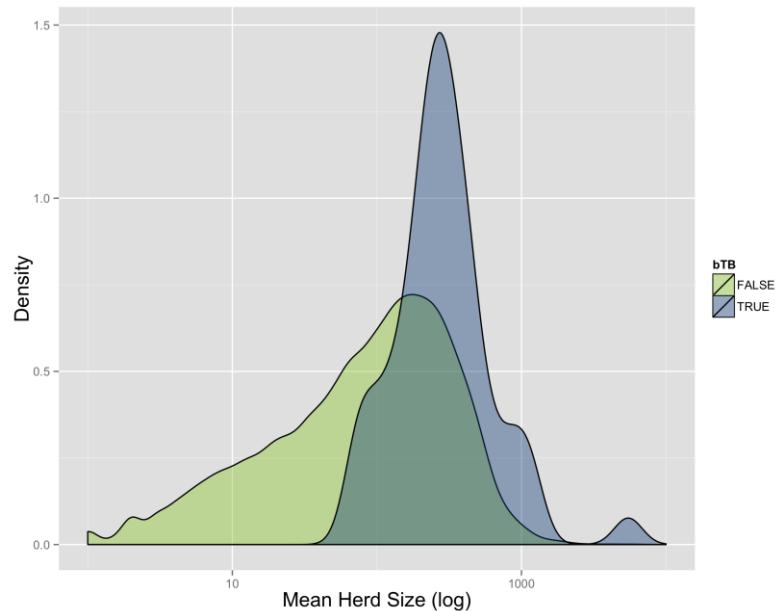
**Figure S2. Receiver Operating Characteristics curve for the model fit for the risk factors in LRAs and in Scotland.** The area under the curve (AUC) is presented

next to each respective model in the legend. The solid black line represents a model that assigns the binary response at random.

**A**

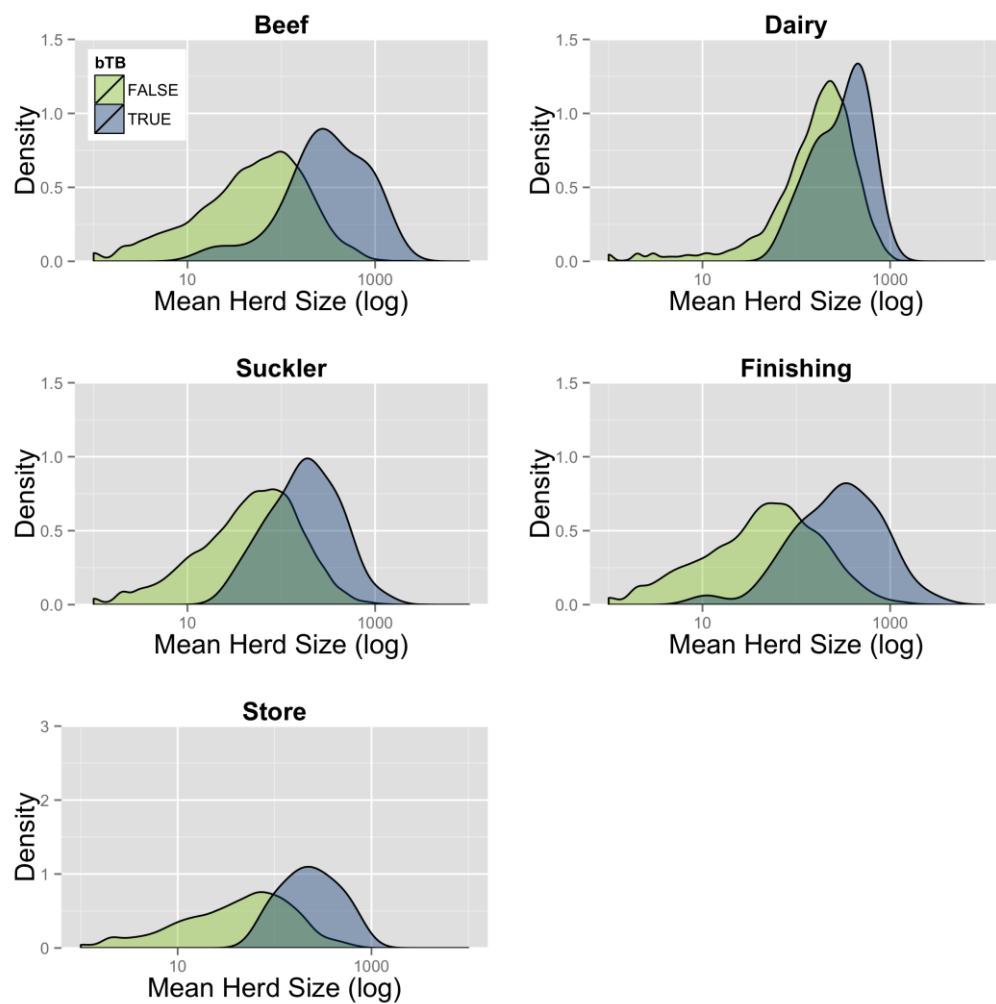


**B**



**Figure S3. Mean herd size versus number of herd breakdowns.** Density distributions of the mean herd size of farms with at least one breakdown (in blue) and without breakdowns (in green) during 2008-2013 in (A) LRAs and in (B) Scotland. The x-axis is in log scale.

**A**



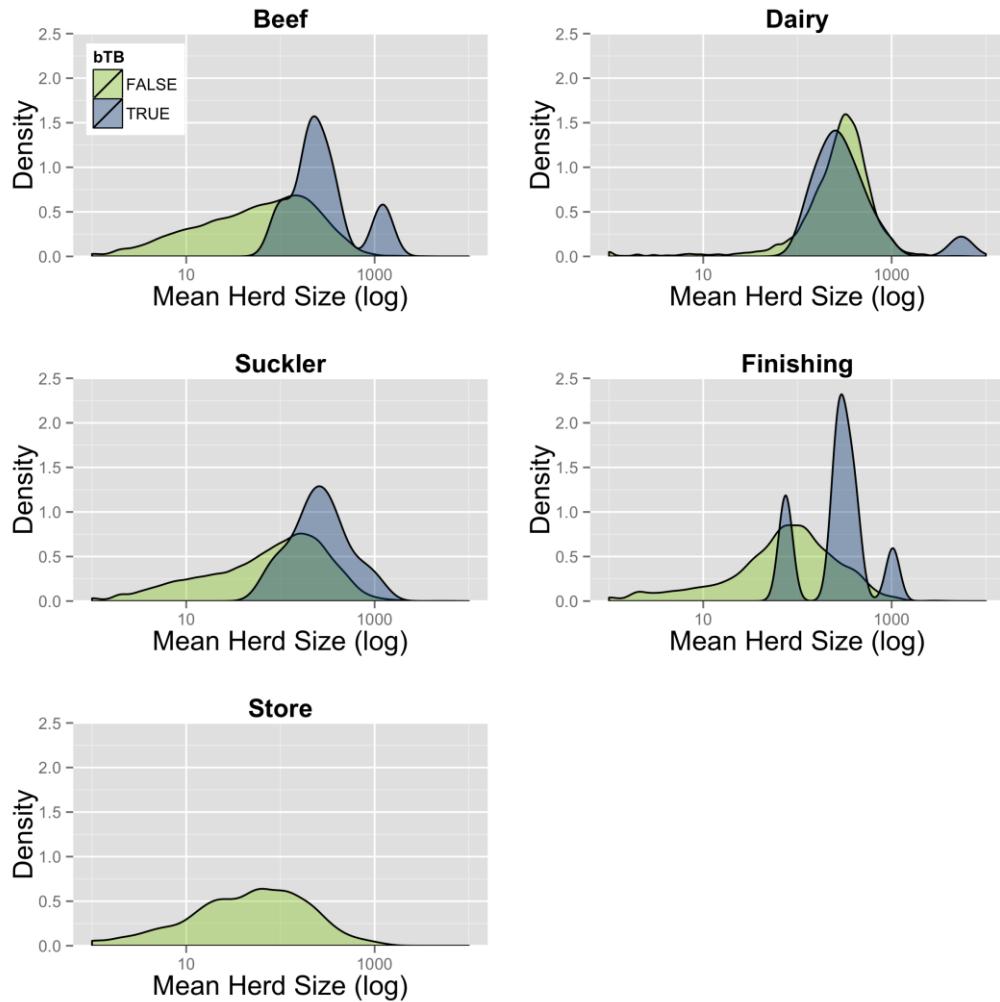
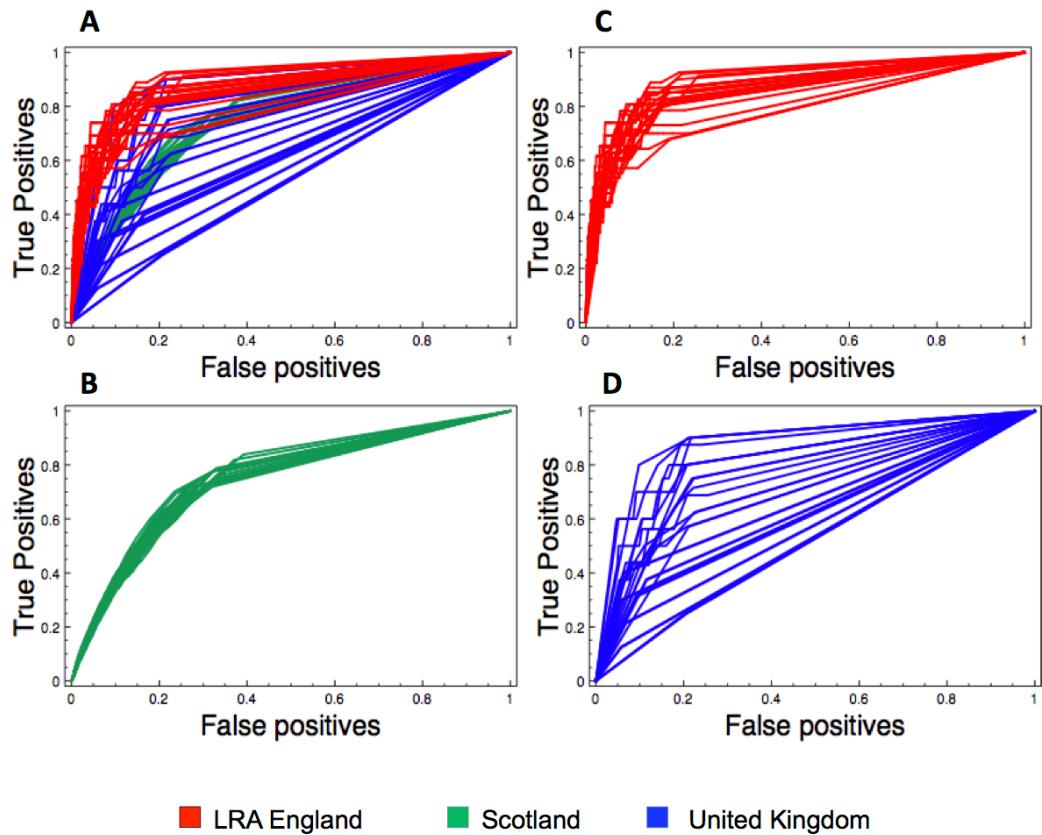
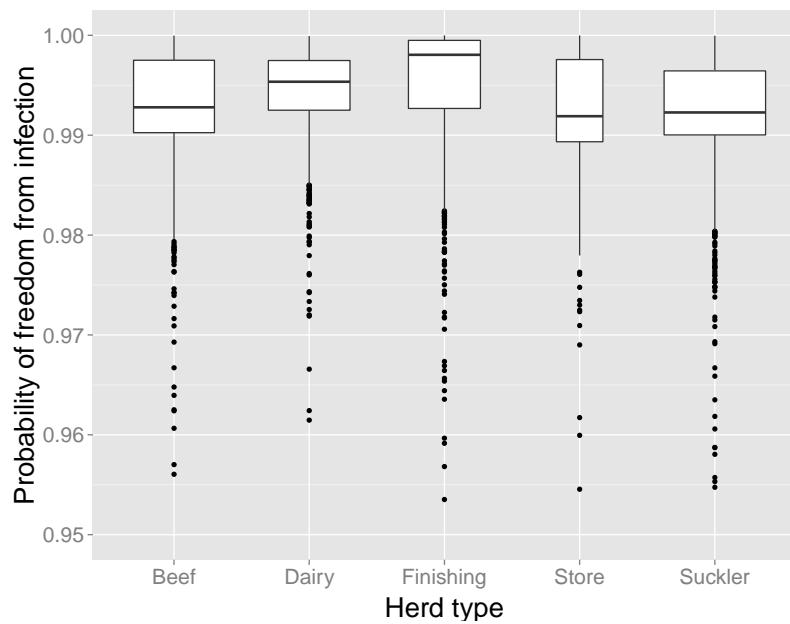
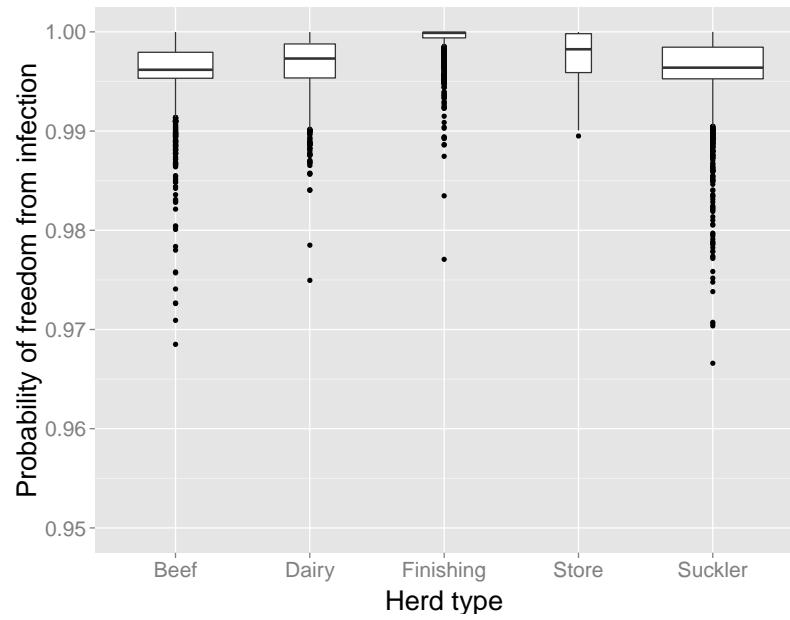
**B**

Figure S4: **Mean herd size versus number of herd breakdowns per herd type.** Density distributions of the mean herd size of farms with at least one

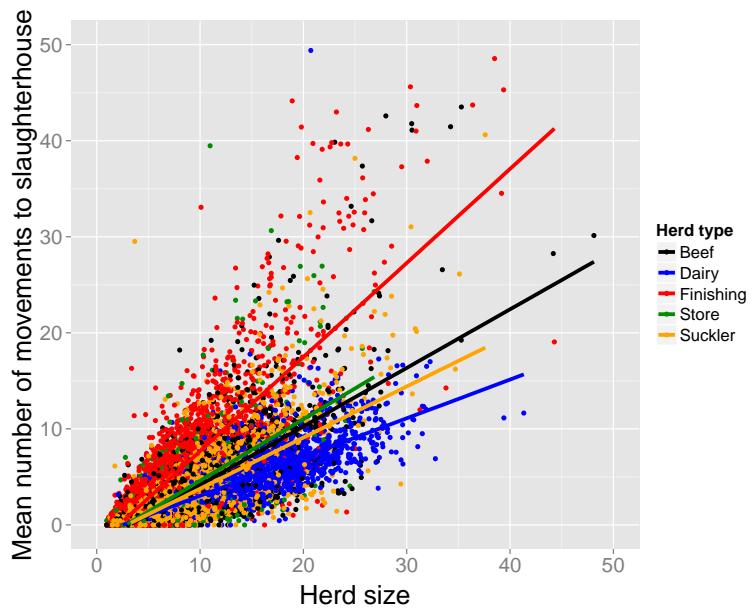
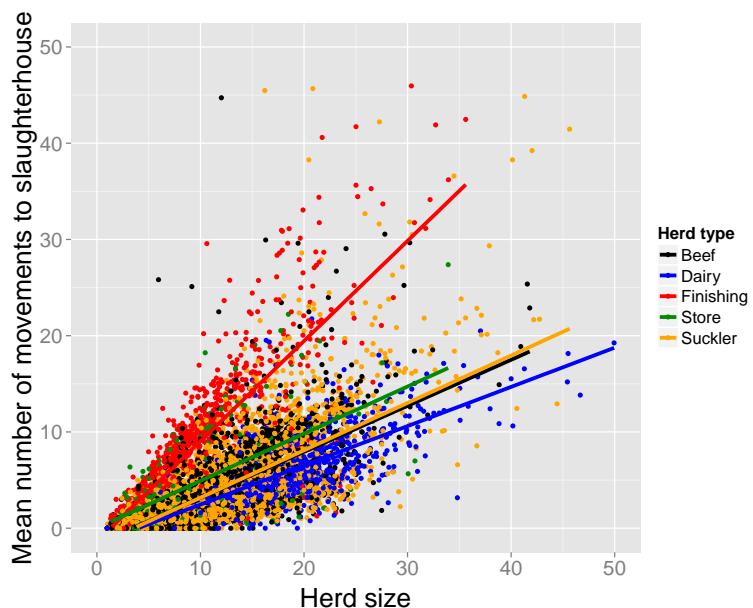
breakdown (in blue) and without breakdowns (in green) separated by herd type in (A) LRAs and in (B) Scotland during 2008-2013.



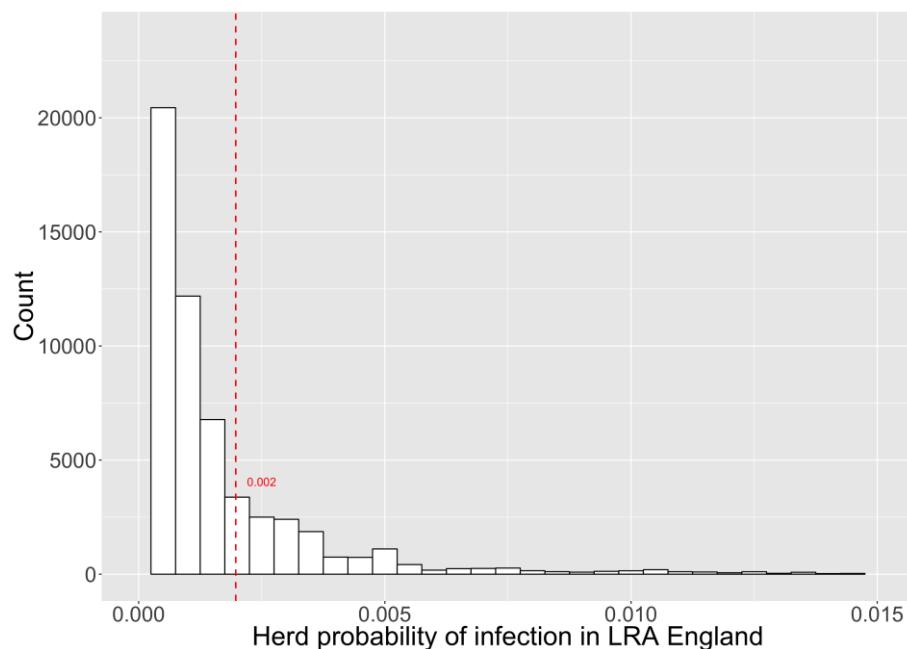
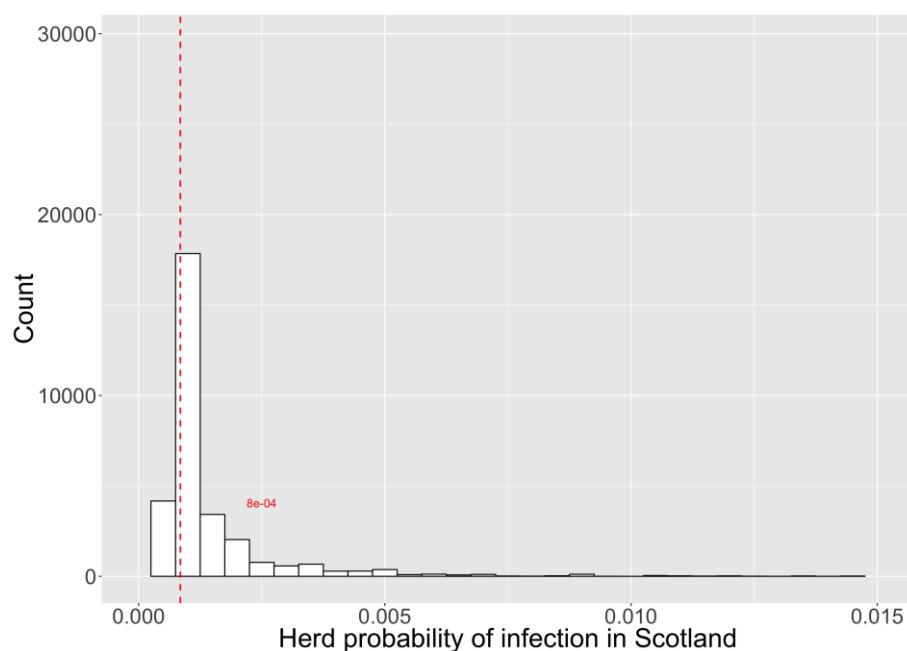
**Figure S5: Cattle movements as risk factors in LRA England, Scotland and UK.**  
 Receiver Operator Characteristic (ROC) curves from all simulation runs of the stump classifier analysis during the time period 2007-2010 for all the three areas together (A), for United Kingdom (B), for LRA England (C), and for Scotland (D).

**A****B**

**Figure S6. Herd type versus the probability of freedom from infection.** Boxplot showing the herd probability of freedom from infection with the slaughterhouse only model by herd type in LRAs (A) and in Scotland (B) during 2009-2013. Probability of freedom of infection is defined as 1-probability of undetected infection. Box widths represent the proportion of data in each herd type category. The y-axis has been truncated for clarity.

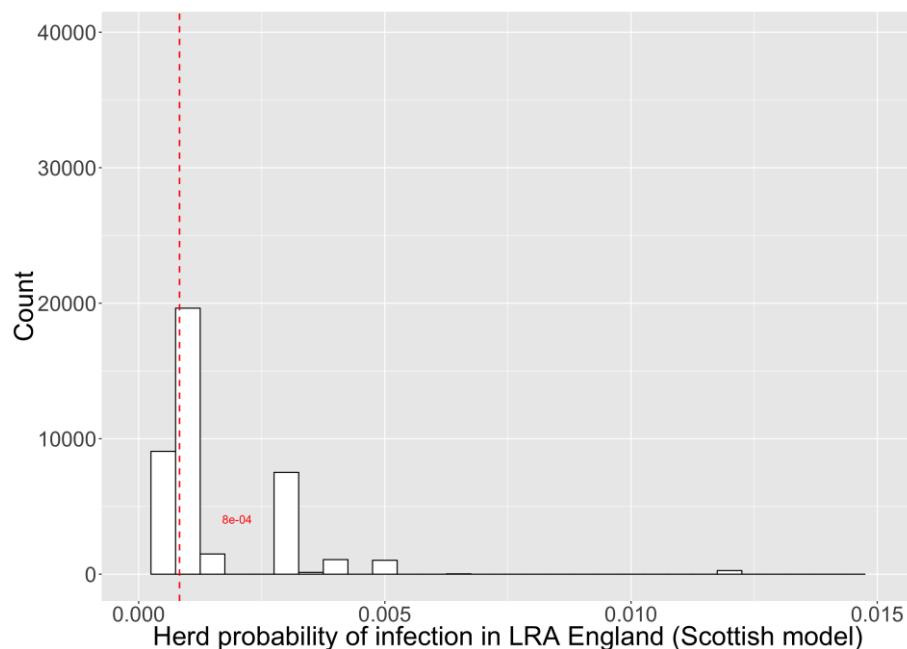
**A****B**

**Figure S7. Movements to slaughterhouse versus herd size.** Scatterplots showing the squared root of mean herd size per herd against the squared root of the mean number of animals moved to slaughter in LRAs (A) and in Scotland (B) in 2009-2013 broken down by herd type as listed in SAM's database. The axes have been truncated for clarity. There is a positive relationship between herd size and number of movements to slaughter with distinct clustering of finishing and dairy herds. Dairy herds are both larger and typically have fewer per capita movements to slaughter compared to finishing herds.

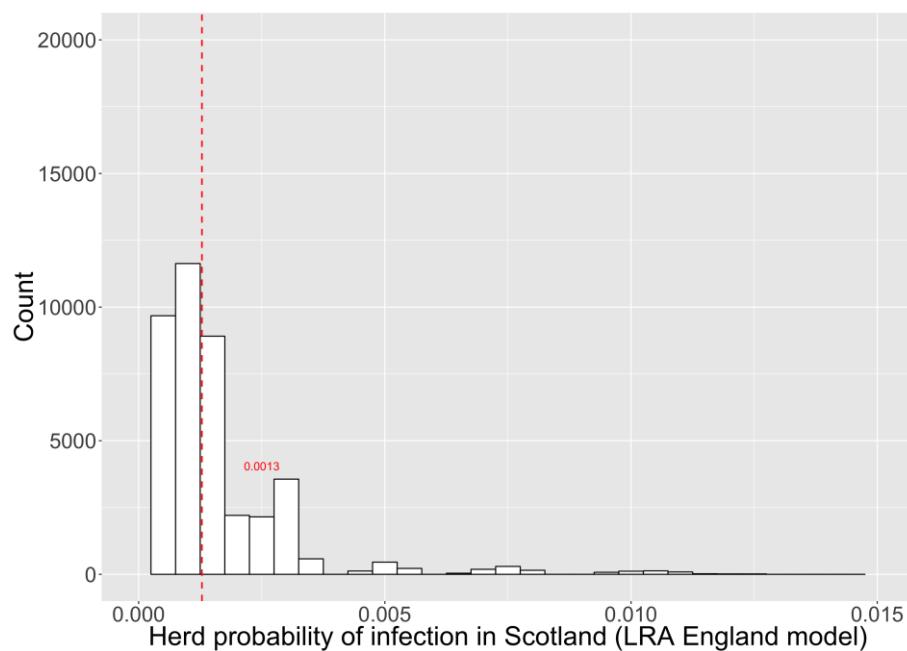
**A****B**

**Figure S8. Histogram of the herd probability of infection estimated by the GLMs used for LRA England (A) and for Scotland (B).** The dashed red vertical lines represent the mean values of the herd probability of infection. The axes were truncated for clarity.

**A**



**B**



**Figure S9. Histogram of the herd probability of infection estimated by the GLMs used for herds in LRA using the Scottish model predictor (A) and for herds in Scotland using the LRA model predictor (B).** The dashed red lines represent the means values of the herd risk of infection. The axes were truncated for clarity.

## Supplementary Tables

Herd type	Specific herd categories
Beef	Beef, BEEF, Beef Bull Hirer, Beef Dealer, Beef, Heifer
Dairy	Dairy, DAIRY, Dairy Bull Hirer, Dairy Dealer, Dairy Heifer
Store	Stores
Finishing	Finishing
Suckler	Suckler, BEEF SUCKLER
Other	All the other categories in SAM's database

Table S1. **Herd type categories.** Characterization of herd types in their sub-categories according to SAM's database. The 'Other' category is not used in our analyses.

A

Predictor	Unit	Odds (95% CI)	Z value	Pr(> Z )
Intercept	0	0	23.83	<0.001
Herd size	1-50	1	-	-
	51-100	3.74 (1.7-8.2)	3.31	0.001
	101-200	5.43 (2.60-11.34)	4.50	<0.001
	201-350	8.25 (3.94-17.28)	5.59	<0.001
	351-500	12.30 (5.55, 27.23)	6.19	<0.001
	>500	17.02 (7.99, 36.27)	7.34	<0.001
Batches from HRAs	1	0	-	-
	1-10	3.38 (2.26, 5.07)	5.92	<0.001
	>10	18.27 (11.75, 28.41)	6.19	<0.001
Irish imports	False	1	-	-
	True	2.34 (1.36, 4.02)	3.06	0.002

B

Predictor	Unit	Odds (95% CI)	Z value	Pr(> Z )
Intercept	0	0	-17.44	<0.001
Herd size	1-100	1	-	-
	101-350	5.23 (2.88-23.58)	3.93	<0.001
	351-500	11.31 (3.43, 37.33)	3.93	<0.001
	>500	14.75 (4.55, 47.75)	4.49	<0.001
	False	1	-	-
Batches from	True	3.20 (1.62, 6.30)	3.35	0.001
	False	1	-	-
	True	4.22 (2.17, 8.22)	4.23	<0.001

Table S2. **Risk factor model results for LRA in England and Scotland.** Results of a mixed logistic regression model that compute the herd risk of infection to determine the risk factors associated with bovine Tuberculosis breakdowns in LRAs (A) and in Scotland (B) during 2008-2013. Odds ratio, 95% confidence intervals express the

contribution of each one of the significant risk factors, Z-score and respective p-values are used to determine whether a certain predictor variable is significant or not.

		Herds from Scotland		Herds from LRA England	
Category	Unit	<=0.025	>0.025	<=0.025	>0.025
Herd Size	0-50	0.335	0	0.411	0
	51-100	0.160	0.013	0.201	0.033
	101-200	0.207	0	0.202	0.085
	201-350	0.161	0.324	0.115	0.326
	351-500	0.071	0.216	0.038	0.198
	>500	0.065	0.446	0.033	0.388
Herd Type	Beef	0.270	0.135	0.215	0.143
	Dairy	0.121	0.081	0.215	0.033
	Finishing	0.087	0.189	0.163	0.613
	Store	0.033	0.027	0.072	0.071
	Suckler	0.489	0.568	0.335	0.139
Irish Imports	False	0.968	0.378	0.991	0.832
	True	0.032	0.622	0.009	0.168
Batches from HRAs	0	0.959	0	0.770	0
	1-10	0.041	0.203	0.217	0.009
	>10	0	0.797	0.013	0.991

**Table S3.** Table showing the proportion of herds in Scotland and in LRA England that fall in each category for low (<=0.025) and high (>0.025) herd probabilities of

infection. The herd probabilities of infection were computed using the LRA England model predictor and the 0.025 value was chosen as the threshold that separates a well mixed number of LRA England and Scottish herds from mainly LRA England herds (Figure 4).

## References

- [1] A. J. Hanley and J. B. McNeil, "The Meaning and Use of the Area under a Receiver Operating Characteristic (ROC) Curve," *Radiology*, vol. 143, pp. 29–36, 1982.
- [2] DEFRA-Publications, "The RADAR Cattle Book 2007," 2007.
- [3] J. J. Dziak, D. L. Coffman, S. T. Lanza, and R. Li, "Sensitivity and specificity of information criteria," *PeerJ Prepr.*, 2015.