Risk-based Surveillance for Tuberculosis in Cattle (bTB)

UGW/003/10

The Scottish Government

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The Scottish Government, Edinburgh 2011

This document is available from our website at **www.scotland.gov.uk**.

ISBN: 978-1-78045-248-7 (web only)

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St Andrew's House
Edinburgh
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Produced for the Scottish Government by APS Group Scotland
DPPAS11761 (06/11)

Published by the Scottish Government, June 2011

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1. PROJECT INFORMATION

1.1 Project Title : Risk-based surveillance for Tuberculosis in cattle (bTB)
1.2 Commission Number : CR/2009/47
1.3 Project Manager (Co-ordinator for large projects) :Martyn Blissitt
1.4 Project start and end dates : April 2010 to March 2011
1.5 Reporting period : April 2010 to March 2011
1.6 Project contractors (Institution and contact names) : Rowland Kao, University of Glasgow

2. EXECUTIVE SUMMARY

Scotland records very few incidences of bTB and the majority of those can be traced back to imports from endemic areas of England, Wales or from Ireland. Scotland has recently been declared as having OTF (officially bTB free) status for the purposes of cattle trading. However, in order to maintain its OTF status Scotland must continue to report few cases whilst maintaining its vigilance to potential new ones. This requires demonstration that new cases will be identified rapidly.

Currently all eligible cattle herds in Scotland are tested on a four-year routine herd testing (RHT) cycle. Four year RHT identifies approximately one third of the incidences of bTB, but accounts for the majority of active screening that takes place. In addition to RHT, all carcasses are inspected at the slaughterhouse for evidence of bTB lesions and this detects around another one third of cases. The remainder of the breakdowns are detected through other forms of surveillance including epidemiological tracings and movement tests.

The aim of this study was to develop a more selective risk-based method of routine herd testing in order to reduce the amount of testing that is undertaken. This should be a supplement to existing surveillance systems, most importantly detection at slaughterhouse. Therefore, a natural consideration of risk targeting is herds that are likely to become infected but unlikely to be detected at the slaughterhouse.

Potential strategies were explored using a stochastic simulation model. These simulations are informed by the probability of breakdowns due to bTB derived from a statistical risk factor model for historical breakdowns in Scotland. A variety of risk-based testing strategies were investigated in combination with slaughterhouse meat inspection. The combination of risk factors that identifies risky herds that are unlikely to be detected at slaughterhouse were defined.

Risk-based surveillance strategies were evaluated by comparing them to a simulated four year testing strategy that mimics current surveillance. The statistic evaluated is the number of infected herds that go undetected (latent infections). The number of undetected infections, number of herds and number of animals tested were compared under different strategies. Strategies were developed that required fewer herd tests and performed better, similar and worse at demonstrating freedom relative to four year testing.

Of the four surveillance scenarios that produce similar freedoms from infection compared to current surveillance, the best gives a 24% saving in terms of the number of herds and animals tested. In this strategy, all herds that slaughter less than 25% of their stock annually or regularly import animals from high risk areas are tested every four years, unless these herds slaughter more than 40% of their stock. This strategy is deemed attractive because it utilizes simple metrics that are easily monitored, and these metrics implicitly reflect the historical risk factor model.

Crucially, under this strategy 35 of the 36 breakdowns that were detected under current four year routine herd testing between 2002 and 2008 would have been required to have been tested. The one that would not have been required to undergo testing slaughters a large proportion of its stock. Therefore, it would have had a high likelihood of being rapidly identified under slaughterhouse surveillance.

Furthermore, this strategy reduces the number of unconfirmed breakdowns or "false positives" by 25%. This saves on the financial and surveillance resources of following up these suspect breakdowns.

Staggered, risk-based timescales for herd testing were explored. However, retaining four year testing of at risk herds was found to be the best solution. This is likely to reflect relative homogeneity in both the risk of infection and the risk of detection at the slaughterhouse.

The strategies modelled in this study are based upon the continued use of the standard tuberculin skin test. Although the skin test has relatively poor sensitivity and requires repeated visits to the farm it does have very high specificity. Sensitivity analysis using the gamma-interferon test produced a very high number of false positives due to the lower specificity of the gamma-interferon test.

As described above, a risk-based surveillance system needs to consider risk of infection and the risk of infection being missed. This study demonstrates that risk of infection is relatively homogeneous, however holdings at greater risk of infection are those that receive animals from high incidence areas. The risk of detection at slaughterhouse is defined by the proportion of stock sent to slaughter. The risk-based system presented here balances the two sources of risk. By discounting the risk of those herds that slaughter more than 40% of their stock annually, this model formalises the current exemptions from surveillance based upon slaughter of stock. This offers a saving of 24% in terms of testing effort and continues to demonstrate freedom from disease. Furthermore, it would have detected almost all breakdowns that were detected under RHT and was robust to a number of assumptions.

Outside of the scope of this report is the monitoring of wildlife and unusual patterns of herd breakdowns, as these were not within the project remit and would require separate analytical tools to those described here. Further, we note that, while these scenarios are robust over the years evaluated, any implemented system should be closely monitored for changes in the epidemiology of the disease in Scotland and as a result of changes elsewhere. An advantage of our approach is that our scenarios are based upon a continuum, so the strategy can be easily adapted should the surveillance goals or the disease situation change.

3. INTRODUCTION TO THE PROJECT AND BACKGROUND INFORMATION

3.1 Brief statement of overall aims of the project, background and objectives

Surveillance for bovine tuberculosis (bTB) in Scotland currently consists of a combination of pre- and post- movement testing of cattle moving from England, Ireland and Wales into Scotland, regular whole herd testing of all herds once every four years, contact tracing and slaughterhouse surveillance. In addition to the previously implemented testing of movements from one and two year whole-herd testing areas in England and Wales, as of 28th February 2010, "a clear (b)TB test prior to movement to Scotland will be required for bovine animals from all 3 and 4 yearly tested herds in England and Wales no more than 60 days before movement and no less than 60 days after any previous test unless: (i) they can be shown to have spent their whole lives in low incidence areas; (ii) they are being sent to Scotland for direct slaughter; or (iii) they are less than 42 days of age (these need to be tested post movement if they originate from a high incidence area)."[1]

Testing and surveillance for bTB in Scotland currently costs government an estimated £2m per annum in testing and compensation costs, with breakdowns identified via a variety of methods (Figure 1). The numbers of new confirmed breakdowns in Scotland are relatively few in number (Figure 1) and there are typically a small number of reactors on these breakdowns, although one breakdown involved 15 of 21 tested cattle. In ongoing breakdowns at that time, 59 of 4958 cattle were reactors. These snapshot figures suggest that, while breakdowns are few relative to the number of cattle tested, a few herds have large numbers of reactors and have the potential to cause further breakdowns, most likely if they sell on cattle to other operations. Strikingly, regular four year herd testing only directly accounts for only 30% (42/137) of breakdowns from 2002 to 2008 (Figure 1).

In 2008 there were 37,932 movements of cattle from England and Wales to Scottish premises recorded on CTS (excluding movements to slaughter), and 6,383 from Ireland (Republic of Ireland and Northern Ireland). A total of 33,355 Agricultural holdings are listed for Scotland in 2008, of which 15,881 are reported as holding stock in the 2008 Agricultural census, for a total cattle population of 1,895,867, all on regular quadrennial testing. Such figures are of course approximate at best. However, given the contribution of regular testing to total breakdowns this suggests that the effort and cost associated with regular herd testing, of the order of over 200,000 cattle per year, may be disproportionate to its impact, even if one considers the additional impact of tracing from breakdowns identified by regular testing. Using identified data on herd risk of infection, the identified risks of infection and ongoing surveillance through slaughterhouse inspection, this study will develop a surveillance strategy based upon risk of infection and detection as an alternative to four year routine herd testing.

Any revised risk-based surveillance would have to continue to provide sufficiently robust evidence to demonstrate official TB freedom (OTF) in Scotland, and cost less than the existing regime, without increasing either the average speed of detection of affected herds, or the expected incidence of breakdowns. Previous work has demonstrated that adopting a risk-based approach to surveillance can dramatically reduce the necessary sampling intensity, and thus the cost, for documentation of freedom from non-highly contagious diseases of livestock.

[1] http://www.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/bTB/premovement/index.htm

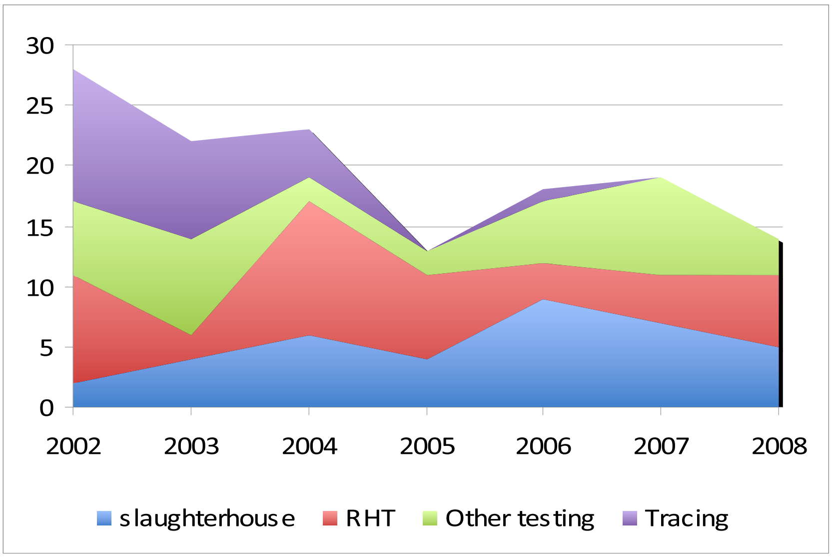

Figure 1. New confirmed breakdowns in Scotland from 2002 to 2008 as of Jan 2009. Breakdowns are attributed to identification at slaughterhouse, regular herd testing (RHT), other regular testing (e.g. post-import Irish testing and post-movement testing) and tracing (Martyn Blissitt, pers. comm.)

3. 2 Staff employed on this project

Professor Rowland Kao (Glasgow, Professor of Mathematical Population Biology), the P.I., is a Wellcome Trust Senior Research Fellow, studying the spread and persistence of infectious livestock diseases (including bTB) in GB.

Dr. Paul Bessell (Glasgow) is the named researcher on the grant, and brings expertise on GIS and spatial statistics, and has worked extensively with Scottish livestock data and the CLAD database describing rural land parcels.

Professor David Logue (Glasgow, Professor of Food Animal Disease) is a highly regarded member of the veterinary profession with detailed knowledge of the cattle industry and the veterinary profession, including over thirty years experience of working with government, the cattle industry and education.

Professor Dominic Mellor (Glasgow, Professor of Epidemiology and Veterinary Public Health) provides expertise on risk-analysis frameworks, surveillance, the interaction between epidemiology and policy, and a working knowledge and experience of cattle farming and slaughterhouse operations in Scotland.

Professor Ivan Morrison (Edinburgh, Roslin Institute, Professor of Immunology) will provide input on cattle immunology, and possible implications of changing the testing regime, including more extensive use of serological testing approaches.

Dr. Richard Orton (Glasgow) is a funded PDRA working on bTB in GB (see below), who will provide input into the further developments of the probabilistic likelihood model described in this proposal.

3.3 Timelines and milestones as in the original proposal.

1. **By Week 2:** meeting with project advisors
2. **Week 2:** decide upon range of risk factors to be initially included in model runs (objective 1, 2 and 3)
3. **Week 4:** complete literature review on bTB testing (objective 4)
4. **Week 12:** incorporation of additional spatial measures – risk by area, risk by spatial association (objective 3)
5. **Week 18:** incorporation of additional demographic factors – cattle age, herd size, herd type (objective 1 and 2)
6. **Week 24:** Determine best fit test sensitivity and specificity under current regime (objective 4)
7. **Week 24:** Initial analysis of risk factors (Objective 5)
8. **Week 26:** progress report in meeting with project advisors
9. **Week 32** Integration of stochastic within-herd simulations into national herd simulation model. (Objective 6)
10. **Week 36:** Analyse different testing regimes (combinations of Gamma-interferon and tuberculin testing) within simulation model (Objective 4).
11. **Week 38:** Development of a preliminary set of surveillance scenarios for further refinement (Objective 7)
12. **Week 44:** Production of final set of surveillance scenarios (Objectives 5, 6, 7)
13. **Week 48** complete forward projection models – what would happen if incidence in GB increases/declines? (Objective 6, 7, 8)
14. **Week 48** meeting with project advisors to discuss direction of final outputs
15. **Week 48** draft version of final report to project advisor for comment and revision of analyses
16. **Week 52** submission of finalised report.

4. RESULTS

These analyses use a stochastic simulation model developed by the Veterinary Laboratories Agency, to calculate the probability of freedom from infection, but refined and tailored to Scottish needs. Probability of freedom is calculated because no holding can be said to be free from infection with 100% confidence. This is due both to the constant risk of infection and imperfect diagnostic tests. This model incorporates data on the risk of infection, the testing regime employed and the efficacy of diagnostic tests to calculate the probability that the herd is free from infection. Based upon analyses of the freedoms of infections of the current surveillance scenarios, risk-based alternatives to current surveillance can be developed. These are developed by adjusting the herds that are tested, and the way in which the surveillance is implemented.

4.1.1 Model description

To demonstrate herd level freedom of infection with bTB during a specified time period (*t*) the model requires that the following parameters are defined by the user:

1. The probability of the herd becoming infected during *t* (*p(Intro)*).
2. The number of animals in the herd (*N*).
3. The bTB surveillance implemented on the farm. Three types of surveillance can be considered
    a. Slaughterhouse meat inspection of animals sent to slaughter.
    b. Part herd testing. However, due to the practicalities of identifying a subset of animals from a herd this is not considered in these analyses.
    c. Whole herd testing. Testing the entire herd.
4. The herd level prevalence of infection p_{star}

The efficacy of the surveillance system is evaluated by calculating the test system sensitivity (se_{system}):

$$se_{system} = 1 - (1 - se_1)(1 - se_2)...(1 - se_n)$$

in which se_1, se_n, are the herd sensitivities of individual components of the test system. The herd sensitivity for a whole herd test is calculated as:

$$se_{herd} = 1 - (1 - se_{animal})^d$$

in which se_{animal} is the sensitivity of the test and *d* is the number of infected animals in the herd defined as:

$$d = N \times p_{star}$$

The sensitivity for a part herd test or the proportion of the herd that is sent to the slaughterhouse is:

$$se_{herd} = 1 - (1 - \frac{n \times se_{animal}}{N})^d$$

where *n* is the number of animals tested.

The corresponding specificity is:

$$sp_{herd} = sp_{animal}{}^n$$

where *n* = *N* for whole herd tests and sp_{animal} is the specificity of the test.

The probability of freedom (the posterior) at *t* is given by:

$$p(free) = \frac{1 - prior_t}{(1 - prior_t) + prior_t \times (1 - se_{system})}$$

where $prior_t$ is the prior probability that he herd is infected. The *prior* for *t+1* is:

$$prior_{t+1} = ((1 - p(free)_t) + p(Intro)) + (((1 - p(free)_t) * p(Intro))$$

4.1.2 Risk of infection

The risk of infection term (*p(Intro)*) for this model is defined by the fitted values from a mixed logistic regression model. The outcome was whether each herd recorded a breakdown in each year between 2002 and 2008. This was tested against a number of putative predictors including the x and y coordinates of the holding (from VetNet), the type of herd (beef, dairy, fattening, suckler or store – from VetNet), the number of animals on the holding on the 1st January that year (from CTS), the number of batches of animals the holding received from high incidence parishes (1 or 2 year testing parishes) in England and Wales in the previous year, and separately whether the holding received animals that originated in Ireland. To allow for clustering at the level of the herd, spatial clustering and temporal clustering, herd nested in parish and the year were included as random effects. The model was reduced and just the predictors that were significant at $p < 0.05$ were included in the final model, interactions and associations between variables were monitored and allowed for where necessary.

The Final model is presented in Table 1. The x and y coordinates were both protective – meaning that the further south and west the greater the risk, however they also had an interaction to allow of clustering in the north-east. Fattening herds were at significantly greater risk than other herd types, as were herds with greater than 100 animals, and herds that received animals from high risk areas including from England and Wales and from Ireland were at increased risk. This includes all cattle that would have spent any time in these areas, including both direct and indirect exposure (i.e. via one or more other premises). The distribution of the fitted values from this model is shown in Figure 2.

Predictor	Unit	Odds (95% CIs)	Z value	P
Intercept			3.948	<0.001
x-coordinate	x/100000	0.010 (0.003, 0.040)	-6.565	<0.001
y-coordinate	y/100000	0.094 (0.046, 0.191)	-6.536	<0.001
Herd type	Other	1		
	Fattening	2.127 (1.293, 3.501)	2.971	<0.001
Size	0 - 9	1		
	10 - 99	0.839 (0.367, 1.921)	-0.414	0.346
	>=100	3.445 (1.749, 6.784)	3.577	<0.001
Movements from HRAs	0	1		
	1 – 10	1.407 (0.883, 2.243)	1.436	0.145
	>10	4.203 (2.503, 7.058)	5.430	<0.001
Irish imports	No	1		
	Yes	6.248 (4.133, 9.445)	8.691	<0.001
x * y		1.851 (1.518, 2.258)	6.075	<0.001

Table 1. Risk factor model for breakdowns in Scotland.

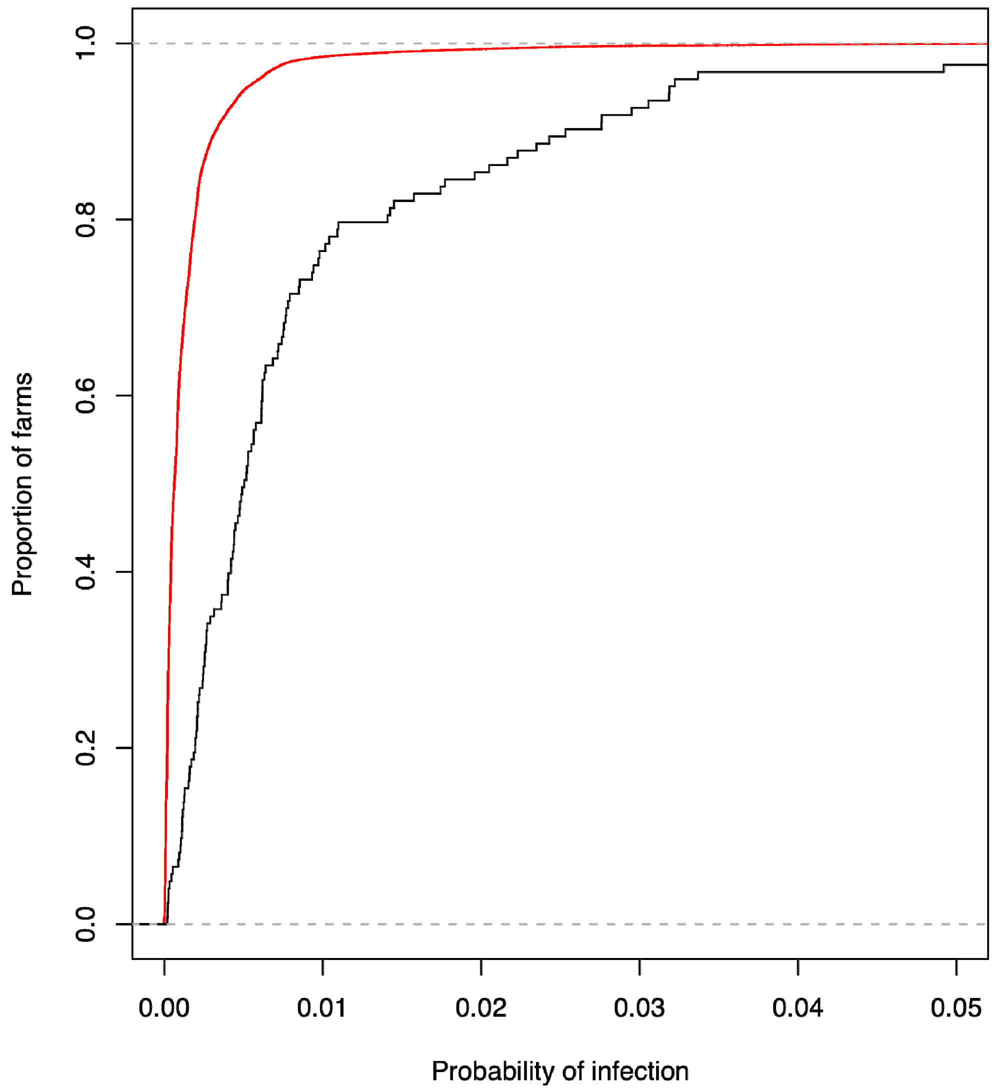

Figure 2. Cumulative distribution plot of the mean of the fitted values for the probability of infection from the mixed logistic regression model of bTB infection between 2002 and 2008. The red line represents non-breakdown herds and the black line herds that did breakdown. The x-axis has been truncated.

4.1.3 Data

The data used in these analyses were derived from VetNet and the British Cattle Movement System (BCMS) Cattle Tracing System (CTS). The following steps were used to derive the data:

1. All herds (identified by CPH number) in Scotland from the VetNet herd table that were active in all years between 2002 and 2008 (inclusive). This comprised 12,016 herds.
2. Of the herds identified above, only those were included that had animals recorded on CTS – this comprised 11,730 herds. For these the number of animals on the herd on January 1st was calculated.
3. Calculating the number of animals sent to slaughter from the herd in each year. A holding is defined as sending an animal to slaughter if

the holding is the last holding on which the animal spent at least seven days prior to slaughter.

4.1.4 Stochastic model implementation

The model was run for Scotland for all years between 2002 and 2008. Proxy data for 1998 to 2001 were derived from the observed data from 2002 and 2003, this was to enable a “burn-in” period for the model to ensure that it was stable for the period of simulation. Model stability was further tested by comparing the results from 2003 to 2008 with those from just 2005 to 2008 in a sensitivity analysis. The defined time period for implementation (*t*) is one year. The derivation of p(Intro) is described above. The actual number of reactors on each holding (*d*) is described by Figure 3a and the herd prevalence (p_{star}) by Figure 3b.

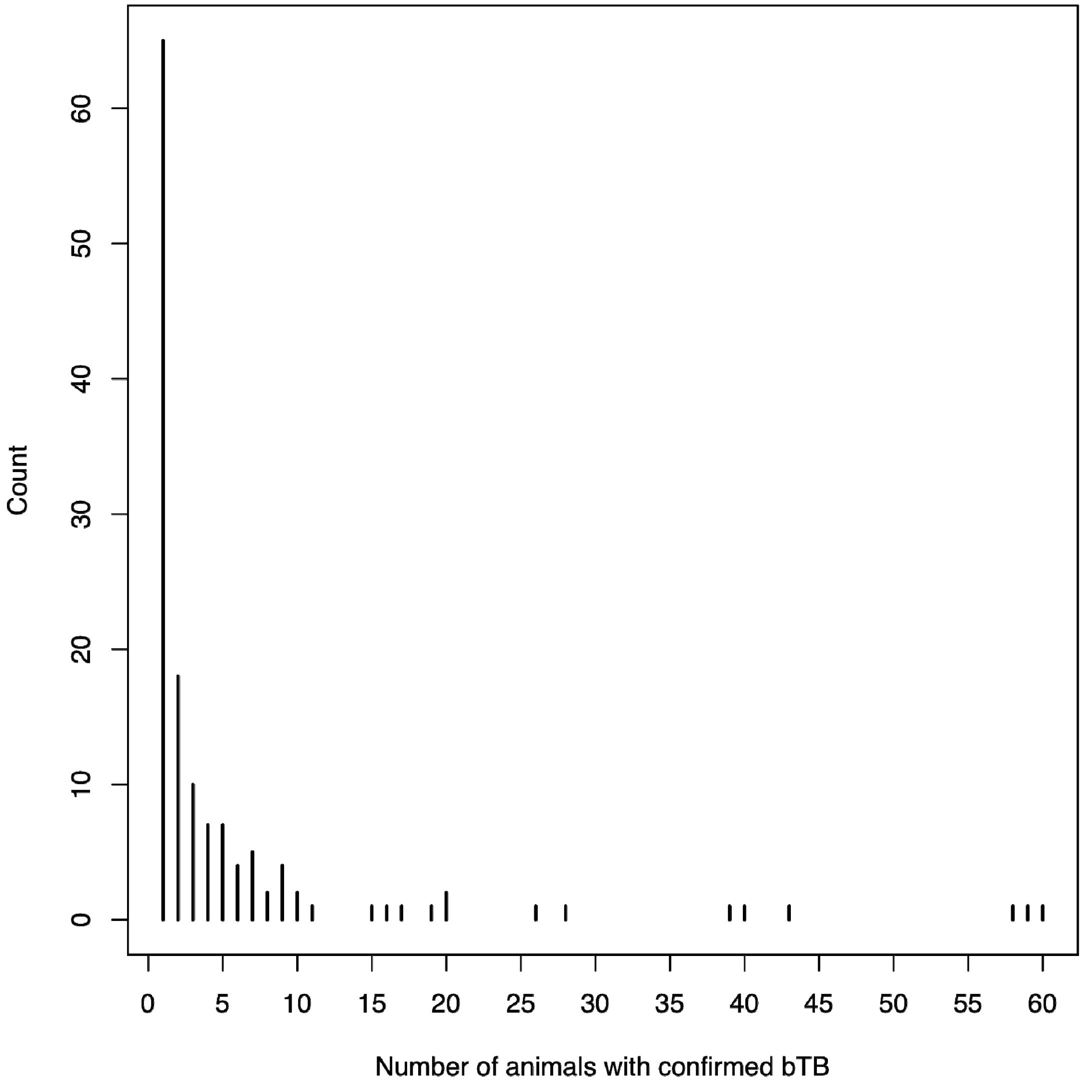

Figure 3a. Distribution of the numbers of animals on each breakdown holding with confirmed bTB on Scottish holdings between 2002 and 2008 inclusive. This comprises the number of reactors at skin test that were confirmed by culture and lesioned animals at slaughterhouse that were confirmed by culture.

The parameter *d* was generated by sampling from a beta(2, 90) distribution (in the beta distribution, the first parameter (α) is equivalent to the putative number of successes – 1, and the second parameter (β) to the putative number of failures - 1), multiplying by the herd size and rounding up to the nearest whole number (generating the parameter *d*). The value of p_{star} is generated by dividing *d* by *N*. the fitted distribution for the Scottish cattle population is shown by Figure 4.

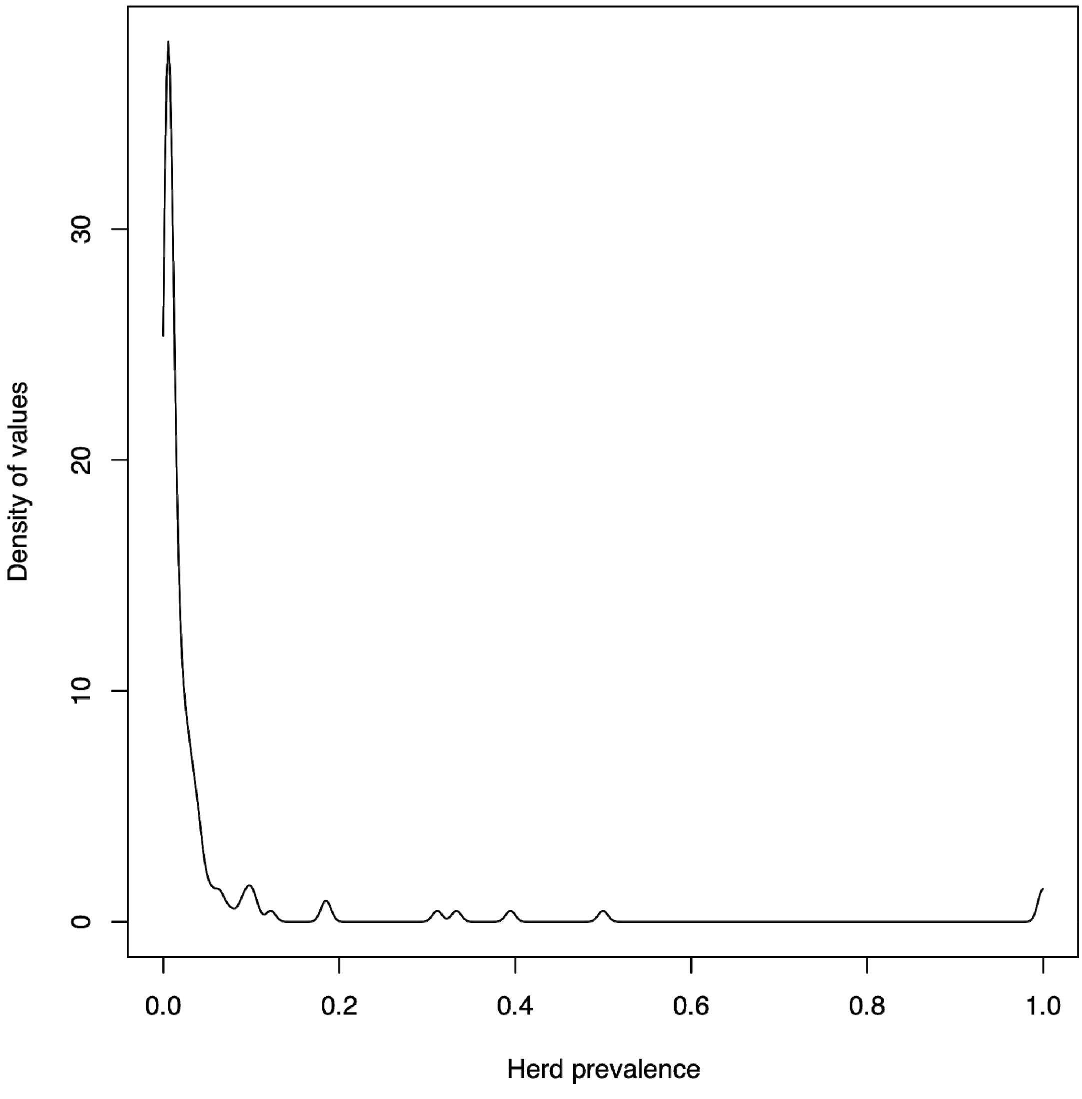

Figure 3b. The herd prevalence for breakdown herds in Scotland.

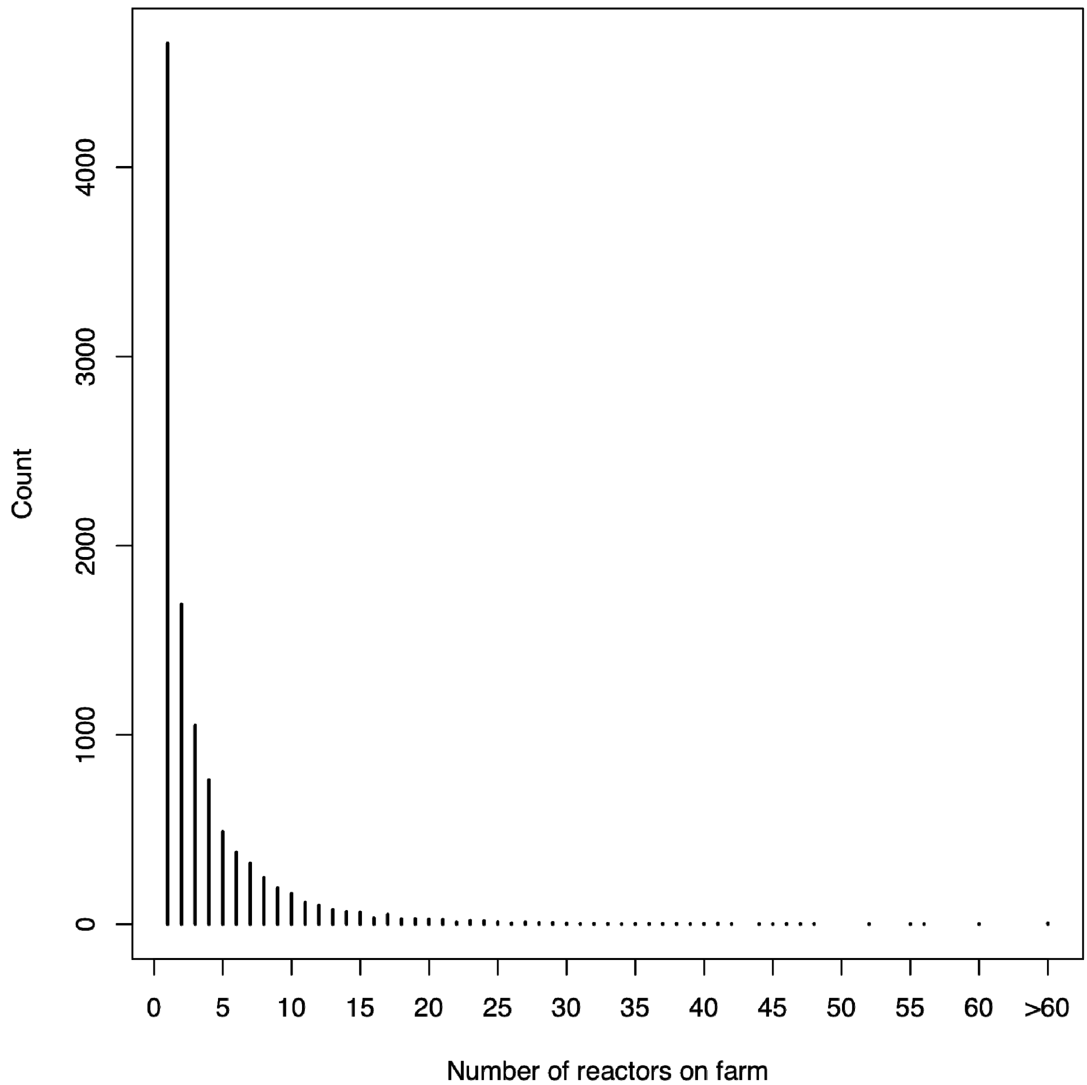

Figure 4. The distribution of the fitted number of infected animals.

The distributions of the sensitivity and specificity parameters are taken from a bTB diagnostic test meta-analysis (Jessica Parry, VLA, personal communication). The mean sensitivity and specificity of the single intradermal comparative cervical test (SICCT - standard implementation) are taken to be 51.11% and 99.58% respectively, described by beta(6.66, 6.37) and beta(1.188, 0.005) distributions. The sensitivity and specificity of the SICCT relate to the effective field values for these tests. For slaughterhouse meat inspection the mean sensitivity is 69.30%, described by a beta(6.784, 3.006) distributions (Figure 5).

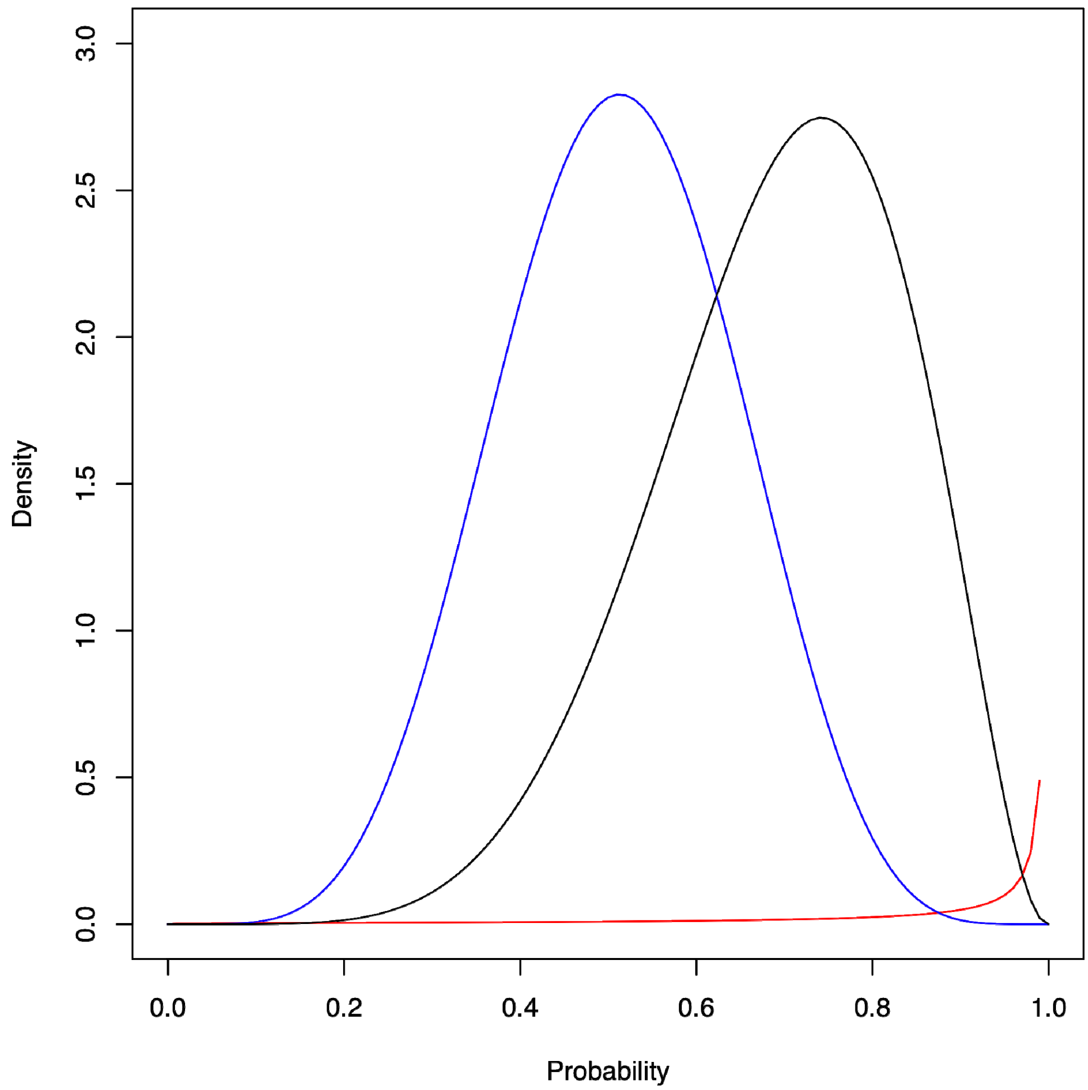

Figure 5. The distribution of sensitivity (blue line) and specificity (red line) for the standard SICCT and the sensitivity distribution of the slaughterhouse meat inspection (black line).

The model was implemented in the R statistical environment and run for 100 iterations. Herd prevalence and test sensitivities were sampled for each holding from the distribution. For whole herd tests over a regular repeat period (such as four year testing) the start year of the herd testing cycle (for instance from between year 1 to four for four year testing) was generated randomly for each distribution.

As 2002 was the first year for which there was actual data and as this was a “rebound year” from the 2001 Foot and Mouth Disease epidemic the statistics from this year were found to be unstable. As a result the fitted values from 2002 were discarded.

4.1.5 Variables

A number of risk-based surveillance options were explored based upon both how likely a holding is to become infected and how likely an infection is to be detected at the slaughterhouse. We require that any system replacing RHT would need to largely identify the same set of breakdowns; it is less important to check the herds that would be identified by other means such as slaughterhouse inspection, expected to continue under any new system. The following were identified as likely determinants of the risk of detection:

1. The size of the holding.
2. Whether or not it is a dairy holding.
3. The proportion of stock that is sent to slaughter.
4. Where the holding sources its stock – whether the holding is buying in animals from high risk (one year testing) areas in England, Wales and Ireland.

These variables were plotted against the baseline risk from slaughterhouse surveillance and combined to understand their importance in determining missed infections at slaughterhouse.

4.1.6 Scenarios

Three different baseline scenarios can be modelled based upon an annual timeframe for surveillance and assuming that slaughterhouse surveillance will continue:

1. Minimal model – slaughterhouse surveillance only.
2. Current scenario – four year and slaughterhouse surveillance.
3. Maximal model – annual whole herd testing and slaughterhouse surveillance.

The maximal and minimal scenarios represent the bounds for what can be achieved in this model. Herds with a low probability of disease freedom in the minimal model are those that should be targeted in any risk-based surveillance scheme. The risk-based combinations will be compared with the current (four year testing) surveillance scenario. This represents the scenario that is to be improved upon (if possible). Depending on whether the herd is deemed to be at-risk and the identified level of risk (herds may have different level of risk assigned), the following timeframes for testing were explored:

1. Four year testing for all risk herds.
2. Staggered four and two year testing depending upon the level of risk.
3. Staggered four, two and one year testing depending upon the level of risk.

4.1.7 Statistics

The key statistics for evaluation of the effectiveness of the surveillance strategy were the number of infections that are detected and the number of infections that remain undetected. The objective of the study was to ensure that these statistics remain similar to or at a better level than the current surveillance effort whilst testing fewer herds and animals.

The number of latently infected premises was derived from 1-p(free). The following were calculated over the period 2003 – 2008 (2002 is dropped as a burn-in):

1. The number latently infected in 2008.
2. The annual mean between 2003 and 2008.
3. The minimum and maximum value between 2003 and 2008.

The total number of detected breakdowns in each year between 2003 and 2008 was calculated as the difference between the model prior and posterior. The difference between the number detected by the different scenarios being explored and the current surveillance, and between the minimum surveillance (slaughterhouse only) and scenarios explored. This gives a measure of the relative improvement in the different scenarios. The total number of false positives (i.e. unconfirmed reactors) was calculated for each year as the sum of the herd specificity. This tells us the sampled number of herds recording one or more reactors.

Additionally, it is important to identify whether herds that recorded a historical bTB breakdown are included under risk-based surveillance. Therefore, the proportion of herds that had confirmed bTB that are included in the risk-based surveillance system was calculated. In particular, the number of breakdowns that were first detected at RHT were calculated. From the VetNet test table those confirmed breakdowns that were inconclusive by RHT at first test and later confirmed were identified and included in these counts.

The probability of freedom is derived from the risks of infection and the probability of detection at the slaughterhouse. Therefore, combinations of risk-based surveillance mechanisms will be derived by exploring combinations and cut-offs of the risk factors defined in 4.1.5. Depending upon the temporal window for surveillance and the herds selected for surveillance, the risk-based surveillance models were evaluated to test whether they are better, similar or worse than current surveillance. By identifying scenarios that require fewer annual tests than current surveillance, the following scenarios will be evaluated relative to the number of latent infections produced by current surveillance:

1. <u>Improved detection</u> The mean number of latently infected herds is more than 5% lower than produced by current surveillance. This can only be achieved using a temporal window that includes surveillance over periods lower than 4 years.
2. <u>Similar surveillance</u> The mean number of latently infected herds is within 5% of the current surveillance, for fewer herds tested.
3. <u>Lower detection surveillance</u> The mean number of latently infected herds is between 5% and 15% greater than current surveillance, the latter figure taken as a cut-off above which no surveillance system would be considered.

Thus, three scenarios can be developed that ensure that at worse any selected system will be no more than 15% less effective than current surveillance. Following identification of the optimum from each category the three strategies will be further analysed.

4.1.8 Risk combination searching

In order to find the best combination of these risk factors for surveillance, the relationship of these factors was analysed against the probability of freedom following slaughterhouse only surveillance. Subsequently, the combinations of these factors were analysed by constructing matrices in which:

- The rows are cut-offs for the ratio of stock to slaughter. Herds below the cut-off are tested.
- The columns are the herd size cut-offs. Herds larger than the cut-off are tested.

The systems are explored using a simple point system in which points are assigned for having the risk factor in question. Four different combinations of the risk factors described in section 4.1.5 were explored:

1. A baseline matrix in which one point is awarded for each of the ratio slaughtered and herd size. This produces a two-point scale.
2. Three matrices incorporating herd size, ratio slaughtered and the number of batches of movements from high incidence areas between 2002 and 2008 – 1, 2 and 3 batches (one point each for: being below the ratio, being above the herd size and having imported more than the number of batches of animals). This produces a three-point scale.
3. One point is awarded for each of herd size and the optimal high risk move cut-off identified above. This is reduced by 1 point for having slaughtered more than 25% of stock. This produces a three-point scale.
4. One point is awarded for each of being a dairy herd, the ratio slaughtered and the optimal high risk move cut-off identified above. This produces a three-point scale.

These scenarios will be explored across three different temporal windows:

1. Four year testing for all herds that score > 0 on the risk scale above.
2. Four year testing for all herds scoring one point, two year testing for those scoring two or three.
3. Four year testing for all herds scoring one point, two year testing for those scoring two, one year testing for those scoring three.

This produces 18 separate analyses – each of the six analyses above (these are from points 1-4 above with point 2 comprising three analyses) replicated for each of the three temporal windows outlined above in section 4.1.8. The following statistics will be calculated for each of the 18 matrices:

- The annual mean number of latently infected premises for each year between 2003 to 2008.
- The number of herds tested in each year.
- The number of animals tested each year.
- The number of bTB incidences and the number of RHT detected breakdowns that would have tested under these criteria between 2003 and 2008.

These matrices will be evaluated in terms of the three scenarios– the improved detection, similar surveillance and lower detection surveillance. These will be identified through analysis of the mean latent infections and the number of herds tested and the number of breakdown identified.

4.1.9 Assumptions

These analyses are dependant upon a number of assumptions:

1. That all herds are tested. Some herds are eligible for no eligible stock (NES) status. These are herds that have a high turnover of stock (typically specialist fattening herds) and are indirectly incorporated in these analyses by incorporating slaughterhouse inspections.
2. The entire herd is tested under routine herd tests. Under current surveillance in four year testing areas only breeding bulls, females that have calved and younger animals that have been bought in and could be used for breeding (and are over 42 days of age) are eligible for testing. In these analyses comparison between testing strategies is made on the basis of all animals being tested, this requires that differences in the distribution of eligible stock does not have a significant impact on the analysis.
3. That slaughterhouse meat inspection will continue to be carried out in the same manner as is currently employed.
4. That current "additional" tests will continue to be used such as tracings, pre- and post-movement tests and post-import tests.
5. The temporal windows remain the same. The model is run between 2003 and 2008, however sensitivity to this time period should be invested.
6. The standard interpretation of the SICCT is the only appropriate test. In a very low prevalence setting such as Scotland in which a large number of tests are being conducted near perfect specificity is essential. The SICCT is the only test that offers this, however, sensitivity analysis will be run using the Gamma Interferon test that offers better sensitivity but lower specificity.
7. The high risk areas in England and Wales will remain the same, and that all of Ireland will remain under one year testing.
8. That it is more important to minimise the number of herds being tested rather than the number of animals tested.

9. All testing is random and independent. For example, while there will be some variability in the test sensitivity and specificity, this is not meaningfully clustered, and therefore no herds or herd types have an inherently higher sensitivity than others. It is also assumed that consecutive tests occur with a sufficient gap between them, so that the result of the second is uncompromised by the first.

Sensitivity of the resulting models to these assumptions are explored in appendix 1.

4.2 Results

4.2.1 Basic models

The results of the three baseline scenarios – the maximal, minimal and current surveillance models are presented in Figure 6 and the results summarised in Table 5.

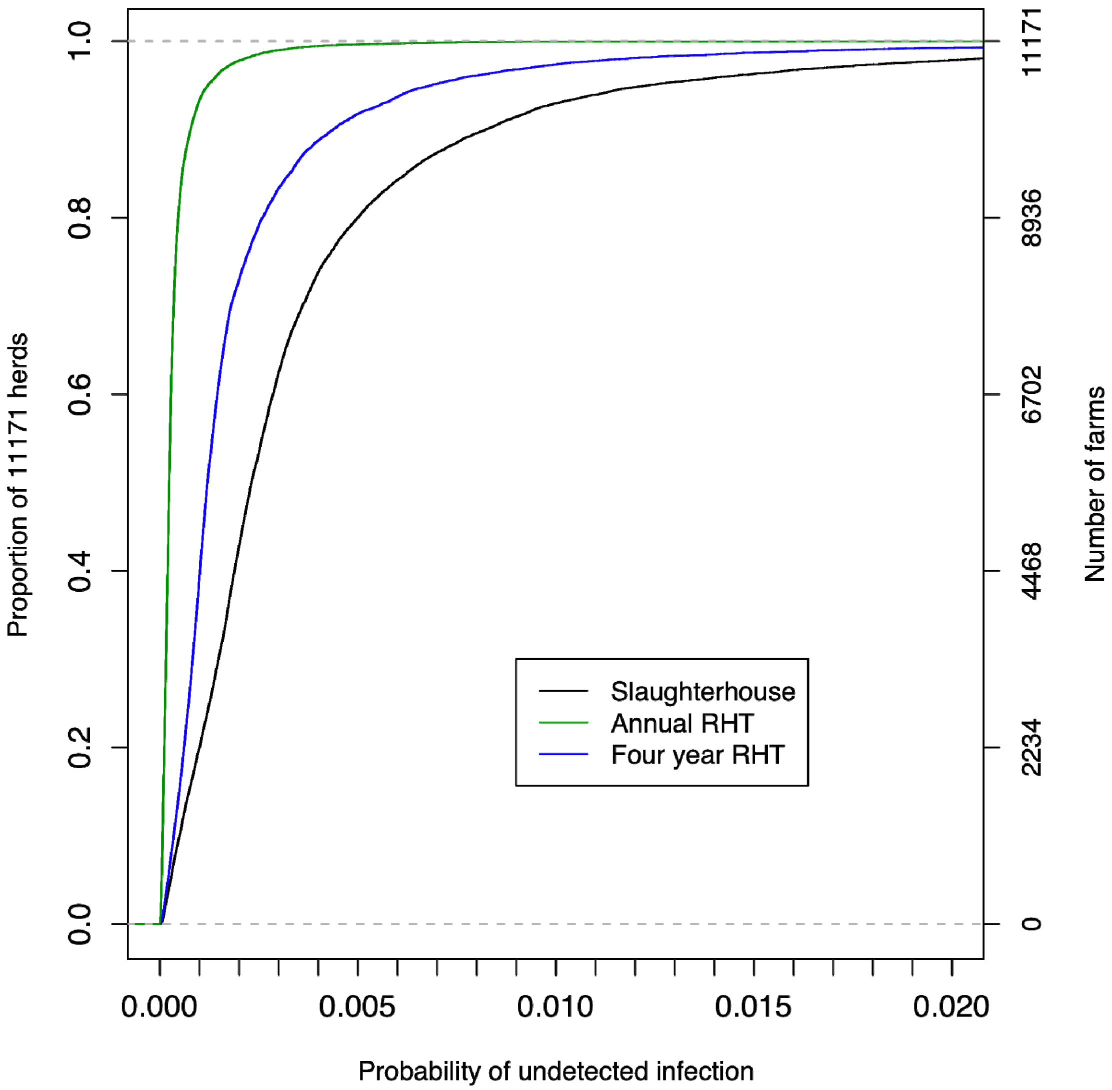

Figure 6. Cumulative distribution plot of the three baseline models.

From the null (slaughterhouse only) model it can be seen that herds that recorded a breakdown had a lower probability of freedom from infection than those that did not record a breakdown (Figure 7).

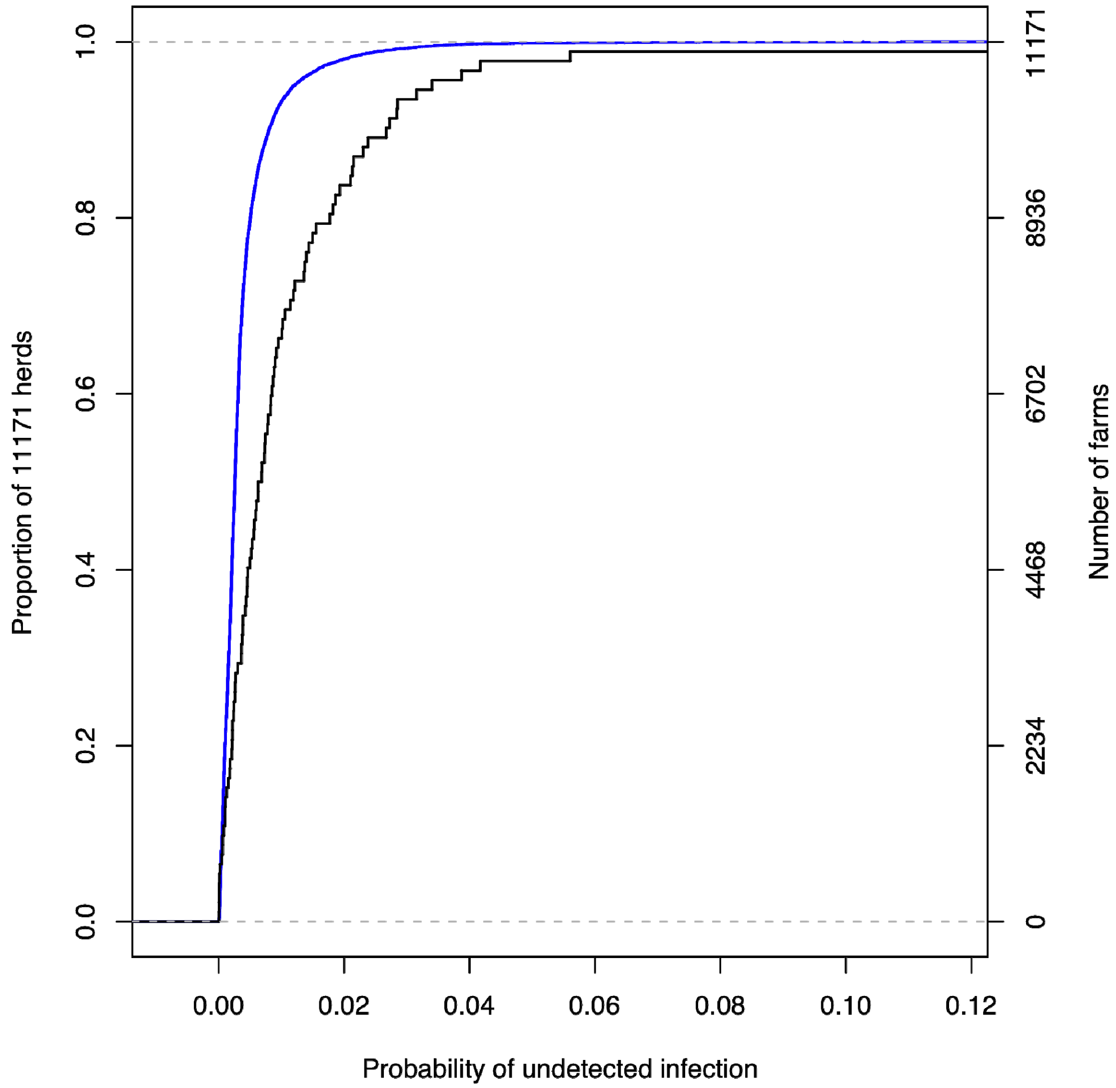

Figure 7. Cumulative distribution plot of the distribution of minimum probability of freedom from the slaughterhouse surveillance only model. Blue line is non-breakdown herds, black line is herds that recorded a breakdown.

4.2.2 <u>Factors for risk-based models</u>

The characteristics of herds that have a low probability of freedom from slaughterhouse surveillance alone must be analysed in order to identify the types if herd that require surveillance. The following are analysed in relation to the probability of freedom from slaughterhouse surveillance only:

1. The herd size.
2. The herd type.
3. The proportion of the herd that is slaughtered.
4. Receiving animals from high incidence areas either directly or indirectly.

Analysis of the mean number of animals sent to slaughter per year during the period 2002:2008 against the mean herd size on January 1st shows a linear relationship with distinct clustering of fattening and dairy herds (Figure 8). Dairy herds tend to have fewer per capita movements to slaughter, while Fattening herds tend to have more.

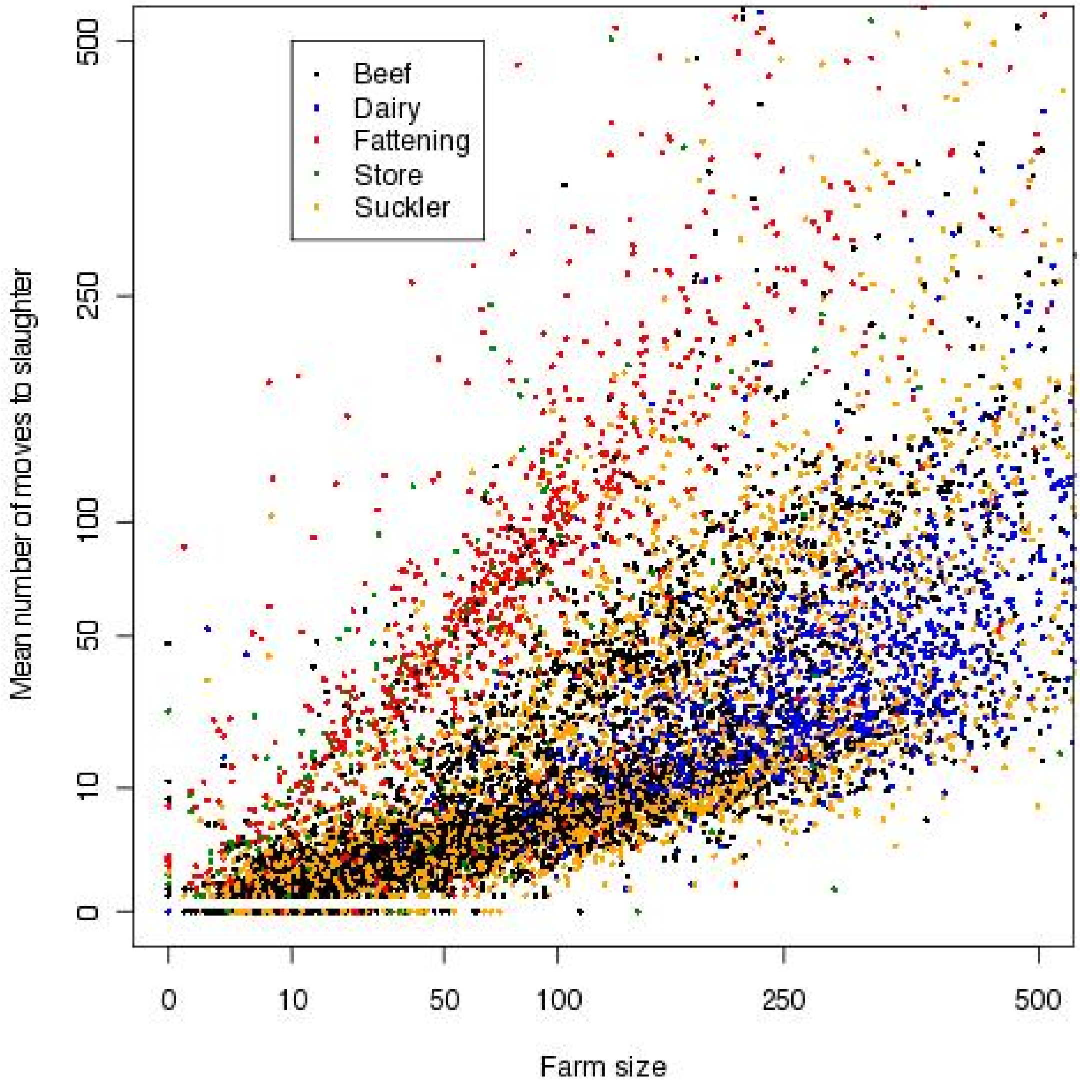

Figure 8. Scatterplot showing farm size on January 1st against the mean number of animals moved to slaughter between 2002 and 2008 broken down by herd type as listed in VetNet. The axes have been truncated for clarity

When plotted against the freedom of infection following slaughterhouse only surveillance, holdings that slaughter a smaller proportion of their stock have a lower probability of freedom (Figure 9).

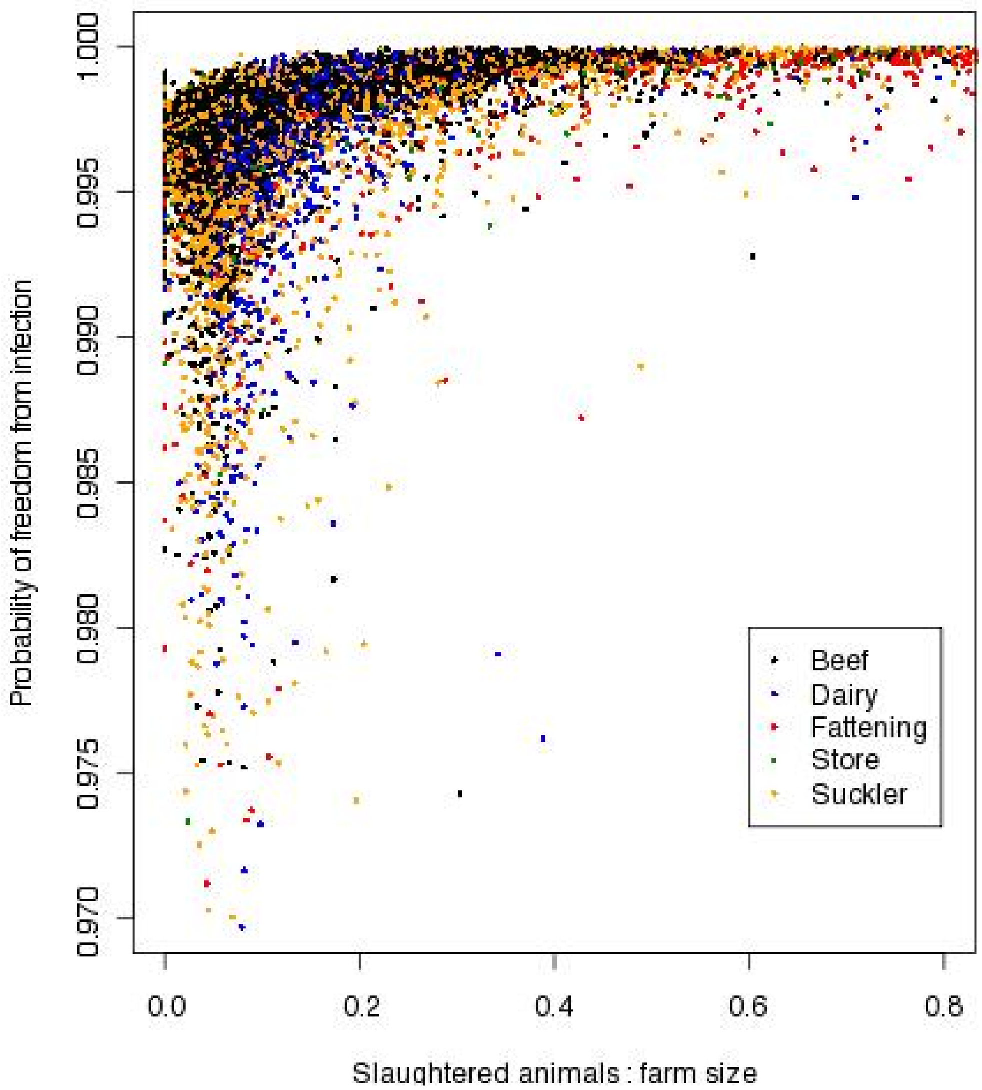

Figure 9. Plot of the ratio of slaughtered animals to probability of freedom from infection. Note the axes on this plot have been truncated to ease interpretation. The axes have been truncated for clarity.

While not a particular risk group for acquiring infection, when the probability of freedom is broken down by farm type from VetNet it is clear that this probability is substantially lower for dairy holdings, than for the other holding types (Figure 10).

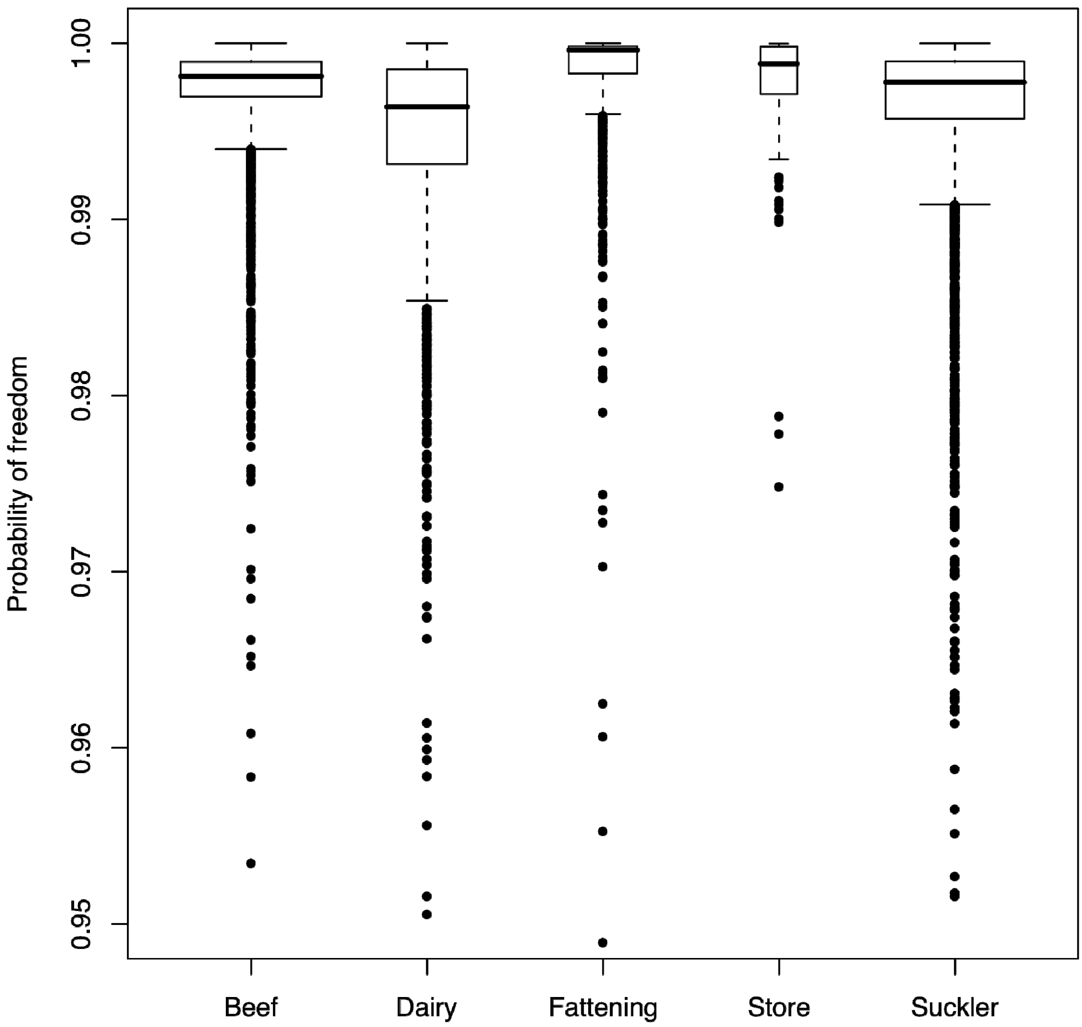

Figure 10. Boxplot of probability of freedom from the slaughterhouse only model in 2008 by herd type. Box widths represent the proportion of data in that category. The y-axis has been truncated for clarity.

Furthermore, and not independent of the dairy relationship (dairy farms generally being larger premises) larger farms also have a lower probability of freedom (Figure 11). However, this is not as important as might be expected considering that herds with more than 100 animals have more than a 3x greater probability of infection from the risk factor model (Table 1).

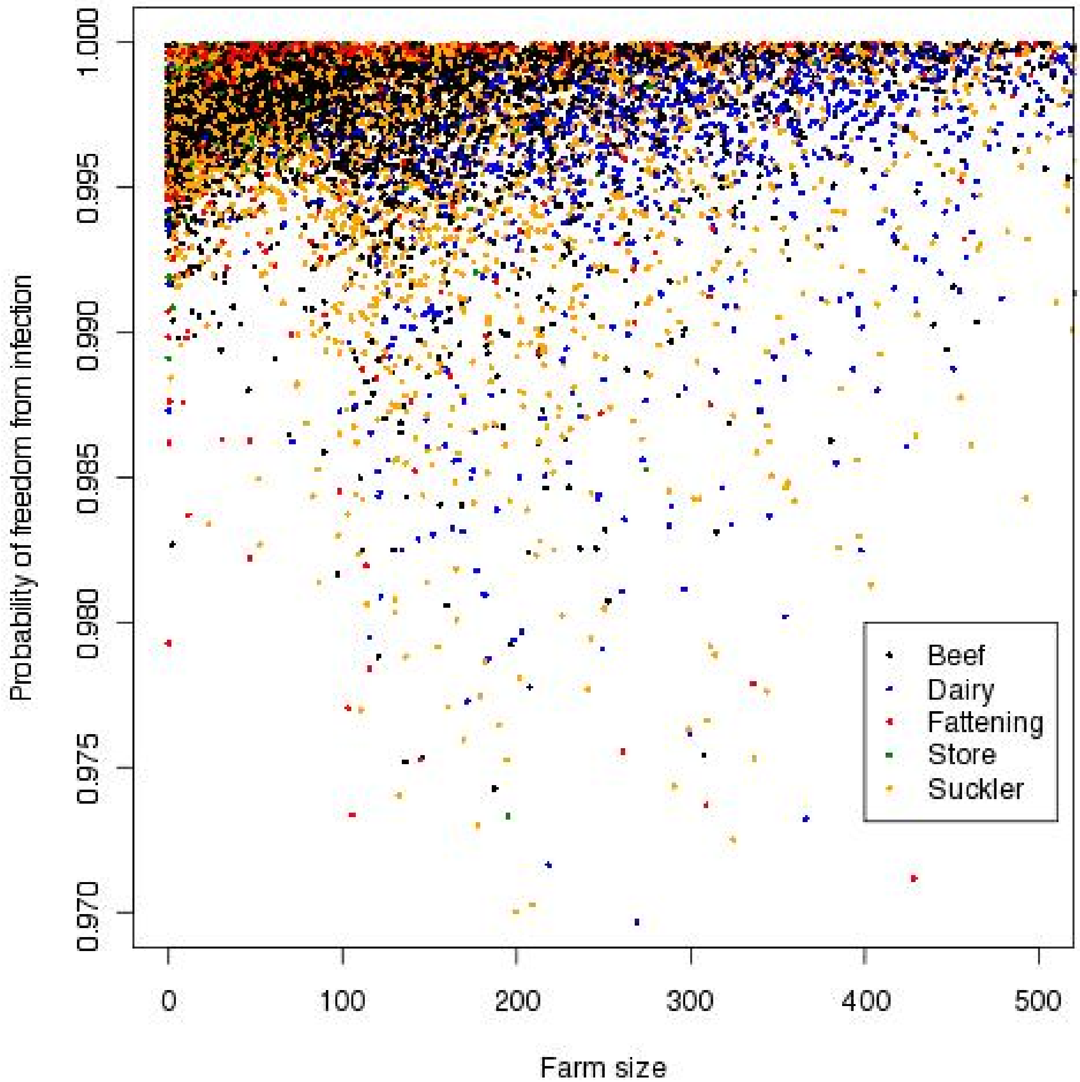

Figure 11. Boxplot of the farm size categories by probability of freedom in 2008 from slaughterhouse only surveillance. Axes have been truncated for clarity.

An analysis of the number of years in which holdings received animals from high incidence areas in England, Wales and Ireland shows a decrease in the probability of freedom as the number of years goes up (Figure 12). Furthermore, there is a marked step increase in risk (particularly noting the tail of the distribution) at 3 batches.

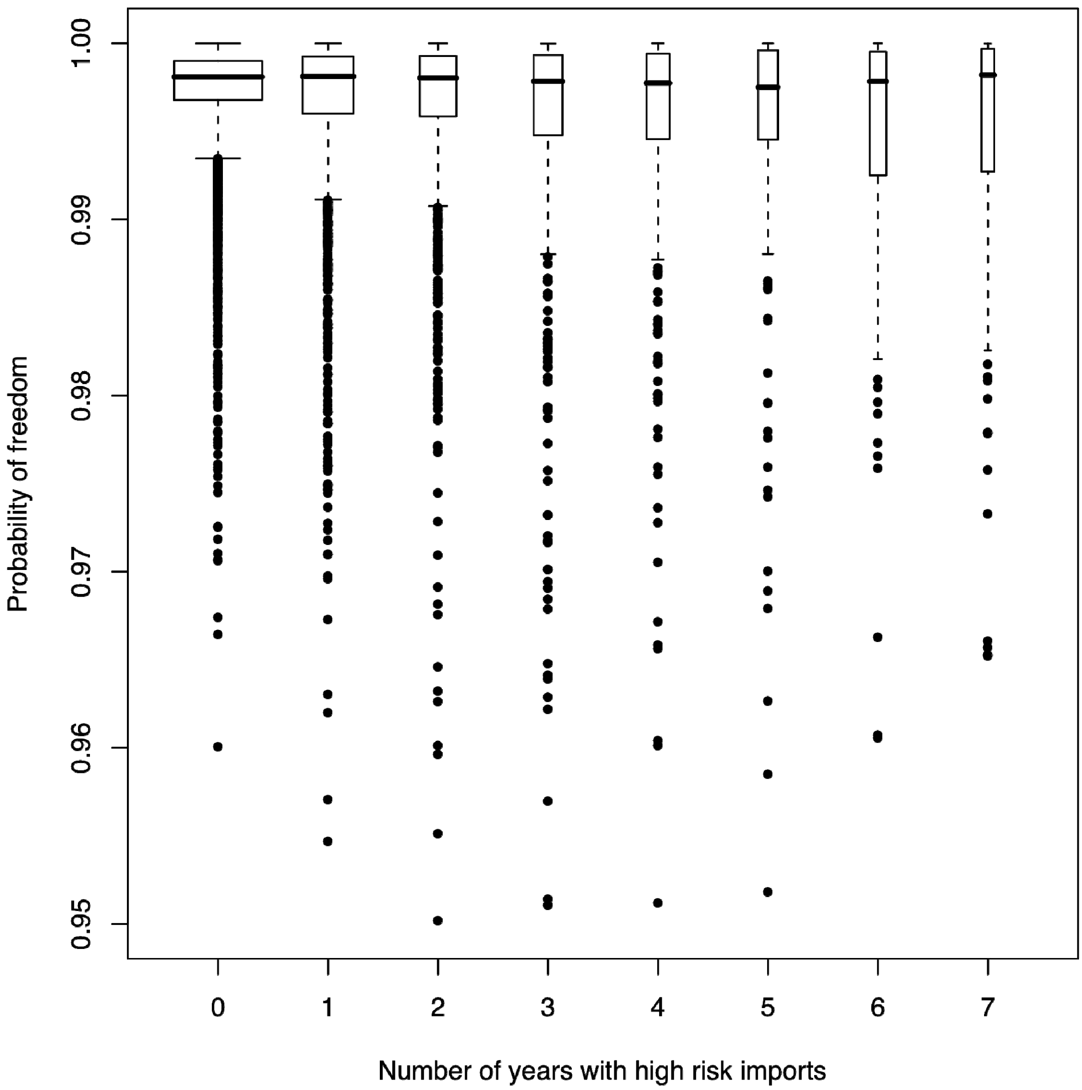

Figure 12. The probability of freedom by slaughterhouse surveillance in 2008 by the number of years in which animals were bought on to the farm from high incidence areas. The box widths represent the relative proportion of data points in each group. The y-axis has been truncated for clarity. When these categories are analysed in terms of the number of bTB breakdowns and the number that were identified by RHT whilst the proportion in each category declines, the percentage of bTB incidences remains similar (Table 2).

Number of years HR animal imports	Number of herds (%)	bTB (%)	RHT
0	6677 (56.9)	18 (18.4)	7
1	2119 (18.1)	9 (9.2)	4
2	1097 (9.4)	15 (15.3)	7
3	690 (5.9)	8 (8.2)	3
4	438 (3.7)	6 (6.1)	1
5	333 (2.8)	12 (12.2)	8
6	224 (1.9)	11 (11.2)	3
7	152 (1.3)	19 (19.4)	3

Table 2. The numbers of years with high risk imports on to a holding by whether the holding recorded an incidence of bTB.

From these analyses it can be seen that there is a relationship between herd size and the probability of freedom from infection following slaughterhouse surveillance. However, the key determinants are the ratio of herd size to animals slaughtered, dairy herds and receiving animals from high incidence areas. Combinations of these factors that determine risk of detection will be explored below.

4.2.3 Risk-based methods

From the matrix analysis of these risk measures, four different scenarios have been identified for further consideration. These are the optimal testing scenarios for the better, similar and lower detection scenarios (two lower detection scenarios presented) are:

1. Better: A two-point scale with testing of herds that score one point on a four year cycle and testing herds that score two points on a two year cycle. All other herds are not tested. Points are allocated as follows:
    - + 1 point for slaughtering fewer that 25% of stock.
    - - 1 point for slaughtering more than 50% of stock.
    - + 1 point for bringing on high risk animals in three or more years between 2002 and 2008.
2. Similar: Four year testing for herds that score one or two points. All other herds are not tested. Points are allocated as follows:
    - + 1 point for slaughtering fewer that 25% of stock.
    - - 1 point for slaughtering more than 40% of stock.
    - + 1 point for bringing on high risk animals in three or more years between 2002 and 2008.
3. Lower detection 1: Four year testing for herds that score one or two points. All other herds are not tested. Points are allocated as follows:
    - + 1 point for slaughtering fewer that 12.5% of stock.

- - 1 point for slaughtering more than 25% of stock.
- + 1 point for bringing on high risk animals in three or more years between 2002 and 2008.

4. Lower detection 2: A three-point scale with testing of herds that score one point on a four year cycle, testing herds that score two points on a two year cycle, and annual testing of herds that score three points. All other herds are not tested. Points are allocated as follows:
    - + 1 point for slaughtering fewer that 5% of stock.
    - - 1 point for slaughtering more than 25% of stock.
    - + 1 point for bringing on high risk animals in three or more years between 2002 and 2008.
    - + 1 point for having more than 100 animals

    The ratio of animals slaughtered to herd size is calculated from the total over the period 2002:2008. By doing this, herds are classified into one risk category for the entire period rather than a variable risk category depending upon the classification for that or the pervious year.

Including dairy as an additional risk factor and adjusting the slaughterhouse ratio cut-offs accordingly produces results that were very similar to those presented above. This is because the majority of dairy herds are included in the listed factors in the model above (Table 3) and so the dairy categorisation was left out for parsimony.

Two lower detection scenarios were selected because scenario one requires that fewer herds are tested (lower detection 1). However under lower detection two 33 of the breakdown herds that were detected by RHT between 2002 ans 2008 would continue to be tested, compared to 21 under lower detection 1 one (Table 4).

	Non-risk (%)	Risk (%)
Beef	757 (16.6)	3807 (83.4)
Dairy	143 (10.1)	1275 (89.9)
Fattening	872 (80.4)	212 (19.6)
Store	176 (54.0)	150 (46.0)
Suckler	840 (19.4)	3498 (80.6)

Table 3. The breakdown of risk category from the “similar” surveillance strategy broken down by VetNet herd type.

	Better		Similar		Lower 1		Lower 2	
Points score	Number of herds (%)	bTB (RHT)	Number of herds (%)	bTB (RHT)	Number of herds (%)	bTB (RHT)	Number of herds (%)	bTB (RHT)
0 (Not tested)	2687 (22.9)	26 (1)	2788 (23.8)	29(1)	4658 (39.7)	55 (15)	4971 (42.4)	19 (3)
1	8052 (68.6)	52 (26)	7951 (67.8)	49 (26)	6350 (54.1)	27 (15)	5340 (45.5)	58 (22)
2	991 (8.4)	20 (9)	991 (8.4)	20 (9)	722 (6.2)	16 (6)	1288 (11.0)	20 (11)
3	NA	NA	NA	NA	NA	NA	131 (1.1)	1 (0)
Total	**11730**	**98 (36)**	**11730**	**98 (36)**	**11730**	**98 (36)**	**11730**	**98 (36)**

Table 4. The points allocation for the four scoring systems described above. This is broken down by the number and percentage of herds falling into each score level ("Number of herds" columns). The "bTB (RHT)" columns gives the numbers of herds with each points score that recorded bTB breakdowns and the number of these breakdowns were detected by RHT.

The comparison of these four risk-based surveillance systems to the baseline scenarios is presented in Figure 13. These results are summarised in Table 5. Better surveillance is achieved through testing slightly fewer herds and animals. Reproducing similar levels of detection to those seen currently can be achieved through testing 697 fewer herds and 122,184 fewer animals.

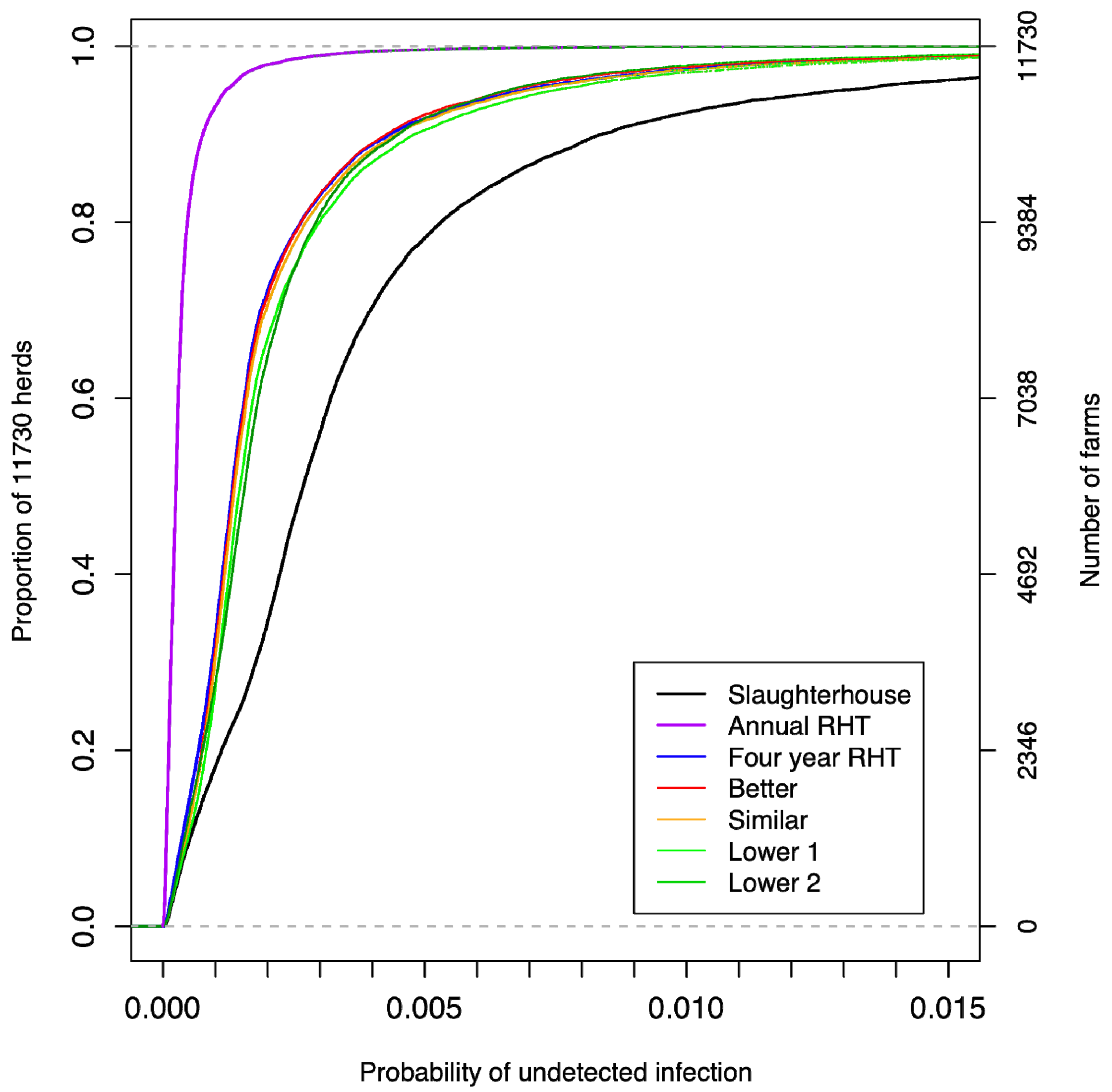

Figure 13. Cumulative distribution function of the latent (undetected) infections from the risk-based surveillance systems. The x-axis has been truncated for clarity.

Surveillance scenario	Interval	Herds tested	Cattle tested	Number detected (out of 98 breakdowns)			Latent infections			False positive herds ie UC Breakdowns
		pa	Pa	Total	Difference[1]	Additional[2]	2008	mean	Min, max	2008
Baseline scenarios										
Slaughter-house only	NA	0	0	76.25	NA	NA	43.60	33.78	19.67, 48.89	NA
Current	4 yr	2,933	439,292	95.08	NA	NA	19.00	16.96	9.98, 25.85	64.27
Maximum	1 yr	11,730	1,757,168	104.39	NA	NA	2.81	2.69	1.58, 4.72	255.19
Risk-based scenarios										
Better	2/4yr	2,509	388,812	96.59	1.51	20.34	17.62	16.03	9.26, 25.70	56.03
Similar	4yr	2,236	317,108	94.53	-0.55	18.28	19.74	17.51	10.24, 26.78	48.69
Lower detection 1	4yr	1,768	209,425	92.81	-2.27	16.56	21.71	18.86	10.93, 28.80	37.37
Lower detection 2	1/2/4 yr	2,110	441,823	95.17	0.09	18.92	19.56	17.30	10.30, 26.95	53.86

[1] The difference between the number detected for this scenario and the number of breakdowns detected under the "current" surveillance strategy.
[2] The additional detections above slaughterhouse detections.

Table 5. Summary of test results. The current system and the recommended system are highlighted.

4.2.4 Sensitivity analyses

The full sensitivity analysis is presented in Appendix 1, but are summarised here.

1. Adjusting the herds and the numbers of animals that were tested does not substantially change the results above. These adjusted counts include 197,102 animals on 2,576 herds for the current four year RHT. The performance of the risk-based surveillance mechanisms does not change substantially relative to the current four year RHT.
2. With the exception of the second lower-detection scenario there was no sensitivity to the adjustment of the temporal window from 2003 to 2008 to 2005 to 2008. In the second lower detection scenario there was a large increase in the number of herds and animals tested. This is likely to reflect a change in herd level demographics to include more large herds.
3. Implementation of these scenarios using the Gamma-Interferon test shows a slight improvement in disease detection (from 95.08 using SICCT to 97.70) due to the improved sensitivity of Gamma-Interferon. However due to the low prevalence and the large numbers of animals being tested the lower specificity there produces an unacceptably large increase in the number of false positive herds (from 64.27 under SICCT to 2137 using Gamma-Interferon).

4.2.5 Summary of results

1. Risk-based surveillance can be as or more effective at detecting infections than the current 4 year RHT.
2. The levels of detection under current surveillance can be replicated by testing 76% of the herds and animals. This strategy would have included all but one of the breakdowns that were identified through RHT and in the model provides statistically equivalent results.

5. CONCLUSIONS

5.1 Discussion

In this project, a model of holding level risk of infection with bTB was developed to demonstrate that certain holdings are at greater risk of infection with bTB than others. The predictors of infection included the size of the herd and the number of batches of animals being bought on to the holding from high incidence areas in England, Wales and Ireland.

Once the risk of infection had been established on individual holdings a simple surveillance model was developed to model the risk of undetected infections. This model is populated with data derived from the BCMS to determine the holding size and the number of animals being sent to slaughter either directly or indirectly. It was used to explore the current surveillance systems, the baseline being slaughterhouse meat inspection based upon the number of animals being sent to slaughter. These results were analysed to identify the types of holdings that had a low probability of freedom following this baseline surveillance. The indicators of surveillance that were identified were the proportion of animals that were sent to slaughter, herd size (or being a dairy herd) and the number of high risk imports. By searching through combinations of these factors at different levels, four different risk-based surveillance models were developed. However, three of these scenarios were very similar and differed only in terms of the cut-off for the proportion of slaughtered animals. The better, current and one of the lower detection scenarios were based upon the proportion of stock slaughtered and the number of batches of high-risk animals moving on. The only scenario that differed was the second of the lower detection scenario that included the testing of large herds as well as those that slaughter few animals and import animals from high incidence areas.

Three different testing regimes were investigated: the current four year testing and two staggered systems: one, two and four year testing and two/four year staggered testing. Different solutions emerged from these testing windows, although they suggest that current four year testing is the most effective. Increasing the frequency of testing according to the level of risk does not necessarily improve the probability of freedom from disease. This reflects the relative homogeneity in risk of infection from the risk factor model, so there is insufficient information on the likelihood infection to produce a pay-off from more frequent testing.

The developed scenarios combine the probability of being detected at slaughterhouse with the probability of becoming infected from risk factor analysis. Whilst there were a number of risk factors in the model, the only one that went on to be included in the analysed surveillance strategies was bringing on animals from high risk areas, measured simply as the number of years in which animals were brought onto the herd. Of the seven years between 2002 and 2008 imports in one, two and three of those years were explored and three was found to be the best cut-off. Using one or two as the cut-off left too many animals being tested. However, under these scenarios if a herd slaughters sufficient stock it will still have a lower surveillance category irrespective of the number of years with imports from high risk areas. A total of 1,843 herds import animals from high incidence areas, of which 1,267 would be tested under this strategy, the remainder slaughter more than 40% of stock and are exempt. By testing herds that slaughter less than 25% of stock per year this ensures that all herds that have a mean turn-over period of more than four years ensures that those herds that would not replace their stock over the testing period in question.

During the period 2003 to 2008 there were 98 breakdowns; 32 of the cases were identified by slaughterhouse and 36 by RHT. However, despite comprising only RHT and slaughterhouse surveillance, the model predicts around 95 cases detected (Table 5). This is because the remainder of the surveillance is made up of other types of testing not made up for here, such as pre- and post-movement tests and tracings. As these are not included in this analysis the model is allowing for their detection at slaughterhouse or by routine surveillance at a later time point.

Of the four scenarios developed there were two scenarios that produced up to 15% lower surveillance. Two “lower” scenarios were chosen for illustration because they offered different advantages. Lower detection one misses 15 of the herds that were detected by RHT but involved many fewer tests, while lower detection two performed better but required the testing of many more animals (Table 4). The similar and the better detection scenarios were variants of each other and both detect 35 of 36 RHT breakdowns. Therefore, the “similar” scenario that requires less testing is recommended. The distribution of the herds tested on a four year cycle under this strategy is presented in Figure 14 and it can be seen that a large number of the holdings that are exempt from testing are in the north-east.

Figure 14. The distribution of the at risk farms from the similar scenario. Red points represent at risk farms, black points represent not-at-risk holdings.

This risk-based system detects all bar one of those that were detected by RHT even when testing significantly fewer herds every year. The one missed turned over 78% of stock to the slaughterhouse annually, so would likely have been detected by slaughterhouse testing and not gone on to cause further undetected infection. When the similar risk system is broken down by herd type it can be seen that the majority of fattening herds are not included in the risk system, whilst the majority of dairy herds are (Table 3). This is due to the large proportion of stock that fattening herds send to slaughter.

The recommended solution requires the continued implementation of the standard SICCT and has the disadvantages of requiring repeat visits to the farm and poor sensitivity. However, at present there are no credible alternative tests. The mean specificity of the Gamma-Interferon test is 96.6% (appendix 3). Whilst the improved sensitivity of the test means that there is greater detection, the lower specificity in a low prevalence setting with a very large number of animals means that around 50% of herds are returning at least one false positive. A number of serological tests are being developed, however, these tests either have a lack of data for estimating field specificity, or have a low specificity similar to the Gamma-Interferon. However, the development of such tests and test combinations should be continually monitored and tested to investigate whether they offer an improvement to the scenarios presented here.

The surveillance scenarios presented here are taken from a continuum and the scenarios can be adapted and tailored to specific needs, or if the goal of the surveillance strategy were to be changed. For instance, it may be desirable to test herds that import animals from high incidence areas and slaughter under 25% of stock on a two year cycle as an incentive to change farmers' sourcing policy. By testing these farms on a two year cycle still leaves a saving in terms of herds tested – 2,483 herds per year rather than 2,933 with all herds under four year testing. In these analyses the risk status of the herd is established and remains for the entire period. An appropriate interval over which the risk category is to be reassessed must be identified.

5.2 Consequences

These surveillance systems are very effective at ensuring that not only are the herds with the highest risk of harbouring infected tested, but also herds that recorded a breakdown are detected, thereby validating the model. In addition to this, the improved targeting of surveillance means that fewer false positives are produced. As the strategies are based upon the proportion of stock slaughtered, herds that are not detected by routine surveillance are sending sufficient animals to slaughter to ensure that the slaughterhouse picks up infections.

These strategies depend on the model assumption that herd composition is homogeneous, particularly regarding the ages of animals, that the animals are recycled with equal probability and that all animals in the herd are at equal probability of infection. In reality, a number of herds, particularly suckler herds may have a number of considerably older animals that could harbour infection for a long time without their infection being detected. In such instances this system requires that infection is passed to another animal for detection at the slaughterhouse.

Differences in the risk of infection for animals of different ages is one of the reasons for the selection of animals for RHT. If the heterogeneities described above were a major problem with these analyses then the sensitivity analysis would have showed differences when herds and numbers of animals from VetNet were included in the analysis. However, the model was robust to this interpretation of the data. Furthermore, there were no substantial changes to the results when the period of analysis was changed from 2003-2008 to 2005-2008, suggesting that the model is robust to the timeframe employed (appendix 1). The sensitivity analysis also shows that the cut-off for the number of movements from high-incidence areas in previous years can be scaled according to the time frame being used.

These models have demonstrated that a risk-based surveillance strategy can save surveillance effort and ensure that freedom from endemic disease can be demonstrated. However, this model has only considered the routine herd surveillance with the back-stopping of slaughterhouse surveillance, and therefore requires that current slaughterhouse surveillance remains at least as vigilant as the current levels. While infected animals that pass through the slaughterhouse obviously have no further impact, they are useful sentinels for infected herds, triggering a chain of testing on the source farm and subsequent tracings that identify further breakdowns. This chain is not explicitly modelled here since the risk-based system effectively replicates the triggering mechanism.

Slaughterhouse surveillance will be assisted by pre-movement testing which will minimise the movement of infected animals between holdings within Scotland. Pre- and post-movement testing is also routinely carried out on imports from England and Ireland. In spite of these movement tests, the risk factor model demonstrates that the type of holdings that import higher risk animals are more likely to become infected, however, these holdings should be tested by the risk-based RHT in addition to continued pre and post movement testing. Thirty five out of 36 breakdowns that were identified by RHT are included in the “similar” surveillance strategy. However, only 18 out of 32 slaughterhouse identified breakdowns and 6 out of 14 tracings are included for RHT surveillance in the “similar” risk-based system and therefore, these other testing systems must continue to be implemented, in order to detect these breakdowns.

5.3 Recommendations

The ‘similar’ scenario offers a saving of 24% of the surveillance effort whilst not compromising the current detection effectiveness. Such recommendations are based on historical patterns of breakdowns, and ongoing monitoring of the situation in Scotland is required. If necessary, the thresholds in the system may be adjusted to match changes in the disease situation. As well as being a surveillance system that reduces the surveillance effort required, this system offers formal quantification to the policy of not testing high throughput NES herds and could replace the use of NES status.

Outside of the scope of this report is the monitoring of wildlife and unusual patterns of herd breakdowns, as these were not within the project remit and would require separate analytical tools to those described here. Further, we note that, while these scenarios are robust over the years evaluated, any implemented system should be closely monitored for changes in the epidemiology of the disease in Scotland and as a result of changes elsewhere. An advantage of our approach is that our scenarios are based upon a continuum, so the strategy can be easily adapted should the surveillance goals or the disease situation change.

6. COMMUNICATED OUTPUTS

6.1 Refereed Publications :

At this stage, two reports are being drafted for peer review. First, a risk factor analysis for breakdowns in Scotland, and second, the risk-based surveillance strategy. Both will be submitted to the Scottish government at a preliminary stage.

6.2 Popular and trade articles :

6.3 Presentations at scientific meetings :

The results of this project have been accepted for an oral presentation at the International Conference on Animal Health surveillance meeting to be held in Lyon, France, in May 2011 (www.animalhealthsurveillance.org)

6.4 Other reports/publications/communications :

6.5 Technology Transfer:

6.6 Patents applied for :

7. RESOURCES

7.1 Project spending for the lifetime of the project in the same format as the costs shown in the contract

7.2 Investigators funded by this project, and related studentships

See section 3.2 above for all staff funded.

7.3 Other staff contributing to this project

None.

8. ACKNOWLEDGEMENTS

Dr. Jessica Parry at the VLA, Dr. Angus Cameron (AusVet Animal Health Services) for use of the surveillance model, and the meta-analysis of test results.

9. Appendix 1– sensitivity analysis

Sensitivity of the risk-based surveillance scenarios that were developed to the following situations has been investigated:

1. Demographics. Excluding herds with no eligible stock (NES) status and excluding stock not eligible for RHT surveillance. These herds and numbers of animals were identified from the VetNet test table based on the RHT testing history between 2002 and 2008.

2. Adjusted temporal windows to check for the impact of changes in the force of infection over time. Rather than evaluating over the period 2003-2008, the time period was reduced to 2005-2008.

3. The use of the Gamma-Interferon tests - a more sensitive but less specific test than the SICCT.

1. Demographics

From the VetNet herd test table, records for routine herd tests in Scotland between 2002 and 2008 were extracted. For each herd the maximum number of animals tested at RHT was calculated, herds that are exempt from testing record a zero in this field. The model for the four risk-based surveillance scenarios was remodelled using these numbers as the number of animals tested and herds with no animals tested were excluded. Thus, the herd prevalence remained the same, but it was assumed that just the animals at risk of having disease were tested.

The results are shown in Figure 1 and Table 1. The difference between the risk-based scenarios and the current surveillance strategy in terms of number of herds tested is lower, but the risk-based scenarios still represent a saving in terms of surveillance effort. The “similar” risk-based scenario gives a saving of around 20% in terms of number of herds tested. Therefore the strategies appear to be robust to the assumption of including all animals and tests in the strategies.

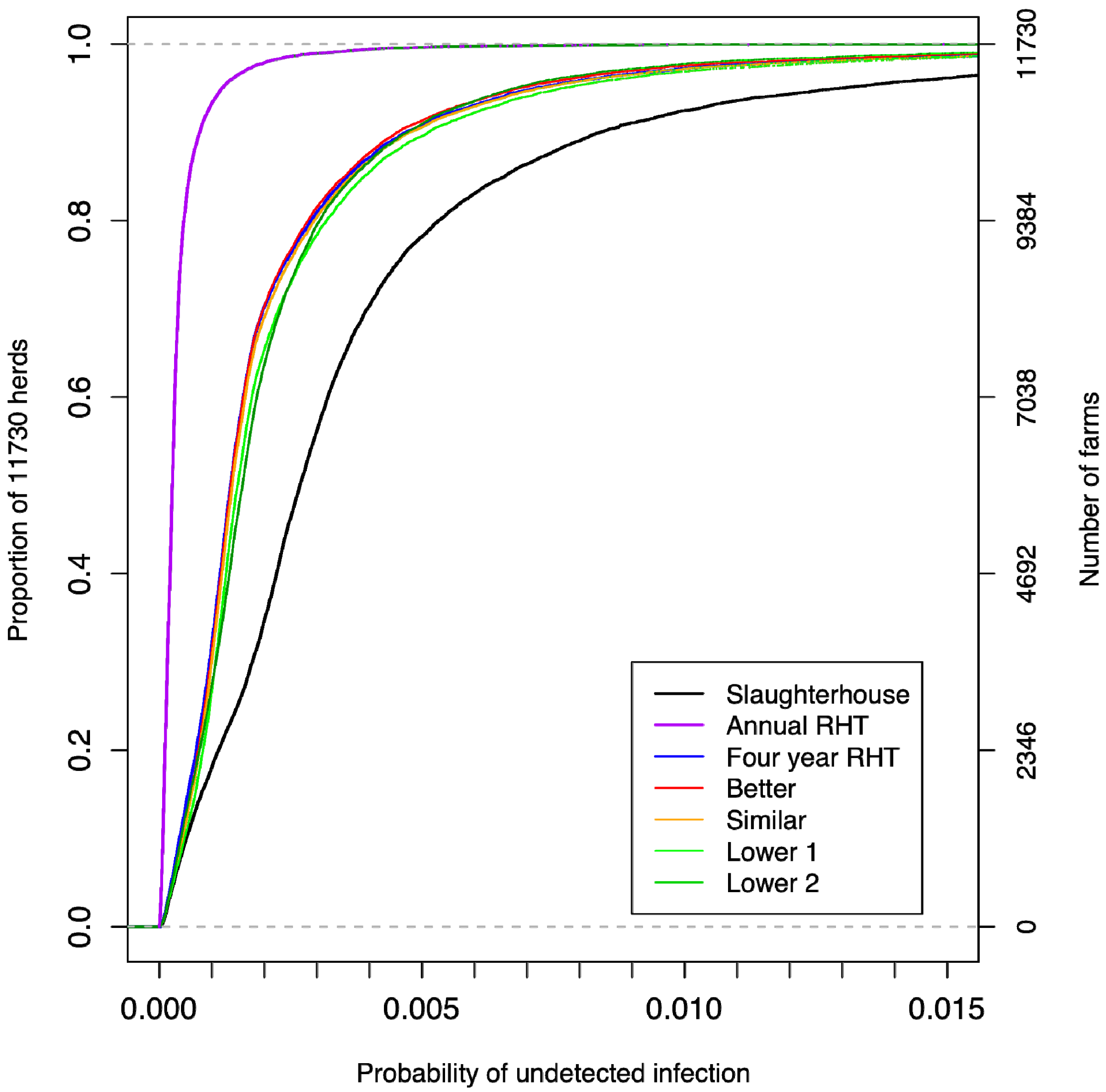

Figure 1. Cumulative distribution plot of the four scenarios with the revised number of herd and animal tests.

Surveillance scenario	Interval	Herds tested	Cattle tested	Number detected out of 98 breakdowns			Latent infections			False positive herds i.e. UC breakdowns
		pa	Pa	Total	Difference[1]	Additional[2]	2008	mean	Min, max	2008
Baseline scenarios										
Slaughter-house only	NA	0	0	76.25			43.60	33.78	19.67, 48.92	NA
Current	4 yr	2,576	197,102	94.23			20.28	17.86	10.48, 27.21	51.95
Maximum	1 yr	10,304	788,406	104.40			2.80	2.68	1.58, 4.70	206.74
Risk based scenarios										
Better	2/4yr	2,406	193,454	94.95	1.72	19.69	18.63	16.78	9.72, 26.62	50.22
Similar	4yr	2,141	160,325	93.83	-0.40	17.57	20.81	18.27	10.69, 27.88	42.70
Lower detection 1	4yr	1,688	112,724	92.16	-2.07	15.91	22.71	19.56	11.35, 29.82	34.17
Lower detection 2	1/2/4 yr	2,002	200,114	94.55	0.33	18.30	20.53	17.97	10.71, 27.83	45.30

[1] The difference between the number detected for this scenario and the number of breakdowns detected under the "current" surveillance strategy.
[2] The additional detections above slaughterhouse detections.

Table 1. Summary table for the revised results following adjustment of the number of herds and animals tested according to previous RHT surveillance.

2. <u>Temporal window</u>

Adjustment of the temporal window to include analysis of just 2005 to 2008 required a reduction in the acceptable number of high risk imports from 3 to 2 to allow for the change in window. The “better” scenario became better still at detecting breakdowns, at the cost of testing more herds, as did the lower detection 2 scenario (Figure 2 and Table 2). However the “similar” and lower detection 1 scenario remained similar to that form the 2003 to 2008 window.

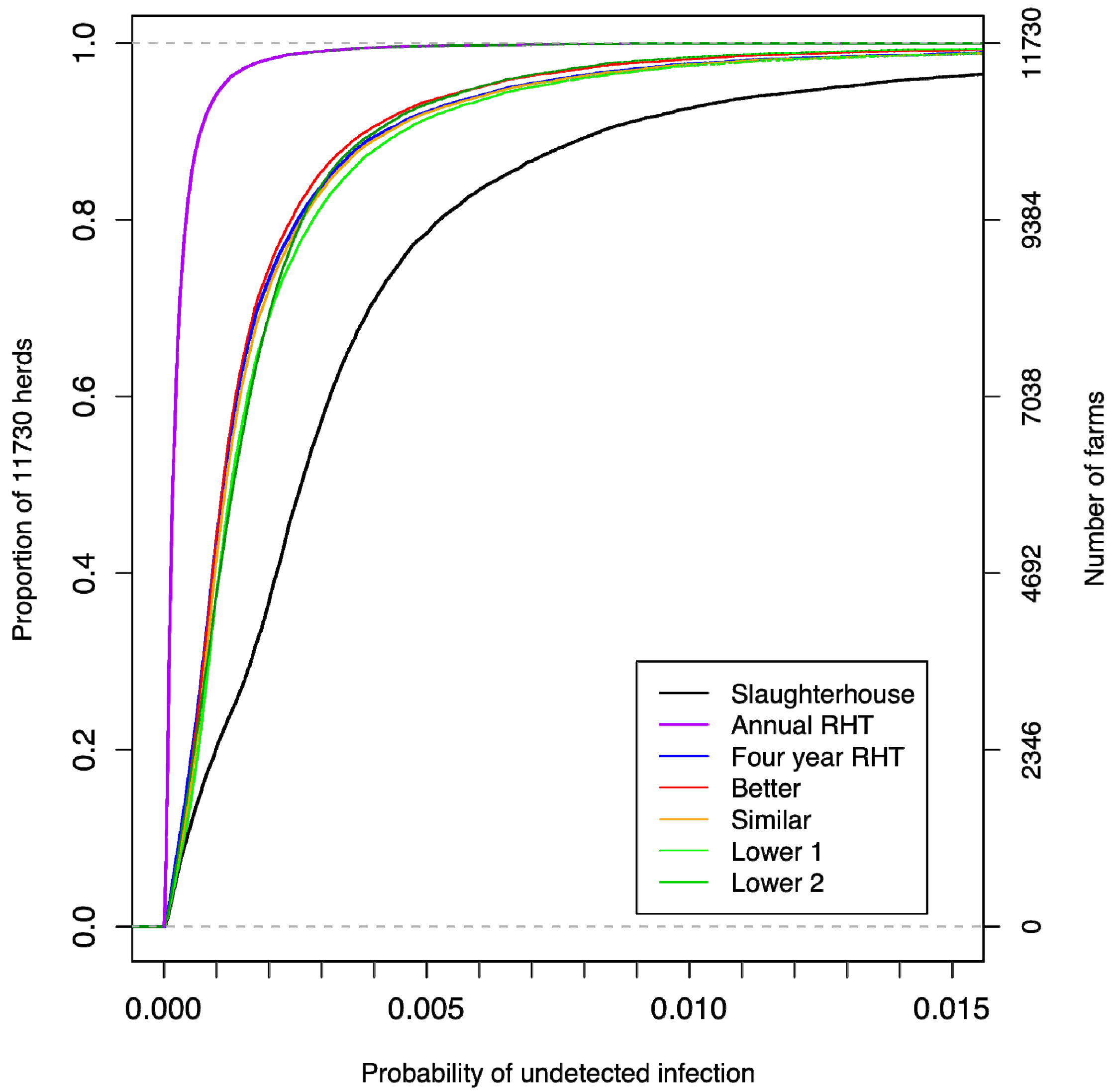

Figure 2. Cumulative distribution plot of the four scenarios with the reduced temporal window of 2005 to 2008.

Surveillance scenario	Interval	Herds tested pa	Cattle tested Pa	Number detected out of 98 breakdowns *			Latent infections			False positive herds i.e. UC breakdowns
				Total	Difference[1]	Additional[2]	2008	mean	Min, max	2008
Baseline scenarios										
Slaughter-house only	NA	0	0	55.42			43.60	38.29	29.14, 47.92	NA
Current	4 yr	2,933	439,292	68.31			19.04	18.20	13.30, 24.60	63.80
Maximum	1 yr	11,730	1,757,168	71.62			2.81	2.72	1.83, 4.03	256.5
Risk based scenarios										
Better	2/4yr	2,770	441,682	69.93	1.62	14.51	16.23	15.92	10.94, 22.47	58.70
Similar	4yr	2,290	327,842	68.28	-0.03	12.86	19.57	18.72	13.63, 24.82	50.02
Lower detection 1	4yr	1,865	234,331	67.79	-0.52	12.37	20.92	19.96	14.57, 26.34	39.00
Lower detection 2	1/2/4 yr	2,493	518,573	69.04	0.72	13.61	18.02	17.30	12.29, 23.63	61.06

[1] The difference between the number detected for this scenario and the number of breakdowns detected under the "current" surveillance strategy.

[2] The difference between this and the number of breakdowns detected under the "current" surveillance strategy. The additional detections above slaughterhouse detections.

* Breakdowns between 2003 and 2008.

Table 2. Summary table for the revised results following alteration of the temporal window to 2005 to 2008.

3. <u>Sensitivity to diagnostic test choice</u>

Different diagnostic tests are available for bovine TB, one of which is the Gamma Interferon test. The mean sensitivity and specificity of the Gamma Interferon test are 86.19 and 96.63% respectively. The distributions are described by a beta(30.147, 4.831) and a beta(219.149, 7.623) for the sensitivity and specificity respectively (Figure 3). Adjustment of the surveillance strategy to incorporate the Gamma Interferon test rather than the SICCT does not result in substantial changes in terms of the number of true positives (Figure 4 and Table 3). The main change with the use of the Gamma Interferon relative to the SICCT scenarios is the large increase in the number of false positives, which is due to the poorer specificity of the Gamma Interferon test.

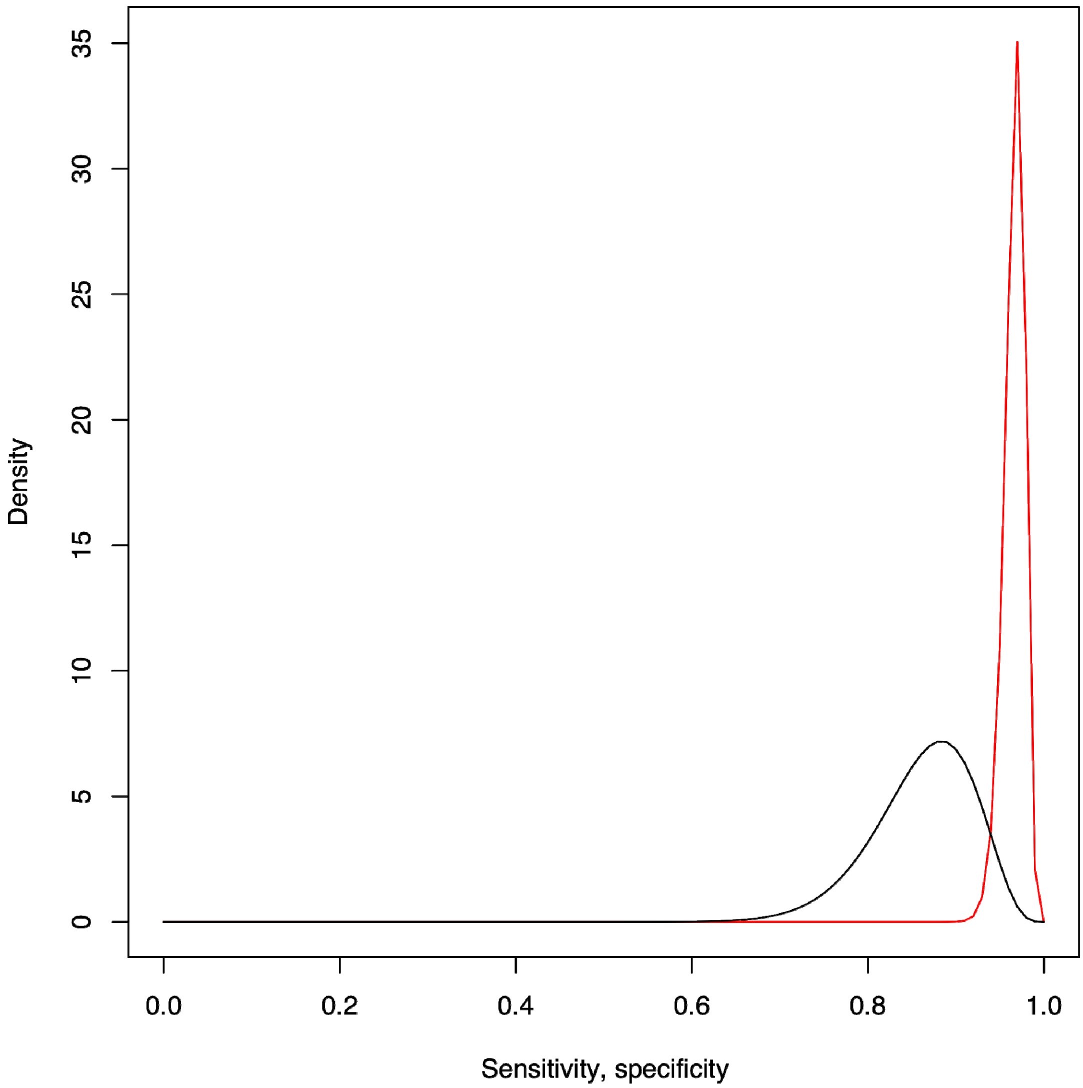

Figure 3. The distributions of the sensitivity (black line) and specificity (red line) of the Gamma Interferon test for bovine TB.

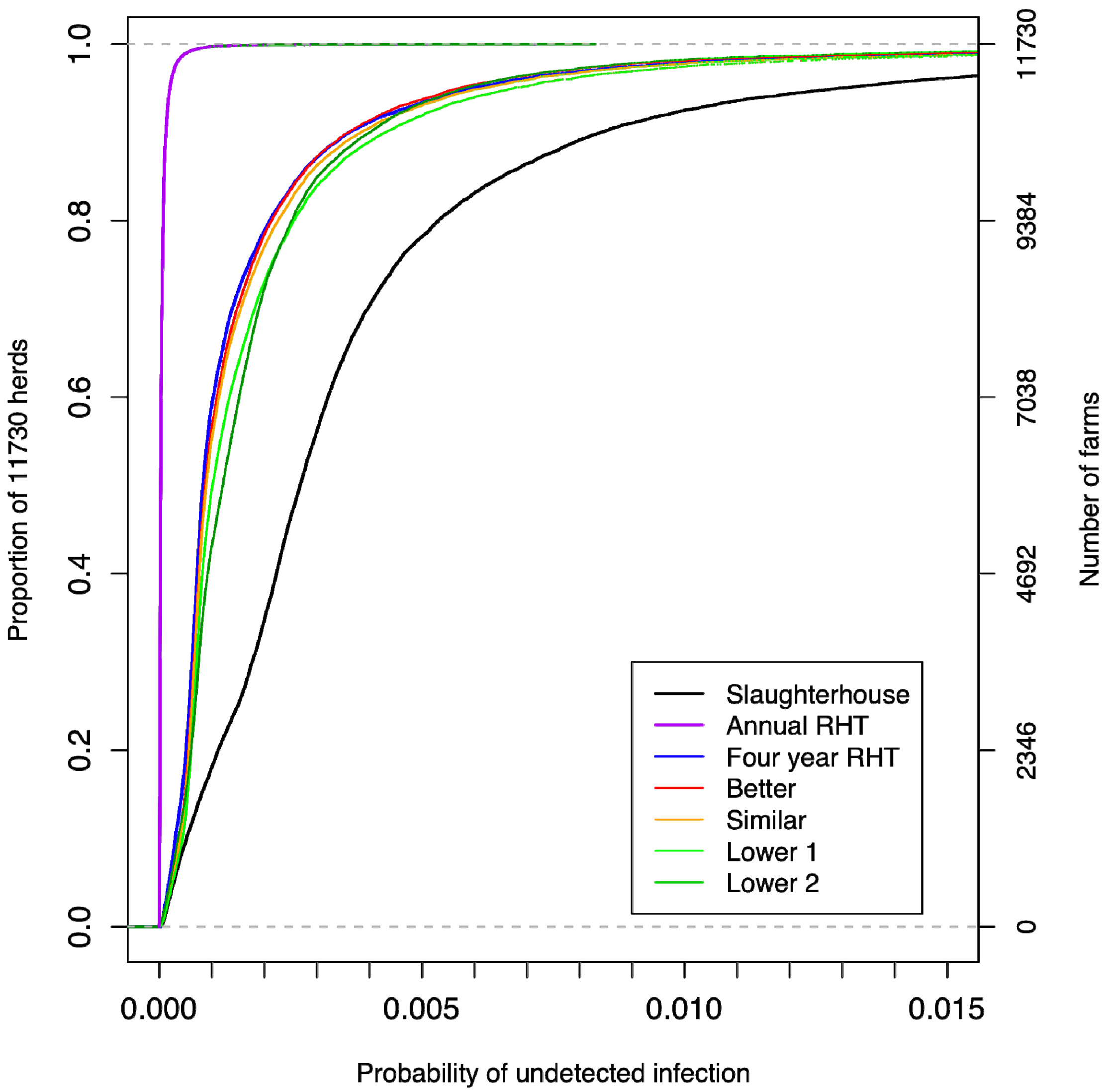

Figure 4. Cumulative distribution plot of the four scenarios tested using the Gamma Interferon test.

Surveillance scenario	Interval	Herds tested	Cattle tested	Number detected out of 98 breakdowns			Latent infections			False positive herds ie UC breakdowns
		pa	Pa	Total	Difference[1]	Additional[2]	2008	mean	Min, max	2008
Baseline scenarios										
Slaughter-house only	NA	0	0	76.26			43.60	33.78	19.66, 48.90	NA
Current	4 yr	2,933	439,292	97.70			13.85	12.62	6.98, 20.79	2137
Maximum	1 yr	11,730	1,757,168	104.79			0.43	0.40	0.22, 0.74	8545
Risk based scenarios										
Better	2/4yr	2,509	388,812	99.10	1.40	22.85	12.76	11.80	6.29, 20.80	1826
Similar	4yr	2,236	317,108	96.98	-0.73	20.72	14.85	13.36	7.32, 22.03	1588
Lower detection 1	4yr	1,768	209,425	94.94	-2.76	18.68	17.23	15.01	8.18, 24.45	1209
Lower detection 2	1/2/4 yr	2,110	441,823	96.94	-0.77	20.68	15.65	13.85	7.76, 22.97	1767

[1] The difference between the number detected for this scenario and the number of breakdowns detected under the “current” surveillance strategy.

[2]The additional detections above slaughterhouse detections.

Table 3. Summary table for the revised results following use of the Gamma Interferon test instead of the SICCT .

The Scottish Government

ISBN: 978-1-78045-248-7 (web only)

APS Group Scotland
DPPAS11761 (06/11)

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