Risk-based surveillance in animal health

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Abstract

Animal health surveillance is an important part of animal health care, particularly in countries dependent on livestock for food production and international trade. There are two major issues related to the provision of effective surveillance activities. Firstly, for good information to become available, the design and conduct of data collection activities should be carried out following sound statistical principles. In reality, constraints such as imperfect tests and unavoidably-biased sampling strategies hinder straightforward analysis and interpretation of survey results. Risk-based surveillance is used to target high-risk sub-populations to increase efficiency of disease detection; however, biased datasets are generated.

This thesis develops methodologies to design risk-based surveillance systems and allow statistically valid analysis of the inherently biased data they generate. The first example describes the development of a method to analyse surveillance data gathered for bovine spongiform encephalopathy (BSE). The data are collected from four different surveillance streams of animals tested for BSE, with each stream containing unavoidable biases and limitations. In the BSurvE model, these data are combined with demographic information for each birth cohort to estimate the proportion of each birth cohort infected with BSE. The prevalence of BSE in a national herd can then be estimated using the method of moments, whereby the observed number of infected animals is equated with the expected number. The upper 95% confidence limit for the prevalence is estimated both for infected countries and for those where no BSE has previously been detected.

A similar approach to that used in BSurvE is then applied to surveillance data for trichinellosis, for which risk-based post-mortem testing is also performed. Negative results from multiple species using different, imperfect tests are combined to give an estimate of the upper 95% confidence limit of the national prevalence of trichinellosis in a reference population. This method is used to provide support for freedom from trichinellosis in Great Britain.

A different approach to risk-based surveillance is explored as the surveillance strategy for detection of exotic causes of abortion in sheep and goats in New Zealand is examined. Using a geographic information system (GIS) maps of disease risk factors were overlain to produce a risk landscape for the lower North Island. This was used to demonstrate

how areas of high- and low-risk of disease occurrence can be identified and used to guide the design of a risk-based surveillance programme.

Secondly, within one surveillance objective there may be many ways in which the available funds or human resources could be distributed. This thesis develops a method to assess BSE surveillance programmes, and provides tools to facilitate BSE detection on the basis of infection risk and to increase the efficiency of surveillance strategies.

A novel approach to allocation of resources is developed, where portfolio theory concepts from finance are applied to animal health surveillance. The example of surveillance for exotic causes of sheep and goat abortion is expanded upon. Risk of disease occurrence is assessed for a population over different time periods and geographical areas within a country, and portfolio theory used to allocate the number of tests to be carried out within each of these boundaries. This method is shown to be more likely to detect disease in a population when compared to proportional allocation of the available resources.

The studies presented here show new approaches that allow better utilisation of imperfect data and more efficient use of available resources. They allow development of surveillance programmes containing an appropriate balance of scanning and targeted surveillance activities. Application of these methods will enhance the implementation and value of surveillance in animal health.

Publications

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Prattley, D., McIntyre, L., Morris, R.S., Stevenson, M.A. and Howe, M. 2006. Clinical practice as a source of veterinary surveillance data - what is it worth? Presented at the Annual Conference of the New Zealand Veterinary Assocation.

Prattley, D., Cannon, R.M., Wilesmith, J.W., Stevenson, M.A. and Morris, R.S. 2006. Scoring points - an objective method to evaluate BSE testing data and optimise surveillance activity. Presented at the Annual Conference of the New Zealand Veterinary Assocation.

Prattley, D., Morris, R.S., Stevenson, M.A. and Thornton, R. 2006. Matching risk and resources in design of surveillance strategies. Presented at the Annual Conference of the New Zealand Veterinary Assocation.

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Chapter 1

Introduction

Animal health surveillance activities have increased in recent years as the focus on food production, international trade and public health has intensified. Factors such as disease characteristics, imperfect diagnostic tests, data availability and resource constraints limit the effectiveness of surveillance programmes. These issues are explored in a literature review presented in Chapter 2. This thesis then addresses some of the problems raised in Chapter 2 by developing methods applied to bovine spongiform encephalopathy (BSE) and trichinellosis. In Chapter 3, a spreadsheet model (BSurvE) for estimating the prevalence of BSE in a national herd using the biased data generated by post-mortem testing is described. For countries where no cases of BSE have previously been detected, the upper 95% confidence limit for prevalence is estimated. Chapter 4 explains a point system developed to allow evaluation of national surveillance systems for BSE. Tests on animals of different ages and leaving the national herd through different surveillance streams are given points reflecting the likelihood of detecting BSE in each group. These sub-populations are ranked according to points per unit cost, allowing resources to be allocated accordingly. This facilitates the design of more efficient surveillance programmes.

The versatility of the methods developed for BSE is demonstrated in Chapter 5, which focuses on surveillance for trichinellosis. This further illustrates the usefulness of the techniques in utilising surveillance data for diseases with low or zero prevalence. The method of prevalence estimation used in BSurvE is applied to a national dataset where subgroups of foxes, pigs and horses have been tested and found negative. The test sensitivities for each species are taken into account, and the spatial distribution of test results are examined in relation to each of the populations at risk. Strong evidence is provided in support of a claim of freedom from trichinellosis in Great Britain.

New Zealand's surveillance programme for detecting exotic causes of abortion in sheep and goats is the subject of Chapter 6. The current surveillance strategy is described and evaluated. An alternative, risk-based approach is explored by demonstrating how risk factors such as climate and stock density can be assessed using rules

applied to layers of spatial data.

In Chapter 7, an alternative, risk-based approach to surveillance resource allocation is developed from theories used in financial investment. Basic portfolio theory is described and the concepts are applied to produce surveillance portfolios for a series of examples. An appropriate level of resource investment is calculated for each disease or geographical area and time period given the degree of disease risk and uncertainty present. Constraints can be set to allow inclusion of all groups, so that while most effort is targeted to high-risk areas, an appropriate level of scanning surveillance is maintained over the rest of the population.

Chapter 8 concludes this thesis with a discussion of the methodologies and findings of the work. Opportunities for future research are outlined.

This thesis consists of a series of papers, which have either been published in peer-reviewed journals or submitted as reports to contracting agencies. Collectively, these papers present a number of alternative ways in which surveillance systems can be enhanced, either by improving the utilisation of data gathered by current programmes, or by using new methods to guide decision-making in surveillance resource allocation.

Chapter 2

Literature Review

Effective animal health surveillance is essential for the health and well-being of both animal and human populations. This review of published literature introduces the background and requirements of modern animal health surveillance, followed by descriptions of various types of surveillance activities that have been implemented throughout the world. Examples are given to illustrate the application, advantages and disadvantages of surveillance programmes. The concept and rationale for risk-based surveillance is introduced, and some of the challenges of analysing the resultant data are addressed. Most surveillance programmes include a combination of activities, and ways in which the data from multiple components can be integrated are considered. The evaluation of surveillance activities is necessary to ensure they fulfil their objectives, provide high quality information and operate efficiently. Funding for animal health surveillance is usually limited, therefore ways in which resources can be distributed between competing demands are reviewed.

2.1 Introduction to animal health surveillance

The World Organisation for Animal Health (OIE; previously known as the Office International des Epizooties) was formed in 1924 with the purpose of 'informing Member Countries on epizootic outbreaks, in order to help protect themselves and exchange scientific information essential to the fight against animal diseases' (OIE 2008a). At its inception in 1924, OIE membership comprised 28 nations; by January 2008 the number of member countries had grown to 172. With this growth the role of the OIE has developed to 'encompass all problems of animal health and welfare, as well as their possible impact on human health'. Guidelines include those for general animal health surveillance, and for surveillance of certain specified diseases, including bovine spongiform encephalopathy (BSE), rinderpest, avian influenza, classical swine fever and foot-and-mouth disease (OIE 2008b). Official agreements exist between the OIE and a number of other international organisations including the Food and Agriculture Organisation

of the United Nations (FAO), the World Health Organisation (WHO), the World Bank and the World Trade Organisation (WTO) (OIE 2008a).

The WTO was established in 1995 following signing of the General Agreement on Tariffs and Trade (GATT) (WTO 2008). One of the founding agreements of the WTO was the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) which specified rules for animal and plant health standards and food safety. The main aim of the SPS agreement is to facilitate trade of agricultural products while allowing countries to protect their human, animal and plant health status. Countries can require sanitary measures for exotic diseases or those under official control programmes in their own country. This necessitates the use of well-designed surveillance systems with a valid scientific basis in order to demonstrate control efforts or absence of disease.

Surveillance is therefore used for three main purposes. Firstly, it is used to detect the presence of disease, for example the incursion of an exotic disease that has not previously been detected in an area. Secondly, surveillance can be used to quantify the level of disease that is present, which involves calculation of measures of disease frequency such as prevalence or incidence. These, and other more complex measures, may be repeatedly estimated in order to monitor the spread of disease or the effects of control strategies. Surveillance used for this purpose is sometimes referred to as monitoring. Finally, if an eradication programme has been in place or if a disease is not known to have existed in a country, surveillance can be used to provide evidence in support of disease freedom. While the word 'disease' is appropriately used, surveillance may in fact not look for clinical disease, but can be used to detect the presence of pathogens or to measure factors that alter the risk of occurrence of the disease (Doherr and Audige 2001).

Modern surveillance systems might have similar goals worldwide (i.e. disease detection or monitoring) but the circumstances in which they are applied are wide-ranging. There is extensive variation in animal production and husbandry systems between different countries, particularly between developing and developed nations. Factors such as climate, economic and political status, education levels and cultural beliefs contribute to the diversity of animal management and agricultural practices. In developing countries, disease management is often focussed on highly contagious diseases, with lack of funding compromising prevention and control and resulting in production losses in communities that are already poor (Perry et al. 2001). These factors affect the design, implementation and efficacy of animal health surveillance activities.

2.2 Classification of surveillance activities

Surveillance activities have historically been divided into passive and active systems, depending on how data are obtained (Salman 2003). Passive systems depend on the inclinations of the people involved to report their information, which may be influenced (and therefore biased) by factors such as ease of reporting, financial reimbursement and the consequences of notification (Hadorn and Staerk 2008; Ranjan and Lubowski 2005; Doherr and Audige 2001; Doherr et al. 2001). Passive surveillance includes, for example, compulsory disease notifications by veterinarians and the accumulation of data via routine laboratory testing of samples submitted for any reason. Even compulsory notification systems are imperfect, as disease recognition depends on the level of knowledge and experience of the diagnostician (including members of the public, farmers and veterinarians), which would be expected to be lower for diseases that were not present in a country for some time (Christenson 2003). Diseases that have long incubation and preclinical periods or gradual development of clinical signs (such as bovine spongiform encephalopathy, BSE) can be overlooked as animals are often slaughtered prior to reaching a pathological state where disease can be detected. Under-reporting is therefore a common yet unwanted side-effect of passive reporting systems. However, as was the case for BSE in the United Kingdom in the late 1980s, passive data collection can identify changes in disease patterns that alert officials to new outbreaks (Salman 2003). Compilation of data from multiple passive systems for the same disease can improve coverage and increase overall surveillance sensitivity, whereas parallel interpretation increases the risk of false positive results.

Active surveillance involves the planning of sampling activities where data is gathered through specific studies. The most straightforward study design involves simple random sampling. The principles of sample size calculations applicable to simple random sampling were first published by Cannon and Roe (1982), with more recent consideration of sampling issues published by Levy and Lemeshow (2008) and Lumley (2004). Simple random sampling assumes that all members of the population have the same probability of selection, so that a sample representative of the population can be obtained. This implies a level of knowledge about the base population (so that a sampling frame can be produced), and requires the capacity to access the required randomly selected study units within the limitations of the resources available. Reporting rates are likely to be increased and data should be more representative of the population compared to non-randomised selection methods. However, greater effort and cost is involved in these studies as compared to passive surveillance. This is particularly the case for diseases with low prevalences, as larger sample sizes are required to identify diseased individuals. For very low prevalences, it becomes more prudent to sample to detect disease above a defined level. If disease is not found, the study population is said to be free of

disease at the defined threshold level, with a stated level of confidence. This situation could apply to exotic diseases when a region or country wants to provide evidence of disease freedom (to support international trade, for instance) (see for example Martin 2008; Corbellini et al. 2006; Canon et al. 1998; Garner et al. 1997), or during the final stages of an eradication campaign (Kaneen et al. 2006; Radunz 2006).

Stratification of the population is used to increase the representation of subgroups within a population and to provide more precise estimates of the parameter of interest. Strata must be mutually exclusive and are based on factors that might affect the results of the study. A random sample is then taken from each stratum. Risk-based surveillance can be implemented as an example of stratified sampling when the strata are constructed according to risk. This risk may relate to the occurrence of a hazard in each stratum (quantifiable by epidemiological investigations), or to the consequences of the presence of the hazard (Staerk et al. 2006). The probability of selection of the sampling units within each stratum is known. In practice, multi-stage cluster sampling methods are commonly used in surveys as they take into account heterogeneous distribution of disease in populations (Ziller et al. 2002; Cameron and Baldock 1998). One-stage cluster sampling involves randomly selecting groups of animals (for example herds or litters), where all of the individuals in the group are then tested. Two-stage sampling occurs when groups are randomly selected, and then individuals from within each group are randomly selected for sampling. While cluster sampling is more efficient than simple random sampling (Ziller et al. 2002; Cameron and Baldock 1998), it is not based on risk. This is inconsequential if the aim is to measure disease prevalence, but for the purposes of disease detection the application of cluster sampling techniques to high-risk populations (for example, within geographical areas more susceptible to exotic disease incursion) would further enhance the process.

The term targeted surveillance has more recently been used in the literature (Salman 2003; de Koeijer et al. 2002; Doherr et al. 2001). This is defined as focusing surveillance activities on sub-populations at higher risk of disease in order to increase detection efficiency (Salman 2003). Risk factors must therefore have already been identified by other epidemiological studies (for example Coelho et al. 2008; Tiwari et al. 2008; Binns et al. 2002; van der Fels-Klerx 2000; Parry et al. 1998). Doherr et al. (2001) described the effects of targeting high-risk populations to detect BSE infection. They considered it unlikely that passive surveillance (compulsory reporting of animals showing clinical signs consistent with BSE infection) would identify more than 50% of detectable cases in Switzerland. In countries with a very low prevalence of BSE, such low detection sensitivity could mean that infection remained unrecognised (Anon. 2000). Doherr et al. (2001) showed that the odds of detecting BSE were significantly higher in fallen stock and cattle slaughtered on an emergency basis compared to passive surveillance (49 times

higher and 58 times higher, respectively). Implementation of a combined strategy, using both passive and targeted surveillance, was recommended. This would mitigate some of the effects of variables affecting the likelihood of clinical suspect cases being reported (such as awareness of farmers and veterinarians, the amount of compensation paid and the consequences of reporting). However, the appropriate level of active surveillance was not discussed, other than that it should be 'sufficiently large', and conducted on animals >24 months old. The study provided evidence for the benefits of targeted surveillance, but highlights a requirement for other studies to further define high-risk groups and quantify the number of animals in each category that should be tested. Hopp et al. (2003) also compared different classes of surveillance activities, using Monte Carlo modelling to determine that surveying fallen stock was more efficient than abattoir testing in detecting scrapie-infected flocks in Norway. Hadorn et al. (2002) found that smaller sample sizes could be used in repeated surveys designed using a risk-based approach, while still maintaining a desired level of confidence.

A risk-based approach facilitates the study of rare disease events, as sampling can be targeted towards groups at highest risk of disease occurrence. This not only increases the likelihood of detecting disease, but is likely to decrease the costs of detection. Rare diseases could include incursions of exotic diseases, the appearance of emerging diseases or the declining incidence of diseases that are subject to eradication programmes. For incursions of exotic disease, risk-based surveillance can decrease the time-lag between disease incursion and detection. As high-risk strata may involve only a small part of the population, samples allocated in proportion to stratum size may not be adequate to support the study objectives. Sampling in proportion to risk (Thurmond, 2003) is one suggested way of overcoming this. Paisley (2001) assessed the viability of a national survey to estimate the prevalence or determine the absence of bovine paratuberculosis in the dairy cow population in Norway. Monte Carlo simulation modelling was used to show that a randomised survey would have a low likelihood of detecting infected herds, due to low test sensitivity, low herd prevalence and small herd sizes. Paisley (2001) also estimated a high monetary cost for a programme required to detect one infected herd (with prevalence <0.2% and confidence level 99%). However, there was no discussion of alternative surveillance strategies that might enhance detection efficiency. Given that Norway had apparently been free of bovine paratuberculosis for many years until it was detected in some previously imported cattle, surveillance targeting herds in similar geographical locations or with traceable contacts from the infected herds could have been carried out with greater efficiency than a randomised survey. Bates et al. (2003) considered that a foot-and-mouth disease detection system that relied on passive surveillance was inadequate, particularly for early detection of disease incursions into the United States. Laboratory samples submitted from animals with suspicious

vesicular disease were also judged to be inadequate for early infection detection in high-risk groups. Proposed strategies to overcome this included targeting high-risk groups (garbage-feeding piggeries, for example); using PCR assays to obtain rapid results; increased efficiency of detecting various pathogens using multiple-testing arrays for the same sample; and pooling samples to reduce costs. In 2006, Thurmond and Perez proposed bulk tank testing of dairy milk to facilitate detection of foot-and-mouth disease virus prior to the appearance of clinical signs. Within-herd transmission of foot-and-mouth disease was modelled (see also Heuer et al. 2007) to determine at what stage PCR analysis would detect viral particles. The aim was to decrease reliance on passive surveillance in detecting disease incursions, as using clinical diagnosis alone was likely to lengthen the time between the virus arriving into the country and its recognition, thereby increasing the likelihood of a large outbreak or epidemic occurring. Enhanced communication between government veterinarians using an intranet forum was another technique aiming to facilitate the recognition of emerging diseases in the United States (Bridges 2000). Vourc'h et al. (2006) described three computerised information systems designed to utilise clinical observational data in detecting emerging diseases, using syndromic surveillance or recognition of atypical cases. This is another way in which passive surveillance could be enhanced, providing field veterinarians could be persuaded to utilise the methods necessary for data input. Examining atypical cases could arguably be considered a risk-based approach to detecting new diseases, while assessing syndromic patterns could also be done on the basis of risk (for example, animals from a particular geographic region, or patterns occurring at particular times of the year).

In targeting surveillance for rare diseases, further challenges arise when imperfect diagnostic tests are used. Test sensitivity and specificity can have considerable influence on interpretation of the results and consequent actions. During the hoax foot-and-mouth disease outbreak in New Zealand in 2005 (Stone 2005), it was thought very unlikely that virus would actually be present on Waiheke Island (the location where virus was reported to have been released). The design of a sampling strategy had to take this into account, together with the likely cycling of virus within the population, a concept discussed in general terms by Thurmond (2003). Heuer et al. (2007) modelled outbreak scenarios in order to determine the most effective time for detection of foot-and-mouth disease, given the reported time of virus release and known disease transmission parameters and pathological characteristics. The inherent difficulties of this were compounded by imperfect test sensitivity and specificity. Heuer et al. (2007) modelled clinical examination of animals, which is likely to have lower sensitivity and specificity than testing of biological specimens (McLaws et al. 2006; Honhold et al. 2004). As an example, a test with sensitivity of 70% would be expected to return 30

negative results from testing 100 infected animals. When the number of truly infected animals is likely to be very small, the possibility of not identifying diseased individuals can be detrimental in detecting disease incursions or in control and eradication activities. This was of concern in New Zealand, an agricultural nation otherwise uninfected with foot-and-mouth disease and where complete eradication is highly desirable. An imperfect test specificity would also be problematic, as a known proportion of false-positive test results would be expected. Any positive outcomes must be followed up to provide definitive evidence that the animals are in fact disease-free; using a series of diagnostic laboratory tests would increase overall specificity (at the expense of sensitivity). Communications about positive test results in cases such as these must be carefully handled, to avoid public panic and unnecessary consequences such as international trade sanctions. The modelling work done by Heuer et al. (2007) allowed the New Zealand disease response team to efficiently reach 95% confidence of detecting clinical infection by designing a sampling strategy that would be carried out when clinical signs were more likely to be present (if virus had in fact been released on the island).

A deficiency in the veterinary surveillance literature is that risk-based surveillance is often concentrated on high-risk targets, while low-risk groups are ignored. While it is intuitively sensible and efficient to look for disease in the places it is most likely to be found, estimates of risk come with inherent uncertainty, and zero risk is unlikely to exist. Salman (2003) regards zero risk as an unacceptable concept with regard to providing evidence of freedom from disease. Bates et al. (2003) considered that it would be prudent to maintain a baseline level of surveillance for foot-and-mouth disease outside of targeted, high-risk groups. Sampling strata that are defined according to risk is one method of overcoming this, whereby the number of animals tested in each stratum is proportional to the risk of the stratum (Thurmond 2003). Scanning surveillance can be considered as the complement of targeted risk-based surveillance. Literature focusing surveillance on high-risk populations does not generally consider how to allocate sampling between high-risk groups and those in other risk categories. The desire to include low-risk groups in a surveillance programme would depend on the objectives of the system and the levels of resource available. For example, surveillance for BSE in European Union countries includes testing of lower-risk, healthy slaughter animals over the age of 30 months, which are processed in large numbers at a consequently high total cost (Heim and Mumford 2005). This is a requirement for public health reasons. In comparison, in New Zealand (considered BSE-free) BSE surveillance is limited to compulsory notification and testing of suspect cases and a relatively small targeted annual sample of slaughtered animals (McIntyre 2008). It could be argued that passive surveillance covers low-risk sub-populations, but as previously explained this method

of disease detection cannot be considered reliable.

2.3 Data analysis in risk-based surveillance

The methods of data analysis that are widely used today were developed on the premise that data were collected using random sampling following standard statistical principles. The purpose of a sample is to estimate measurements about the study population without having to test every individual in that population. Ideally, an unbiased (or representative) sample will be selected from the study population. A sample that is biased will likely lead to an estimated measure that is quite different from the true population value. In targeting surveillance activities, sampling is deliberately biased, usually towards high-risk individuals. This is not problematic if the purpose is to detect disease — simply identifying whether or not it is present. However, if a population parameter is to be estimated, the use of standard analysis techniques gives results that can only be applied to the high-risk group and not to the population as a whole.

For some diseases (including the spongiform encephalopathies and trichinellosis), post-mortem tissue sampling is the only diagnostic procedure available. In practice, post-mortem data are generally biased with respect to the underlying population. For example, cattle slaughtered for human consumption are selected on the basis of good health status and are younger animals that do not represent the age demographic of the general population. Other stock may be culled for health reasons or low production, with the majority being older than those slaughtered for human consumption. The purposes of the surveillance programme might be to protect human health by detecting infection in carcases, but also to monitor disease levels in the living population. Biased post-mortem sample data must be analysed to satisfy the latter requirement. Webb et al. (2001) used data from an abattoir-based survey to supply a model estimating the true prevalence of scrapie infection in the national population. Although sampling was targeted by age, other factors that may have affected either the presence of infection in the national population (e.g. breed susceptibility) or in the slaughter population (e.g. reason for slaughter) were not considered. Nonetheless, the authors did acknowledge that standard statistical interpretation of abattoir surveys required caution, and that careful selection of the target population was necessary. Other authors (Doherr et al. 2001; Ducrot et al. 2003) acknowledged the difficulty of extrapolating findings from targeted surveillance data to the general population with regard to BSE. Ducrot et al. (2003) also considered that using combined compulsory notification and targeted screening for BSE was necessary to decrease the possibility of bias, compared to using either system alone, although this would not eliminate all sources of bias as discussed above.

2.4 Combining data sources

Multiple components of surveillance systems can be used to contribute to the overall knowledge about the disease status of the population (Stevenson et al. 2007). Information gathered from sentinel herds, veterinary practices, laboratories, saleyards and rendering plants were used by Alves and McEwen (1997) to contribute to investigation and surveillance for a bovine viral diarrhoea outbreak in Ontario. Different surveillance activities were considered to have different strengths, and active surveys were used to validate the findings from other data. The importance of weaknesses of each data source were thought to be decreased as each provided consistent information. Although multiple data sources were used, their contributions were not quantified in any way, and the overall sensitivity of the surveillance system was not calculated.

In New Zealand, surveillance for arboviruses and their diseases was implemented using a multi-faceted approach and included elements of risk-based surveillance (Ryan et al. 1991). A passive component involved reporting of suspect clinical cases by veterinarians, while active elements consisted of surveying cattle for signs of infection and carrying out surveillance for *Culicoides* vectors. The programme included targeting veterinarians in areas where vectors were more likely to survive, in order to increase practitioner knowledge of the clinical signs of disease and therefore their likelihood of detecting infection. Sentinel herds were established in districts considered most at risk after districts were ranked according to suitability for vector survival following modelling of climatic conditions. Testing was carried out on an annual basis, as was placement of light traps for *Culicoides*. While this may have been considered an economically efficient programme for detection of disease, the minimum expected prevalence of disease was 25%. Detection would rely solely on practitioner surveillance for much of the year, and early detection was not facilitated. There was limited mention of seasonal variation and other factors such as host density were not discussed. Other parts of New Zealand were presumably dependent on unenhanced passive surveillance.

All of the components of the surveillance programme described above contribute to knowledge about New Zealand's arboviral disease status. Could they be combined into one overall measure? Salman (2003) listed methods of combining different sources of evidence, including scenario tree analysis with stochastic simulation, eliciting expert opinion and Bayesian approaches.

Hueston and Yoe (2000) outlined a probabilistic event tree model to evaluate the ability of surveillance systems to detect disease. This was developed as scenario tree methodology and applied to demonstrating disease freedom by Martin et al. (2007a; 2007b), and has subsequently been implemented in further research (Hadorn and Staerk 2008; Martin 2008). Different components of a surveillance system are evaluated using stochastic scenario trees, and the overall sensitivity of the system is calculated. This

provides a single measure that can be used to compare the value of surveillance systems for different diseases, or the sensitivity of different surveillance activities for a single disease can be assessed. Scenario trees are a useful tool for evaluating surveillance, however they only apply to evidence supporting claims of disease freedom and do not cater for diseases that are detected or are being monitored. There may also be difficulty in obtaining the large amounts of data required for a scenario tree, where probabilities, proportions and/or risks must be numerically represented at each step. Altering the number of nodes in the tree would affect the final outcome, so the effects of combining steps should be carefully considered. For example, whether or not a farmer identifies there is a problem and considers it severe enough to warrant calling their veterinarian represents two separate events, however Martin et al. (2007a) combined these steps into a single node.

Expert opinion can be used to add information to problems where data are lacking, and to make overall assessments of surveillance programmes that are made up of various components (Martin et al. 2007a). This is generally a qualitative evaluation that is more subjective than other methods, and the amount of uncertainty around the result is not always measured. Bridges et al. (2007) used various sources to develop a tool for qualitatively assessing likely emergence of infectious diseases. Although experts were consulted (along with published literature), no formal method was used to capture expert opinion. A straightforward probability estimation method of eliciting expert opinion was used by Gustafson et al. (2005) to identify risk factors for infectious salmon anaemia outbreaks in the United States and Canada. Thirty experts were individually interviewed and asked a series of questions about two different infection scenarios (infected versus uninfected farms, and infected farms with mild versus severe outbreaks). The experts nominated farms they had knowledge of, and supplied information as to the number of sites that did or did not have each risk factor. Likelihood ratios were calculated for each characteristic, as a measure of the perceived importance of each risk factor. This was a subjective process that revealed differences according to vocational affiliations (government versus industry workers).

The Delphi method structures communications between a panel of experts in an iterative manner and provides feedback to the participants after each stage (Arnold et al. 2008; Slocum 2005; Dufour 1997; Webler et al. 1991; Dalkey and Helmer 1963). Advantages of the Delphi method include the ability to have multiple rounds of assessment with feedback (and sometimes discussion) in between each round; this allows for clarification of the question and its interpretation, and discussion of any points of difference so that agreement (or compromise) might be reached. Face-to-face meetings can be used, or the process can be carried out by post or e-mail. The Delphi method has been applied to a variety of problems. Dufour (1997) used the

Delphi process to produce an evaluation scale for surveillance programmes, so that they could be compared. The work was done by mail, allowing international experts to participate in two assessment rounds. It can be more difficult to find a consensus using this approach, where the experts were unable to discuss the survey questions. Evaluating the risks associated with applying sewage sludge to farmland was carried out using a group Delphi process by Webler et al. (1991). This was done face-to-face, with resulting loss of anonymity and the possibility of more opinionated, vocal participants influencing the inputs of their colleagues. Risk factors to human health and the environment were rated, and experts were asked to rate their confidence for the answer they gave in an effort to quantify uncertainty around the evaluation. The Delphi method has also been used in clinical medicine, for diseases where definitive research is lacking. Guidelines for diagnosis and management of a congenital metabolic disorder in babies were produced using the Delphi method by Arnold et al. (2008). Two postal surveys were completed by 15 experts, followed by a face-to-face meeting. The postal rounds would allow people to freely express their opinion without being influenced by the other experts; however, this could result in people interpreting the questions differently from each other, resulting in greater variation in the panel's answers. The final face-to-face meeting would overcome this, but might result in large changes to the scores previously given to some questions. The experts were chosen from a range of pertinent fields (including clinical biochemical geneticists and clinicians) to help avoid panel selection bias. It was pointed out that future research would likely over-rule the guidelines produced in the study, as expert opinion is not a replacement for factual information.

van der Fels-Klerx et al. (2000) combined Delphi and adapted conjoint analysis (ACA) techniques in quantifying risk factors for bovine respiratory disease in the Netherlands. Four postal rounds using the Delphi method took eight months to complete, and aimed to define clinical bovine respiratory disease and define and rank risk factors for its incidence. A one-day workshop completed the process, where the 21 participants used individual computer-based questionnaires and the ACA method to quantify the relative importance of the risk factors. Farms were characterised by levels of risk factors, for example the levels of the risk factor 'house type' might be 'closed barn' or 'open front stall'. The levels of each risk factor were ranked, and then the relative importance of each risk factor was rated. The objective was for the experts to judge the impact of the risk factor on the incidence of respiratory disease on the farm. Pair-wise comparisons of levels of risk factors were also made, to try and elicit further information. A final step involved computer-generated farm profiles, based on the previous answers of the expert, designed to check their answers for internal consistency. Least squares regression analysis was used to assess the contribution of the risk

factor scores for the various scoring procedures. Overall, this method (Delphi followed by ACA) minimised discussion between experts, but allowed a more in-depth examination of risk factor importance. Conjoint analysis was also used by Staerk et al. (2002) in characterising infection and transmission of *Salmonella enterica* in pigs. Written questionnaires were completed by 36 experts from various countries, with discussion between participants disallowed. Although this is a more rapid process than completing multiple Delphi rounds, greater variation between experts can occur as there is no endeavour to reach consensus. There was a low proportion of valid answers to some of the questions, which would likely have been avoided using a Delphi method. On the other hand, information was gained regarding internal consistency of each expert's answers, and those with low consistency were able to be excluded from further analysis, thus reducing variation. Horst et al. (1998) used three-point estimation, conjoint analysis and the ELI technique to gauge expert opinion regarding the risks of introducing several infectious viral diseases into The Netherlands. Three-point estimation (estimating the minimum, most likely and maximum values) was used to assess the length of the high-risk period (the time between infection of the first animal and control or eradication) for virus transmission. The comparative importance of risk factors (for example, importation of livestock or animal products) was measured using conjoint analysis. The ELI technique, a graphic computer programme, helped the experts produce probability density functions representing the likely number of disease outbreaks. Both the most likely value and the uncertainty around that value could be elicited for each participant using this technique. The latter two methods were considered particularly useful by the authors.

Bayesian techniques combine previously known information (encapsulated by the prior distribution) with current data to produce a revised estimate (known as a posterior distribution) describing the parameter under investigation. The use of probability distributions to represent both prior and posterior information allows uncertainty to be taken into account. Selecting an appropriate prior distribution can be challenging, particularly when it represents unquantified expert opinion. With recent increases in computing power, Bayesian techniques have been applied to a range of problems (Bland and Altman 1998), including human and animal health surveillance. Jiang et al. (2008) developed a Bayesian network model to predict epidemic curves and applied this to data from *Cryptosporidium* and influenza outbreaks. Epidemic curves are normally produced once an outbreak is over, but there would be benefits for disease management if the epidemic curve could be estimated in advance. Counts of observable events (for example, sales of over-the-counter medicines) were correlated with the daily counts of cases. The model included factors such as outbreak severity and duration, disease counts from previous days, counts of correlated observable events, and

background counts of observable events (i.e. sales of over-the-counter medicines that would have occurred in the absence of an outbreak). The accuracy of the predicted curve increased over subsequent days, as further information was added to the model. Audige et al. (2001) employed a Bayesian approach to estimate the probability that Switzerland was free from infectious bovine rhinotracheitis. The prior probability of disease freedom was combined with serological survey results to substantiate a disease-free status. A hierarchical Bayesian model was used by Suess et al. (2002) to estimate the disease parameters for Newcastle disease and porcine reproductive and respiratory syndrome in Switzerland. The probability of country freedom, proportion of infected herds and within-herd prevalence were estimated. Prior distributions based on published literature and expert opinion were combined with diagnostic test results from previous surveys. Simulated datasets were also used, and it was shown that the model could not always determine unequivocally whether or not the country was free from disease when the number of infected animals was low. Increasing the number of herds sampled was expected to mitigate this outcome. An inaccurate prior was also shown to adversely affect the posterior distribution, decreasing the likelihood of it including the true population value. This is a disadvantage of using priors that cannot be quantified; otherwise, the Bayesian approach is a useful method for incorporating multiple data sources while taking uncertainty into account.

An additional method of combining information from various data sources was put forward by Cannon (2002). A point-based approach was developed, where points gained equalled the test sensitivity multiplied by the number of tests done. Test sensitivity was weighted by the disease prevalence at the time of testing, divided by the design prevalence (a prevalence that it is desirable to be able to detect with the required confidence). Effectively, each completed test was valued as a fraction of an animal sampled. The total number of points reflected the level of confidence of disease freedom. Target scores could be set if required, to ensure that adequate amounts of testing were done. Points could be lost by buying in animals, or by other activities that were high-risk for disease introduction. This is a flexible approach, allowing different testing regimes to be used as appropriate for a given situation and taking into account testing at various grouping levels (herd, region, zone etc.). Testing could include activities such as clinical examination, providing the diagnostic sensitivity were known. The method does assume that a positive unit (herd, region etc.) would be removed from the system if disease was detected. Unlike the scenario tree approach, this is a probabilistic, deterministic method, focusing on the confidence achieved by surveillance activities rather than their sensitivity of disease detection. Hadorn et al. (2002) implemented Cannon's (2002) concept of maintaining the required confidence level in designing repeated surveys to document freedom from enzootic bovine leucosis and *Brucella melitensis* in sheep and

goats in Switzerland. Using the results of previous national surveys, the probability of disease freedom was estimated. Over time this probability was considered to decrease, by an amount that depended on the risk of importing the pathogens of concern. Sample sizes for subsequent surveys were therefore able to be decreased.

2.5 Evaluation of alternative surveillance strategies

Increasing demands for veterinary surveillance have recently been attributed to increases in international trade and the emergence of animal and zoonotic diseases (Staerk et al. 2006). One hundred and seventy-five human pathogens are currently considered to be emerging or re-emerging (affecting a new host population or increasing in incidence), and 75% of those are known to be zoonotic (Taylor et al. 2001). The need to prioritise surveillance activities within a country is likely to grow in importance as surveillance demands increase faster than the resources available to fulfil them - a situation that has already been reached in New Zealand (Ministry of Agriculture and Forestry, 2008). Resources available for use in national surveillance programmes are almost always limited. Within a national surveillance portfolio there are usually many surveillance systems operating simultaneously for different diseases, and resources have to be divided amongst these. Any new requirement for surveillance (for example, following a threatened or actual exotic disease incursion) can cause redirection of resources normally used to monitor other diseases that remain a risk. Reduction of budgets for animal health activities will also have an effect on the distribution of resources, which has been an issue particularly in developing countries (Perry et al. 2001). Perry et al. (2001) describe how epidemiology and economics could contribute to priority setting, decision-making and disease control, but the same principles could equally be applied to disease detection and surveillance. In New Zealand, Sanson and Thornton (1997) used stochastic models to estimate the delay in detection of an incursion of an exotic *Salmonella* strain if decreased funding for animal health surveillance adversely affected surveillance activities in place at the time. Economic constraints are perhaps the most obviously limiting resource, but practical limitations can include staffing levels, laboratory capacity and access to sampling units. In order for resources to be allocated within an overall surveillance portfolio, disease risks and alternative surveillance strategies must first be evaluated.

Risk assessment procedures for food safety and animal diseases are required by the SPS Agreement. International standards for food safety are set out by the Codex Alimentarius Commission (Codex 2008). Food-borne disease risks are assessed in a stepwise process, including hazard identification (including biological, chemical and physical agents), hazard characterisation (qualitative or quantitative evaluation of the hazard under study), exposure assessment (evaluation of the likely intake of the haz-

ardous organism or substance by consumers) and risk characterisation (estimation of the probability of occurrence and severity of adverse effects in the population). Risk management and risk communication complete the exercise (Codex 2008; Murray 2002). Using similar concepts, risks and consequences of disease incursion are commonly assessed using a risk analysis procedure comprising hazard identification (what might go wrong), risk assessment (how likely is to go wrong and what the consequences would be if it did), risk management (controlling the risks and providing an appropriate level of protection from the hazard) and risk communication (informing decision-makers and stakeholders) (OIE 2008b; MacDiarmid and Pharo 2003). Standards for this procedure are published by the OIE (2008a). Risk assessment consists of release, exposure and consequence assessments, and risk estimation (Murray 2002; OIE 2008b). Risk analysis is required for each pathogen of concern, following each of the possible pathways of entry into a country. Many factors affect the likelihood of a disease entering a country, for example the epidemiology of the agent, whether or not a country has suitable hosts or vector habitats, or whether a country imports products likely to harbour the agent. The likely effects of an incursion (for example, epidemic size, morbidity, mortality, public health implications, effects on trade) should also be taken into account, as these would affect the need for, and characteristics of, any response. Risk analysis is a complex procedure, often involving quantification of processes that have insufficient data available to describe them (MacDiarmid and Pharo, 2003), although qualitative and semiquantitative approaches are also acceptable and are frequently used. Expert opinion can be used where data are unavailable (Slocum 2005; Murray 2002; Staerk et al. 2000; Clemen and Winkler 1999), although there can be a great deal of variability in expert's answers to the same questions (Staerk et al. 2002; Staerk et al. 2000; Clemen and Winkler 1999). McKenzie et al. (2007) developed a rapid risk analysis method to assess and rank wildlife pathogens so that surveillance priorities could be established. Only one expert was used to score each pathogen, which avoided the problem of combining scores from multiple experts but potentially limited the range of knowledge and experience that the scores were based on. The assessments were also subject to the biases of the individuals involved, which could be mitigated by using multiple experts with different industry backgrounds or affiliations.

As in surveillance, a desire for efficiency of resource use can drive the application of techniques to evaluate the benefits of gathering further information about risk. Value-of-information methodology was used by Disney and Peters (2003) to help determine when further information about the risk of disease transmission (using avian influenza in poultry as their example) does not increase economic benefit. Firstly, the probability of a disease outbreak was modelled using a probability tree structure and Monte Carlo simulation techniques. An agricultural economic model that estimates changes

in producer and consumer surplus was then used to evaluate four scenarios representing import and outbreak event combinations, in terms of the payoff of each combination. The values of increased surveillance and/or further research (two options to reduce uncertainty of the disease outbreak probability estimates) were assessed using the value-of-information process. This is where the maximum expected payoff given the probability of a state of nature (import/outbreak event) occurring is subtracted from the expected payoff after receiving further information (surveillance data/research) about the state of nature. This method takes into account uncertainty of input parameters and gives results in easy-to-understand dollar terms. As in other studies (Prime and Nimmo-Bell 2002), the consequences of disease outbreak did not include factors such as alteration of trade agreements in the face of an outbreak, and this may have altered the outcome. However, the set of all possible consequences of a disease outbreak is infinite and it is not reasonable to expect that all options can be considered. The concepts of confidence-increasing, probability-reducing and consequence-reducing actions were also introduced by Disney and Peters (2003), with regard to increasing confidence in the estimated probability of a disease incursion. These concepts, particularly the first, could also be applied to surveillance activities, even at an individual test level — what is the value to the overall surveillance system of an additional test on a given animal?

The results of a risk analysis will guide whether or not diseases require ongoing attention, and how best to mitigate the possible entry of disease. With regard to the latter, import restrictions or biosecurity measures might be appropriate and all that is necessary. However, high-risk and high-consequence diseases may also be under surveillance in the animal population in effort to detect an incursion or re-emergence at an early stage. Given limited resources and multiple diseases for which pre-border measures alone are insufficient, how should it be decided which diseases are of sufficient importance to be included in the surveillance portfolio? Expert opinion could be used but is subject to the biases, experience and motivations of the individuals involved. Diseases could be ranked according to risk of incursion, likely size of outbreak, public health risk, cost of detection, control or eradication, or a number of other factors. Standardised evaluation methods are necessary so that multiple and very different diseases can be compared. Value-of-information methodology could be applied (Disney and Peters 2003). Another option is cost-benefit analysis. Two consultancy companies were jointly employed in New Zealand to identify priorities for surveillance and propose an economic framework to determine optimal funding levels for surveillance (Prime and Nimmo-Bell 2002). They used a series of varied disease types (pathogens were not explicitly stated) to show that cost-benefit analysis was considered most appropriate when quantification of the costs and benefits was possible. In this case, money would be allocated to surveillance projects with the highest net benefit. With an upper

limit on spending, the net benefit to capital cost ratio was regarded as most suitable. Unfortunately, quantification of costs and benefits is rarely accurately possible. Prime and Nimmo-Bell (2002) modified their quantitative results using multi-criteria analysis to assess factors that could not be valued in monetary terms. Experts weighted the chosen factors using a Delphi survey process. The economic and multi-criteria analysis rankings were compared, but the final ranking was dependent on judgment which would therefore be subject to bias and open to criticism. It was stated that comprehensive risk analyses would be required for their model to be weighted by the probability of an incursion occurring, but that few of these existed for the diseases of concern. The document did not discuss the surveillance scenarios in any detail, so although different options for a given disease were evaluated (for example, high, medium and low levels of infection with the options of allowing a pest to become endemic, versus eradication or containment), the likelihood of occurrence of a given level of infection was not discussed. Also, the uncertainty of the input values and results for both the quantitative and qualitative methods was not taken into account. Galligan et al. (1987) took into account expected utility (return), uncertainty around the expected return, and defined the confidence interval as an attitude towards risk. These concepts were applied to decision tree evaluation of treatment options for two medical conditions in dairy cattle. As Galligan (1987) pointed out, simply selecting the option with the best monetary return is appropriate for people who are risk neutral. However, most people either prefer risky options or are risk averse, depending on the situation. Government agencies would be expected to be risk averse in order to protect animal and human health and international trade; however, this would be tempered by budget constraints.

Once it has been decided which diseases are of sufficient importance to be included in the surveillance portfolio, alternative surveillance strategies for each disease should be evaluated. There are several methods that have been used for this, from epidemiological to economic modelling approaches. Monte Carlo simulation models were used by Hopp et al. (2003) to evaluate alternative surveillance strategies for scrapie in sheep in Norway. This process allowed evaluation of the success of surveillance for varied (unknown) true infection prevalences, and variation in surveillance variables such as test sensitivity. This method also allows different sample sizes to be evaluated. As previously discussed, Paisley (2001) used Monte Carlo methods to evaluate a randomised survey for paratuberculosis in cattle in Norway, and calculated the costs of different surveillance options. Hasler et al. (2006) also used Monte Carlo simulation to estimate the costs of *Neospora caninum* infection in dairy cattle in Switzerland. In addition, four control strategies were evaluated over a simulated time period of 25 years. Calculation of the cost-benefit ratio and net present value was done for each option. Factors such as effects on international trade or market supply were not included in the anal-

ysis. This illustrates another use for these methods in evaluating control options as well as surveillance strategies. Akhtar et al. (1988) wrote a computer algorithm to simulate four sampling strategies, the aim being to assess the optimum sampling strategy for four dairy herd health and production variables. The strategies tested were simple random, stratified (by herd size), random with proportional sample allocation, and stratified random with Neyman allocation. Neyman allocation took into account both population size and variability in response among the strata, and was shown to be more efficient than the other strategies when variability was heterogeneous across strata. For the one variable tested with constant variability across strata, the three sampling plans were equally precise. A stochastic bio-economic optimisation model was used by van Asseldonk et al. (2005) to evaluate several surveillance strategies for bovine tuberculosis. Strategies varied in the detection method and sampling frequency used. The epidemiology of bovine tuberculosis infection was modelled to simulate outbreaks using a state transition model (susceptible, exposed but not detectable, exposed and detectable and infectious). The costs of the various surveillance strategies and control efforts for the simulated outbreaks were calculated. The efficiency frontier was determined for the expected overall costs and expected number of infected farms (as a measure of risk). An efficient set of alternatives was constructed, composed of options with the same level of risk but lower costs than inefficient options. Decision-makers were then able to select a desirable strategy according to expenditure and risk. Effects of large outbreaks (such as loss of international trade) and public health impacts were not evaluated. The methodology used by van Asseldonk et al. (2005) is appropriate for comparing different possible surveillance system components, but could be unwieldy at the more detailed level of finding the optimal number of surveillance tests to carry out in a given group.

Scenario tree methodology (Martin et al. 2007a; 2007b; see previous discussion) can also be used to assess alternative actual or proposed surveillance strategies, as the sensitivity of each component is estimated and these can be compared. This is only applicable to demonstrating freedom from disease and not to estimating population parameters; nevertheless it is a useful way to identify gaps in knowledge that can be filled by further studies.

There are some factors not commonly included in economic assessments. The cost of re-distributing previously allocated resources (Roy 1952) is often not taken into account. Rich (2007) describes a systems dynamics simulation model representing both epidemiologic and economic factors in a disease outbreak, which also includes the influences of feedbacks from the disease itself (for example, a zoonotic disease might decrease product consumption) and from incentives (for example, compensation for slaughtered animals) or control policies (such as slaughter, re-stocking or vaccination)

that affect how livestock producers behave. Such feedback factors are often overlooked in models of animal health economics (Rich 2007), but would be a more complete representation of an animal production system in the face of a disease outbreak.

2.6 Allocation of resources

After suitable methods have been used to evaluate disease risk and surveillance options, the task of allocating resources remains. Hurwicz (1973) described the properties of allocation mechanisms as efficiency, optimality and feasibility. The size of a resource allocation problem depends on the number and complexity of objectives, constraints and variables. Hurwicz (1973) pointed out that in economic problems goal conflicts are due to multiplicity of consumers, which is akin to the veterinary surveillance allocation problem. Other fields as diverse as military operations, manufacturing, computing, finance, logistics and plant ecology also require division of finite resources, with a variety of methods being applied to finding solutions. Hurwicz (1973) proposed that ideas from administration, control sciences, computer theory and game theory (the mathematical representation of strategic situations, where the success of one party's decisions depends on the choices made by another party) could be used to solve economic resource allocation problems. A recent review of the history and applications of various algorithmic approaches to solving resource allocation problems in multiple fields was published by Patriksson (2008).

Matlin (1970) reviewed the literature of the time addressing the problem of optimal allocation of missiles to targets. A number of relevant parameters were identified, such as missile availability, reliability and reaction time, and target locations, location uncertainty and defence programmes. Such characteristics could be translated to a veterinary surveillance problem, for example as test availability, sensitivity and processing time, and host location, uncertainty around population parameters and national or farm level biosecurity, respectively. Matlin (1970) listed several methods of determining the optimal allocation, including game theory, linear and dynamic programming, exhaustive searches and Monte Carlo techniques. However, the characteristics of the models of missile allocation were reviewed rather than the methods used to drive them. More recently, Erdem and Ozdemirel (2003) used genetic and repair algorithms in an evolutionary approach to assigning friendly combat units to enemy units. Assumptions around the ability to divide units and the effects of dividing units were taken into account. Ghose (2002) used game theory in model the distribution of multiple resources in a military air campaign. Two-person game theory was applied to the resource allocation problem by Hohzaki and Nagashima (2009), where a fixed budget was used by one player to purchase missiles that varied in effectiveness depending on the target. The second player was allowed to hide valuable goods in the desired facilities given the

knowledge of the missile allocation used by the first player. This models the receipt of intelligence information in the real world. A further step was taken by Belfares et al. (2007), where multiple defined tasks, each with space and time constraints, required multiple types of resources to be assigned to them. Tasks could be carried out at the same time and it was assumed that they had already been scheduled. This scenario represents a difficult problem to solve, but is one that characterises a common, real-world dilemma. It was considered that there would be no one optimal solution, but a set of efficient possible solutions could be produced. A progressive resource allocation procedure was developed, where one viable solution was found and then used to generate other possible solutions. The Tabu Search algorithm (Glover 1989, as cited in Belfares et al. 2007) was employed, which makes moves from the initial solution to create new, neighbouring solutions. Haapalinna (2003) developed a decision support system that allowed different allocation strategies to be evaluated, by graphically displayed the difference between a desired outcome and the outcome that was likely given the allocation decision made. This concept is one that is practical and could be used by decision-makers in real-time situations where resource allocation strategies needed to be implemented. Other recent examples of the application of resource allocation concepts in the military realm have focused on the distribution of health care resources (Fulton et al. 2007), and management of disrupted and overloaded systems in disaster response situations (Baker 2007a; 2007b). With continuing decreases in military defence budgets (Forder 2004), these 'operational analysis' activities are likely to continue, and may provide useful analogies for applying new concepts to the planning and delivery of veterinary surveillance programmes.

van der Waaij (2004) described a resource allocation model in the field of animal physiology. He assumed that selecting animals for production under limited energy intake means that individuals are being selected for the ability to use that energy for production at the expense of fitness (defined as maintenance, health and reproduction). Fitness also requires more resources in a sub-optimal environment. Stochastic simulation over 40 generations of selecting for observed production illustrated the negative effects on reproductive rate and increased environmental sensitivity. Another physiological application hypothesised that reproductive activity decreased immunocompetence (Lehmer et al. 2007). However, the work in deer mice with chronic Sin Nombre virus infection did not support this hypothesis; instead the results suggested that infection with the virus decreased immunocompetence, with differences in effects between males and females. Other resource allocation investigations of this type could show different results, depending on the animal, pathogen and outcomes studied.

Ecologists are interested in how organisms distribute resources. Venable and Lloyd (2004) discuss the limitations of plants to resources necessary for function. While some

resource allocation models consider allocation of a single limiting resource and use cost-benefit analysis (Prime and Nimmo-Bell 2002), Venable and Lloyd (2004) address multiple limiting constraints using a graphical model to show that such problems could be reshaped as single resource issues. This would be increasingly difficult as the number of constraints increased. In any case, it could be argued that veterinary surveillance issues are a single resource, multiple recipient problems (i.e. several entities competing for one limiting resource), as generally resources such as manpower or laboratory tests are ultimately defined in monetary terms.

Resource allocation is an important consideration in economics and finance. Well before 1952, people would invest in a diversity of assets. However, there were no developed theories as to how this affected the overall risk level to which they were exposed, the balance of risk versus return, or the overall properties of investment portfolios. Roy (1952) defined a safety first methodology to describe how people invest their money under uncertain conditions, with a desire to minimise disastrous outcomes. In a 1956 paper, Roy described how models of economic behaviour that include uncertainty need to specify expectations (formed by experience), objectives that are to be achieved, and opportunities that may arise with which to achieve those objectives. A lack of precise information to form probability distributions that measure future characteristics is overcome by representing a distribution using two parameters — an expected value and a measure of uncertainty around the expected value. This potentially loses information, but two parameters are more straightforward to estimate than an entire distribution. Historical data (previous experience) can be used to guide parameter estimation. Despite Roy (1952) and Markowitz (1952) both developing portfolio theory techniques, only Markowitz has been credited as the 'father of modern portfolio theory', presumably due to his substantial further work in the area (Markowitz 1999). Markowitz has been considered the first to define risk and return (Miller 1999). Markowitz (1952) used the expected return, its variance and covariance between assets to allow the investor to select a portfolio with levels of return and risk that suited individual requirements. The methods of both researchers reduce large volumes of complex information to a more manageable and comprehensible set of options.

Galligan et al. (1991) used portfolio theory in conjunction with decision tree analysis to evaluate various intervention strategies for reproductive management in a dairy herd. The advantages of using portfolio theory included consideration of the risks of taking different decision options, and potentially reducing costs by diversifying the choices made for different animals within the herd. Although used in the context of veterinary medicine, application of this methodology to the wider questions of animal health surveillance was not considered.

Which of the many available methodologies should be applied to the allocation of veterinary surveillance resources? To answer this, the characteristics of the problem

and the desirable characteristics of the outcome should be identified. The objectives of each surveillance system component should be clearly stated. A resource allocation problem generally involves finite assets, which for most purposes can be ultimately regarded as limited finance, although conceptually the limiting factor could be other entities (skilled labour, laboratory capacity, etc.). In any case it can generally be assumed in the surveillance context that there is only one limiting resource. Conversely, there are multiple possible recipients (and combinations of recipients). Uncertainty and variability in the knowledge and data describing the recipients is often high. Both should be taken into account, as should the fact that these change over time. Uncertainty relates to both uncertain knowledge about the current situation, and what conditions will be like in the future (Webler et al. 1991). Quantitative and qualitative data may both need to be incorporated in finding a solution.

The outcome of a resource allocation exercise in the context of animal health surveillance should be a practical and achievable surveillance strategy. The required number of sampling units in a geographic area or time frame must be available, and both of the latter factors should be appropriately delimited. Efficient disease detection, in terms of the cost of detection and the time taken to find disease if it were present, is the overall objective. Portfolio theory techniques were considered to meet these requirements, and have not previously been applied to veterinary surveillance problems.

Animal health surveillance systems vary widely and involve many techniques for designing sampling strategies, gathering and analysing data and distributing resources. There is no perfect system, and each technique used has its own advantages and disadvantages. Some of the methods used in other disciplines show suitability for application to veterinary surveillance, and further research is required to explore and implement these.

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Chapter 3

A model for estimating the prevalence of BSE in a national herd

3.1 Abstract

We developed the BSurvE spreadsheet model to estimate the true prevalence of bovine spongiform encephalopathy (BSE) in a national cattle population, and evaluate national BSE surveillance programmes. BSurvE uses BSE surveillance data and demographic information about the national cattle population. The proportion of each cohort infected with BSE is found by equating the observed number of infected animals with the number expected, following a series of probability calculations and assuming a binomial distribution for the number of infected animals detected in each surveillance stream. BSurvE has been used in a series of international workshops, where analysis of national datasets demonstrated patterns of cohort infection that were consistent with infection control activities within the country. The results also reflected the timing of known events that were high-risk for introduction of the infectious agent.

Prattley, D.J., Cannon, R.M., Wilesmith, J.W., Morris, R.S. and Stevenson, M.A. 2007. A model (BSurvE) for estimating the prevalence of bovine spongiform encephalopathy in a national herd. Preventive Veterinary Medicine 80 330-343.

3.2 Introduction

Surveillance for bovine spongiform encephalopathy (BSE) in a national herd may be undertaken to detect the infection or monitor disease prevalence, and to support claims of BSE-status. Mandatory reporting of clinical suspect cases has been the mainstay of BSE surveillance in many countries. However, the effectiveness of such passive systems depends on factors including disease awareness in the country of concern, policies for dealing with infected herds and diagnostic capabilities. Guidelines for BSE surveillance

are published by the World Organisation for Animal Health (OIE) (World Organisation for Animal Health 2005), and were originally founded on the results of passive clinical surveillance for BSE in Great Britain. These guidelines are periodically revised and have moved towards requiring a targeted, risk-based approach to surveillance. This is on the basis of accumulated BSE surveillance data and the results of targeted screening programmes, which have shown variation in the odds of detecting infection in different sub-populations of adult cattle (Doherr et al. 2001).

Calculating the apparent BSE prevalence of a country is straightforward. However, characteristics of the disease, surveillance programmes and current detection capabilities mean that apparent and true prevalences can be very different, and estimation of the true BSE prevalence is a much more challenging proposition. Definitive diagnosis is only possible post-mortem. The disease has a long incubation period and infected animals can be removed from the national herd (via slaughter or death) for unrelated reasons before the appearance of clinical signs. This can occur either in the latent period (when BSE is undetectable by current means) or during the preclinical period when infection is detectable but not clinically expressed. Animals that die or are slaughtered are not selected or tested for BSE on a random basis and are therefore a biased sample upon which post-mortem surveillance is performed.

Animals leaving the national herd can be categorised into one of four surveillance streams (World Organisation for Animal Health 2005): healthy slaughter (healthy cattle slaughtered for human consumption), fallen stock (animals that died on farm), casualty slaughter (animals that are injured or abnormal but eligible for slaughter under special restrictions) and clinical suspects (animals reported as showing neurological signs that might have been due to BSE). Each stream is inherently biased with respect to the national population by factors such as age distribution, BSE prevalence and availability for testing. These biases also vary according to the surveillance systems in place in a country and how well those systems are carried out. Therefore, there is no straightforward method that can be used to estimate prevalence in the national population.

In this paper we present an approach to estimating BSE infection prevalence, which uses demographic and surveillance data to estimate the proportion of each birth cohort that was infected and hence the prevalence in the national population. To achieve this the relative prevalence of BSE in each of the four surveillance streams by age is determined using four sets of data: the age-culling distribution of animals; the incubation period of BSE; conditional age-stream exit probabilities for clinically infected animals; and conditional age-stream exit probabilities for other animals.

Our specific objectives were to: describe a method for estimating BSE infection prevalence in a national herd; evaluate current national surveillance programmes; and provide tools to improve surveillance strategies for infected and uninfected countries.

This paper describes the structure and methods used to produce a spreadsheet model (BSurvE) to obtain estimates of BSE-infection prevalence. Example data are used which is typical of that recorded in EU countries, and is referred to as data from fictional country A. A second paper describes the point system used to quantify surveillance testing and provides tools to aid optimisation of resource allocation.

3.3 Methods

We developed BSurvE as a spreadsheet (Microsoft Excel, Microsoft, Redmont, WA) with four components: Input Data; BSE Status Assessment; BSE Surveillance Assessment; and Surveillance Resource Allocation. The first two components are required to estimate BSE prevalence in the national herd and are described below. The remaining sections are covered in Chapter 4.

3.3.1 Input data

3.3.1.1 Population characteristics

The first data requirement is the age distribution of a typical cohort. This is the number of cattle of one birth cohort (a birth cohort includes all animals born in one year) present in the population at each age of the cohort's lifetime. If unavailable this can be approximated using the age distribution of all cattle in the national population (which contains multiple birth cohorts) in any stated year(s). The model accepts up to 5 years of population data with an age range from 0 to 16 years. From this the average count for each age can be used as a guide to manually producing an estimated count for the age distribution of the typical cohort, from which the probability that an uninfected animal would leave the herd at age t (d_t) is obtained.

Animals are considered to leave the national population by one of the four surveillance streams (healthy slaughter, fallen stock, casualty slaughter and clinical suspect), indexed by subscript j. Two sets of country-specific exit probabilities are required: the probability $d_{j|t}$ that an uninfected (or apparently uninfected) animal would enter surveillance stream j given it left the herd at age t, and the probability $c_{j|t}$ of an infected animal being sent to surveillance stream j at the onset of clinical signs, given that clinical signs developed at age t. The exit probabilities we used as an example were derived from the surveillance data of 2002 from multiple EU countries, with the $d_{j|t}$ values from animals testing BSE-negative and the $c_{j|t}$ data from animals testing positive. For explanatory purposes, other input data (for example d_t) are presented as data for a fictional country (country A), and are based on composite data from EU countries. We assumed that the adult population size in country A was approximately one million animals and there was an apparent BSE prevalence of 0.72 cases per 10,000 animals (72 cases detected in the most recent complete year of testing). For a country

using the model, the values of d_t, $d_{j|t}$ and $c_{j|t}$ would be based on information specific to the country of concern.

3.3.1.2 Surveillance testing

The number of animals tested ($n_{j,t}$) and the number of animals testing positive ($x_{j,t}$) in each age group in each stream are required by the model. EU countries typically collect data for age groups of < 2 years, yearly increments for 2 to 7 years, a cumulative group of ≥ 8 years, and a group of animals of unknown age at testing. Cumulative groups are apportioned to each age based on d_t, with animals recorded as < 2 years old assumed to be 1 year of age.

3.3.1.3 Disease characteristics

The proportion of infected animals that first showed clinical signs at each age (c_t) was derived from the main epidemiological database for BSE in Great Britain (Wilesmith et al. 1991). These values may be adjusted but are considered appropriate for all countries (because Great Britain has vastly more experience with BSE than any other country to date). The incubation period has latent and preclinical phases, and the user can adjust the preclinical period by entering the proportion of animals expected to test positive if they left the population within 1 year prior to the appearance of clinical signs (r). The value of r is user-defined but a value between 0.3 and 0.5 (Wells et al. 1998; Wells et al. 1999; Grassi et al. 2001; European Commission 2002; Wells et al. 2005; G.A.H. Wells, M. Arnold pers. comm.) would be considered applicable to all countries. For example, if $r = 0.5$ then half of all infected animals leaving the population up to 12 months before they would otherwise have shown clinical signs would test positive. We assumed that all such preclinically infected animals were detectable using current testing procedures and that all infected animals would show clinical signs by 16 years of age.

3.3.2 BSE status assessment

This component computes age-specific removal probabilities, and estimates the initial infection prevalence (together with confidence limits) for birth cohorts in the national population of an infected country, or estimates an upper limit to the prevalence in the national population of uninfected countries. As part of this process a point value for each surveillance test undertaken can be calculated (as described below). The value reflects the relative likelihood of detecting BSE in an animal of a given age leaving via a stated stream, and therefore the relative worth of testing such an animal. The total number of points gained can be used to evaluate the surveillance carried out by a country. A point target may also be calculated, which is applicable for both endemic

and non-endemic countries wishing to demonstrate an upper limit for the possible level of disease and is used in other components of the model (not described in this paper). The following steps are performed:

3.3.2.1 Removal probabilities

- $d_{j,t}$: Probability an uninfected (or apparently uninfected) animal would exit at age t via stream j

  The country-specific exit probabilities for uninfected animals $d_{j|t}$ and the estimated age distribution d_t are used to calculate the probability of an uninfected animal being removed at age t from surveillance stream j ($d_{j,t} = d_{j|t} \times d_t$). These probabilities are also applicable to infected animals until clinical signs appear.

- $c_{j,t}$: Probability an infected animal would show clinical signs at age t and exit via stream j if no other culling pressures were operating

  The country-specific exit probabilities for infected animals showing clinical signs $c_{j|t}$ and the proportion of infected animals that begin to show clinical signs at each age c_t are used to calculate the probability of an infected animal showing signs and exiting at age t from surveillance stream j, if no other culling pressures were operating on the animal ($c_{j,t} = c_{j|t} \times c_t$).

- $b_{j,t}$: Probability an infected animal would exit at age t via stream j

  This is the probability that an infected animal left the herd for any reason (either BSE-related or otherwise). Until clinical signs develop, the exit probability for an infected animal is the same as for an uninfected animal. The age at which an infected animal would leave the herd is the minimum of the age it would have left had it not been infected, and the age at which clinical signs appeared. If both of these events occurred at the same age, the animal is assumed to have left the herd because of the appearance of clinical signs. The values of $b_{j,t}$ are calculated as follows:

$$\begin{aligned} b_{j,t} &= d_{j,t} \times (c_{t+1} + c_{t+2} + \dots) + c_{j,t} \times (d_t + d_{t+1} + \dots) \\ &= d_{j,t} \times (1 - C_t) + c_{j,t} \times (1 - D_{t-1}) \end{aligned} \tag{3.1}$$

  where C_t is the cumulative sum of c_t, $1 - C_t$ is the probability of an infected animal still being in the population after the age t and D_t is the cumulative sum of d_t.

- $g_{j,t}$: Probability an infected animal would exit and be detectable

  An infected animal will test positive if it is showing clinical signs or if it is one of the proportion of animals (r) expected to test positive within one year of

becoming clinically infected. The probability that an infected animal exited and was detectable, $g_{j,t}$, is calculated as follows:

$$g_{j,t} = d_{j,t} \times r \times c_{t+1} + c_{j,t} \times (1 - D_{t-1}) \tag{3.2}$$

- $f_{j,t}$: Proportion of exiting infected animals that would test positive

  This calculation takes into account the sensitivity $Se_{j,t}$ of the testing procedure, which we assumed to be 100% in country A. It was also assumed that the testing procedure resulted in 100% specificity for BSE.

$$f_{j,t} = \frac{g_{j,t} \times Se_{j,t}}{b_{j,t}} \tag{3.3}$$

- $a_{j,t}$: Ratio of infected to uninfected animals ($b_{j,t}/d_{j,t}$) that would exit via stream j at age t.

  This ratio $a_{j,t}$ is calculated to simplify calculations in later sections of the model:

$$a_{j,t} = \frac{b_{j,t}}{d_{j,t}} \tag{3.4}$$

- $v_{j,t}$: Point value of a test

  The ratio $v_{j,t}$ of detected infected animals to uninfected animals is calculated as:

$$v_{j,t} = a_{j,t} \times f_{j,t} = \frac{g_{j,t} \times Se_{j,t}}{d_{j,t}} \tag{3.5}$$

  Because the derived approximation for the confidence limits depends on $\sum n_{j,t} \times v_{j,t}$, it is convenient to think of $v_{j,t}$ as a way of measuring the contribution that a single test of an animal in a particular age/stream makes towards the estimate of prevalence. As a result, the values of $v_{j,t}$ can be used as points for surveillance tests performed.

- $w_{j,t}$: Points per euro

  The number of points per euro is calculated by dividing $v_{j,t}$ by the cost per test. These costs are user defined as they are specific to the country under consideration.

- Relative proportion of infected animals

  If p is the unknown proportion of animals that became BSE-infected in their first year of life, then the relative proportion $q_{j,t}$ of animals leaving the herd in class j at age t that are infected is:

$$q_{j,t} = \frac{p \times b_{j,t}}{p \times b_{j,t} + (1-p) \times d_{j,t}} = \frac{p \times a_{j,t}}{p \times a_{j,t} + (1-p)} \tag{3.6}$$

  This proportion needs to be multiplied by $f_{j,t}$ to give the apparent prevalence.

The model assumes that the number of positive animals detected in stream j at age t ($X_{j,t}$) is binomially distributed. The binomial distribution has the parameters (n, p) with the number of trials n equal to $n_{j,t}$ and the probability of success p estimated by the apparent prevalence $f_{j,t} \times q_{j,t}$:

$$X_{j,t} \sim \text{Binomial}(n_{j,t}, f_{j,t} \times q_{j,t}). \tag{3.7}$$

Equation 3.7 is the basis of the prevalence estimation. The method of moments (equating the observed number of positives with the expected number) and maximum likelihood can both be used to estimate p. Both methods give almost identical results for the level of prevalence associated with BSE cases in the EU. For simplicity, we used the method of moments in this paper (see Equation 3.9).

3.3.2.2 Prevalence estimation in endemic countries

This analysis assumes a different infection prevalence for each cohort and combines information for each cohort over all of the years of surveillance data entered.

The testing data for grouped older animals testing negative are distributed by birth cohort according to the proportion of animals of each age in the estimated age distribution, for example $n_{j,t} = n_{8+} \times d_{j,t}/(1 - D_7)$. For test-positive animals the grouped data are distributed according to B_t. If cumulative information is provided for the age group of less than 2 years old, all animals are assumed to be one year old.

An approximate prevalence is found as a starting point for the next step. This is based on an approximation (that ignores the denominator) to Equation 3.9.

$$p = \sum X_{j,t} / \sum n_{j,t} \times v_{j,t} \tag{3.8}$$

The summation is over those testing results that apply to the particular birth cohort.

The estimated proportion of animals infected in the cohort (p) is found by equating the observed number of test-positive animals $x_{j,t}$ with the expected number of test-positive animals, $n_{j,t} \times f_{j,t} \times q_{j,t}$. This results in an equation that must be solved iteratively for p:

$$\sum_y x_{j,t} = \sum_y \frac{n_{j,t} \times v_{j,t} \times p}{1 - p \times (1 - a_{j,t})} \tag{3.9}$$

The summation is over all testing data for animals born in the year y. The process is repeated for each cohort in the national population for which sufficient data is available.

The number of infected animals from a particular age cohort in the national population is found by multiplying the initial prevalence p by the proportion of infected animals remaining ($1 - B_t$), and by the number of animals in the national population. This number is summed over all birth years except for the youngest cohort. These youngest animals are excluded from the estimate due to inadequacy of available data;

few animals in this age group have been tested because there has been insufficient time since birth for infected animals to reach a detectable stage of infection.

Approximate confidence limits are obtained by treating the small number of BSE cases detected as a Poisson distribution with mean λ. The $\gamma\%$ confidence limits for λ ($\lambda_{upper,X,\gamma}$ and $\lambda_{lower,X,\gamma}$) are determined from the observed number of cases ($X = \sum x_{j,t}$). The confidence limits for λ are then substituted for X in Equation 3.9 and solved to give confidence limits for p (p_{upper} and p_{lower}):

$$\lambda_{upper,X,\gamma} = \sum_j \frac{n_{j,t} \times f_{j,t} \times p_{upper} \times a_{j,t}}{1 - p_{upper} \times (1 - a_{j,t})} \tag{3.10}$$

In setting upper limits for countries in which no cases have been detected ($X = 0$), it is convenient to note that $\lambda_{upper,0,\gamma} = -\ln(1-\gamma)$.

3.3.2.3 Estimation of the upper confidence limit of prevalence in uninfected countries

The method used in Section 3.3.2.2 works equally well to estimate the upper confidence limit of prevalence in uninfected countries, or for infected countries in years when new infections were not thought to be occurring. All available surveillance data for cohorts born after a designated year can be used in this calculation, as opposed to considering data on an individual cohort basis as above.

3.4 Results

3.4.1 Input data

Table 3.1 shows the example, hypothetical age input data table in BSurvE. The user can enter age counts for up to 5 years (only two are shown), with the average count for each age across the 5 years being used as a guide to complete the estimated count. We assumed that the number of animals born into each annual cohort is 300,000, and that there is a steady annual decline in the number of animals remaining in the cohort as it ages.

The values we used for $d_{j|t}$ and $c_{j|t}$ in this example were derived from pooled EU data and are shown in Figures 3.1 and 3.2 respectively. We expected that for all ages most uninfected animals would leave via the healthy slaughter stream, with smaller proportions exiting through the fallen stock and casualty slaughter streams and a small percentage leaving as clinical suspects. Most infected animals showing clinical signs were expected to leave as clinical suspects, followed by casualty slaughter and fallen stock with a very small proportion entering the healthy-slaughter stream. The incubation period of infected animals is illustrated in Figure 3.3 (Wilesmith et al. 1991). The preclinical phase is shown as being approximately five months in duration in this example ($r = 0.40$).

Table 3.1: The BSurvE age data entry table for country A. In the model coloured cells are used to indicate user-defined input (i.e. the observed and estimated counts of cattle in this table). Up to 5 years of national population data can be entered as observed counts, which contribute to the average count. The average can be used as a guide to produce the estimated count, which is the age distribution of a typical cohort.

	Number of cattle		Average		Estimated	
Age (years)	2000[a]	2004	count	Total hazard[b]	count[c]	Total hazard[b]
0	294,807	296,629	299,873	0.05	300,000	0.07
1	286,823	276,817	285,947	0.12	280,000	0.11
2	249,985	258,300	252,911	0.18	249,600	0.17
3	207,380	206,824	207,379	0.20	208,400	0.21
4	163,668	169,467	164,989	0.25	164,600	0.25
5	119,425	123,243	124,123	0.29	123,200	0.28
6	89,814	86,467	87,531	0.30	89,000	0.31
7	64,281	59,291	61,506	0.32	61,300	0.31
8	42,164	41,116	41,661	0.33	42,000	0.34
9	28,643	27,041	27,861	0.37	27,800	0.37
10	16,709	18,291	17,665	0.41	17,580	0.41
11	10,629	9923	10,497	0.44	10,420	0.43
12	5721	6082	5856	0.47	5925	0.49
13	3133	3110	3087	0.56	3045	0.55
14	1299	1411	1364	0.61	1365	0.61
15	510	544	530	0.79	528	0.79
16	112	107	110	1.00	110	1.00

[a] In the model up to 5 years of national population data can be entered as original counts. Two years are shown.
[b] The probability of removal given the animal has survived to the specified age.
[c] The typical cohort age distribution expected to be seen in the country, which is entered by the user. These values are used in the calculations in the model.

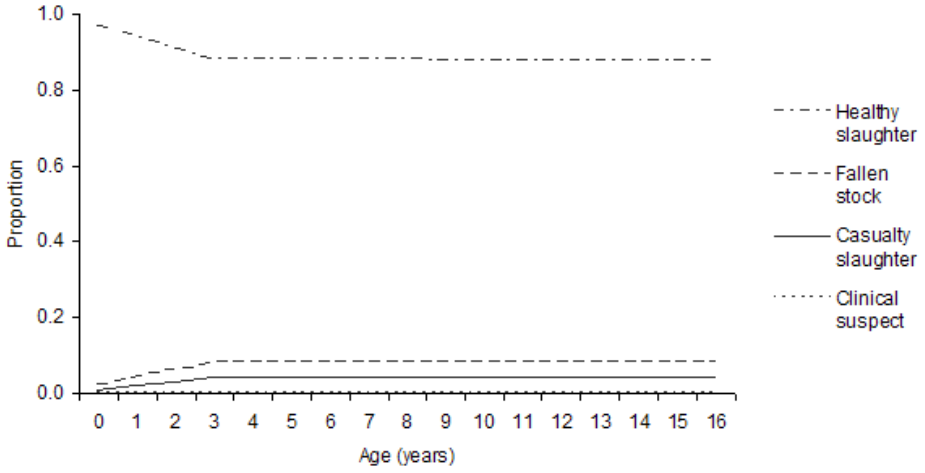

Figure 3.1: $d_{j|t}$: The distribution of exiting uninfected animals apportioned between the four surveillance streams. This is user-defined input to the model. The clinical suspect line is essentially coincident with the x-axis.

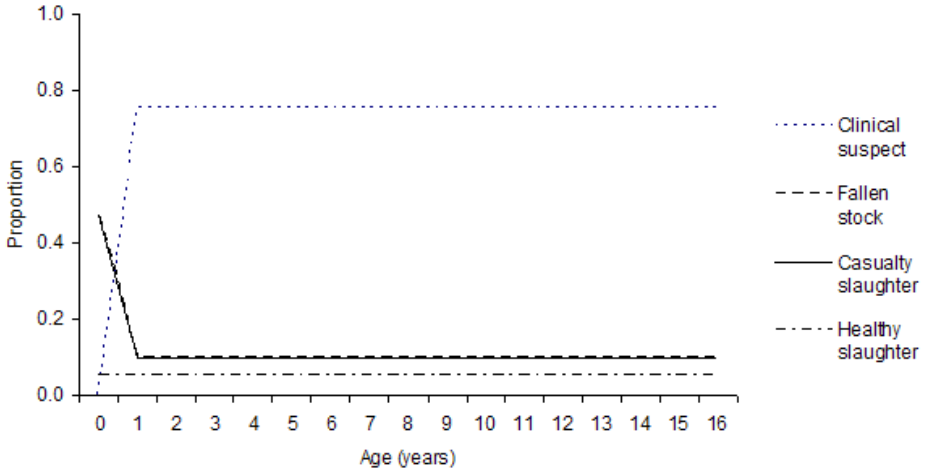

Figure 3.2: $c_{j|t}$: The distribution of exiting BSE-infected cattle apportioned between the four surveillance streams. This is user-defined input to the model. The fallen stock and casualty slaughter lines are essentially coincident.

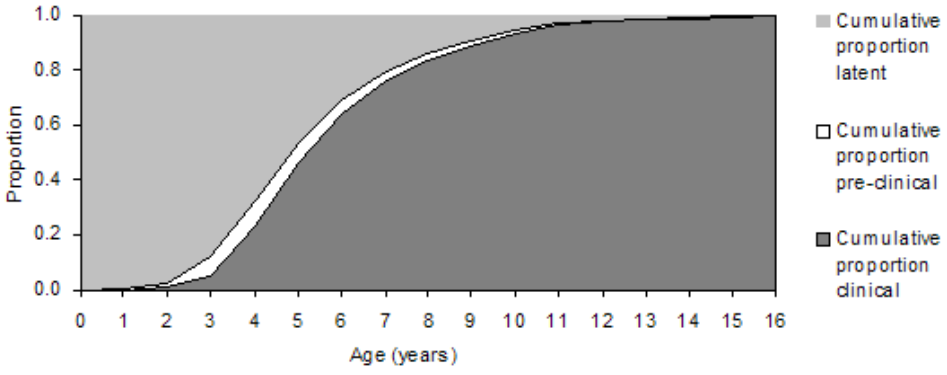

Figure 3.3: Infection status of BSE-infected cattle.

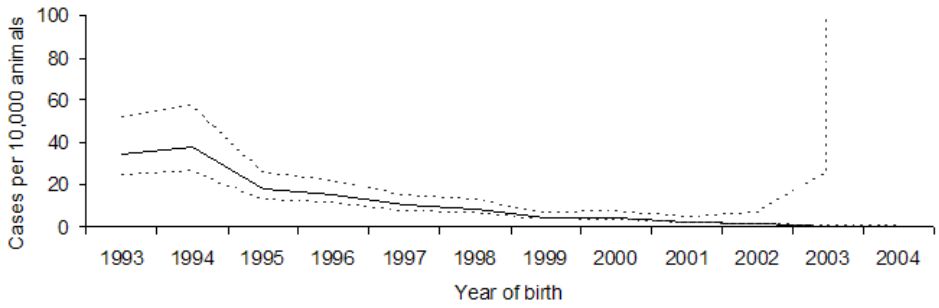

Figure 3.4: Predicted true BSE prevalences for hypothetical country A (cases per 10,000) for each birth cohort. (Interrupted lines are 95% confidence limits.)

3.4.2 BSE status assessment

Surveillance data were entered into the spreadsheet with a cumulative group of ≥ 8 years. Tests in this group were distributed according to the estimated age distribution, with the results for 2004 shown in Table 3.2. Removal probabilities $d_{j,t}$ and $c_{j,t}$ were calculated as above, with all subsequent removal probabilities ($b_{j,t}$, $g_{j,t}$, $a_{j,t}$, $f_{j,t}$, $v_{j,t}$ and $w_{j,t}$) calculated using these values.

The estimated true infection prevalence for each cohort (Section 3.3.2.2) is illustrated in Figure 3.4. A decline in the prevalence of infection is seen from the 1994 to later cohorts. The upper confidence limit increases for the younger cohorts and there is a high upper confidence level on the estimate for the 2003 and 2004 cohorts due to inadequacy of available data - fewer animals in these age groups have been tested and there has been insufficient time since birth for infected animals to reach a detectable stage of infection. The two youngest cohorts were excluded from the prevalence estimate for these reasons and the resulting estimate of true BSE prevalence in this national population was 0.9 cases per 10,000 animals (upper 95% confidence limit 7.57 cases per 10,000).

We estimated the upper limit of true prevalence if the country was uninfected (Section 3.3.2.3) to be 12.20 cases per 10,000 animals. However this method assumes a constant infection prevalence for each cohort and such an assumption is not suitable for this example data set. If the same age data and exit probabilities were used with the same amount of testing, but with no positive cases, the upper 95% confidence limit of the prevalence estimate was 0.08 cases per 10,000 animals.

3.5 Discussion

Fulfilling the objectives of this study involved many challenges and development of the BSurvE model has been an evolutionary process. This culminated in the European Food Safety Authority (EFSA) being invited by the EC in 2004 to provide advice on

Table 3.2: $n_{j,t}$ and $x_{j,t}$: The observed number of animals tested and testing positive in hypothetical country A at age t in surveillance stream j in 2004

Age (years)	Cattle tested $n_{j,t}$				Year of birth of cohort	Cattle testing positive $x_{j,t}$			
	Healthy slaughter	Fallen stock	Casualty slaughter	Clinical suspect		Healthy slaughter	Fallen stock	Casualty slaughter	Clinical suspect
0					2004				
1	0	0	45	0	2003	0	0	0	0
2	79,562	800	76	12	2002	0	0	0	0
3	35,874	870	154	16	2001	1	0	0	1
4	12,965	753	79	22	2000	0	3	1	3
5	13,856	851	85	25	1999	2	7	0	9
6	11,938	678	76	31	1998	2	8	0	10
7	7195	486	67	20	1997	3	4	1	7
8	30,607	1738	23	17	1996	1	1	0	2
9	20,259	1150	15	12	1995	1	1	0	1
10	12,811	727	10	7	1994	0	0	0	1
11	7593	431	6	4	1993	0	0	0	0
12	4318	245	3	2	1992	0	0	0	0
13	2219	126	2	1	1991	0	0	0	0
14	995	56	1	1	1990	0	0	0	0
15	385	22	0	0	1989	0	0	0	0
16	80	5	0	0	1988	0	0	0	0
Unknown	0	0	85	10		0	0	0	0

the general approach used within BSurvE. The EFSA Scientific Expert Group convened for the evaluation reported its findings in October 2004 (EFSA 2004).

In addition to these discussions, three two-day practical workshops have been held. This allowed veterinary epidemiologists from EU Member States and other countries to use BSurvE to analyse their country's surveillance data. As a result of these workshops a number of refinements were made to BSurvE and consideration has been given to providing advice where the available data inputs are lacking in various respects. The following provides a summary of the key issues identified.

National data collection procedures vary and in many countries there is limited availability of data suitable for use in BSurvE. For example, some countries do not record the age of tested animals. Such data can be distributed according to an estimated age distribution but this introduces greater uncertainty in the results, particularly when estimation is done for individual age cohorts. Age and surveillance data are commonly collected within multi-age groups, particularly for older animals, and in order to make prevalence estimations on a cohort basis it is necessary to distribute this data according to an approximation of the age distribution of a cohort, i.e. the estimated count d_t. The estimated count is determined manually, guided by the age data that is available, i.e. the age distribution of the national population for up to 5 years. Automation of the approximation process was attempted but found to be inadequate due to the wide variability in national data and the need for distribution of different multi-age groups. The collection of national data across a wider age range will improve accuracy and

if gathered over a period of time will allow the construction of the current estimated age counts from actual data. BSurvE makes the assumption that the estimated age distribution is applicable to all cohorts considered in the model (which implies that the population is stable over the analysed time period), although a few countries have had wide variation in population size within a short period of time.

Initial versions of BSurvE accepted age data stratified by industry (dairy and beef), because management systems and age structures are very different between the two production sectors and there is a higher prevalence of BSE in dairy animals (Wilesmith et al. 1988; Stevenson et al. 2000, Ducrot et al. 2003). However, unless all input and surveillance data is allocated by production sector it is not possible to estimate the prevalence within each sector; such information was not available to the authors and would in any case be difficult to collect. Hence, we modified the model to accept total population age data without reference to industry. Analyses could be run for each production sector separately if data were available.

Currently, up to 5 years of surveillance data may be entered and analysed by the user. In a situation where it is not necessary to estimate infection prevalence on a per-cohort basis, data from multiple years can be amalgamated. Some countries categorise animals into a larger number of streams or have different eligibility criteria for the streams used in BSurvE. For the analysis of data within a country the user should interpret the results according to their categorisation of the input data.

Country-specific exit probabilities for uninfected animals ($d_{j|t}$) should in principle not be difficult for a country to obtain, regardless of national BSE prevalence. Probabilities for infected animals ($c_{j|t}$) would be more easily obtained for a high prevalence country than a low prevalence/uninfected country because case data can be used to indicate the required values. National studies on the disposal of cattle would assist in providing the required data, and are being undertaken in some countries.

BSurvE assumes that most animals are infected in their first year of life. Epidemiological studies of the BSE epidemic in Great Britain indicate that there is an age-dependent susceptibility, with cattle in their first six months of life being at most risk (Arnold and Wilesmith 2004). Modelling studies of the French BSE epidemic suggest that most cattle were infected between six and twelve months of age (Supervie and Costagliola 2004). The distribution of the time until clinical signs develop reflects these findings. However, allowance for an older age of infection can easily be incorporated into BSurvE by adjusting this distribution. BSurvE also allows the user to set the proportion of preclinical animals that would be detectable if culled in the year prior to the onset of clinical signs. As indicated above, we suggest a range of 0.3 to 0.5, based on current evidence from the validity of the three screening tests that have been used to date, and for which performance characteristics are for practical purposes similar. If more-sensitive screening tests are developed then there is the facility to change the

value of this input parameter.

When BSurvE was used by various countries, prevalence estimation by cohort resulted in realistic curves, whereby increases or decreases in the estimate could be related to events such as implementation of feed bans or other statutory controls. The wide confidence intervals for recent cohorts will decrease over time as these cohorts age and more data become available.

This study was able to capitalise on the results of the very large amount of surveillance carried out within the EU. The use of BSurvE model has been examined for a wide range of scenarios and can accommodate the various demographic and epidemiological situations likely to exist. It is an epidemiological tool with which users can become proficient in a relatively short period of time.

3.6 Conclusions

BSurvE estimates a true population prevalence by combining the sampling information from a number of different sub-populations of animals. Individual cohort prevalence estimates for populations of several countries were biologically plausible, with decreases in the prevalences between cohorts relating to control measures. This method can be used for other diseases, provided that the (mathematical) relationship between the prevalence in each sub-population at the time of testing and the prevalence being estimated can be determined. The current version of BSurvE can be obtained from www.BSurvE.com.

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Chapter 4

A model for evaluating national surveillance programmes for BSE

4.1 Abstract

Our BSurvE spreadsheet model estimates the BSE prevalence in a national cattle population, and can be used to evaluate and compare alternative strategies for a national surveillance programme. Each individual surveillance test has a point value (based on demographic and epidemiological information) that reflects the likelihood of detecting BSE in an animal of a given age leaving the population via the stated surveillance stream. A target sum point value for the country is calculated according to a user-defined design prevalence and confidence level, the number of cases detected in animals born after the selected starting date and the national adult herd size. Surveillance tests carried out on different sub-populations of animals are ranked according to the number of points gained per unit cost, and the results can be used in designing alternative surveillance programmes.

Prattley, D.J., Morris, R.S., Cannon, R.M., Wilesmith, J.W. and Stevenson, M.A. 2007. A model (BSurvE) for evaluating national surveillance programmes for bovine spongiform encephalopathy. Preventive Veterinary Medicine 81 225-235.

4.2 Introduction

The intensity and pattern of BSE surveillance testing varies greatly between countries and until recently there has been no standard method of evaluating such surveillance programmes. The World Organisation for Animal Health (OIE) provides guidelines for BSE surveillance, which were initially based on the results of passive clinical surveillance for BSE in Great Britain (World Organisation for Animal Health, 2004). Standards were revised to take into account the findings of the initial active surveillance of fallen stock in Switzerland, which revealed a greater prevalence of BSE than that estimated from clinical surveillance (Doherr et al. 1999). Between May 1999 and April 2000, a

targeted screening programme in Switzerland showed the odds of detecting a case of BSE in fallen stock was 49 times higher compared to detection via mandatory reporting of clinical suspects (passive surveillance); in emergency slaughter stock the odds were 58 times higher (Doherr et al. 2001).

The 2004 OIE guidelines required testing a minimum number of cattle showing clinical signs consistent with BSE, with the number adjusted according to the size of the cattle population > 30 months of age. Article 3.8.4.2 of the Animal Health Code 2004 (OIE) stated that the minimum numbers of animals to test were a 'subjective interpretation' rather than statistically derived, due to the non-randomness of sampling animals exhibiting clinical signs. Cattle can be considered to leave the national herd via one of four 'surveillance streams': clinical suspects (animals reported as showing neurological signs that might have been due to BSE), fallen stock (animals which died on farm), casualty slaughter (animals that are injured or abnormal but eligible for slaughter under special restrictions), or healthy slaughter (healthy cattle slaughtered for human consumption). If insufficient numbers of clinically affected animals were available, cattle showing clinical signs that were not necessarily those of BSE should be tested. This sub-population included fallen stock and casualty slaughter cattle. Healthy slaughter animals were used to make up any shortfall in a country with insufficient numbers in the above two categories. A surveillance programme based exclusively on random sampling from healthy slaughter animals was not recommended but permitted if sufficient numbers were tested to detect infection at a prevalence of less than one case in 1 million animals. Even if the assumption was made that each infected animal would test positive, this would require sampling of over 2.2 million animals to achieve 95% confidence of detecting one of five infected animals in a population of 5 million adult cattle. These requirements addressed a range of situations in different countries, but did not provide a way to demonstrate the prevalence of infection or allow uncomplicated comparison between countries.

The development of rapid screening tests for BSE and the evaluation of the first three tests by the European Commission (Moynagh and Schimmel 1999) led to the widespread use of these screening tests in the European Union (EU) countries in 1999 and in other countries at the end of 2000. Within the EU, compulsory large-scale surveillance for BSE in all Member States began in July 2001 (Regulation (EC) No. 999/2001 of the European Parliament). According to current EU regulations most member countries are required to test all animals showing clinical signs, all healthy slaughter stock > 30 months of age and all fallen stock and casualty-slaughter animals > 24 months old at the time of death. As a result, approximately 11 million cattle per year are tested within the EU (European Commission 2004). This has provided useful insights into the relative efficiencies of the four surveillance streams, and has indicated that due

to geographic, logistic and other factors, testing 100% of eligible animals is not always possible. The economic and case-detection efficiency of a surveillance programme might be improved if the animals most likely to be infected are identified and targeted.

We developed the BSurvE spreadsheet model to: (1) estimate BSE infection prevalence in national herds (Prattley et al. 2007), (2) evaluate current national surveillance programmes, and (3) provide tools to improve surveillance strategies for infected and uninfected countries. Improving a surveillance strategy refers to increasing the efficiency of case detection within economic constraints. We used a hypothetical example country (and typical European input data) to illustrate the point system used in the BSurvE model. Points are allocated for each surveillance test carried out and a point target calculated for a country according to the national adult-herd size, a chosen design prevalence (the BSE prevalence a country would like to show is not exceeded in the national herd), a required level of confidence and the observed number of cases detected in animals born after the selected starting date. The point system is a further development of the concept described in Cannon (2002), which aimed to estimate the overall confidence level of detection of infection for a surveillance regime using multiple methods of detection (with varying sensitivities), while accounting for changes in infection prevalence over time.

4.3 Methods

We developed BSurvE as a spreadsheet (Microsoft Excel, Microsoft, Redmont, WA) with four components: Input Data; BSE Status Assessment; BSE Surveillance Assessment; and Surveillance Resource Allocation. The first two components were described previously (Prattley et al. 2007) while the two latter sections are discussed below. The required input data are the age distribution of a typical birth cohort (to 16 years of age), up to 5 years of surveillance data, the incubation period of BSE, and conditional age-stream exit probabilities for clinically infected animals and for all other animals. The input data used for our fictional country (country A) are based on composite data from EU countries and are the same as that used in Prattley et al. (2007). Surveillance data for country A are shown in Table 4.1.

4.3.1 BSE surveillance assessment

For a range of user-defined input prevalences, the expected numbers of different sub-groups of animals that will be removed from the population are calculated. These estimates illustrate the removal probabilities for the different sub-groups (described in Prattley et al. 2007) in terms of actual numbers of animals. For each age of the cohort, the expected number of infected animals removed, the expected number of undetected

Table 4.1: $n_{j,t}$ and $x_{j,t}$: The observed number of animals tested and testing positive in hypothetical country A at age t in surveillance stream j in 2004

Age (years)	Cattle tested $n_{j,t}$				Year of birth of cohort	Cattle testing positive $x_{j,t}$			
	Healthy slaughter	Fallen stock	Casualty slaughter	Clinical suspect		Healthy slaughter	Fallen stock	Casualty slaughter	Clinical suspect
0					2004				
1	0	0	45	0	2003	0	0	0	0
2	79,562	800	76	12	2002	0	0	0	0
3	35,874	870	154	16	2001	1	0	0	1
4	12,965	753	79	22	2000	0	3	1	3
5	13,856	851	85	25	1999	2	7	0	9
6	11,938	678	76	31	1998	2	8	0	10
7	7195	486	67	20	1997	3	4	1	7
8	30,607	1738	23	17	1996	1	1	0	2
9	20,259	1150	15	12	1995	1	1	0	1
10	12,811	727	10	7	1994	0	0	0	1
11	7593	431	6	4	1993	0	0	0	0
12	4318	245	3	2	1992	0	0	0	0
13	2219	126	2	1	1991	0	0	0	0
14	995	56	1	1	1990	0	0	0	0
15	385	22	0	0	1989	0	0	0	0
16	80	5	0	0	1988	0	0	0	0
Unknown	0	0	85	10		0	0	0	0

infected animals removed and the expected proportion of detectable infected animals removed via each of the four surveillance streams are calculated.

The surveillance programme is also evaluated by dividing the actual number of animals tested in each age group and surveillance stream by the number expected to leave the herd in each of those age groups via the four streams. The number expected to leave is calculated using a user-defined design prevalence (referred to as p_{design}) for the number of animals in the cohort that were infected, and the exit probabilities $d_{j,t}$ (the probability an uninfected (or apparently uninfected) animal would leave the national herd at age t via stream j) and $b_{j,t}$ (the probability an infected animal would exit at age t via stream j) (see Prattley et al. 2007).

4.3.2 Surveillance resource allocation

4.3.2.1 Surveillance system evaluation

The component of the model for surveillance system evaluation was designed to quantify the value of the surveillance programme currently undertaken by a country, and to provide tools to aid the design of an alternative programme that might improve BSE detection efficiency and cost. The values of $v_{j,t}$ (the ratio of detected infected to uninfected animals leaving the national herd, calculated as described in Prattley et al. (2007)) are used as the number of points gained for each test carried out. These values reflect the relative likelihood of detecting BSE in each age/stream combination, and the estimation of prevalence depends on $v_{j,t}$ and the number of animals tested. Therefore,

$v_{j,t}$ can be considered a way of measuring the contribution one surveillance test makes towards the overall prevalence estimate. The total number of points achieved by a country is calculated by multiplying the number of tests done for each of the four surveillance streams at each age by the appropriate $v_{j,t}$ value, and summing the result. For example, if testing a 5 year-old casualty slaughter animal was worth 1.6 points, 2400 points would be gained when 1500 such animals were tested. A starting date would be set by the country, with points only being accumulated for tests on animals that were born after that date.

Each combination of exit stream and animal age is sorted according to the economy of testing (points per euro). Combined with the number of animals estimated to be available in each surveillance stream, the resulting table helps the user to develop an alternative surveillance programme that would improve the case detection efficiency and reduce the cost of surveillance.

4.3.2.2 Demonstrating maximum infection prevalences

A point target for the country is set that depends on the adult ($>$ 24 months) population size, the desired design prevalence and confidence level, and the number of cases (X) of BSE that have been detected in animals born after the nominated starting date. The target T is the total amount of testing that must be done with no further cases of BSE detected. The target is calculated by dividing $\lambda_{upper,X,\gamma}$, the upper γ% confidence limit for a Poisson distribution for which X cases had been observed, by the design prevalence:

$$T = \lambda_{upper,X,\gamma}/p_{design} \tag{4.1}$$

The country would select a p_{design} and carry out sufficient testing to show that their BSE prevalence was below the nominated p_{design}. Because countries with smaller cattle populations are disadvantaged in comparison with countries that have large populations, for national herds of less than one million animals the p_{design} is adjusted to represent a chosen number of infected animals in the population (referred to as an adjusted prevalence). Thus the time needed to test sufficient animals in order to reach the target is independent of population size. For populations of $>$ 1 million adult animals, the p_{design} is expressed as the number of infected cattle per million animals. The model output includes point targets for a user-defined range of p_{design} values and confidence-level settings. The model also calculates the total number of points accumulated by the current surveillance programme and determines the confidence levels achieved to date for various p_{design} values. These calculations summarise all years of surveillance data entered by the user.

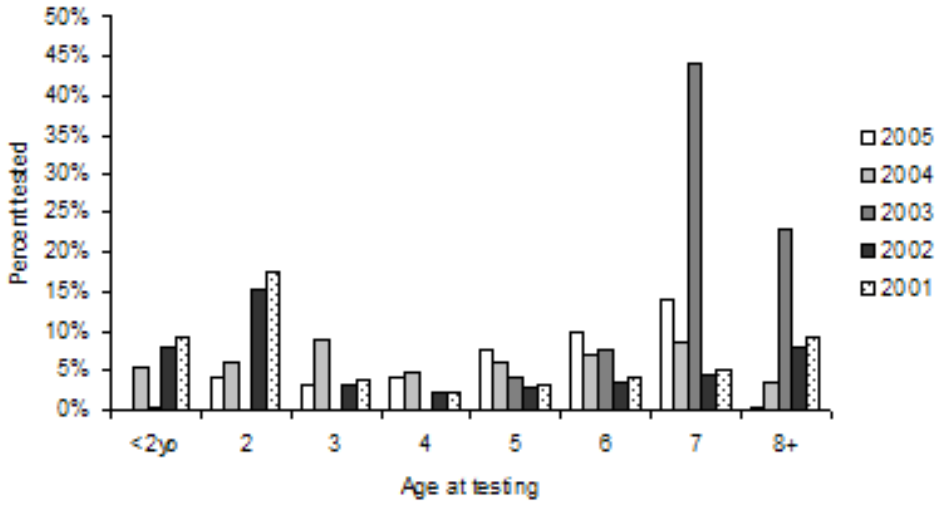

Figure 4.1: Results for the proportion (actual number tested divided by expected number entering the stream) of each age group tested in the casualty slaughter stream if the chosen design prevalence was 4 infected animals per 10,000.

4.4 Results

The results relate to an adult population in country A of approximately 1 million animals with a BSE prevalence of 0.72 cases per 10,000 animals (72 cases detected in the most recent complete year of testing).

4.4.1 BSE surveillance assessment

Figure 4.1 shows the number of animals actually tested as a percentage of the number of animals that would be expected to enter the casualty-slaughter stream when the user-defined prevalence was four cases per 10,000 animals. The results are a reflection of testing policies and can also highlight areas where adjustment of input parameters might be necessary (for example, if the proportion tested is greater than 100% of the number of animals expected to enter the stated stream). Equivalent calculations were made for each of the other three streams.

4.4.2 Surveillance resource allocation

The values $v_{j,t}$ (calculated as outlined in Prattley et al. (2007)) were used as the number of points gained for each surveillance test carried out by country A (Figure 4.2). The highest points were gained for testing clinical suspects, because there was a high ratio of detectable infected to uninfected animals entering this stream, particularly at ages 4 to 6 years. Lowest points were gained by testing very young animals in any

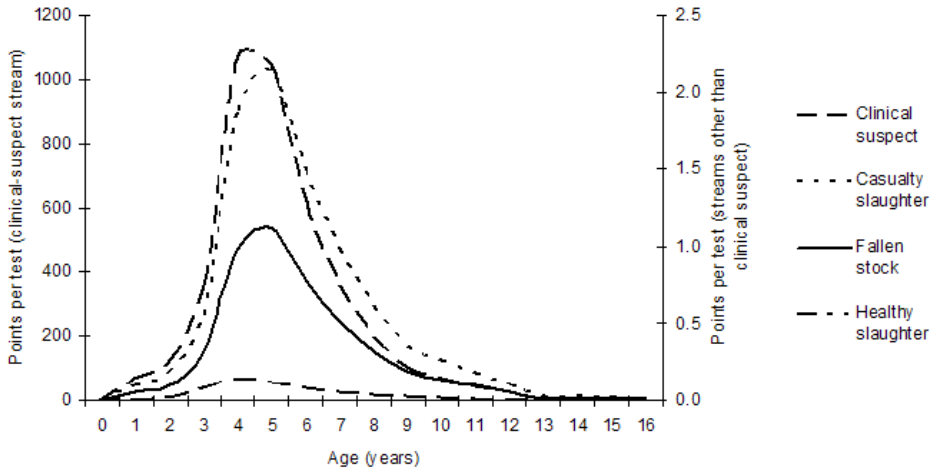

Figure 4.2: $v_{j,t}$: The calculated points associated with the value of testing an animal leaving the population via stream j at age t.

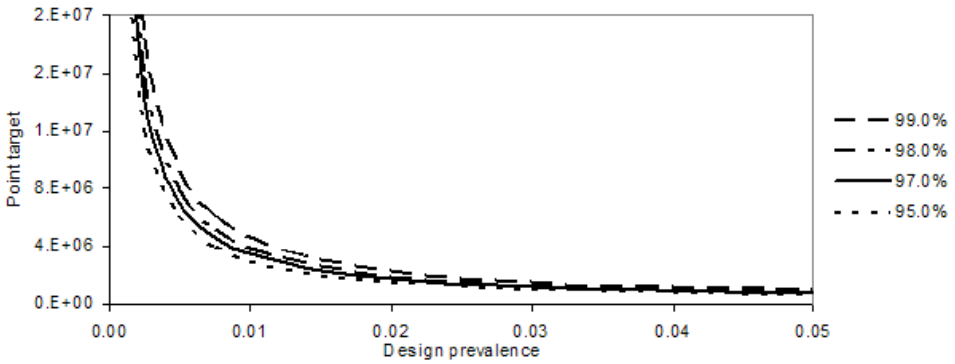

Figure 4.3: Calculated number of points required to reach the desired confidence that prevalence (number of infected animals per 10,000) is below the required prevalence when no BSE cases have been found ($X = 0$) in a population greater than one million.

stream, with the healthy-slaughter stream being least rewarding on average across all ages. Note that the points for clinical suspects are greater than the points for the other streams, and use a secondary y-axis. The cost per point may also be relevant.

The point targets for country A are illustrated in Figure 4.3 for a range of p_{design} values and confidence levels. A desire to have a high degree of confidence in demonstrating that estimated prevalence is below a very low user-defined threshold prevalence results in a higher target. Table 4.2 shows the adjustment in the point target for a country where X positive cases are born after the starting date, with varying p_{design} and confidence levels.

Table 4.2: The calculated number of points required to reach the desired confidence that estimated prevalence (cases per 10,000) is below the user-defined design prevalence for countries that have identified X number of BSE cases in a population of 1 million or more adult animals

Design prevalence (cases per 10,000)	Number of cases detected (X)	Confidence required			
		90%	95%	97.50%	99%
0.01	0	2,302,585	2,995,732	3,688,879	4,605,170
	1	3,889,720	4,743,865	5,571,643	6,638,352
	2	5,322,320	6,295,794	7,224,688	8,405,947
	3	6,680,783	7,753,657	8,767,273	10,045,118
	4	7,993,590	9,153,519	10,241,589	11,604,626
	5	9,274,674	10,513,035	11,668,332	13,108,484
0.02	0	1,151,293	1,497,866	1,844,440	2,302,585
	1	1,944,860	2,371,932	2,785,822	3,319,176
	2	2,661,160	3,147,897	3,612,344	4,202,973
	3	3,340,392	3,876,828	4,383,637	5,022,559
	4	3,996,795	4,576,760	5,120,794	5,802,313
	5	4,637,337	5,256,517	5,834,166	6,554,242
0.04	0	575,646	748,933	922,220	1,151,293
	1	972,430	1,185,966	1,392,911	1,659,588
	2	1,330,580	1,573,948	1,806,172	2,101,487
	3	1,670,196	1,938,414	2,191,818	2,511,279
	4	1,998,397	2,288,380	2,560,397	2,901,156
	5	2,318,668	2,628,259	2,917,083	3,277,121
For other prevalence values, divide the values below by the prevalence (per 10,000):					
	0	23,026	29,957	36,889	46,052
	1	38,897	47,439	55,716	66,384
	2	53,223	62,958	72,247	84,059
	3	66,808	77,537	87,673	100,451
	4	79,936	91,535	102,416	116,046
	5	92,747	105,130	116,683	131,085

Table 4.3: Summary of the calculated number of points gained by hypothetical country A for surveillance testing over the five year period

	2005	2004	2003	2002	2001	Total
Number of animals tested	169,635	250,503	245,685	255,133	255,140	1,176,096
Number of points achieved	75,058	107,448	104,363	104,129	72,621	463,618

Table 4.4: Calculated time to achieve point target (years) for country A for a range of p_{design}s and confidence levels using the 2004 testing pattern, and the level of confidence achieved by the total number of points gained for testing across all years to date

	Time required (years) to reach level of confidence				Confidence achieved
Design prevalence [a]	90%	95%	97.5%	99%	to date (%)[b]
0.0025	86	112	137	171	11
0.0050	43	56	69	86	21
0.0075	29	37	46	57	29
0.0100	21	28	34	43	37
0.0125	17	22	27	34	44
0.0150	14	19	23	29	50
0.0175	12	16	20	24	55
0.0200	11	14	17	21	60
0.0225	10	12	15	19	65
0.0250	9	11	14	17	68

[a] Prevalence expressed as number infected per 10,000 animals.
[b] Confidence level achieved for the total points accumulated for all years of testing.

Table 4.3 summarises the number of points gained for each year of surveillance testing in country A. The number of tests and points gained in 2005 reflect an as-yet incomplete year of testing.

The level of confidence achieved from the total number of points gained over the 5 years (463,618 points) was calculated for a range of p_{design}, and increased as p_{design} increased. In Table 4.4 it can be seen that the time taken for country A to achieve the point target (assuming that the pattern of future years of testing matched that of 2004 and that no cases were detected in animals born after 2001) increased as lower p_{design} and higher confidence levels were required.

4.5 Discussion

BSE has caused considerable public health concerns and has had serious economic consequences in several countries. The development of rapid screening tests for BSE and their use in surveillance have identified BSE in a greater number of countries than had been determined by the examination of clinically suspect animals. Surveillance for BSE is complex because infection can only be detected by post-mortem examination

and only in the late stages of the incubation period. Animals available for testing are not random samples and the prevalence estimates obtained from each class of stock are biased. In addition, the cost of surveillance is expensive because of the relatively low prevalence in most affected cattle populations and the costs associated with securing the animals for sampling and the sample collection itself.

The choice to test animals from a particular age/stream combination remains with the country concerned, so that resources may be used most appropriately in the given situation. Sorting each age/stream combination according to the economy of testing (points gained per unit of currency spent) provides a starting point for designing an alternative surveillance programme. Consideration must be given to the availability of animals entering each stream, as although it may be more economical to test, for example, larger numbers of fallen stock, the current infrastructure in a country may not allow for the collection and subsequent testing of this group of animals. While acknowledging that different countries may have slightly different definitions for the four streams, efforts should be made to classify animals into the appropriate stream. Misclassification of large numbers of animals into streams that have previously been awarded the highest points would have the effect of diluting the relative prevalence in that age/stream cell, thereby decreasing the number of points gained per test.

BSurvE cannot overcome the basic limitations of sampling theory which mean that large sample sizes are inevitably required to detect infected animals in cattle populations with a very low prevalence, and even larger sample sizes are required to estimate the prevalence with narrow confidence limits. The appropriate p_{design} remains as a matter of political and epidemiological judgement. Were formal targets to be set (i.e. a required p_{design} and confidence level), then it is possible that the required confidence level could be adjusted according to the risk-mitigation measures operating in a country. In other words, the p_{design} would remain the same regardless of the perceived confidence but the level of confidence required would reflect the country's efforts to prevent or control the infection. Table 4.2 provides examples of the point targets for various p_{design}, confidence levels and number of cases detected. A greater level of confidence (and consequently a higher target) would be required for a country with relatively poor control measures. If an animal born after the starting date were detected as BSE-positive, the target would be increased. For example, the target would increase from 2,995,370 (X=0) to 4,743,870 (X=1) after the first detection of BSE in a country wishing to demonstrate 95% confidence that the prevalence was < 1 in 1 million. The points represent the status of the national population over the period they were accumulated, and hence they would gradually expire as the cattle population changed over time. We propose that points expire at the rate of 5% per year, so that over 20 years they would have to be totally renewed in order for a country to maintain

the same status. This represents the maximum time over which a cow is likely to live, therefore the turnover time for points matches the maximum turnover time of the cattle population. This proposal is obviously open to further discussion.

In 2005, the OIE reviewed their BSE-surveillance guidelines and adopted a simplification of the point system in the BSurvE model (World Organisation for Animal Health 2005). "Type A" surveillance has 95% probability of detecting one BSE case in 100,000 adult cattle, while "Type B" maintenance surveillance (for countries with very low risk of BSE) has 95% probability of detecting one case in 50,000 adult animals. The point target depends on the adult population size and type of surveillance. The points gained per test are categorised according to the age of animal tested (five categories) and surveillance stream (four categories), and represent a mean value based on surveillance data from different countries. Points remain valid for 7 years. Although not taking full advantage of data available within some countries, this implementation is a move towards more efficient, risk-based surveillance strategies for BSE.

4.6 Conclusions

The use of BSurvE model has been examined for a wide range of scenarios and can accommodate the various demographic and epidemiological situations likely to exist. It can be used to evaluate current national surveillance programmes and improve surveillance for infected and uninfected countries. The point system used in BSurvE can potentially be applied to other diseases to evaluate surveillance and monitoring programmes.

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Chapter 5

Integration of diverse surveillance data to evaluate national disease status

5.1 Abstract

Surveillance for *Trichinella* species is required under European Commission regulations, which have recently allowed for a reduction in the amount of national testing providing a negligible risk to human health can be demonstrated. Extensive surveillance for trichinellosis has been performed on multiple species over several years in Great Britain, including pigs, foxes and horses. This paper describes our method of integrating surveillance data from the different species and from sub-populations within species. Data from each population and sub-population were weighted according to the population's risk of infection relative to that of low-risk grower pigs, which were regarded as an indicator group. Low-risk grower pigs were those housed indoors and therefore classified as low-risk for contracting *Trichinella*. A national prevalence estimate for trichinellosis was produced for the indicator population based on the weighted surveillance data from all species and sub-populations. No *Trichinella* was detected by the surveillance. The method of moments was used to estimate the prevalence of trichinellosis, and the upper 95% confidence limit was found by using a Poisson distribution to represent the number of positive animals found. The 95% upper confidence limit for the prevalence in the national pig population was 0.000036% based on the data collected from 2000-2005.

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5.2 Introduction

Surveillance for a given disease may require testing of animals of different species, or animals belonging to distinct sub-populations of the same species. The size of each population is likely to differ, as are the numbers tested, test sensitivities and disease prevalence. Obtaining an overall measure of the disease status in a country or area can be difficult unless all of these factors are taken into account.

Surveillance for trichinellosis in Great Britain (GB) has been carried out on various animal populations for several decades. There have been no porcine cases detected since 1979, no confirmed cases in foxes since 1957 and there are no recorded equine cases. No cases of human trichinellosis have been attributed to meat originating from GB since records began in 1965. This accumulated evidence provides support for the claim that GB has negligible risk of autochthonous cases of *Trichinella* infection in the human population. While prevalence estimates can be produced for individual species, the diverse sources of surveillance data have not been integrated to provide an estimate of prevalence with associated confidence limits in an indicator species.

There are similarities between surveillance for BSE and *Trichinella*. Both use multiple surveillance techniques which need to be integrated into a single assessment, and in both cases animals in some categories provide much stronger evidence than others. Post-mortem testing is used to provide information about the prevalence of disease in the population, and that prevalence might be very low. To interpret multiple sources of BSE surveillance data, a spreadsheet calculation model (BSurvE) (Prattley et al. 2007) was developed to combine information from four different surveillance sources (clinical suspects, fallen stock, casualty slaughter and healthy slaughter stock). In this model, the method of moments is used to determine the underlying prevalence of BSE in the standing cattle population that gives the best fit to the prevalence of BSE-positive animals in the surveillance streams tested. Simply combining the estimates numerically from the surveillance streams is inappropriate due to the non-random entry of animals into each of the streams, and it is necessary to minimise those biases. Estimates of the confidence limits around the prevalence are produced by assuming the small number of BSE cases follow a Poisson distribution, and substituting Poisson confidence limits into the method of moments equation.

We applied the concepts developed in the BSurvE model to integrate *Trichinella* surveillance data from multiple species and sub-populations within species. Our aim was to provide estimates of prevalence for all species both for defined areas within GB and for GB as a whole. As there have been no recorded cases of trichinellosis in the species under surveillance the point estimates of prevalence are all zero. However, 95% upper confidence limits (UCLs) for the prevalence estimates were required in order to indicate the upper value of the number of cases of disease that would be expected given

zero cases were found on testing.

5.3 Methods

Surveillance testing data were available for pigs, horses and foxes. Estimates of the total population at risk for each species and geographical distribution data for GB were also obtained. Humans become infected by consuming pork or horsemeat products, so they are considered to be secondary cases and were not included in the analysis.

5.3.1 Fox data

5.3.1.1 Fox population

A fox density grid was provided by the Central Science Laboratory, Sand Hutton, York, YO41 1LZ, England. The fox population was estimated using faecal density counts (Webbon et al. 2004), whereby fox faeces were counted in 444 one-kilometre squares throughout mainland Britain. Seven landscape types were identified and the estimated fox density for each type was applied as appropriate across GB.

5.3.1.2 Fox sampling

Several surveys for *Trichinella* in foxes were carried out between 1999 and 2006. We were provided with data from these surveys, including kill date, easting and northing coordinates of kill location, sex, estimated age and condition at the time of slaughter.

5.3.2 Horse data

5.3.2.1 Horse population

Equine population data were purchased from the National Equine Database (NED, National Equine Database, Stoneleigh Park, Kenilworth, Warwickshire, CV8 2TF, England). Counts of horses by year of birth (1967 to 2006) and counts of horses of unknown age were listed by county and postcode area (the first two digits of the postcode), as at 16 November 2006. The location information related to the owner rather than the horse as it is only mandatory for owners to supply their own locations and not that of their horses. However, as we were only able to map the provided data at county level, we considered that the owner location would in most circumstances be a sufficiently accurate representation of horse location. The number of horses per owner was not provided.

A horse population density map was created after allocation of horses within their county location. The 120,469 horses where the county location was unknown were allocated to counties in proportion to the county location distribution of the rest of the horse population. Horses were then allocated to a property within the appropriate

county, with the number of horses per holding determined using a pert distribution with a minimum of 1, maximum of 20 and most likely value of four. This was considered likely to adequately represent the majority of horse-grazing properties.

5.3.2.2 Horse sampling

Data from six abattoirs included the total number of horses processed per year between 2000 and 2005, although not all abattoirs provided data for each of the six years. In total there were 21 abattoir-years of data. The locations of origin of the slaughtered horses were not provided. It was assumed that all slaughtered horses were tested for *Trichinella* as this is a requirement for horse meat export.

The total number of horses slaughtered per abattoir across the whole time period was mapped and analysed. To define locations of origin for the slaughtered horses, for small abattoirs (those who slaughtered ¡1000 horses) horses were allocated at random to holdings within a 50 km radius of the abattoir. For all other abattoirs, 75% of slaughtered horses were located according to the equine population density and 25% randomly across the whole of GB. The number of horses slaughtered per holding was allocated according to a pert distribution with minimum and most likely values of one and a maximum value of five. It was considered unlikely that many properties would send multiple horses for slaughter.

5.3.3 Pig data

5.3.3.1 Pig population

A written description of the British pig industry (Fowler 2003) included summary data up to and including 2002. Part of this document included results of research by Sheppard (2002) which was used to guide the production of denominator populations for the sub-populations of pigs.

Data provided by Defra (Department for Environment, Food and Rural Affairs, 1A Page Street, London, SW1P 4PQ, United Kingdom) locating farm holdings classified as piggeries were combined with agricultural census data. Mis-matched holdings (those present in one dataset but not in the other) were mapped and examined for spatial patterns. Pig herds identified only in the census data were allocated to piggery sites that were part of the Defra dataset but had a pig population size of zero. Any remaining piggeries in the Defra dataset with zero population were excluded from further work. Each piggery was classified as grower only, breeder only or mixed, and as indoor (low-risk) or outdoor/other housing (high-risk) (Table 5.1). The total number of pigs and the number of breeder and grower pigs on breeder and mixed farms were calculated. Grower pigs were classified as those weighing up to 110kg and the remaining pigs

Table 5.1: Categorisation of high- and low-risk accommodation for weaner, grower and breeder pigs

Pig class	**Low risk**	**High risk**
Weaner/grower	Houses with fully slatted floors/flat decks	Deep straw yards
	Houses with partly slatted floors	Outdoors
	Houses with solid lying area and solid dung passage	Other
Breeder (including dry sows/served gilts)	Breeding sows in indoor farrowing accommodation	Breeding sows in outdoor farrowing accommodation
	Cubicles and free access stalls	Yards with electronic sow feeders
		Yards with individual sow feeders
		Yards or kennels with short stall feeders
		Yards or kennels with floor/trough feeders
		Outdoor accommodation
		Unspecified or other

were classified as breeders, representing older animals with an increased time at risk of infection.

The classification system resulted in four risk-groups of pigs: low-risk (indoor) grower, high-risk (outdoor/other) grower, low-risk (indoor) breeder and high-risk (outdoor/other) breeder. The risk level was considered lowest for low-risk growers, followed by low-risk breeders then high-risk growers, with high-risk breeders as the highest-risk group. The densities of indoor and outdoor breeder pigs and indoor and outdoor growers were mapped.

5.3.3.2 Pig sampling

A survey of licensed pig abattoirs in 2003 encompassed 192 abattoirs and demographics of slaughtered pigs, testing of slaughtered pigs for *Trichinella* and the testing methods used (Food Standards Agency (FSA) 2003). The data included the total number of pigs slaughtered by year for each abattoir and classified the number of pigs slaughtered by type, rearing method (indoor, outdoor or combination), and location of origin. Data were available for 1990 to 2003. The number of pigs slaughtered per year was estimated for 2004 and 2005 for each holding according to the estimated number and classes of pigs present in the denominator population, taking reproductive and management parameters into account. Additional slaughter data were provided by the British Pig Executive Limited, Winterhill House, Snowdon Drive, Milton Keynes, MK6 1AX, England.

Records of the number of pigs tested for trichinellosis were similarly examined (FSA 2003). We estimated the numbers and locations of sub-populations of pigs tested for *Trichinella*. The FSA (2003) survey data was used to determine the percentage of slaughtered pigs that were tested in each region. Fourteen percent of slaughtered grower pigs and 86% of slaughtered breeders were assumed to be tested. In each class, 76% of pigs were estimated to be indoors and 24% outdoors. Outdoor (high-risk) pigs included those kept in combinations systems (55%).

5.3.4 Species and sub-population weighting

The method used to integrate species data relies on evidence from the scientific literature (see Appendix 2) that there is a known relationship between the prevalence in each population being sampled, i.e. that infection levels in the host species are linked because of the epidemiology of *Trichinella*. The relationship between the species is treated as linear, which is realistic and simplifies the mathematical calculations, but is not critical. We can treat one of these prevalences as the "reference" prevalence - if we can obtain an estimate of the reference prevalence, then we can automatically calculate all the other prevalences of interest.

The fundamental source of infection for all of the tested species is wildlife, and the level of wildlife infection could be used as a reference point. However, since the prevalence in wildlife reservoirs is difficult to measure directly, an alternative is to use one particular category of animals as a reference group - in this study low-risk grower pigs - and to use evidence from infected countries to calculate weighting factors that reflect the likelihood of finding infection in each of the other categories of animals being tested. For example, a negative finding from a fox is much more valuable than a negative result from a grower pig, because foxes are much more likely to be exposed to *Trichinella* during their lifetime than individual grower pigs, and are therefore more likely to test positive. Within species, sows have had a longer exposure compared to grower pigs and some sows have been in a higher-risk environment (outdoor compared to indoor sows). Therefore, negative test results from some animals provide greater support that the disease is not present than do negative results from other animals. On this basis, each data source contributes to the overall surveillance portfolio by different weightings.

The relative prevalence value (v_j) of the three species and sub-populations to the reference group were determined from a literature review (see Appendix 2). We used these weightings to combine the data from the different categories of animals and estimate the overall prevalence.

5.3.5 Theory for estimating prevalence

Suppose that X_j is the number of infected animals found when sampling n_j animals from population j in which the apparent relative prevalence is $p \times v_j \times Se_j$ when the prevalence in the reference population is p. The values of v_j reflect the relative prevalence for the species (i.e. horse, pig, fox) or sub-class of animals (e.g. age group). The values of Se_j represent the sensitivity of the test used for the species. These values were determined for each species following a review of published literature (Zimmer et al. 2008; Webster et al. 2006; Smith et al. 2003; Gamble et al. 2000). X_j has a Binomial$(n_j, p \times v_j \times Se_j)$ distribution.

One method of estimating the reference prevalence p is to use the method of moments which equates the observed number of positives with the expected number. The expected number of infected animals found in the entire survey is:

$$\text{Expected} = \sum n_j \times v_j \times p \times Se_j \tag{5.1}$$

By equating this with the observed number of positives:

$$\text{Observed} = x_j \tag{5.2}$$

we get an estimate for the reference prevalence p of:

$$p = \sum x_j / \sum n_j \times v_j \times Se_j \tag{5.3}$$

This is equivalent to the points approach outlined in Prattley et al. 2007; the number of points a test is worth is equal to the sensitivity of the test multiplied by the relative prevalence in the population group at the time of the test. The estimate of prevalence is the number of positives divided by the total number of points from all the testing.

A second method is to find the value of p that maximises the likelihood function:

$$\prod (pv_j Se_j)^{x_j} (1 - pv_j Se_j)^{n_j - x_j} \tag{5.4}$$

From Equation 5.4, using calculus, the maximum likelihood estimator for p can be found by iteratively solving:

$$\sum n_j = \sum \frac{n_j - x_j}{1 - pv_j Se_j} \tag{5.5}$$

The two methods give similar results when the prevalence is low.

The number of positive animals found in all the surveys can be approximated by a Poisson distribution with a mean given by Equation 5.1. Hence, approximate confidence limits for the reference prevalence can be found by replacing the $\sum x$ in Equation 5.4 with the Poisson confidence limits corresponding to the value of $\sum x$. The UCL for the prevalence in another population is equal to the UCL of the reference population multiplied by v, the relative prevalence of that population.

5.3.6 Analysis

5.3.6.1 Sampling effort

For each species, numerator and denominator data were converted into density grids. Sampling effort for horses, foxes and pigs was assessed by dividing the slaughter density by the population density. We assumed that all slaughtered horses and all foxes were tested. Sampling effort for pigs was similarly assessed for each sub-population for an average year of testing.

5.3.6.2 Upper confidence limit (95%) for the estimate of prevalence

All surveillance carried out from 2000 to 2005 was included in producing estimates of the maximum *Trichinella* prevalence for each species. For analytical purposes, GB was divided into one hundred and fifty equi-pig areas which contained similar numbers of pigs; county or parish boundaries were followed where possible. The mean number of pigs per area was 31,883 with a range of 27,316 - 39,990 for all but one area, which had 48,013 pigs. This maximum number was high due to the presence of one very large farm that resulted in the designation of its parish as one equi-pig area.

Two sets of analyses were performed. Firstly, the 95% UCL was calculated for each species and sub-population using the number of positive tests for *Trichinella* and the number of animals tested from that population in each equi-pig area. This analysis was not weighted in relation to the reference population. Secondly, 95% UCL was calculated for each equi-pig area using the number of positive tests for *Trichinella* and the number of points (equal to the number of animals of all species and sub-populations tested multiplied by the weighting values per test). Similar calculations were done for GB as a whole. Maps were created illustrating the 95% UCL by equi-pig area for the prevalence of each species/sub-population for both unweighted and weighted testing done from 2000-2005.

5.4 Results

There were no positive tests for *Trichinella* in any of the species under surveillance.

The relative worth of testing different species is based on the relative prevalence (v_j) and test sensitivity (Se_j). Test sensitivity was estimated to be 0.85 for each species. The weighting values used for each species and subgroup are given in Table 5.2, with the low-risk grower pig being used as the reference population (see Appendix 2). Tested foxes had a greater surveillance value than any other group, with high-risk breeder pigs weighted most heavily within the pig sub-populations.

Table 5.2: Weighting values (v_j) assigned to surveillance tests for each species and sub-population

Species	**Test sensitivity** (Se_j)	**Class**	**Weighting** (v_j)	**Point value** ($v_j Se_j$)
Pig	0.85	Low-risk grower	1.0	0.85
		Low-risk breeder	2.0	1.70
		High-risk grower	5.0	4.25
		High-risk breeder	10.0	8.5
Fox	0.85	Any age	75.0	63.75
Horse	0.85	Any age	0.5	0.43

5.4.1 Sampling effort

5.4.1.1 Fox data

Webbon et al. (2004) estimated the total rural fox population in GB to be 225,000 foxes (95% confidence interval 179,000-271,000). The population was estimated to be highest in central and southern Scotland and southwest England. Urban foxes were not included in the population density map.

A total of 2945 wild foxes were sampled for *Trichinella* between 1999 and 2006. Ten foxes did not have location, date or age information recorded. These were excluded from further analysis. The highest densities of sampled foxes were in the north, southeast and southwest of England.

The sampling effort for foxes included foxes tested between 1999 and 2006 (see Figure 5.2 in Appendix 1). The highest level of sampling in relation to estimated fox population density was in the Scottish Borders.

5.4.1.2 Horse data

The horse population data included 873,596 horses. There were 10.7% for which the age was unknown. Of horses whose age was known, the average age was 11.8 years, with a median of 10.0 years and a mode of 8.0 years. There was a long tail to the right of the distribution, with the oldest horses aged 39 years (n = 1383).

The NED data was supplied as the number of horses by county, with location information being unavailable for 13.8% of horses. The highest count of horses was in Devon (n = 45,206; 5.2% of all horses) followed by Lancashire (3.5%). Across all ages, horses were widely distributed across England. There were low-density areas in the east and north and across Scotland. Wales had a relatively high density of horses in the south (following the pattern of human population density) but few elsewhere.

We received data from six abattoirs but expect there are others where horses are slaughtered. The distribution of horses slaughtered across GB was weighted by the population density, abattoir size and abattoir location. This led to the highest densities

Table 5.3: Estimated number of pigs present by sub-population in England, Scotland and Wales

Country	Low-risk breeder	High-risk breeder	Low-risk grower	High-risk grower	Total pigs
England	381,617	142,015	2,846,923	934,917	4,305,472
Scotland	55,569	0	383,280	0	438,849
Wales	4,604	0	26,053	0	30,657
Great Britain	441,790	142,015	3,256,256	934,917	4,774,978
	9.25%	2.97%	68.19%	19.58%	100.00%

of slaughtered horses around the West Midlands, Tyne and Wear and the south of Wales. A total of 45,005 horses were slaughtered.

Sampling effort for horses included horses slaughtered across all years of data provided (see Figure 5.3 in Appendix 1). It was assumed that all slaughtered horses were tested for *Trichinella*. The highest sampling densities were seen in Scotland and Wales.

5.4.1.3 Pig data

The pig population in Great Britain was estimated at 4,774,978 pigs (Table 5.3). The population was most densely concentrated in the Norfolk/Suffolk, Humberside/Yorkshire and Grampian regions. The Defra records of properties classified as piggeries included 21,887 English holdings, 1153 Scottish holdings and 2509 Welsh holdings (total number of properties 25,549). Approximately 10,000 commercial piggeries exist, with around 2000 providing 92% of total pig meat production (A. Knowles, pers. comm.). Census 2005 data included records for 794 holdings where pigs were kept outdoors.

The pattern of both grower and breeder pigs being reared in low-risk accommodation was similar to that of the whole pig population. Grower and breeder pigs living in high-risk accommodation are found mainly in the east of England and Cumbria.

Abattoir throughput increased each year, with 7,654,466 pigs slaughtered in 2002 by the 192 abattoirs that responded to the FSA survey (FSA 2003). The estimated numbers of pigs slaughtered by sub-population and country for 2005 are given in Table 5.4. Slaughtered low-risk breeders were mainly from the east coast, from Suffolk, Norfolk, Humberside, Yorkshire and Grampian regions. High-risk breeder pigs were mainly from Suffolk, with smaller clusters in Cumbria and a few other counties. Low-risk grower pigs were slaughtered from locations in a similar pattern to low-risk breeders, although there were higher densities of grower pigs slaughtered in the western and southern areas. There were fewer high-risk grower pigs slaughtered, and these were mainly located in the east of England. The density pattern for all pigs slaughtered was similar to that for low-risk grower pigs, which was expected due to the large proportion of this group of pigs in the population.

Table 5.4: Estimated number of pigs slaughtered per year by sub-population and country

Country	Low-risk breeder	High-risk breeder	Low-risk grower	High-risk grower	Total pigs
England	148,638	55,382	7,967,696	2,837,824	11,009,540
Scotland	21,681	0	1,092,330	0	1,114,011
Wales	1,757	0	82,189	0	83,946
Great Britain	172,076	55,382	9,142,215	2,837,824	12,207,497

Table 5.5: Estimated number of pigs tested in 2005 by sub-population and country

Country	Low-risk breeder	High-risk breeder	Low-risk grower	High-risk grower	Total pigs
England	126,437	39,927	916,291	289,355	1,372,010
Scotland	6,759	0	48,979	0	55,738
Wales	173	0	1,256	0	1,429
Great Britain	133,369	39,927	966,526	289,355	1,429,177

There were a total of 43 records from 13 abattoirs that tested pigs for *Trichinella* between 1993 and 2002. Not all abattoirs indicated that they tested pigs in all years. There was a peak of testing in 1998 with 2,914,651 pigs sampled, whereas in 2002 1,228,520 pigs were tested. Fourteen percent of slaughtered grower pigs and 86% of slaughtered breeders were estimated to be tested. Seventy-six percent were estimated to be kept indoors with the remainder either outdoors or in combination systems. Table 5.5 gives the estimated number of tested pigs by country and sub-population in 2005.

Pig sampling effort was calculated for each of the four sub-populations (high- and low-risk breeder and grower pigs) using the estimated number of pigs slaughtered in one year. Low-risk grower pigs were uniformly sampled across the country, with the exception of west and northern Scotland (see Figure 5.4 in Appendix 1). High-risk grower pigs were slaughtered in a uniform pattern across England in relation to the underlying population (see Figure 5.5 in Appendix 1). Relative to their sub-population low-risk breeders were most highly sampled in the north-west of Scotland (see Figure 5.6 in Appendix 1). Sampling effort for high-risk breeders (see Figure 5.7 in Appendix 1) followed a similar pattern to the high-risk grower population.

5.4.2 Upper confidence limit (95%) for the estimate of prevalence

The analysis was performed using all data for the six years 2000-2005. Prevalence estimates using unweighted data from each population and sub-population were calculated for each equi-pig area. The fox UCLs were higher in areas across England and the north-east of Scotland than in other areas (Figure 5.8, Appendix 1). Most areas had a UCL of between 0.01% and 0.10% for horses (Figure 5.9, Appendix 1). Low-risk

grower pigs had lowest UCLs in northern England (Figure 5.10, Appendix 1). High-risk grower pigs were not tested from Scotland and Wales or from some areas in central England (Figure 5.11, Appendix 1), as pigs were not expected to be living in outdoor, high-risk systems in these areas. The areas with highest UCLs were in the south of England. UCLs for low-risk breeder pigs were mainly between 0.01% and 0.10% (Figure 5.12, Appendix 1). High-risk grower pigs had lower UCLs than high-risk breeder pigs, because of the larger numbers of grower pigs tested (Figure 5.13, Appendix 1).

Group prevalence estimates for each equi-pig area were calculated based on the combined, weighted data collected for that equi-pig area, as discussed below and shown graphically in Appendix 1. From 2000-2005, 2450 foxes were sampled, covering the majority of equi-pig areas. The UCLs for foxes in each equi-pig area are seen in Figure 5.14 in Appendix 1, with lower values in the north of England. The 95% UCLs were relatively low across GB for all years of horse slaughter data (see Figure 5.15 in Appendix 1).

The 95% UCL for estimated prevalence for the reference population of low-risk grower pigs tested from 2000-2005 in each equi-pig area is shown in Figure 5.1. The maximum estimated 95% UCL in any area was 0.035%, with the lowest being 0.00038%. When compared to Figure 5.10, it can be seen that estimating the prevalence in the reference population using data combined from all species and sub-populations results in lower UCLs, mainly across England.

High-risk grower pigs tested from 2000-2005 had low UCLs across most of GB, with a small number of areas with higher UCLs in the east of England (Figure 5.16 in Appendix 1). The pattern of the estimate for low-risk breeder pigs was similar to that for low-risk growers in Scotland and Wales, with some areas of slightly higher prevalence estimates in central England (Figure 5.17 in Appendix 1). High-risk breeder pigs had generally higher UCL estimates compared to other pig sub-populations, with Wales and Scotland being amongst the highest areas (Figure 5.18 in Appendix 1).

The estimation of prevalence was repeated for GB as a whole using surveillance data from 2000-2005 (Table 5.6). The 95% UCL for the prevalence in the reference group (low-risk grower pigs) in GB is 0.000017% based on all the data collected from the three species during the six-year period. The 95% UCL for the entire pig population is 0.000036%, or about 1.7 pigs in the population of 4.77 million pigs.

5.5 Discussion

As a result of many years of testing for trichinellosis in three animal species, GB has accumulated substantial amounts of surveillance data. Our work shows how this diverse information can be incorporated to produce upper confidence limits for prevalence estimates for the pig, horse and fox populations.

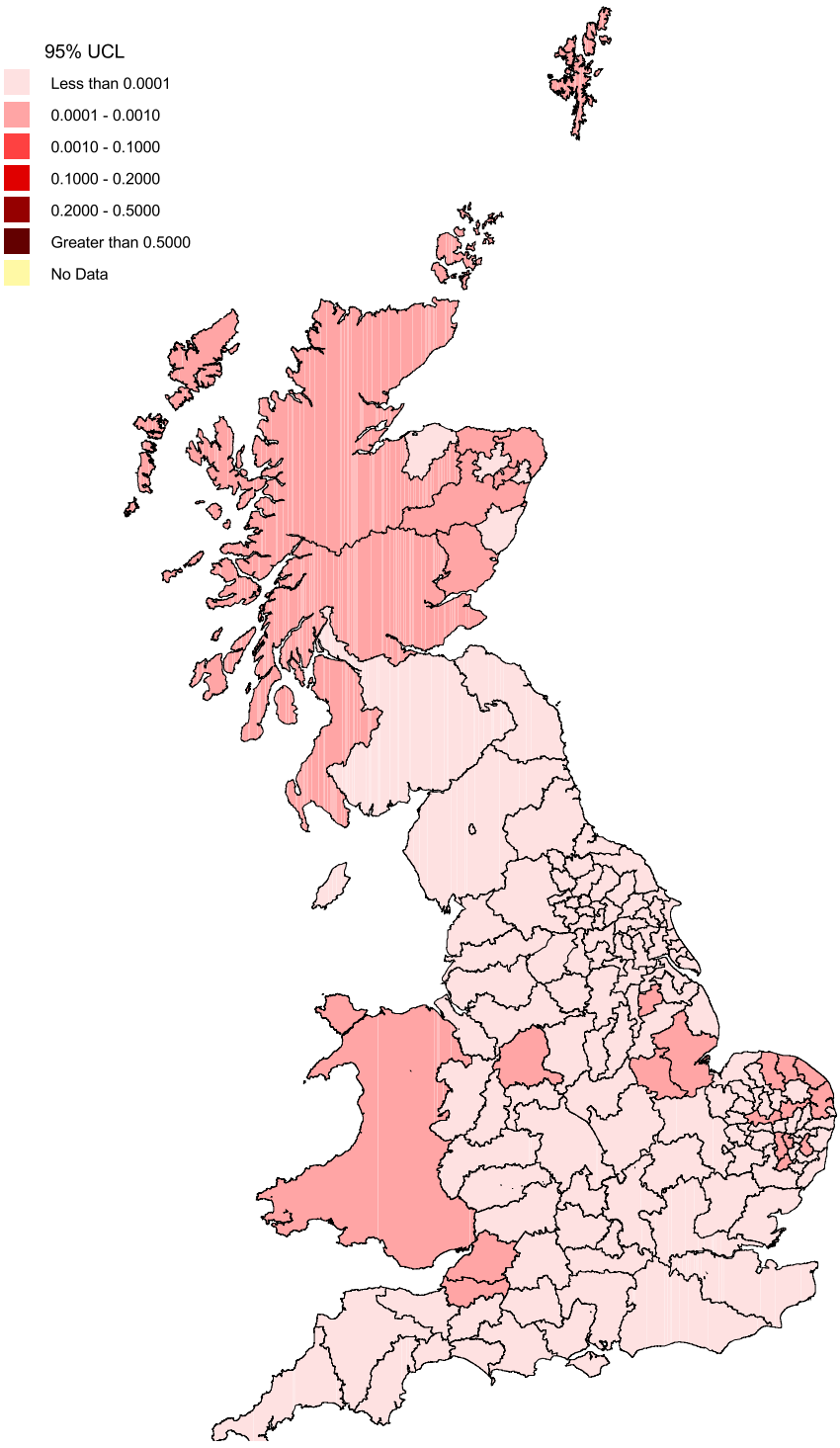

Figure 5.1: 95% upper confidence limit for the prevalence of *Trichinella* in low-risk grower pigs by equi-pig area, based on all animals tested from 2000-2005. No positive samples were found, and the variation in confidence limit between areas reflects greater uncertainty due to a lower amount of testing.

Table 5.6: 95% upper confidence limit for the prevalence estimate for *Trichinella* in Great Britain based on all testing done during 2000-2005

Species/ sub-population	Number positive	Number tested	Point value ($v_j Se_j$)	Total points	95% UCL for group prevalence	95% UCL for number of infected animals
Fox	0	2,450	63.75	156,188	1.25E-05	2.80
Horse	0	45,003	0.43	19,126	8.31E-08	0.07
High-risk breeder	0	294,156	8.50	2,500,326	1.66E-06	0.24
Low-risk breeder	0	971,336	1.70	1,651,271	3.32E-07	0.15
High-risk grower	0	1,940,971	4.25	8,249,127	8.31E-07	0.78
Low-risk grower	0	6,416,914	0.85	5,454,377	1.66E-07	0.54
Reference population (based on all data)	0	9,670,830		18,030,415	1.66E-07	

There were a number of difficulties in obtaining the input data that were desirable for the analyses to be carried out. Structuring of the pig populations was guided by information from a variety of sources, as there were limited data available describing the demographics of pigs, particularly those in outdoor management systems.

The fox population density estimates (Webbon et al. 2004) showed lower populations in the north of England and the north of Scotland. No data were obtained to describe peri-urban fox populations, although Webbon et al. (2004) estimated the total rural and urban fox population to be 258,000. Peri-urban fox populations might be areas of higher fox densities, close to higher-density human populations. It might also be reasonable to expect overlap with higher horse densities and piggeries that exist around the fringes of populated areas. Sampling of foxes for *Trichinella* was concentrated on lowland foxes.

There have been surveys of foxes for *Trichinella* carried out in many countries (see Appendix 2). However, only one study demonstrating the prevalence in foxes and in other species within one country was available (Gottstein et al. 1997). A sensitivity analysis would assist in determining the effects of altering the weighting values for all species and sub-populations. Age-related prevalence information for positive foxes would allow further relative weightings of different sub-populations of foxes to be included in this analysis. This would also be the case for horses, where the longevity of the species would likely add greater value to the surveillance of older horses.

We were fortunate to obtain the first extraction of data from the NED. However, at the time this analysis was performed the NED data was known to be incomplete, with an uncertain number of horses yet to obtain passports and be registered. The total number of horses counted in the NED data was 873,596. This compares to the British Equestrian Trade Association (BETA) National Equestrian Survey 2006 estimate of 1.2 million horses (Swift Research Limited 2006) and the Henley Centre (2004) estimate of 600,000 to 975,000 horses. The assumption that owners and horses are located within

the same county is considered reasonable, as few horse owners would be expected to commute long distances to tend their horses on a regular basis. Owners may of course live near a county boundary and keep their horses in a neighbouring county, but this would not apply to the majority. Owners of Thoroughbred racehorses would be most likely not to fit with our assumption, as racehorses are more likely to be grazed and trained at greater distances from their owner's location of residence, and also in higher numbers per property.

Our allocation of slaughtered horses to locations of origin was largely based on the number of horses processed by the abattoir at which they were slaughtered, and the horse population density. Random allocation was used for 25% of slaughtered horses in order to include horses from all over GB. It was expected that few horses would be trucked long distances to slaughter relative to the number slaughtered locally; however, the locations of all horse-slaughtering abattoirs in our dataset were in the southern half of England. There may be others that were not included in our dataset. It was assumed that all horses slaughtered were tested for *Trichinella*. The analysis of the horse and interspecies data would be improved if the locations of origin of the slaughtered horses were known. It would also be possible to allocate different weighting values to horses in different age groups, providing the ages of slaughtered horses were recorded and there was information available from the literature or from further studies regarding the age-related prevalence of equine trichinellosis.

The mismatch between holdings carrying pigs in the 2005 agricultural census data and the holdings classified as pig-owning in the Defra data could be attributable to a number of factors. Firstly, the agricultural census is not actually complete census but a large sample survey, and therefore subject to greater inaccuracies. A complete census is carried out every 10 years, with the next due in 2010. The Defra data were generally assumed to be more accurate than the census; however, particularly in the case of small backyard herds, there may be frequent fluctuations in the presence of pigs. There is also likely to be a lag time between changes in pig numbers and reporting to Defra. Piggeries may of course also be sold, closed down or started. The method of dealing with the mismatch of piggeries was not ideal, but considered reasonable given the available data.

We received some information from the agricultural census survey of England for pigs in different sub-populations, however these data were not available for all herds. The methods used to estimate the numbers of breeder and grower pigs by CPH (county-parish-herd number) in England utilised the limited information available, and are expected to be less accurate than the census data would be. Outdoor pig numbers in Scotland and Wales are considered to be low, and the lack of data led to an assumption of no outdoor pigs being present. However, fox numbers in some areas within these

countries are relatively high, and outdoor pigs are likely to be at relatively high risk of contracting trichinellosis in these areas. Obtaining accurate data describing the outdoor pig population within GB would be extremely beneficial.

We were provided with limited descriptions of human cases of trichinellosis in England and Wales. Thirty-eight cases were diagnosed between 1975 and 2001. These were located only by the diagnosing laboratory. This might have been some distance from the location at which the person resided, which might also have been disparate from the location at which the person became infected and/or the location of origin of the infective material. There is no evidence to suggest that human cases have arisen due to the consumption of British products. Although human case and demographic data were considered as part of this work, they were excluded from the analysis because of incompleteness and because human cases are secondary to those in meat sources.

Determination of the appropriate test sensitivity was not straightforward as there were variations in the testing methods used in GB, and the sensitivity also varies according to the number of larvae per gram it is desirable to detect. No evidence was found to suggest an appropriate sensitivity for testing of horse meat, but as the same value was used for pig and fox tests it was decided to apply it to horses also. The value of 0.85 is within the ranges of sensitivity values of the tests used for foxes and pigs in GB and within the ranges of published values.

The 95% upper confidence limit was calculated for each equi-pig area in GB. Since no *Trichinella* was detected, areas with a higher UCL reflect greater uncertainty resulting from a lower number of tests being performed. Analysis on a per-year basis is not reported, due to the difficulties of accurately quantifying and classifying the denominator populations and the numbers of animals tested each year. There were also changes in test sensitivity, as different tests were used at different times over the six-year period. The combined data was used to illustrate the application of the methodology, which could easily be applied to individual years of data where all necessary information was available.

The relative densities of at-risk species vary by location and would be expected to influence the risk of infection with *Trichinella* if it were present within the area. Using more precise location data would help to ensure that representation of animal populations was more accurate, and would give a more useful risk profile for trichinellosis.

It would be possible to devise a surveillance programme that optimised the contributions made by testing of the various species and sub-populations. For example, carrying out regular surveys of foxes would contribute more information per animal compared to pigs; however the relative convenience of pig sampling would need to be taken into account. The cost (measured in pounds or time) per "point" provides a way to measure the relative efficiency of different surveillance methods.

5.6 Conclusions

Regulation 2075/2005 (Anon. 2005) requires testing on the annual slaughter swine population. However, testing other species, such as foxes, might contribute more epidemiological value than testing large numbers of low-risk animals. We have shown how such information can be integrated in order to estimate the upper limit of prevalence in a reference population, which can then be used to estimate prevalence in other populations providing the relationship between the various populations is known. The results provide support to GB's claim of negligible risk of human infection by *Trichinella* species.

Acknowledgements

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5.8 Appendix 1: Additional figures

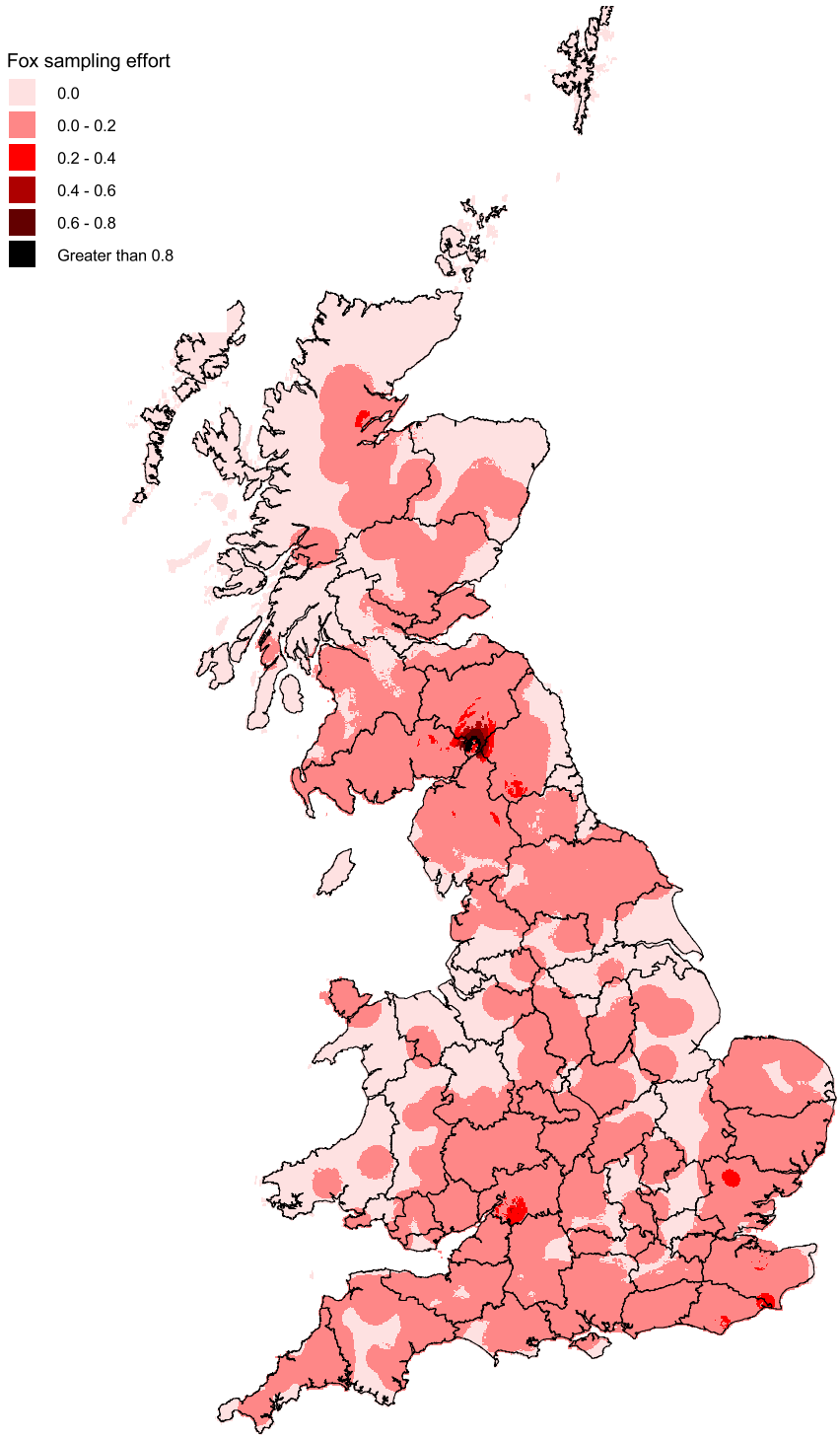

Figure 5.2: Sampling effort for foxes tested across all years of fox survey data

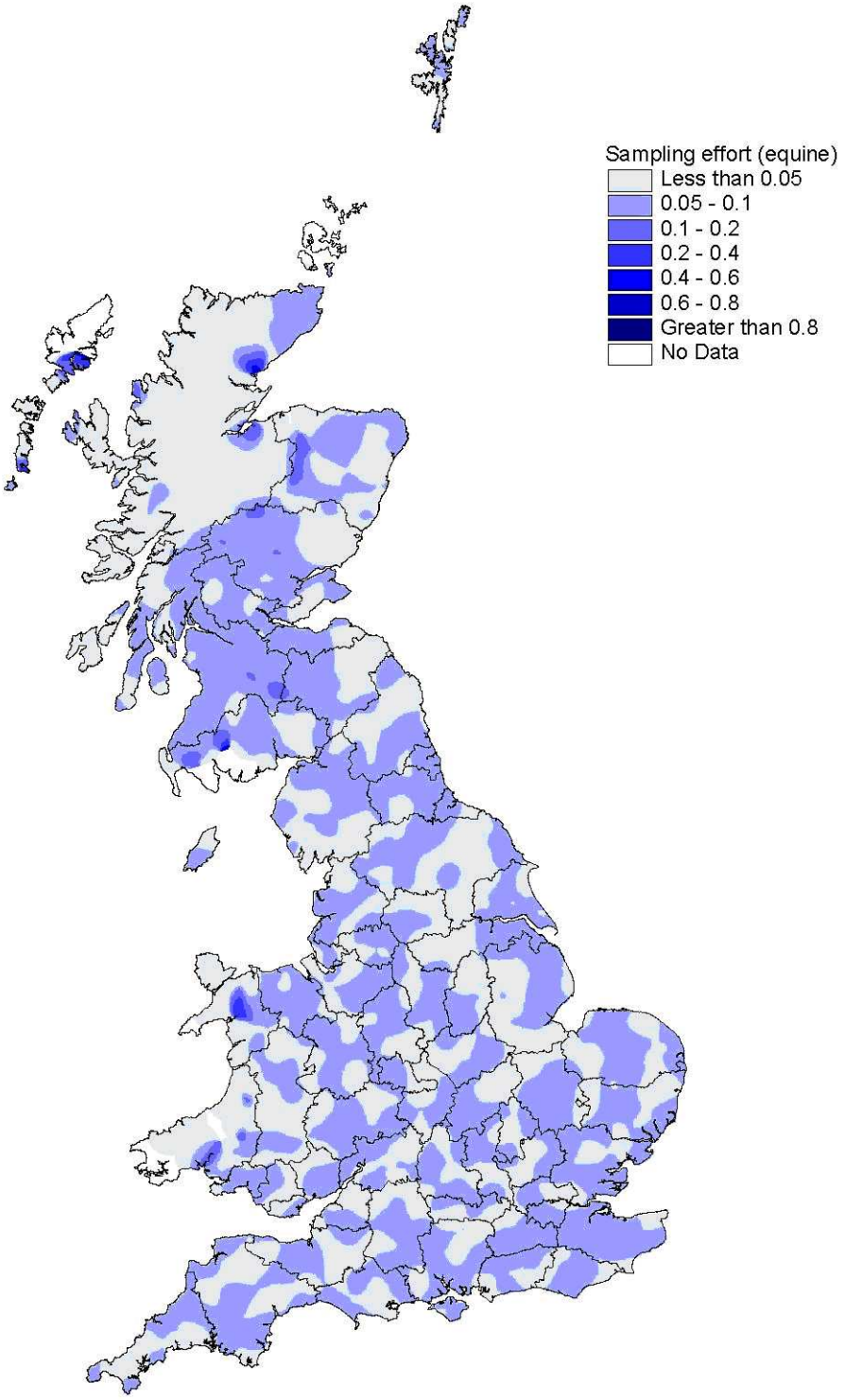

Figure 5.3: Sampling effort for horses including all years of horse slaughter data

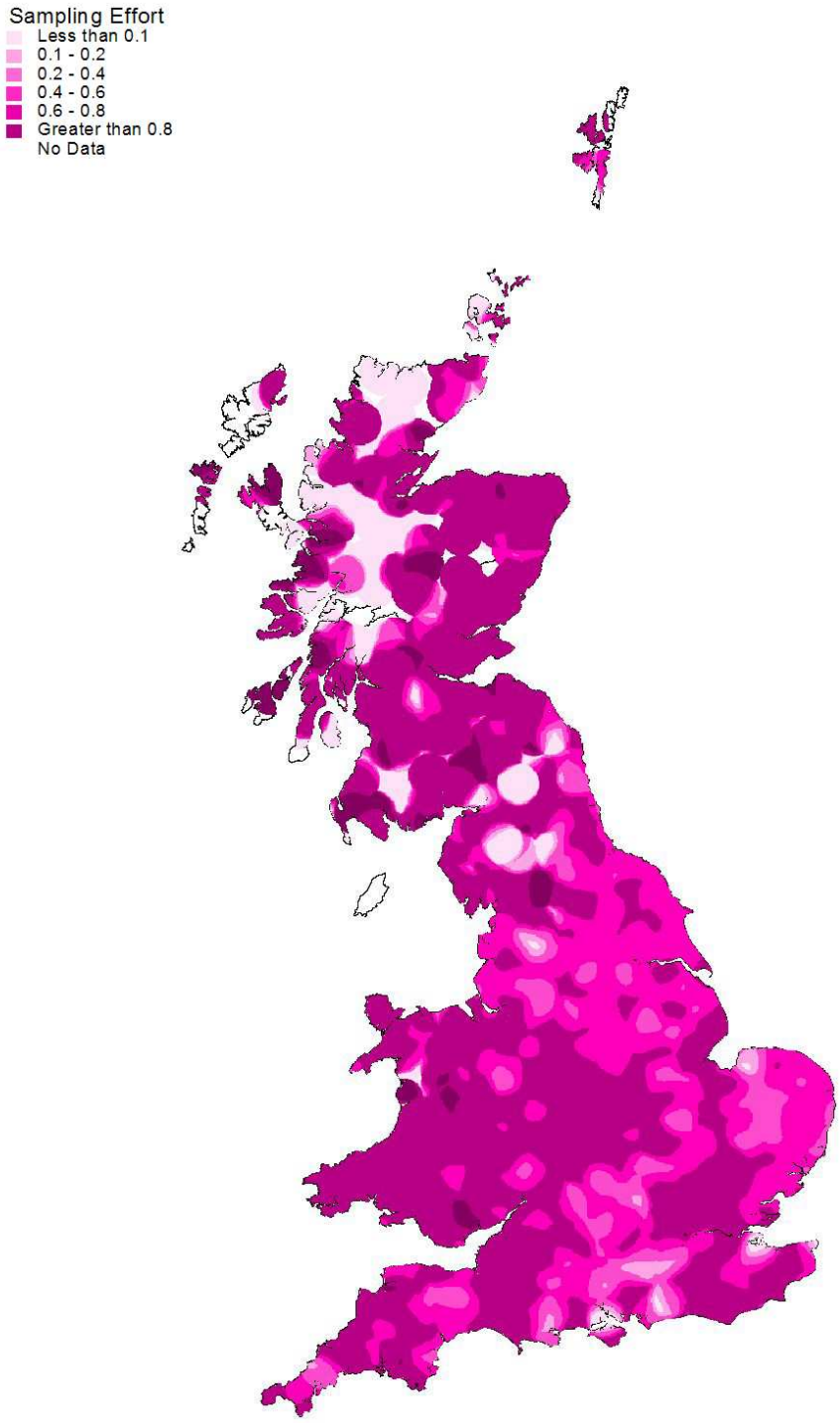

Figure 5.4: Sampling effort for low-risk grower pigs as the estimated density of low-risk growers slaughtered annually divided by the density of the low-risk grower population

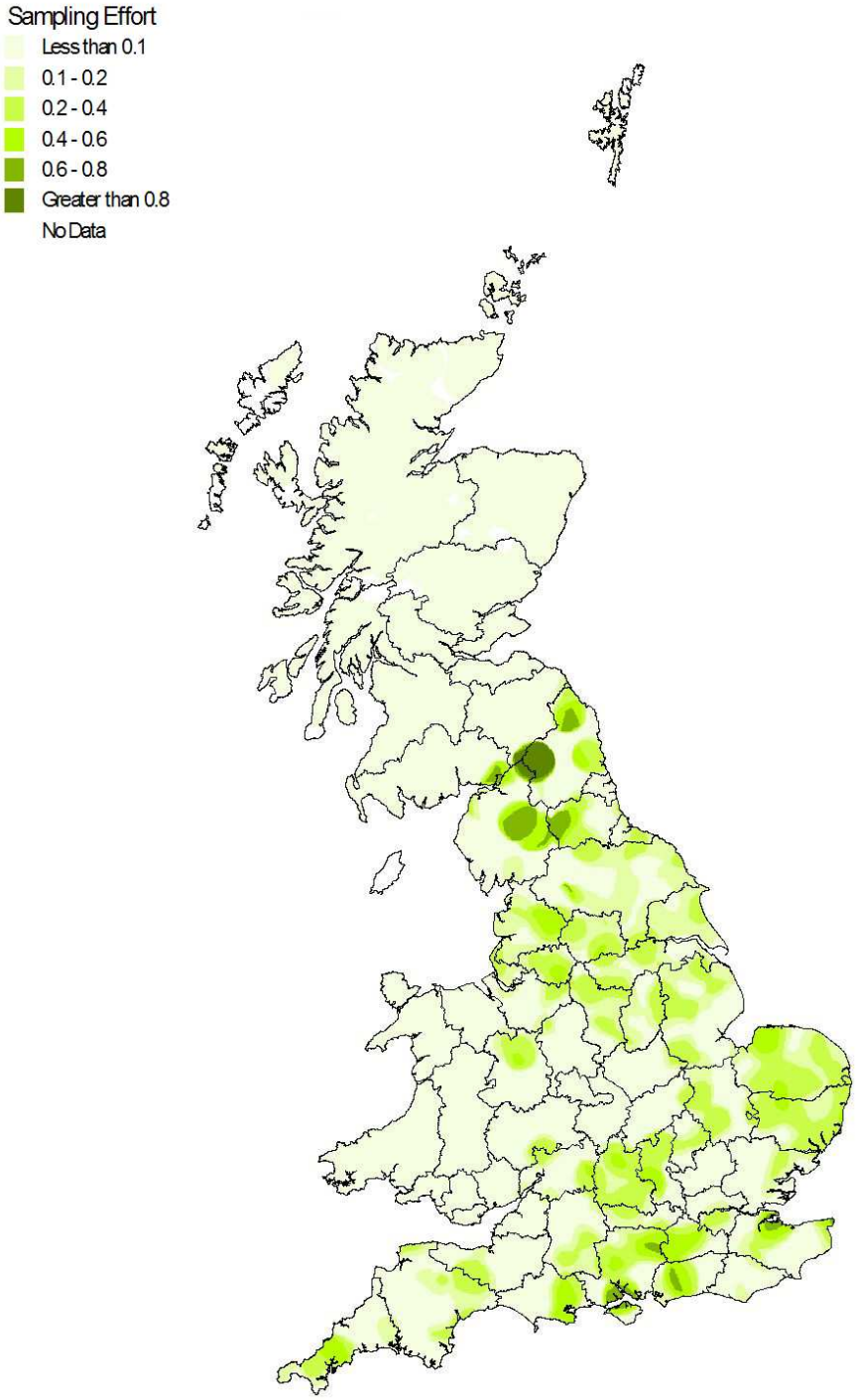

Figure 5.5: Sampling effort for high-risk grower pigs as the estimated density of high-risk growers slaughtered annually divided by the density of the high-risk grower population

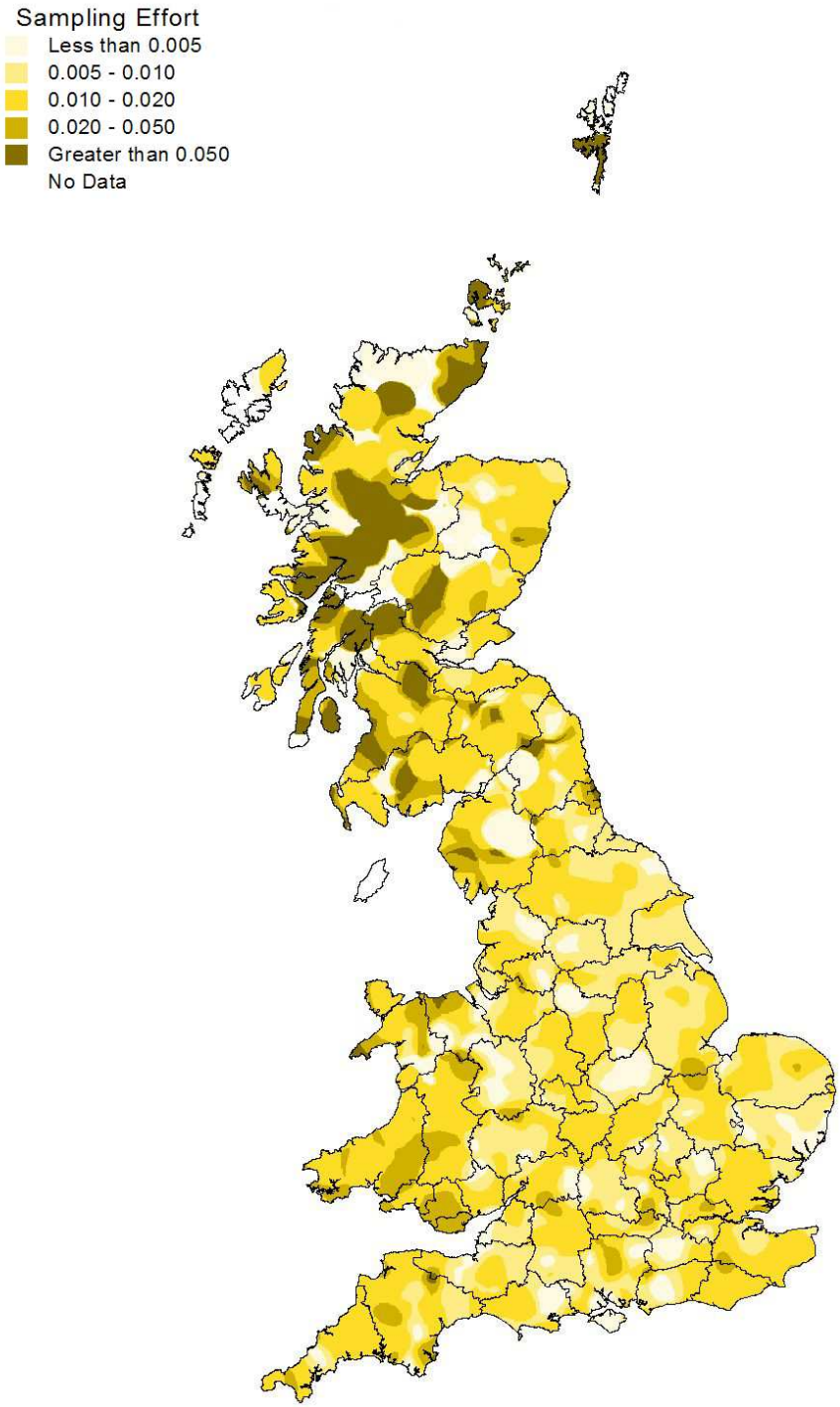

Figure 5.6: Sampling effort for low-risk breeder pigs as the estimated density of low-risk breeders slaughtered annually divided by the density of the low-risk breeder population

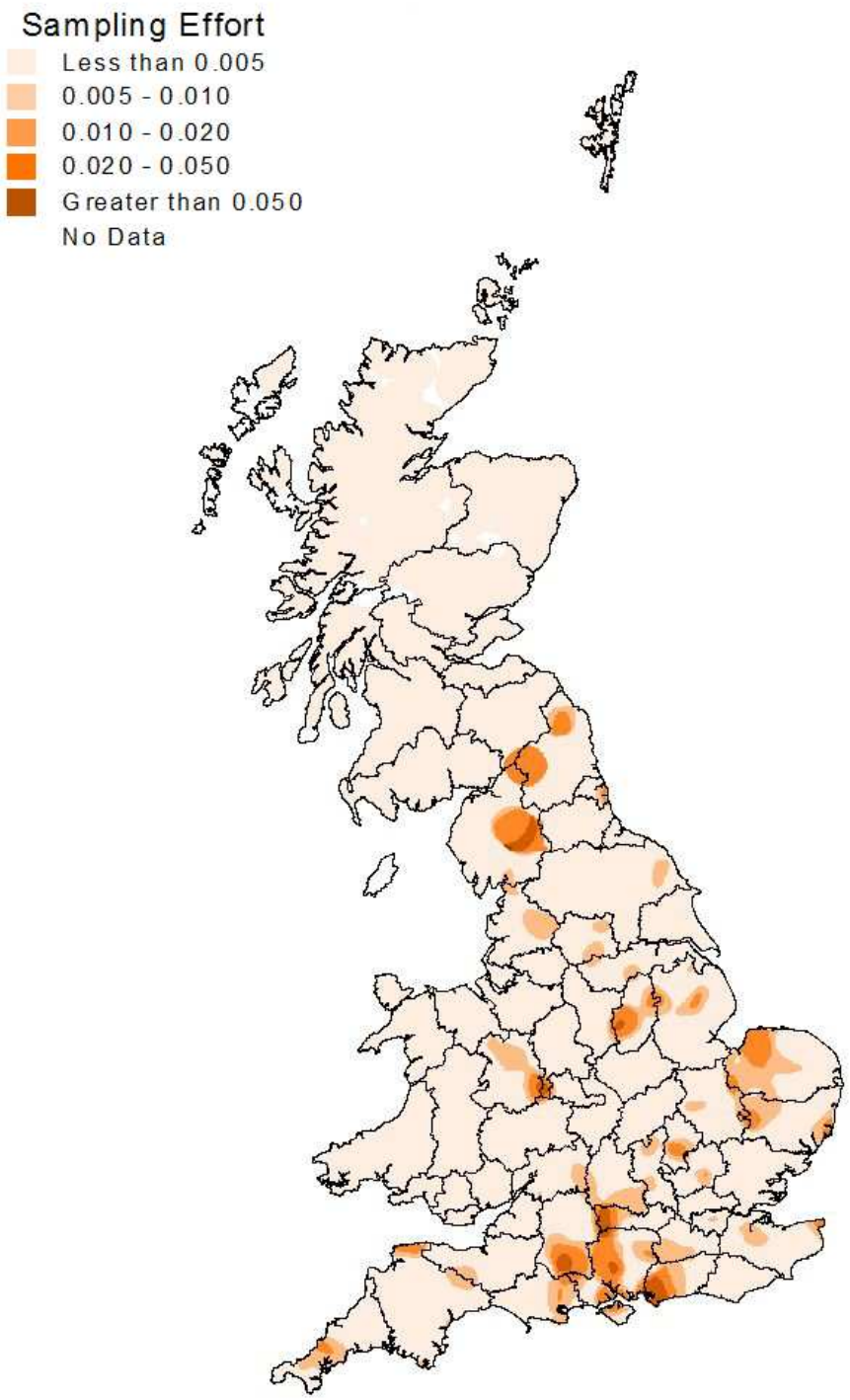

Figure 5.7: Sampling effort for high-risk breeder pigs as the estimated density of high-risk breeders slaughtered annually divided by the density of the high-risk breeder population

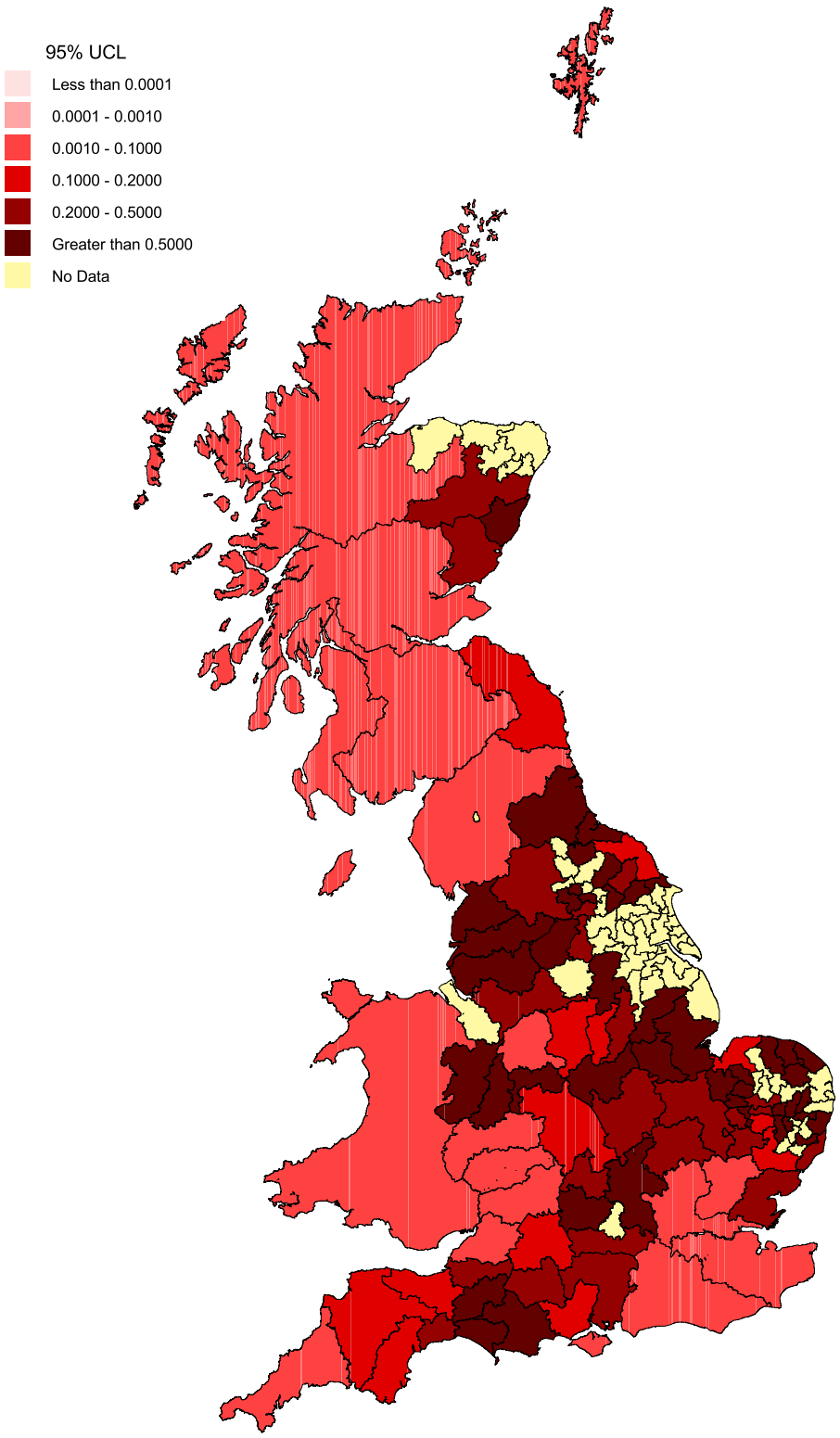

Figure 5.8: Upper 95% confidence limit for foxes tested from 2000-2005 (based on unweighted fox data only)

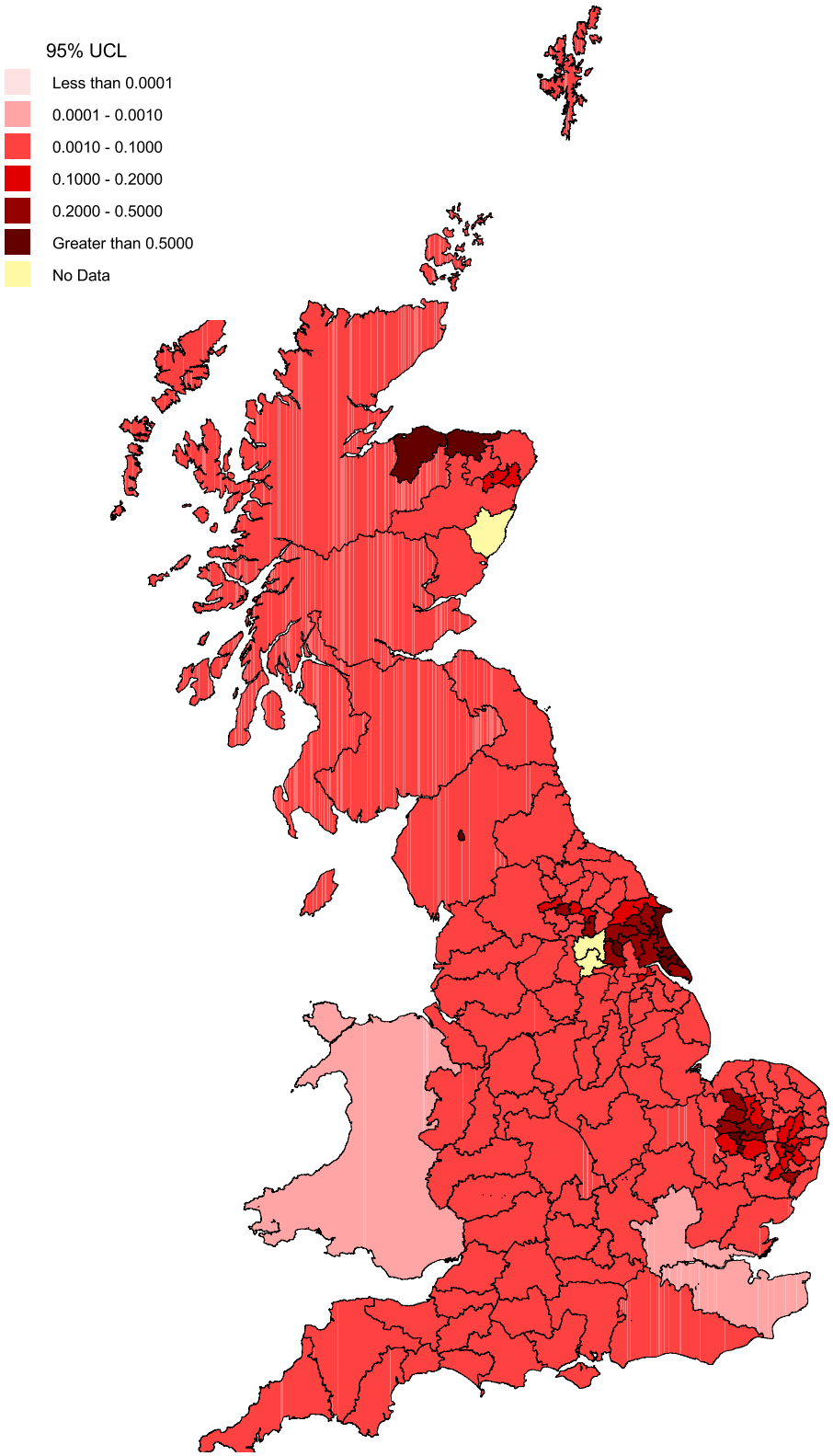

Figure 5.9: Upper 95% confidence limit for horses tested from 2000-2005 (based on unweighted horse data only)

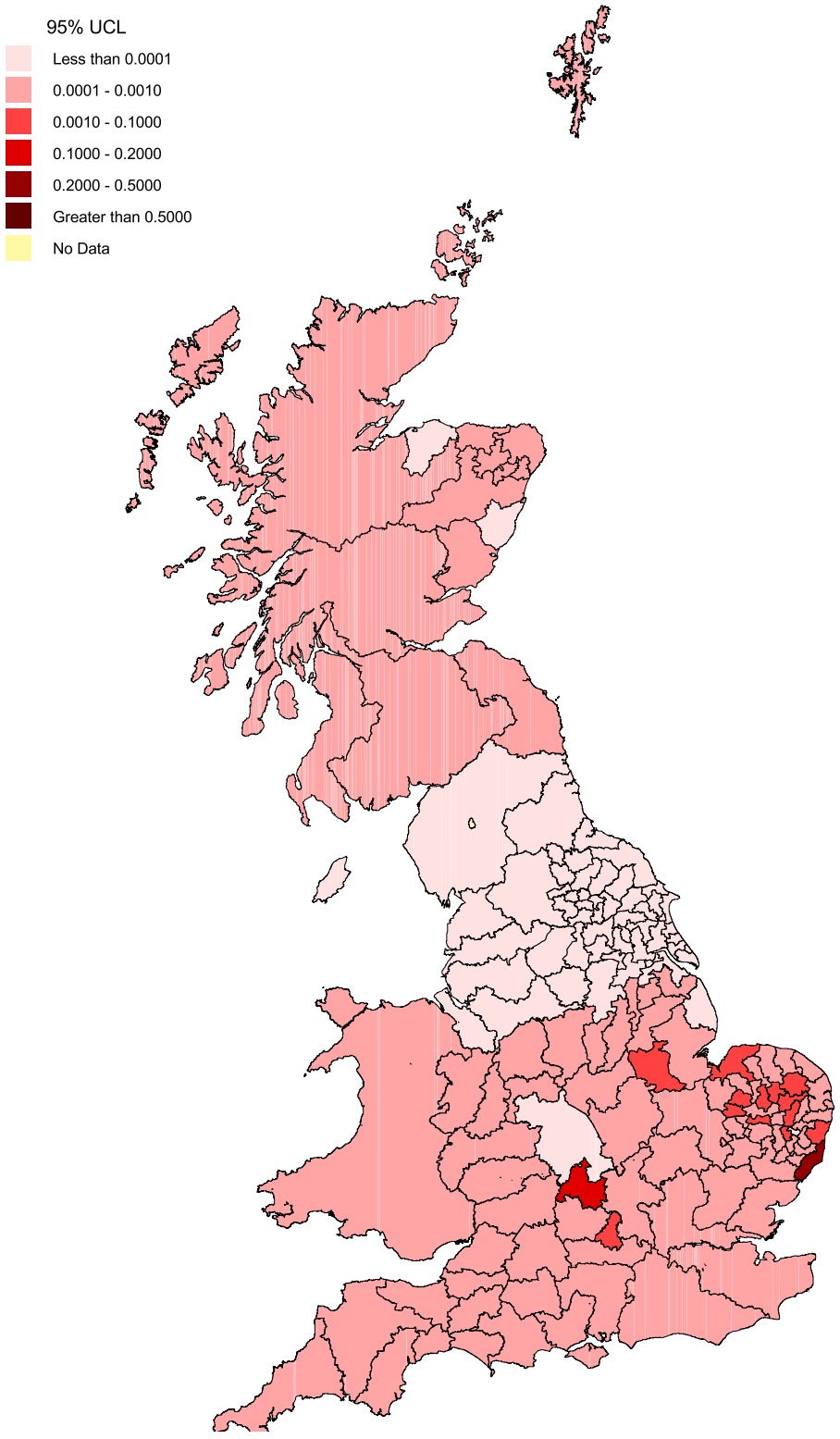

Figure 5.10: Upper 95% confidence limit for low-risk grower pigs tested from 2000-2005 (based on unweighted low-risk grower pig data only)

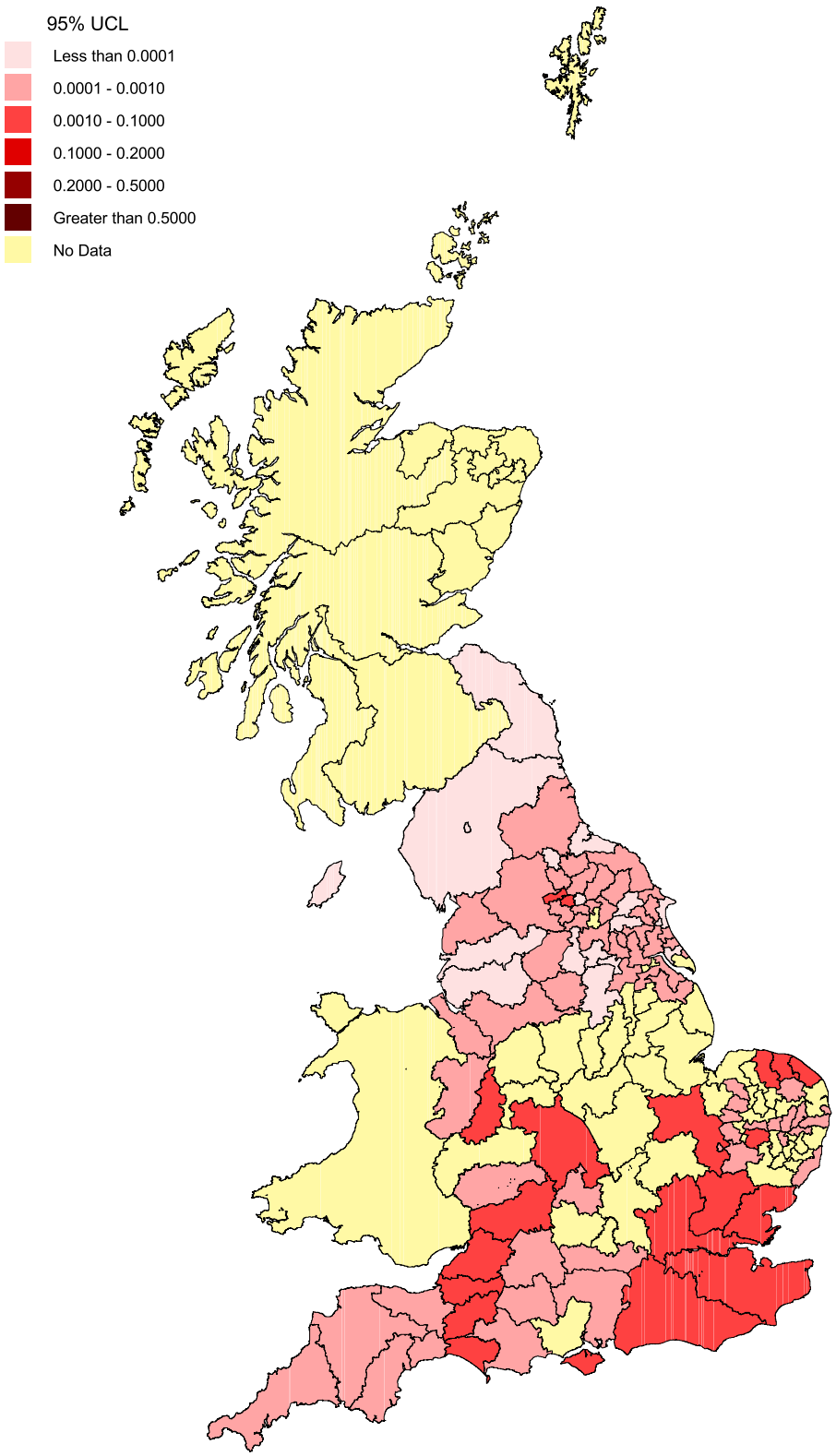

Figure 5.11: Upper 95% confidence limit for high-risk grower pigs tested from 2000-2005 (based on unweighted high-risk grower pig data only)

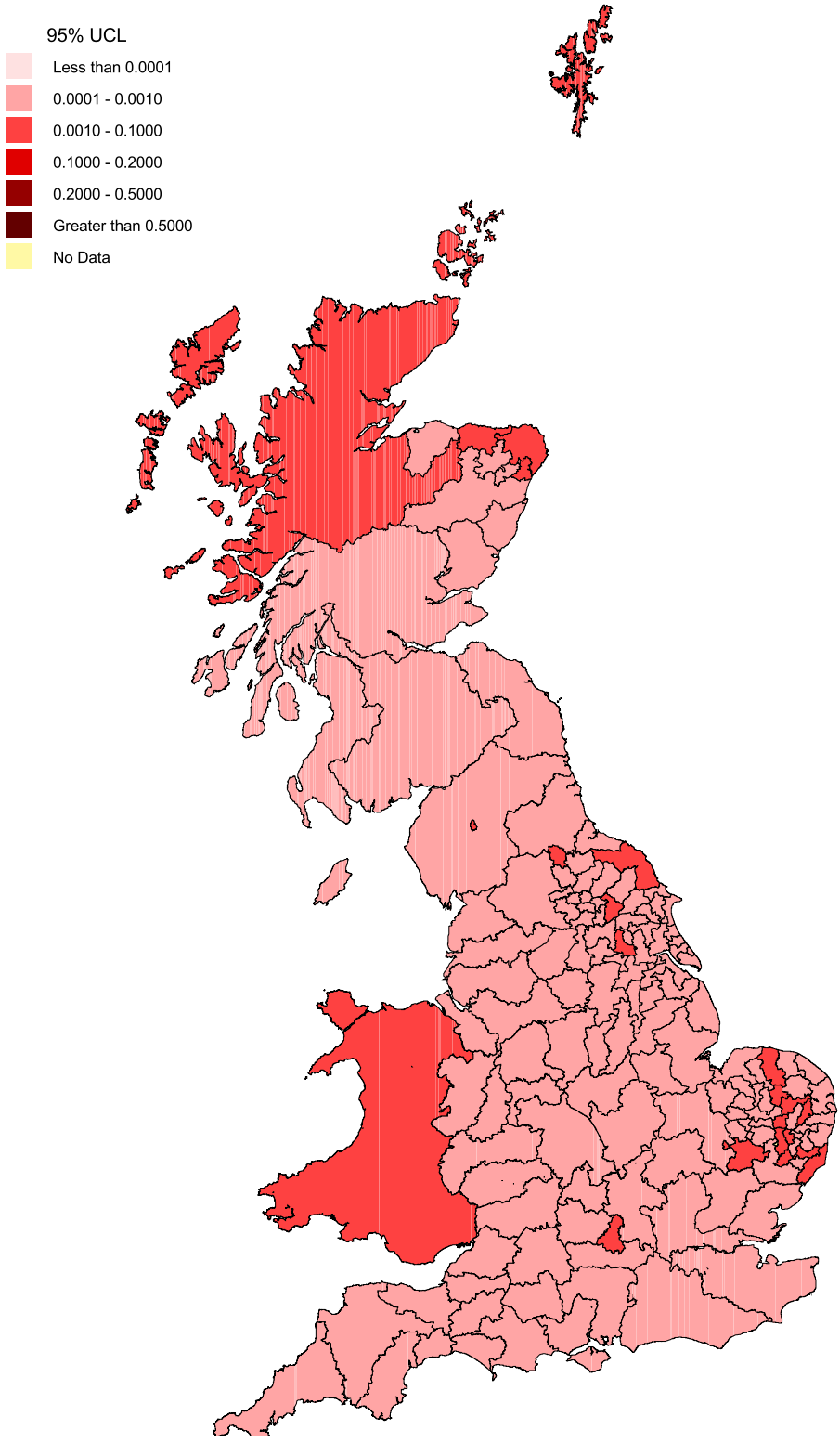

Figure 5.12: Upper 95% confidence limit for low-risk breeder pigs tested from 2000-2005 (based on unweighted low-risk breeder pig data only)

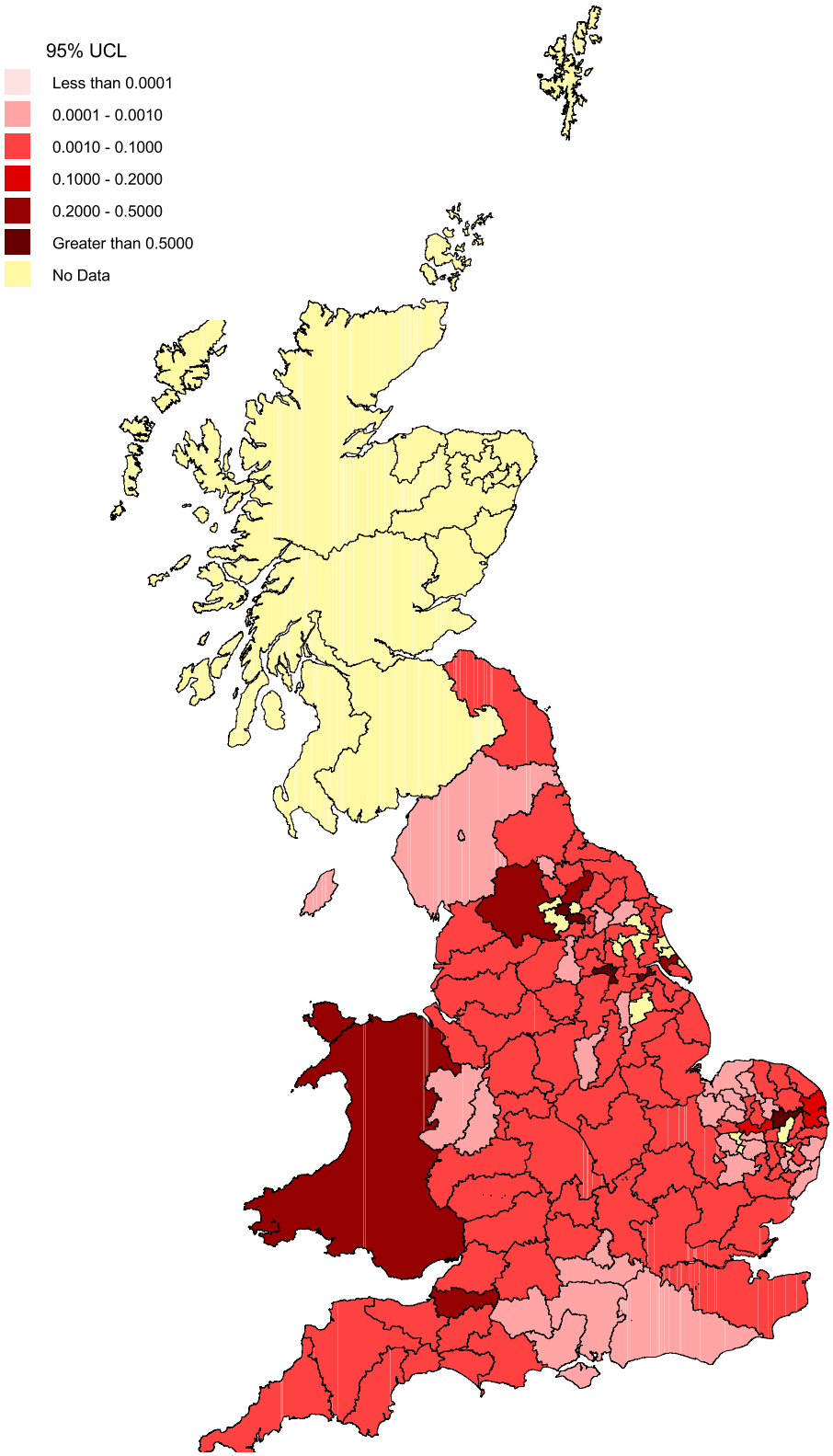

Figure 5.13: Upper 95% confidence limit for high-risk breeder pigs tested from 2000-2005 (based on unweighted high-risk breeder pig data only)

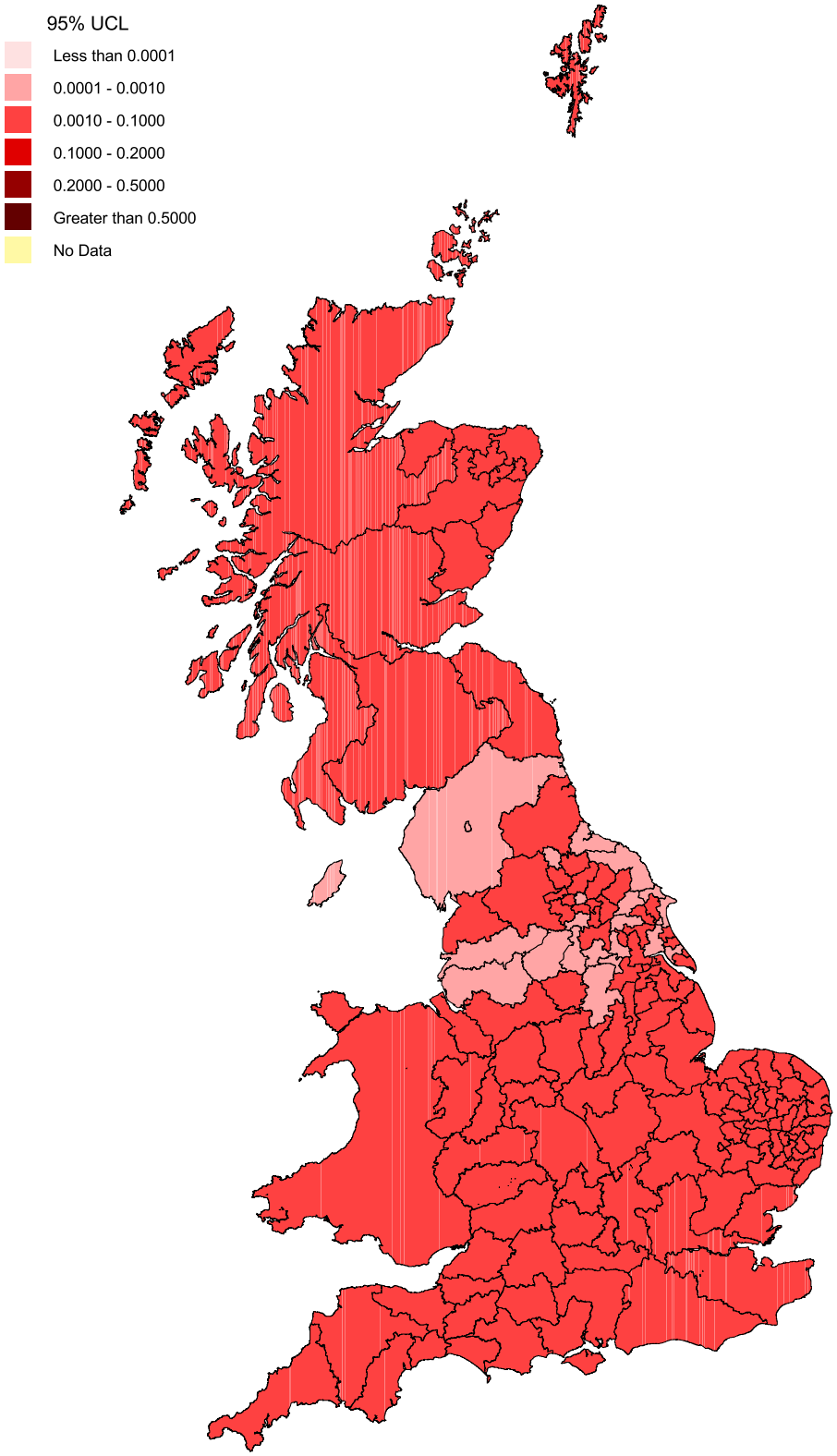

Figure 5.14: Upper 95% confidence limit for foxes tested from 2000-2005, calculated in relation to the reference low-risk grower pig population

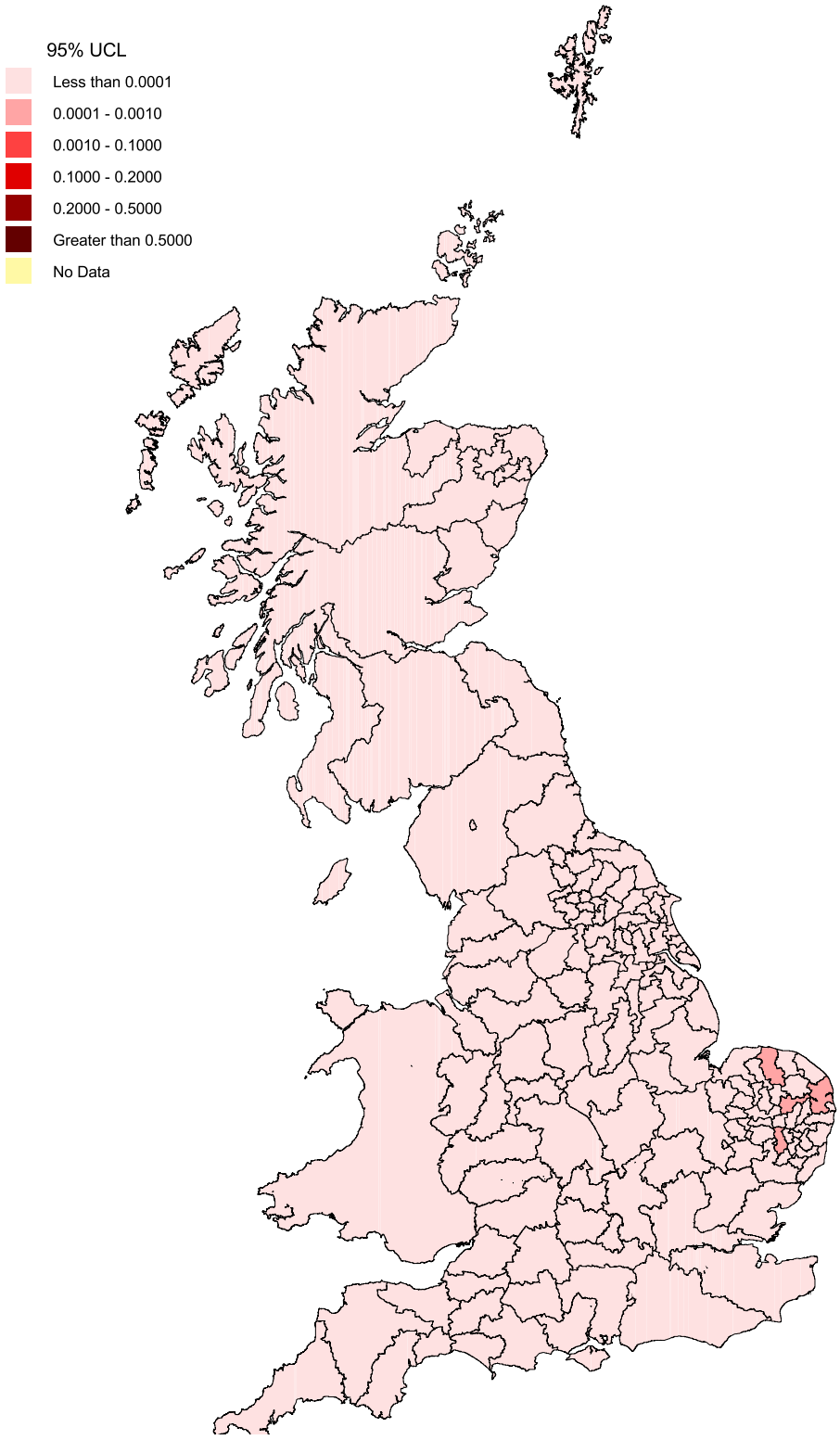

Figure 5.15: Upper 95% confidence limit for horses tested from 2000-2005, calculated in relation to the reference low-risk grower pig population

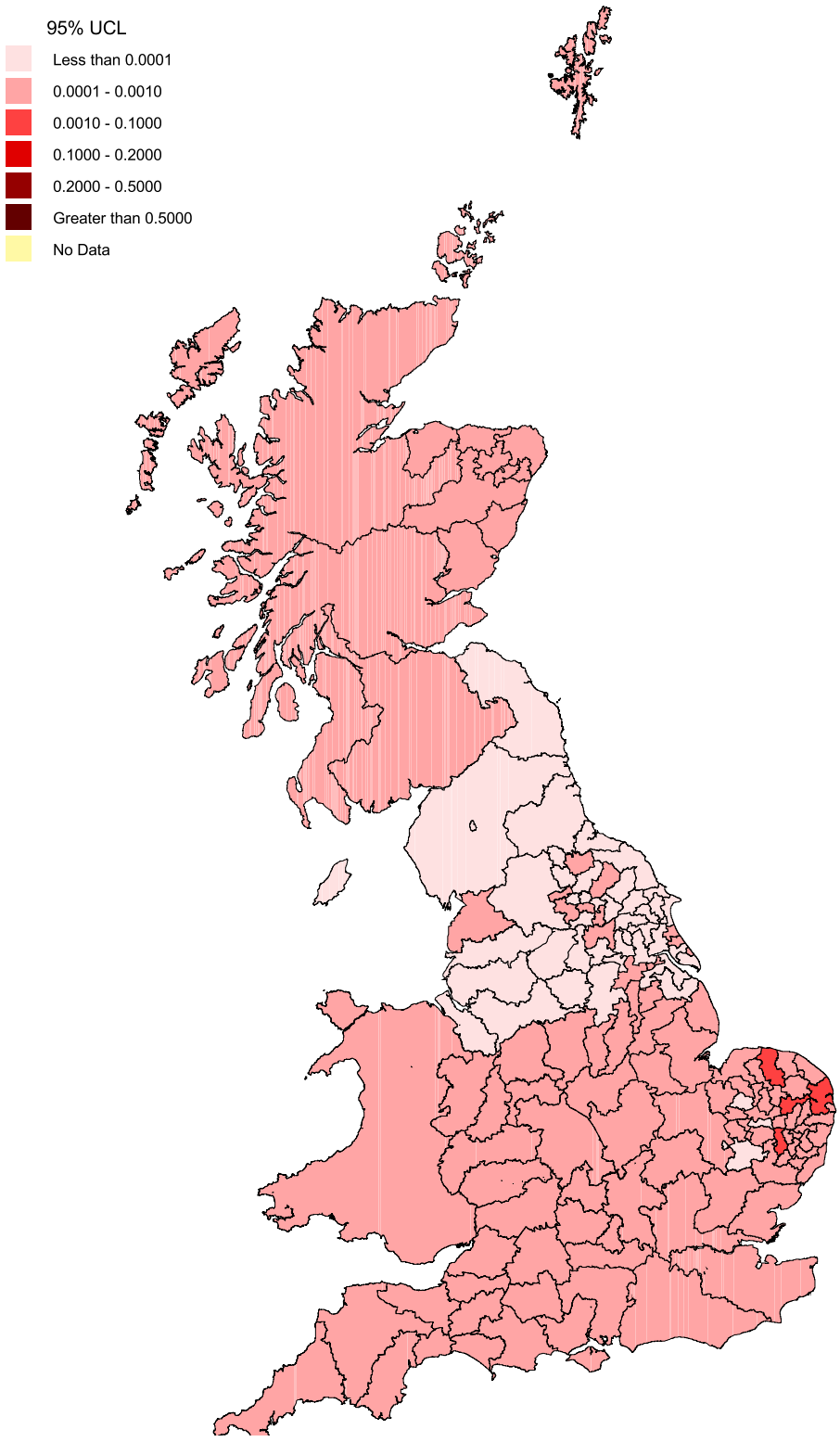

Figure 5.16: Upper 95% confidence limit for high-risk grower pigs tested from 2000-2005, calculated in relation to the reference low-risk grower pig population

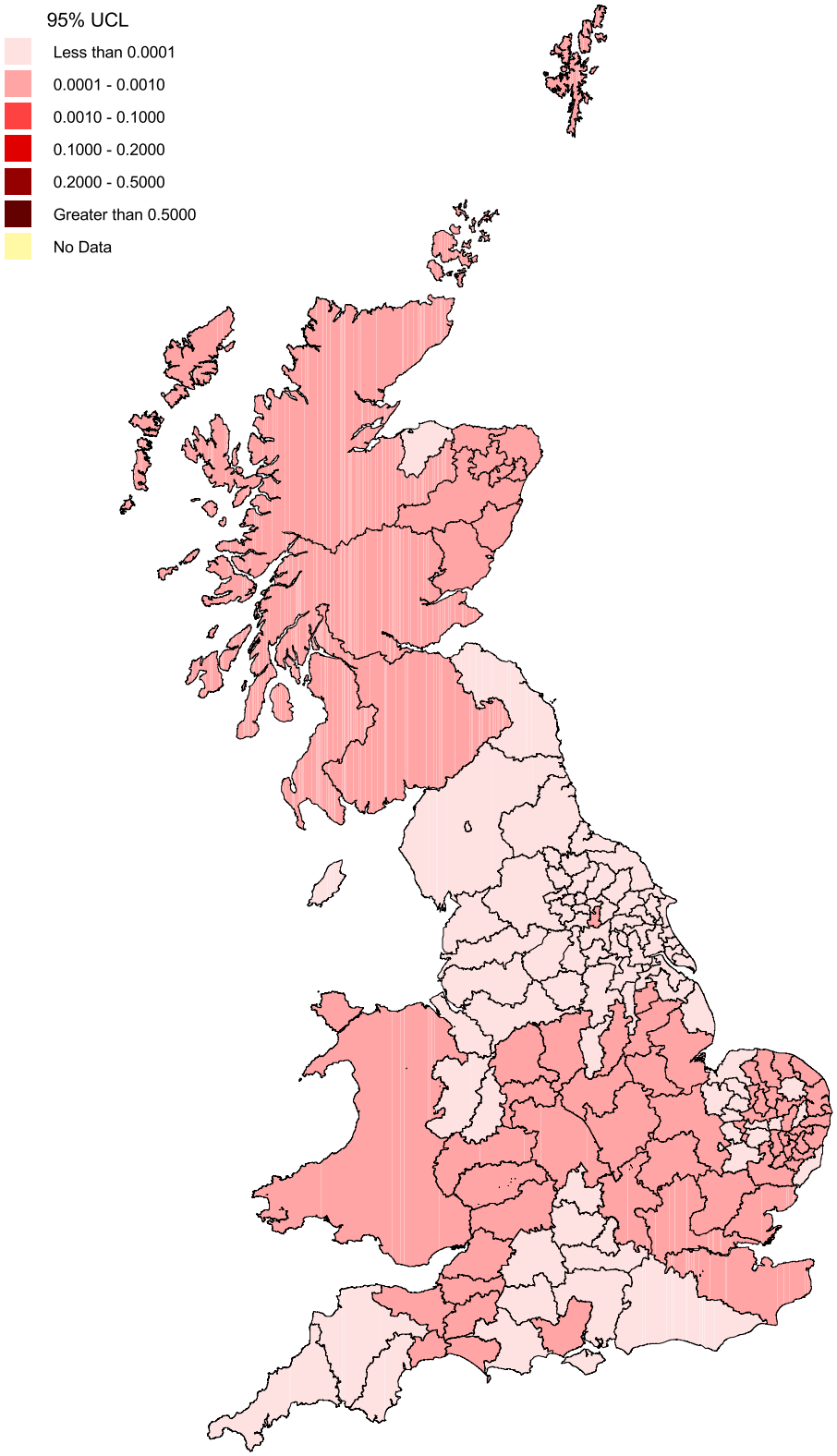

Figure 5.17: Upper 95% confidence limit for low-risk breeder pigs tested from 2000-2005, calculated in relation to the reference low-risk grower pig population

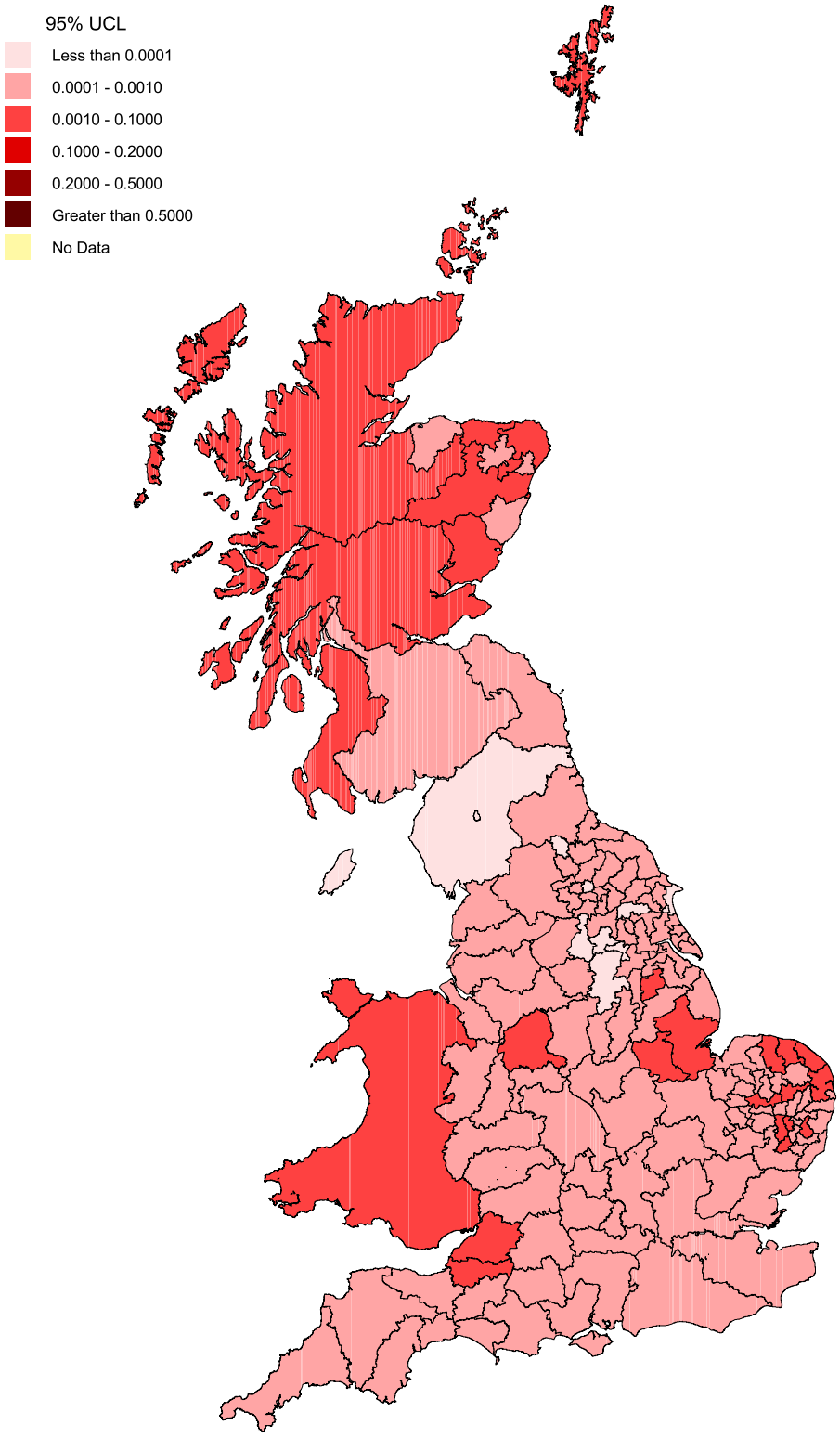

Figure 5.18: Upper 95% confidence limit for high-risk breeder pigs tested from 2000-2005, calculated in relation to the reference low-risk grower pig population

5.9 Appendix 2: Weighting samples in a risk-based surveillance system for *Trichinella*

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The relative value of testing an animal from a particular class is equal to the relative prevalence of the animal class compared to a reference group of animals multiplied by the sensitivity of the test. This appendix summarises data from a range of sources to estimate the relative prevalence in various animal classes as summarised in Table 5.2 of the main report.

Reference population

Pigs are considered the most likely route by which humans in GB would be exposed to *Trichinella*. They are also the species which are most widely and systematically tested in GB, in accordance with EU regulations. Relative to all other groups, the level of infection in pigs is lowest in grower pigs raised indoors. This group is therefore used as the baseline, and surveillance samples from other classes of pig and other species are weighted relatively, according to the findings in the literature.

Red foxes

Summary: A sample from a red fox is equivalent to 75 samples from grower pigs housed indoors

Trichinella infection has frequently been detected in red foxes (*Vulpes vulpes*) in countries that have almost a complete absence of cases of infection in pigs and humans (Table 5.7). Gottstein et al. (1997) was the only study that reported the frequency of infection in both red foxes and domestic pigs. In this study the upper 95% confidence limits for the percentage of foxes and pigs infected in Switzerland were 2% and 0.03%, respectively. Therefore, samples taken from red foxes were weighted at 75 times more than those from a grower pig housed indoors.

Horses

Summary: Samples from two horses are equivalent to a sample from one grower pig housed indoors

The first case of trichinellosis in humans associated with horses was identified in 1975. To date the pathway by which horses, considered herbivores, acquire a meat-borne

Table 5.7: Results of studies investigating the level of *Trichinella* infection in the red fox (*Vulpes vulpes*) population by country

Country	Year	Test method	Number of positives	Number tested	% positive	Source
Belgium	1996-1999	ELISA (sera)	61	130	46.9	(Vercammen et al. 2002)
	1996-1999	ELISA (meat juice)	90	478	19.8	(Vercammen et al. 2002)
Denmark	1995-1996	Digest	3	3133	0.1	(Enemark et al. 2000)
	1997-1998	Digest	0	3008	0	(Enemark et al. 2000)
Estonia	2000-2002	PCR	181	446	41	(Jarvis et al. 2004)
Hungary	N/R[a]	PCR	3	100	3	(Sreter et al. 2003)
Italy	2001-2004	Digestion	8	227	3.5	(Remonti et al. 2005)
Ireland	2002	Digestion	4	454	0.9	(Rafter et al. 2005)
Lithuania	1987-2000	Digestion	9	27	4	(Senutaite and Grikieniene 2001)
Netherlands	1985	Digestion	N/R	N/R	4.3	(van der Giessen and voor de Volksgezondheid en Milieu 2001)
	1995	Digestion	N/R	N/R	13.6	(van der Giessen and voor de Volksgezondheid en Milieu 2001)
Norway	1994-1995 & 2002-2005	Digest	19	393	4.8	(Davidson et al. 2006)
Ireland	2005	PCR	4	454	0.9	(Rafter et al. 2005)
Spain	1997-1999	Trichinoscopy	6	67	8.9	(Criado-Fornelio et al. 2000)
Switzerland	N/R	Digest	4	452	0.9	(Gottstein et al. 1997)

[a] N/R: not reported

parasite remains unknown. One hypothesis is that horses on pasture will graze on the carcasses of wild carnivores. Another hypothesis is that they are fed meat by producers as a way of fattening the animals prior to sale. The latter is supported by interviews with horse producers at local horse markets in Serbia, revealing that feeding of animal products prior to market was common practice (Murrell et al. 2004). The authors also conducted a series of trials and found that 32% of 219 horses would consume meat patties. Furthermore, three horses fed pork balls infected with *T. spiralis* became infected.

The level of *Trichinella* infection appears to be extremely low; in the years between 1975 and 2000 only 25 infected horses were reported worldwide. Twenty-one of the infected horses were imported to France and Italy from Eastern Europe, Poland, the USA, Canada, Mexico and Serbia. Four were identified in horses slaughtered in Mexico (Pozio 2000). The results of a number of studies investigating the level of *Trichinella* infection in horses are summarized in Table 5.8. Some caution is advised when interpreting the estimates of disease frequency because a survey of 150 horses from two slaughterhouses in Mexico showed that results vary considerably depending on the testing regime used (Jimenez-Cardoso et al. 2005). When using artificial digestion methods two positive horses were detected, and PCR identified seven infected animals. In contrast, when the samples were tested using trichinoscopy all horses tested negative. Therefore, when using trichinoscopy, digest or PCR the apparent prevalence was 0%, 1.3% or 4.6%, respectively.

Allowing for issues relating to testing regimes it would appear that horses are not commonly infected with *Trichinella*. Furthermore, the source of infection appears to be the unregulated feeding of meat products to fatten horses before slaughter. In countries such as GB where there is strict veterinary regulation of feeding practices, horses are less likely to be infected with the parasite. Therefore, in a risk-based surveillance system a horse should be weighted at less than a grower pig housed indoors. It was difficult to select the appropriate weighting because of the small number of infected horses, thus a weighting of 0.5 was chosen.

Domestic pigs

Table 5.9 shows the results of a number of studies investigating the level of *Trichinella* infection in domestic pigs. The results of studies conducted in Argentina, Croatia, and Spain show that the level of infection in pigs housed outdoors is higher than in those raised indoors. The increased level of infection in these pigs is likely to be caused by increased exposure to wildlife carcasses. This is supported by a study of 91 swine farms in North Carolina showing that the presence of wildlife on a farm increased the risk a

Table 5.8: Results of testing of horsemeat for *Trichinella* in various countries. Adapted from Boireau et al. (2000)

Country	Year	Test method	Number of horses	Number of positives	% positive
France	1996-1999	Digest	59,600	2	3.36×10^3
Mexico	1996	Digest	80	4	5
Poland	1984-1994	Digest	500,000	0	0
Switzerland	1993	Digest and ELISA	106	0	0
Belgium	1986-1991	Digest	1577	0	0
Italy	1996-1999	Digest	600,000	3	5.00×10^4
USA	1996-1999	Digest	60,697	0	0
Canada	1995-1999	Digest	315,000	0	0

farm would be sero-positive (Cowen et al. 1990b). Gamble et al. (1999) also found an increased risk of *Trichinella* infection on farms where pigs had access to wildlife. Farms where pigs had access to wildlife carcasses were 6.33 (95% confidence interval (CI): 0.82-48.73) times more likely to have sero-positive grower pigs than farms that did not allow pigs access to the outdoors. A study of hogs in the USA between 1933 and 1937 by Schwartz (1940) (in Gamble et al. 1999) found that 1% of hogs fed grain or forage, 6% of hogs fed uncooked garbage and 0.6% of hogs fed cooked garbage were infected with *Trichinella* larvae. In a second study conducted by Schwartz (1952), 0.63% of grain-fed hogs and 11.21% of 1328 garbage-fed hogs tested positive for *Trichinella*. Similarly, in the USA a national survey of 22,451 hogs found that while the overall prevalence of *Trichinella* infection was 0.13%, the prevalence in garbage-fed hogs was 0.51% (Zimmerman and Zinter 1971).

The level of *Trichinella* infection has been reported to be higher in breeding age animals than grower pigs. Zimmermann and Brandly (1965) (reported in Gamble et al. 1999) found that the prevalence of *Trichinella* infection in butcher hogs and breeder hogs was 0.12% and 0.22%, respectively. Thirty years later the 1995 National Swine Monitoring System Survey in the USA also found evidence of higher levels of infection in breeding pigs compared to grower pigs (Gamble and Bush 1999). In this survey a total of 7987 samples, approximately 40% from gestating sows and 60% from grower/finisher pigs, were tested for the presence of antibodies to *Trichinella*. The prevalence was 0.03% in sows and 0.0% in grower/finisher pigs. An increased level of infection in older animals was also detected in a study of pigs in the area surrounding Beijing, China (MeiKun et al. 1997). The levels of infection in piglets, grower pigs and adult breeding animals were 5%, 7% and 17%, respectively.

Given that the prevalence of *Trichinella* infection is affected by housing type and age, it is possible to divide pigs into four risk categories:

- Grower pigs housed indoors
- Breeding-age animals housed indoors
- Grower pigs housed outdoors
- Breeding-age animals housed outdoors.

Relative to all other groups, the level of infection is lowest in grower pigs raised indoors. This group should therefore be considered the baseline, and in a risk-based surveillance system all other samples should be weighted comparatively.

Summary: A sample from a breeder pig housed indoors is equivalent to two samples from grower pigs housed indoors

The decision was made to weight breeding-age animals raised indoors at twice the value of a grower pig raised indoors. This value was selected on the basis of Zimmermann and Brandly (1965) showing the risk of infection being 1.8 times higher in breeding pigs than butcher pigs. Additional evidence for this weighting is provided by Gamble et al. (1999), who found that the upper limit of the 95% CI for the prevalence of infection in sows was 2.5 times that in finisher pigs. The upper 95% confidence interval for the prevalence of infection in sows and grower/finisher pigs in the 1995 Swine Monitoring System survey was calculated using exact binomial limits and assuming that 40% (n = 3195) of the samples were taken from gestating sows and 60% (n = 4792) were taken from grower/finisher pigs.

Summary: A sample from a grower pig housed outdoors is equivalent to five samples from grower pigs housed indoors

A weighting of 14.5 for grower pigs raised outdoors could be justified based on the results of a study of pig farms in Croatia (Nckler et al. 2004). The study found the sero-prevalence of *Trichinella* in pigs raised indoors was 0% (95% CI: 0-2%) while the sero-prevalence of pigs raised outdoors was 17% (95% CI: 9-29%). In countries such as GB that have undetectable levels of *Trichinella* in wildlife the difference between indoor and outdoor farms is likely to be lower. Studies on pig farms in the north-east of the USA have found that farms where pigs had access to wildlife carcasses were 6.33 times more likely to have sero-positive grower pigs than those farms where pigs did not have access to wildlife carcasses. (Gamble et al. 1999) This is supported by a study of 91 swine farms in North Carolina that found the presence of wildlife on the farm increased the risk of the farm being sero-positive by a factor of 1.66 (95% CI: 1.0-2.8) (Cowen et al. 1990b). Based on these results, surveillance tests carried out on grower pigs housed outdoors were weighted five times the value of grower pig housed indoors.

Summary: A sample from a breeder pig housed outdoors is equivalent to ten samples from grower pigs housed indoors

Based on the literature, breeding age animals raised outdoors are most likely to be infected with *Trichinella*. Therefore, the decision was made to weight a breeding age animal housed outdoors at 10 times more than a grower pig housed indoors. This weighting was calculated by multiplying the weighting for breeding age animals housed indoors by the weighting for grower pigs housed outdoors. This is based on the assumption that the effects of housing and age are multiplicative. In the absence of studies describing the prevalence of breeding age animals raised outdoors to: (1) grower pigs raised indoors, (2) grower pigs raised outdoors or (3) breeding age animals raised indoors, this assumption could not be evaluated.

Table 5.9: Results of studies investigating the level of *Trichinella* infection in domestic pigs by country and year

Country/Region	Year	Type of pig	Test type	Number positive	Number tested	% positive	Source
Argentina	2000	Slaughtered pigs	Digest	16	55	29.09	(Larrieu et al. 2004)
	2001	Slaughtered pigs	Digest	5	105	4.76	(Larrieu et al. 2004)
	2002	Slaughtered pigs	Digest	3	140	2.14	(Larrieu et al. 2004)
	2000	Grower pigs	Serology	31	181	17.13	(Larrieu et al. 2004)
	N/R[1]	Grower pigs housed indoors	Serology	N/R	N/R	0	(Ribicich et al. 2005)
	N/R	Pigs housed outdoors	Serology	N/R	N/R	9.27	(Ribicich et al. 2005)
Bolivia	1993	Slaughtered pigs	ELISA	178	1327	13.40	(Brown et al. 1996)
Boliva/ Altiplano	1991	Slaughtered pigs	Digest	21	118	11.20	(Bjorland et al. 1993)
Canada	1985	Slaughter sows	ELISA	4	15,318	0.03	(Smith et al. 1988)
China	N/R	Piglets	ELISA	N/R	N/R	5.10	(MeiKun et al. 1997)
	N/R	Grower pigs	ELISA	N/R	N/R	7.00	(MeiKun et al. 1997)
	N/R	Adult breeding animals	ELISA	34	77	17.20	(MeiKun et al. 1997)
Croatia	2002	Indoor pigs	ELISA	0	163	0.00	(Nckler et al. 2004)
	2002	Outdoor pigs	ELISA	11	63	17.00	(Nckler et al. 2004)
Germany	2002	Indoor pigs	ELISA	0	1176	0.00	(Nckler et al. 2004)
	2002	Outdoor pigs	ELISA	0	225	0.00	(Nckler et al. 2004)
Lithuania	1987-2000	Domestic pig	N/R	N/R	1386	N/R	(Senutaite and Grikieniene 2001)
Poland	1996-2000	Domestic pig	PCR	N/R	19	N/R	(Cabaj et al. 2004)

Continued on next page

[1]N/R: Not reported

Table 5.9 – Continued

Country/Region	Year	Type of pig	Test type	Number positive	Number tested	% positive	Source
	1987	Slaughter pigs	N/R	N/R	N/R	4.56	(Lis 1999)
	1997	Slaughtered pigs	N/R	N/R	N/R	0.0004	(Lis 1999)
Serbia	1999	Domestic pigs	N/R	N/R	N/R	0.17	(Cuperlovic et al. 2001)
Spain	1993	Domestic pig	N/R	0	>40,000,000	0.00	(Bolas-Fernandez and Martinez-Fernandez 1997)
Spain	1993	Family farms	N/R		9,290,501	0.002	(Bolas-Fernandez and Martinez-Fernandez 1997)
Switzerland	N/R	Slaughtered pigs	Digestion	0	11226	0.00	(Gottstein et al. 1997)
	N/R	Sows	Serology	0	25239	0	(Gottstein et al. 1997)
USA	1961-1965	Breeding hogs	N/R	N/R	6,881	0.22	Zimmermann and Brandly 1965
	1961-1965	Butcher hogs	N/R	N/R	9,495	0.12	Zimmermann and Brandly 1965
	1966-1970	Farm-raised butcher swine	Digestion	25	20,003	0.13	(Zimmerman and Zinter 1971)
	1966-1970	Farm-raised breeder swine	Digestion	0	1,858	0.00	(Zimmerman and Zinter 1971)
	1966-1970	Garbage-fed hogs	Digestion	3	590	0.50	(Zimmerman and Zinter 1971)
	1990	Domestic pigs	Serology	5	3048	0.16	(Gamble and Bush 1999)
	1995	Grower pigs[2]	Serology	0	4792a	0.00	(Gamble and Bush 1999)
	1995	Sows[2]	Serology	1	3195	0.01	(Gamble and Bush 1999)
USA/ Florida	1988-1989	Pigs > 6 months	ELISA	23	1,294	1.78	(van der Leek et al. 1993)
USA/	1980-1981	Slaughtered pigs	Digest	1	1,223	0.001	(Hugh-Jones et al. 1985)
	1980-1981	Slaughtered pigs	ELISA	4	1,225	0.003	(Hugh-Jones et al. 1985)

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[2]Based on assumption that 60% of pigs sampled in 1995 swine survey were grower/finisher

Table 5.9 – Continued

Country/Region	Year	Type of pig	Test type	Number positive	Number tested	% positive	Source
	1980-1981	Slaughtered pigs	Digest	0	267	0.00	(Hugh-Jones et al. 1985)
USA/ Mid-Atlantic	N/R	Slaughtered pigs[3]	Digest	196	33,482	0.58	(Schad et al. 1985a)
USA/ Nth Central	1983-1985	Domestic pigs	Digest	0	3245	0.00	(Stromberg and Prouty 1987)
USA/ New Jersey		Grower pigs	ELISA	5	1,946	0.26	(Gamble et al. 1999)
USA/ New England		Grower pigs	ELISA	10	2,132	0.47	(Gamble et al. 1999)
USA/ New England	1983	Slaughtered pigs	Digest	39	5,315	0.73	(Schad et al. 1985b)
USA/ Nth Carolina	1987-1988	Culled swine	ELISA	49	10,765	0.005	(Cowen et al. 1990a)
	1987-1988	Breeding swine	ELISA	105	30,162	0.004	(Cowen et al. 1990a)
	N/R	Grower pigs	ELISA	359	29,947	1.22	(Cowen et al. 1990b)
	1994-1995	Indoor	ELISA	0	2128	0.00	(Davies et al. 1998)
	1994-1995	Outdoor	ELISA	1	54	1.80	(Davies et al. 1998)

[3]Included pigs from a variety of sources, from backyard operations to commercial farms

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Chapter 6

Risk-based surveillance for causes of ovine and caprine abortion exotic to New Zealand

6.1 Abstract

New Zealand's Ministry of Agriculture and Forestry purchases laboratory testing on an annual basis for exotic causes of sheep and goat abortion. Abortion case submission data for 2002-2003 were examined, along with the feasibility of carrying out surveillance on a regional basis. Different types of climatic and population data for the lower North Island were integrated using a geographic information system and a rule-based approach was applied to demonstrate how surveillance needs for vector-borne diseases could be assessed both temporally and spatially.

This chapter consists of a report submitted to the Ministry of Agriculture and Forestry of New Zealand, July 2005.

6.2 Introduction

Demonstrating freedom from exotic diseases of farmed animals is important to the New Zealand economy. Agricultural exports were worth $16,135,634,000 in 2004 (provisional figures) and comprised 53% of total exports, 17% of the total being dairy products and 16% meat (www.stats.govt.nz). With such a heavy reliance on the agricultural sector, it is crucial for New Zealand to maintain effective and efficient surveillance systems in case of an exotic disease incursion. Diseases of concern include bluetongue (an *Orbivirus*), brucellosis (*Brucella melitensis*) and Q fever (*Coxiella burnetii*), among others. Early identification of an outbreak would facilitate prompt containment, control and eradication, with resumption of normal trading activities as soon as possible.

Surveillance systems must be temporally and economically efficient in locating disease if present. Knowing where and when disease is most likely to be found will help

Table 6.1: Composition of surveillance zones

Surveillance Zone	Regional Council
Auckland	Northland, Auckland
Waikato	Waikato, Bay of Plenty
Hawkes Bay	Gisborne, Hawkes Bay
Wellington	Taranaki, Wanganui, Manawatu, Wellington
West Coast	Tasman, West Coast
Canterbury	Marlborough, Canterbury
Southland	Otago, Southland

in the detection and also eradication of disease. Also the results of testing programs will be used to support claims of freedom from disease. Ideally the design of a surveillance system should take account of all available information types, including factors influencing disease occurrence and spread along with results of any testing carried out.

Currently, the Ministry of Agriculture and Forestry (MAF) pay for laboratory testing for exotic causes of abortion from all laboratories in New Zealand. This study includes an exploratory analysis of animal health laboratory data for cases of sheep and goat abortion in New Zealand. It investigates the adequacy of current surveillance for exotic causes of sheep and goat abortion in flocks and herds in New Zealand, and examines the feasibility of carrying out surveillance on a regional basis. The number of sheep and goat abortion case submissions required to allow MAF to establish freedom from notifiable diseases and detect emerging diseases is calculated. A method of integrating various types of available information in developing risk-based surveillance systems and responses to disease incursions is described, using data that would be applicable to a vector-borne disease such as bluetongue.

6.3 Methods

6.3.1 Surveillance zones

Animal health laboratories currently record cases as coming from one of seven surveillance areas. These zones are obtained by amalgamating New Zealand Regional Council boundaries, and have been identified in this report as shown in Table 6.1.

6.3.2 Incursion zones

Entry points for cargo and passengers into New Zealand are high risk areas for the introduction of disease agents or vectors from overseas. A five kilometre radius around international airports and seaports where international cargo is unloaded determined the boundary of each incursion zone. Five kilometres was chosen as the maximum flight distance of a disease vector; however, vectors may be distributed outside this range by

wind or carried by animals, people or fomites. The main entry points are shown in Figure 6.3.

6.3.3 Sheep and goat population data

Agribase data for September 2004 were obtained from Agriquality New Zealand. This comprised a list of farms in New Zealand, each with a unique identifier, details of farm location, area (hectares), enterprise type classification, goat numbers and the number of sheep in each of six classes (numbers of breeding ewes, drystock, sheep grazing off-farm, other sheep (e.g. rams), replacement hoggets and total number of sheep at last update). This data is updated irregularly, as and when opportunities arise to collect information from farmers.

6.3.4 Abortion data

Laboratory data were provided for 2002 and 2003 and included ovine and caprine submissions with a history of abortion, abnormalities of the reproductive system (ARS) or perinatal loss. Cases with a history of ARS but a diagnosis that is not known to cause abortion were excluded, however 125 cases (40 cases in 2002 and 85 cases in 2003) were not diagnosed. These were retained in the dataset. Fourteen cases of perinatal loss were included as the diagnosis did not preclude these cases being abortions rather than post-natal losses. Other data fields included identification of the receiving laboratory, case identification number, surveillance zone (see below), district council of the source farm and diagnosis. The date of finalisation of the case was included for 2002 data. The data contained 62 different diagnoses, which were grouped into nine categories for analysis.

A surveillance case is defined by MAF as one with "one of the designated clinical signs as a major part of the clinical history, with samples and examinations allowing a diagnosis of an endemic disease, or with sufficient material or history to allow the exclusion of relevant notifiable organisms as the cause of the disease incident. The relevant notifiable organisms may be excluded either on the basis of clinical and/or epidemiological history, gross pathology or laboratory testing".

6.3.5 Estimation of abortion and case submission rates

An estimate of the national annual incidence of abortion in sheep was obtained from Quinlivan and Jopp (1982). In this study data were collected from 1975 to 1980 in Hawkes Bay, with the overall individual ewe abortion rate for the region over this time being 1.8%. The highest within-flock incidence risk was 16%, however endemic diseases (such as toxoplasmosis) are known to cause abortion storms of up to 20% within a flock, so this upper limit was used. In the estimation process (Figure 6.1) a beta distribution

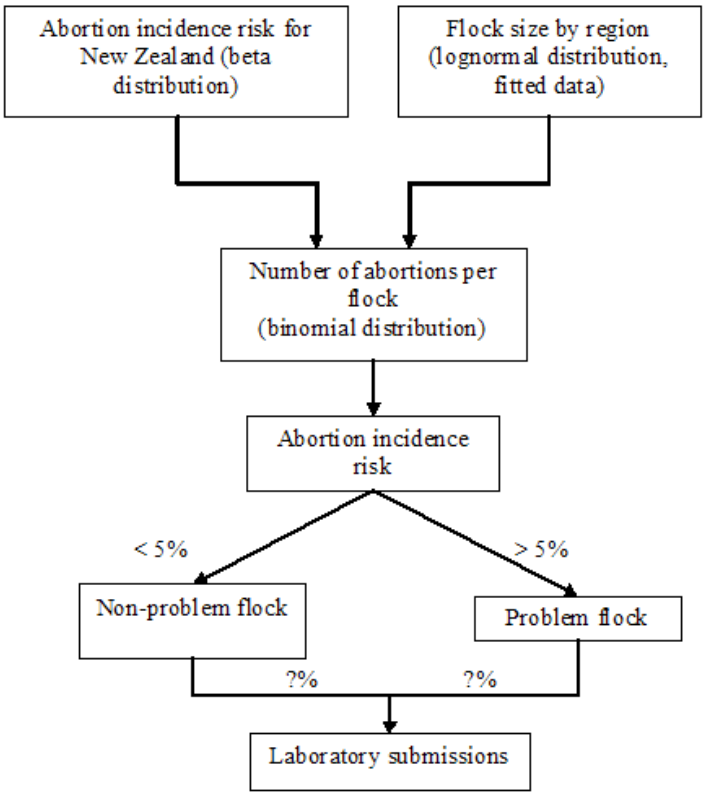

Figure 6.1: Flow chart outlining the simulation of abortion incidence risk in New Zealand sheep flocks. Unknown percentages of problem and non-problem flocks contribute to the total number of laboratory submissions.

was used to simulate the within-flock abortion incidence risk, with truncation at 0 and 0.20. For each region, flock size data from Agribase were fitted in @Risk to find the most suitable distribution. Lognormal distributions were used, with truncation to confine the distributions to the minimum (one sheep) and maximum flock sizes for each region. The number of abortions per flock was then simulated (with 10,000 iterations) using a binomial distribution and the flock counted if the resulting incidence risk was above the cutoff value. The chosen cutoff was five per cent, being the 75^{th} percentile for the percentage of lambs born dead per farm in a study in the United Kingdom (Binns et al. 2002). The number of flocks having an abortion problem was compared with the number submitting cases to laboratories in each region in 2003. Case submissions may also come from flocks with an abortion incidence of less than five per cent but the number of such submissions is unknown.

6.3.6 Number of cases to test to detect disease

The number of flocks to be tested to detect disease was estimated as follows (Dohoo et al. 2003):

$$n = (1 - (\alpha)^{1-D})(N - \frac{D-1}{2}) \tag{6.1}$$

where:

n = required sample size

α = 1 - confidence level

D = estimated minimum number of diseased flocks present (population size $\times$ design prevalence).

N = population size.

When an infinite population is being sampled the following approximation has been used:

$$n = \ln \alpha / \ln q \tag{6.2}$$

where q = 1 - design prevalence.

Having completed the required number of tests and if all results are negative, it can be stated that the disease in question does not exceed the design prevalence in the sampled population, with α level of confidence. Calculations were performed using a range of design prevalences.

Equation 6.3 was rearranged to allow calculation of the maximum number of diseased flocks in a population given that all samples (n) were tested negative:

$$D = (1 - \alpha^{(1/n)}) \times (N - \frac{n-1}{2}) \tag{6.3}$$

6.3.7 Surveillance system design

Variables for which data were available to be incorporated into a surveillance system were sheep and goat population size, laboratory abortion submission data, import of overseas cargo to New Zealand ports and airports, overseas passenger arrivals to New Zealand and climatic factors. National climate grids for monthly temperature and rainfall were obtained from Landcare Research, Hamilton. Temperature surfaces were based on surfaces fitted to long run average meteorological data collected at New Zealand meteorological stations from 1950 to 1980. The rainfall surfaces were calculated using 'Summaries of Climatological Observations to 1980' (New Zealand Meteorological Service).

A geographic information system (GIS) was used to illustrate spatial and temporal considerations of a risk-based surveillance system. The months of January, April, July

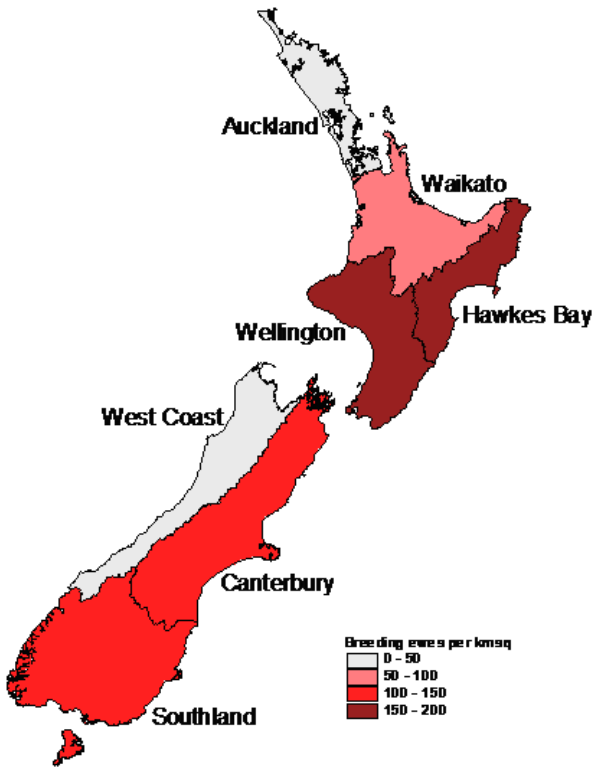

Figure 6.2: Surveillance zones in New Zealand and breeding ewe density in each zone.

and October were chosen as representing the four seasons. For each season the locations in the lower North Island where breeding ewe density was greater than 50 ewes/km^2, minimum temperature was 10^0C and monthly rainfall was greater than 50 mm were identified. These locations are areas of risk where conditions would be suitable for the survival of some species of mosquito or *Culicoides* (potential disease vectors), and comprise a 'risk landscape'. Geographical information from laboratory submissions from 2002 was compared with the risk landscape in order to assess the potential for disease detection by laboratory testing in high risk areas.

6.4 Results

6.4.1 Surveillance zones and population data

The seven surveillance zones and the density of breeding ewes per square kilometre in each zone are shown in Figure 6.2. Wellington and Hawkes Bay have the highest breeding ewe density.

Table 6.2: Characteristics of surveillance zones

Surveillance zone	Number of flocks [a]	Average farm size (ha)	Average flock size [b]	Farm type [c]		
				Goat	Sheep	Sheep and beef
Auckland	4169	73	108	81	594	948
Waikato	5348	140	304	81	330	1755
Hawkes Bay	2741	402	1419	10	474	1783
Wellington	7769	213	725	46	1701	3170
West Coast	1472	140	183	15	261	332
Canterbury	6255	441	763	41	2468	1655
Southland	6359	440	1245	31	3271	1991
Total	34,113			305	9099	11,634

[a] Number of flocks containing breeding ewes.
[b] Average size of breeding ewe flocks in each zone.
[c] Many other farm types are recorded in Agribase; only those relevant to the current study are shown here.

Table 6.3: Stock numbers by surveillance zone

Surveillance zone	Breeding ewes	Total sheep	Total goats	Area (km^2)	Breeding ewe density[a]
Auckland	589,810	866,001	30,382	17,538	35
Waikato	2,079,364	2,914,594	60,454	36,687	58
Hawkes Bay	3,750,207	5,539,041	37,282	22,546	166
Wellington	6,889,666	9,797,378	38,134	37,616	184
West Coast	326,954	447,775	10,059	33,434	10
Canterbury	5,765,124	8,310,874	28,726	55,761	104
Southland	9,011,747	12,000,368	16,749	63,648	142
Total	28,412,872	39,876,031	221,786	267,229	106

[a] Number of breeding ewes per square kilometre

Characteristics of each of the seven surveillance zones are shown in Table 6.2 and Table 6.3. The largest farms (> 400 ha) were in the Hawkes Bay, Canterbury and Southland zones, while the largest flocks (> 1000 ewes) were in Southland and Hawkes Bay. The predominant farm type for each property was recorded in one of 33 categories with the main types involving sheep and goats shown below. However, other types such as lifestyle farms are also likely to carry sheep and/or goats, albeit in smaller numbers.

Stock counts in Table 6.3 include the stated class of stock from all farm types. The number of goats was provided as a total count only. Density of breeding ewes was highest in the Wellington area (which includes Taranaki, Manawatu, Wanganui and Wellington regions), followed by Hawkes Bay and Southland.

6.4.2 Incursion zones

Possible incursion zones are illustrated in Figure 6.3. The main incursion zones within New Zealand and their attributes are shown in Table 6.4 to Table 6.7. In 2004 there were 4167 million visitor arrivals into New Zealand with the largest group (40%) coming from Oceania (Statistics New Zealand, www.stats.govt.nz).

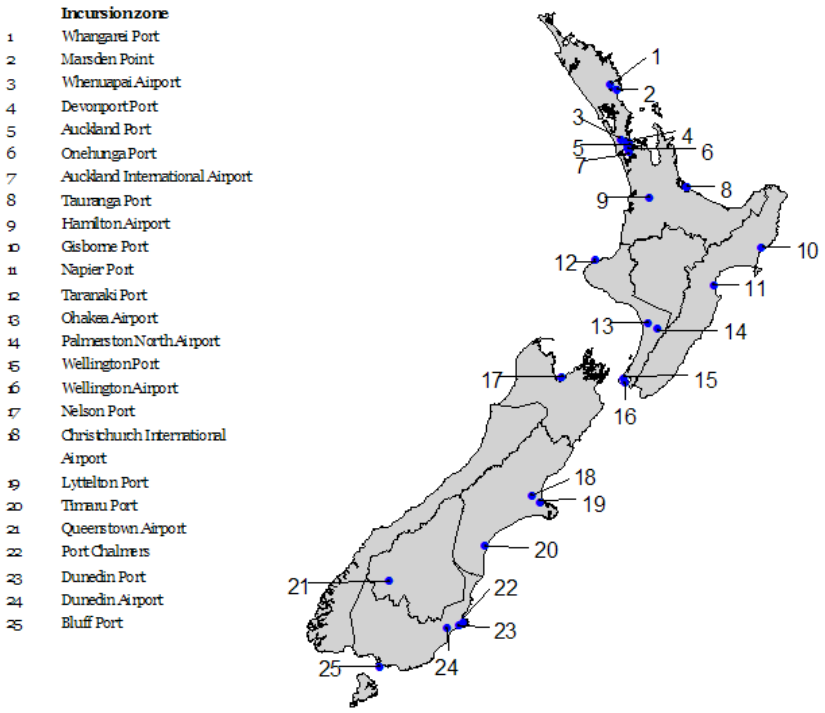

Figure 6.3: The main incursion zones within New Zealand

Table 6.4: Seaports: stock numbers by incursion zone

Incursion zone	Number of ewe flocks	Breeding ewes	Total sheep	Total goats	Total stock count	Breeding ewe density (per km^2)
Auckland	0	0	0	0	0	0
Bluff	13	3916	4171	53	4224	53
Devonport	0	0	0	0	0	0
Dunedin	64	3674	4540	90	4630	58
Gisborne	9	1660	8460	0	8460	108
Lyttelton	25	14,931	18,555	204	18,759	238
Marsden Point	6	33	46	4	50	1
Napier	2	5225	11,272	0	11,272	144
Onehunga	3	443	604	0	604	8
Port Chalmers	76	24,269	30,187	109	30,296	386
Port Nelson	11	461	539	13	552	7
Taranaki	52	543	853	228	1081	11
Tauranga	0	0	0	0	0	0
Timaru	50	5844	9355	142	9497	120
Wellington	3	4000	4445	0	4445	57
Whangarei	33	538	919	11	930	12
Total	347	65,537	93,946	854	94,800	1203

Table 6.5: International airports: stock numbers by incursion zone

Incursion zone	Number of ewe flocks	Breeding ewes	Total sheep	Total goats	Total stock count	Breeding ewe density (per km^2)
Auckland International	3	26	28	1	29	0.3
Christchurch International	36	17,036	24,437	103	24,540	218.1
Dunedin	47	34,733	45,162	7	45,169	444.6
Hamilton	94	5745	10,643	1821	12,464	73.5
Ohakea	66	27,230	40,926	11	40,937	348.6
Palmerston North	117	6604	12,132	101	12,233	84.5
Queenstown	21	14,434	18,026	107	18,133	184.8
Wellington	3	4700	7760	20	7780	60.2
Whenuapai	128	1347	2210	104	2314	17.2
Total	515	111,855	161,324	2275	163,599	1431.9

Table 6.6: Seaports 2003: vessel arrivals and international cargo weights by incursion zone. Data were not available for all ports.

Port office	Number of vessels	% of total arrivals	Cargo unloaded (tonnes)	% of cargo unloaded
Auckland	1300	38.8	3,632,981	22.6
Christchurch	135	4	1,268,545	7.9
Dunedin	39	1.2	263,728	1.6
Gisborne	26	0.8	143	0.0
Hamilton	5	0.1		0.0
Invercargill	146	4.4	1,048,066	6.5
Tauranga	557	16.6	1,864,193	11.6
Napier	87	2.6	684,090	4.3
Nelson	126	3.8	98,072	0.6
New Plymouth	176	5.3	442,071	2.8
Northland/Whangarei	673	20.1	5,444,743	33.9
Timaru	13	0.4	287,243	1.8
Wellington	69	2.1	1,009,075	6.3
Total	3352	100	16,066,754	99.9

There was a 9.6% increase in the weight of cargo unloaded at New Zealand ports in 2004. The relative percentages of cargo unloaded at each port were similar for both years.

A peak of 9.5% of aircraft arrivals occurred in December with a trough of 7.4% in June. Smaller airports included in the 'other' category were Northland/Whangarei, Napier, New Plymouth, Nelson, Invercargill, Gisborne and Mount Maunganui (Table 6.7). Similar percentages of cargo were unloaded by each airport in 2004, with and overall increase of 8.6% on the total weight of imports.

6.4.3 Abortion data

The annual number of abortion case submissions from 1973 to 2003 (Surveillance, Ministry of Agriculture and Forestry) is shown in Figure 6.4, along with the national count of breeding ewes from 1989 to 2003 (Meat and Wool Innovation Limited). A

Table 6.7: Airports 2003: international aircraft arrivals, cargo weights and passenger arrivals by incursion zone

	Aircraft type							
Airport	Commercial	Freight	Private	Military	Total	% total flights	% cargo unloaded	% of passengers
Auckland	16,324	713	104	2	17,143	68.8	87.6	73.2
Christchurch	3628	0	10	117	3755	15.1	10.7	18.6
Dunedin	373	0	0	0	373	1.5		0.9
Hamilton	523	0	8	0	531	2.1		1.1
Ohakea	7	0	0	16	23	0.1		0
Military Palmerston North	350	0	3	0	353	1.4		0.7
Queenstown	111	0	4	0	115	0.5		0.5
Whenuapai	8	0	1	74	83	0.3		0
Military Wellington	2442	0	34	13	2489	10	1.7	5.1
Other	2	0	38	0	40	0.2		0
Total	23,768	713	202	222	24,905	100%	100	100

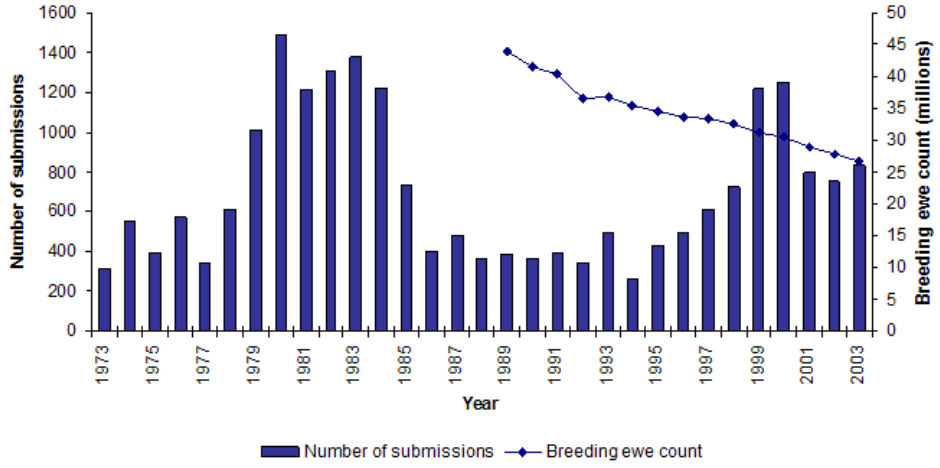

Figure 6.4: Comparison of the national ewe population size with the annual number of abortion submissions.

variety of factors influence the number of case submissions made each year, including emergence of new causes of outbreaks, climatic conditions and cost of laboratory testing. A peak in the early 1980s coincides with investigations for campylobacteriosis, for which vaccines became available in 1981. The number of submissions decreased in 1986 when laboratory fees were introduced, and an increase in the late 1990s corresponds to the emergence of *Salmonella* Brandenburg in the South Island. The size of the national breeding ewe flock has shown a steady decline since 1989.

A total of 793 laboratory records were analysed in 2002 and 655 in 2003. There were

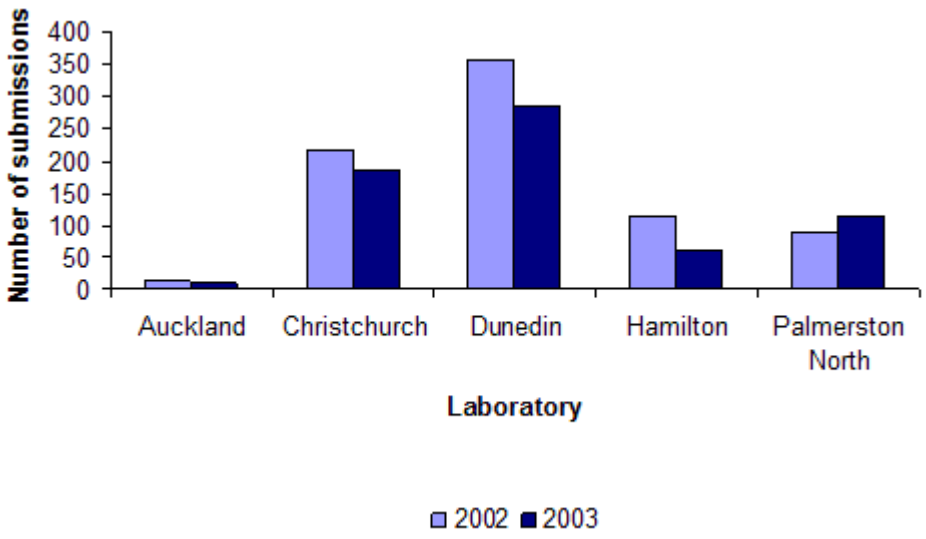

Figure 6.5: Total number of abortion submissions to each laboratory in 2002 and 2003.

21 cases from aborting does in 2002; all remaining records were ovine. Each record of a case submission may have represented samples from multiple animals from the same flock. The history of received cases was either abortion (84%), abnormalities of the reproductive system (ARS) (15%) or perinatal loss (1%), with cases going to one of five centres for diagnosis (Auckland, Hamilton, Palmerston North, Christchurch or Dunedin). Figure 6.5 shows the number of cases submitted to each laboratory in each year. Hamilton received cases from all surveillance zones with a majority of 43% originating in the Waikato zone. The Palmerston North laboratory received the majority of its cases from Wellington and Hawkes Bay zones but also received a small number from Canterbury and Southland in 2003. Most cases submitted to Christchurch were from Canterbury with a small number from West Coast and Southland; Auckland and Dunedin only received cases from the surveillance zone in which they are located.

Most cases (96%) were recorded as being either suitable or unsuitable as a surveillance case; four percent were not categorised. All submissions and surveillance cases per 1000 ewe flocks are shown by source area in Figure 6.6 (two records did not include source location information). Hawkes Bay, Canterbury and Southland have a higher number of abortion case submissions relative to the number of flocks than do other surveillance zones. This observation has been made previously (Gumbrell 1990) but the reasons behind it are unknown.

The temporal pattern of submissions is shown in Figure 6.7. As would be expected for New Zealand pastoral systems, the number of cases peaks in the third (spring) quarter and remains at low levels throughout the remainder of the year.

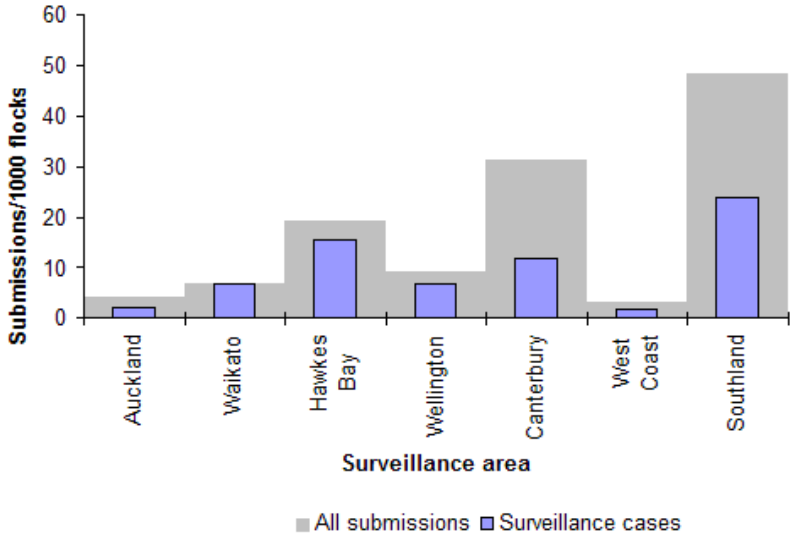

Figure 6.6: Number of surveillance cases and total number of submissions per 1000 ewe flocks in each surveillance zone in 2003.

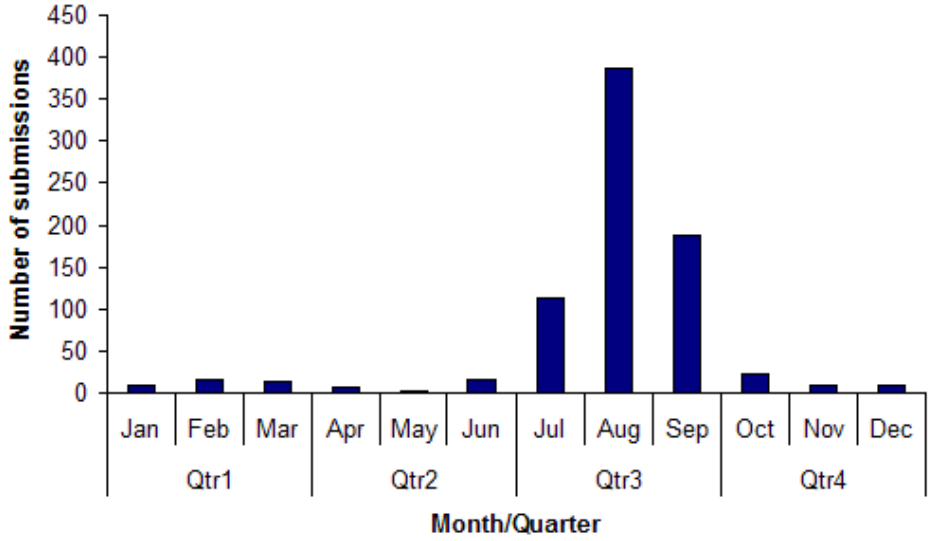

Figure 6.7: Total number of abortion case submissions for each month in 2002.

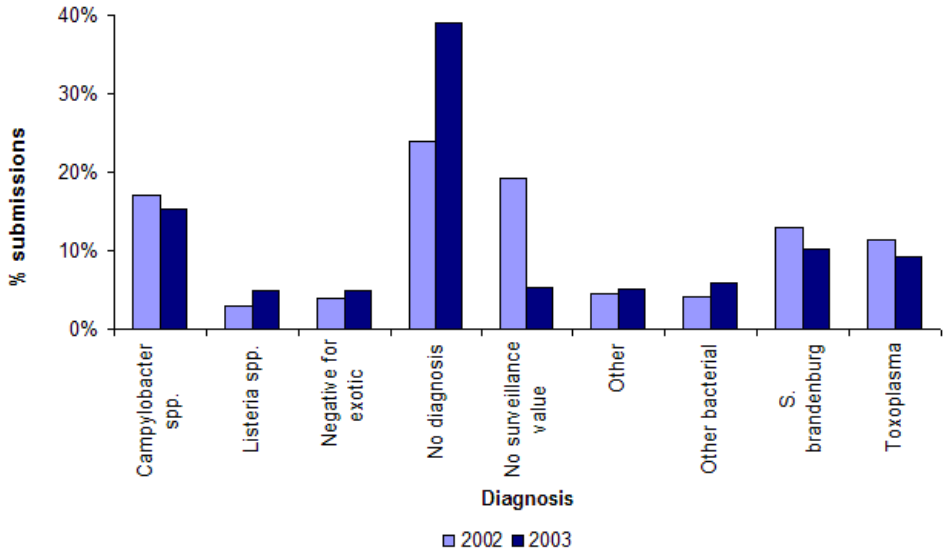

Figure 6.8: Diagnosis of laboratory submissions.

Figure 6.8 illustrates diagnosis of abortion cases for 2002 and 2003. A high proportion of cases (24% in 2002 and 39% in 2003) remained undiagnosed in both years. Cases which were recorded as 'negative for exotic' were ruled out for exotic causes although it is not known whether they were excluded on the basis of history, epidemiology or diagnostic test results. 'No surveillance value' consisted of cases that had insufficient information to be assessed for surveillance purposes and no other diagnosis was entered. 'Other bacterial' causes were all bacterial causes other than campylobacteriosis, listeriosis or *Salmonella* Brandenburg. Cases categorised as 'other' included a range of aetiologies such as mineral deficiencies and Border Disease.

In Figure 6.9 the diagnosed submissions are shown as the per cent of cases given each diagnosis in each surveillance zone in 2003. The actual number of submissions made from each area are given next to the name of each surveillance zone. It can be seen that toxoplasmosis and campylobacteriosis predominate in the North Island, while in the south there are fewer cases of toxoplasmosis but more cases of *S.* Brandenburg.

It can be seen in Figure 6.10 that Hamilton and Palmerston North laboratories recorded a higher proportion of submissions as surveillance cases than other centres (>90% and >70% respectively). Over the two year period, seven percent of cases ruled out an exotic cause on the basis of epidemiology and one percent on histological grounds. The remainder of the records did not have a reason stated. In 2002 57% of cases were categorised as surveillance cases with 53% in 2003.

The main diagnosis of cases suitable to be considered for surveillance purposes was campylobacteriosis (Figure 6.11). The diagnostic success rate for surveillance cases was

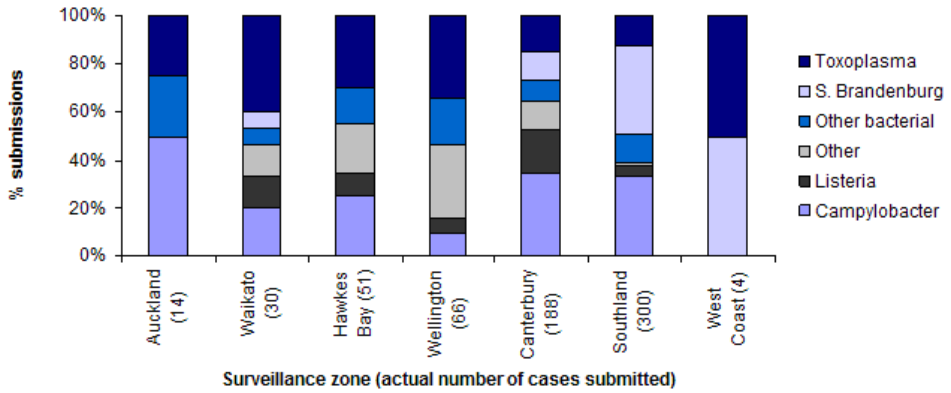

Figure 6.9: Diagnoses by surveillance zone in 2003. Actual number of cases submitted to each zone is shown in brackets.

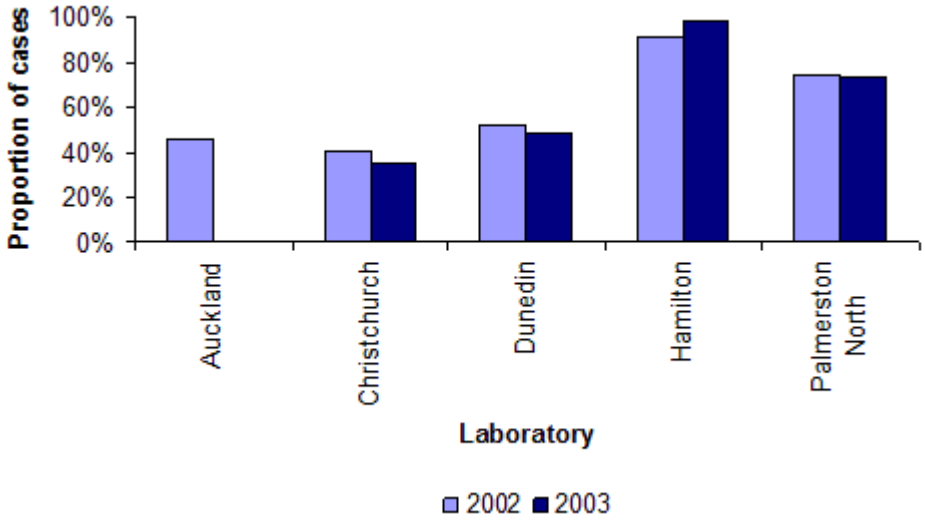

Figure 6.10: Proportion of submissions suitable for use as surveillance cases.

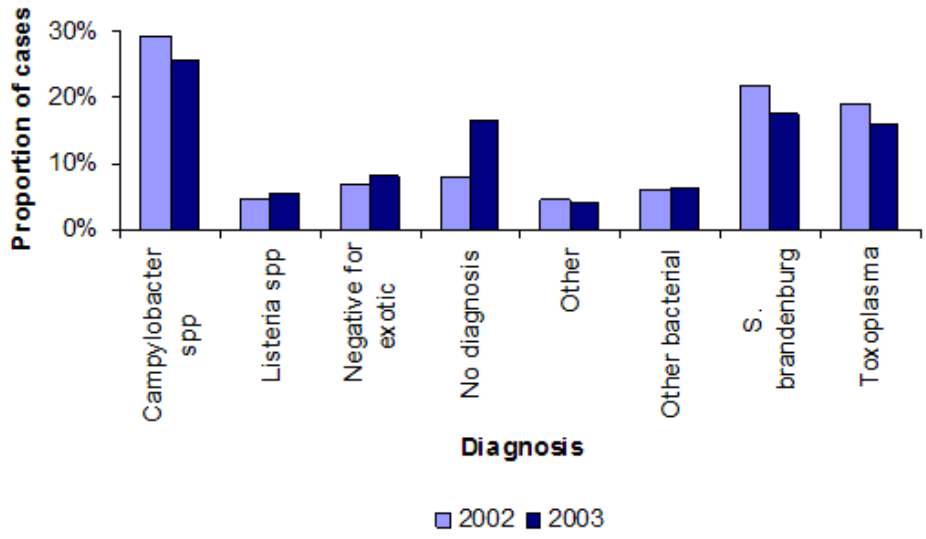

Figure 6.11: Diagnosis of surveillance cases.

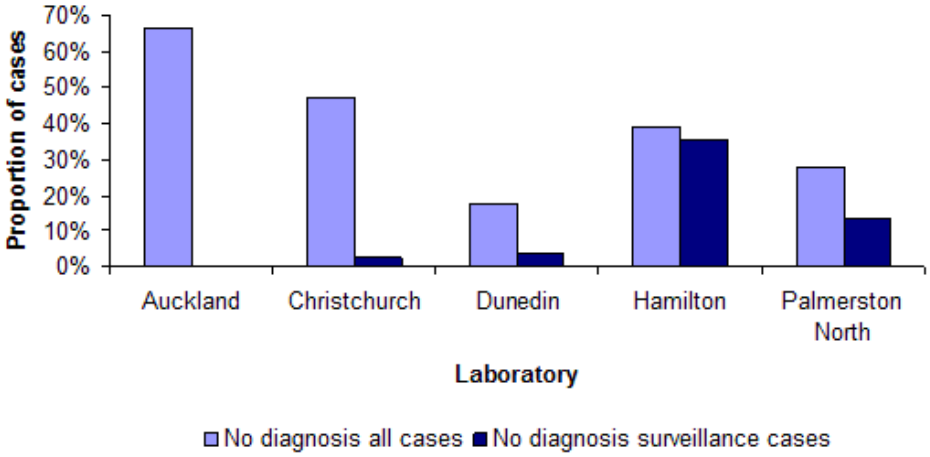

Figure 6.12: Proportion of cases remaining undiagnosed at each laboratory. Data for 2002 and 2003 were combined.

greater than that for all cases, presumably due to the submission being of better quality (which initially enabled consideration for surveillance purposes).

The proportion of cases that remained undiagnosed at each laboratory is illustrated in Figure 6.12. Auckland had the lowest percentage result for diagnostic success, but only 21 abortion cases over the two year period were received at this laboratory.

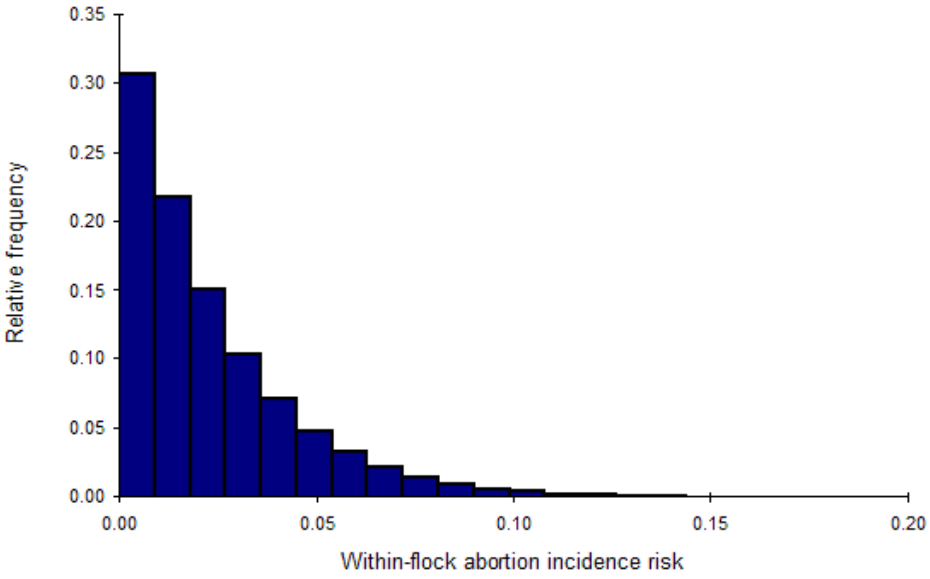

Figure 6.13: Within-flock abortion incidence risk simulated in @Risk using a beta distribution truncated at 0.00 and 0.20. The median incidence risk of abortion was 1.68%. The 95% confidence limits of within-flock abortion incidence risk were 2.32% to 2.41%.

6.4.4 Estimation of abortion and case submission rates

Figure 6.13 illustrates the output distribution of the within-flock abortion incidence risk, which was applied to all regions. The median incidence risk was 1.68% (95% confidence limits 2.32% to 2.41%). The 5^th and 95^th percentiles were 0.13% and 6.95% respectively and the maximum simulated abortion incidence risk was 19.74%.

Descriptive statistics for the actual flock size data (from Agribase) and the simulated flock size distributions for each region are shown in Table 6.8. Median and maximum values for actual and simulated data were closely matched.

The distribution of flock sizes for Southland is shown in Figure 6.14. A truncated lognormal input distribution was used following fitting of actual data in @Risk to find the most appropriate distribution.

The number of abortions per flock was modeled using a binomial distribution and for each iteration of the model the incidence risk (number of abortions per flock divided by flock size) was calculated. Table 6.9 contains the median and maximum number of abortions per flock and output within-flock incidence risk in each region and across New Zealand as a whole. The maximum incidence risk may be high due to the occurrence of abortions in small flocks, i.e. a lifestyle block may have had one ewe that aborted, giving an incidence risk of 100%. The distribution of the incidence risk of abortions in

Table 6.8: Comparison of descriptive statistics for actual and simulated flock size distributions for each region and across New Zealand as a whole. The minimum flock size was one ewe in all regions.

	Input flock size values		Output distribution values	
Surveillance zone	Median	Maximum	Median	Maximum
Auckland	20	45,000	25	43,778
Waikato	35	27,000	35	26,852
Hawkes Bay	785	50,000	781	49,857
Wellington	120	31,000	122	30,922
Canterbury	272	15,000	278	14,979
West Coast	30	5500	31	5494
Southland	700	53,000	709	52,795
New Zealand	120	53,000	124	47,868

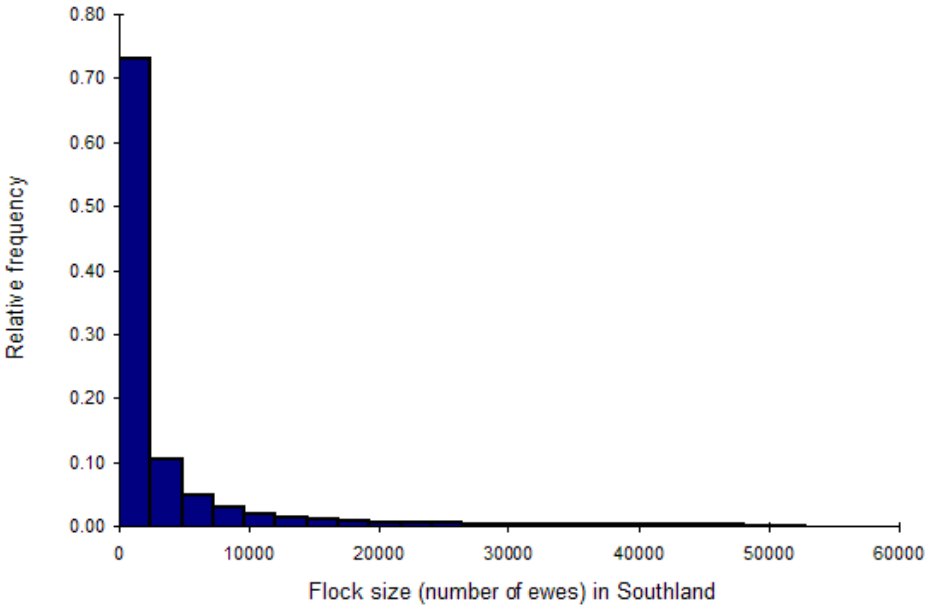

Figure 6.14: Histogram of simulated flock sizes for Southland. A lognormal distribution was fitted to 2003 Agribase flock size data for each region. The median flock size was 709 ewes.

Table 6.9: Number of abortions and within-flock incidence risk of abortion in each region and across New Zealand as a whole

	Number of abortions		Within-flock incidence risk	
Surveillance zone	Median	Maximum	Median	Maximum
Auckland	0	596	0.00%	100%
Waikato	0	1967	0.00%	100%
Hawkes Bay	11	4135	1.52%	50%
Wellington	2	3120	1.00%	100%
Canterbury	4	1375	1.37%	50%
West Coast	0	290	0.00%	100%
Southland	10	3684	1.49%	50%
New Zealand	2	3689	1.28%	100%

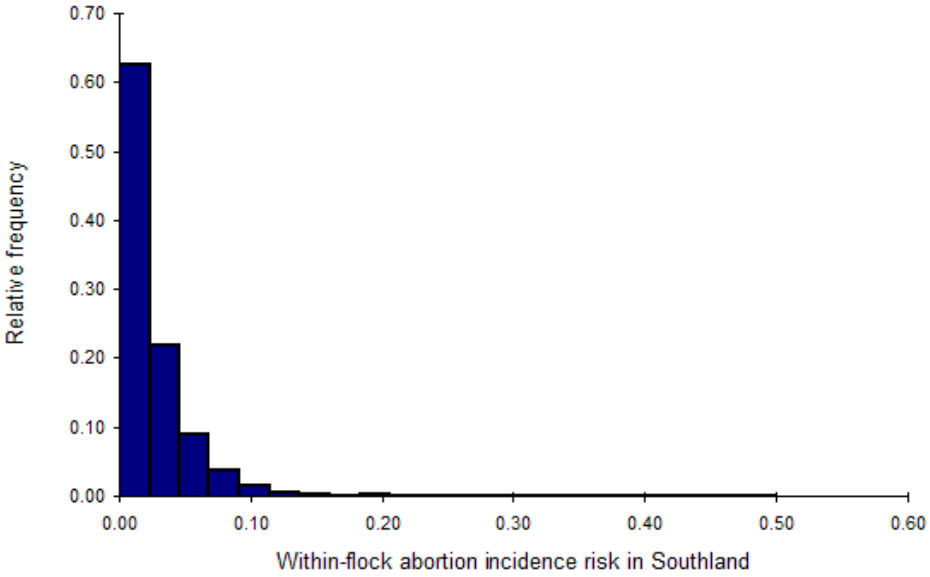

Figure 6.15: Simulated incidence risk of abortions in Southland flocks. The median incidence risk was 1.49% and the 95% confidence limits were 2.29% to 2.39%.

Southland flocks is shown in Figure 6.15.

After 10,000 iterations the number of flocks in each area for which the simulated incidence risk was greater than 5% were counted (Table 6.10). The total value was simulated for the whole of New Zealand and is not the sum of the estimations for the individual regions. All variables in the model converged to less than 4% variation after the 10,000 iterations.

Table 6.10: Number of flocks with estimated abortion incidence risk greater than the cutoff value of 5%

Surveillance zone	Number of flocks with incidence risk >5%
Auckland	484
Waikato	600
Hawkes Bay	343
Wellington	1025
Canterbury	839
West Coast	175
Southland	894
Total	4360

Table 6.11: Number of flocks to be tested to detect disease at varying design prevalences with $\alpha = 0.05$

	p	0.01	0.02	0.03	0.04	0.05	0.08	0.1
Surveillance zone	N							
Auckland	3195	285	145	97	73	58	36	28
Waikato	4323	288	146	97	73	58	36	28
Hawkes Bay	2642	282	144	97	72	58	36	28
Wellington	7193	292	147	98	73	58	36	28
Canterbury	6000	291	146	98	73	58	36	28
West Coast	1253	265	140	95	71	57	35	28
Southland	6220	291	147	98	73	58	36	28
Total	30,826	297	148	98	73	58	36	28

6.4.5 Number of cases to test to detect disease

Table 6.11 shows the number of flocks to be tested to detect disease at $\alpha = 0.05$ and varying design prevalences. The population (N) is the number of flocks in each surveillance area, as one case is assumed to be one outbreak in a flock and it is expected that few flocks would have more than one outbreak per lambing season. The design prevalence in this instance is therefore the between-flock prevalence. It would of course be desirable to detect exotic diseases as quickly as possible and while flock prevalence remains low, although this requires a greater testing effort.

Table 6.12 shows the maximum number of infected flocks in the population given that all samples evaluated for exotic diseases in 2003 were negative. There are very high possible flock prevalences for West Coast (78%) and Auckland (39%). Using the estimated number of flocks with an abortion rate of greater than 5% from the simulation process, between 27% and 29% of problem flocks need to be tested before calculations show 95% confidence that there are no diseased flocks in the population.

Table 6.12: Maximum number of infected flocks given all surveillance cases were considered negative for exotic disease

Surveillance zone	N (number of flocks)	n (number of surveillance cases)	D (maximum number of diseased flocks)	Prevalence
Auckland	3195	6	1255	39.30%
Waikato	4323	29	423	9.80%
Hawkes Bay	2642	41	185	7.00%
Wellington	7193	48	434	6.00%
Canterbury	6000	70	250	4.20%
West Coast	1253	2	972	77.60%
Southland	6220	150	122	2.00%
Total	30,826	346	264	0.90%

6.4.6 Surveillance system design

Figure 6.16 to Figure 6.19 illustrate the use of a GIS in conjunction with animal population and laboratory data (from 2002) to cover both spatial and temporal aspects. Vector-borne diseases are particularly likely to be affected by climatic conditions and in each of the four figures red shading is used to highlight parts of the lower North Island where conditions would allow this type of disease to spread through the sheep population. For each month illustrated the conditions to be met were sheep density of greater than 50 sheep/km^2, minimum temperature of 10^0C and monthly rainfall over 50mm, which would be suitable for the survival and replication of some species of mosquito or culicids. January, April, July and October are shown as representing the four seasons, with each figure also showing the incursion zones in the lower North Island. Because the geographical information supplied with the laboratory data was not detailed enough to allow accurate plotting, the cases within each district were allocated to representative towns or cities that were kept constant for each of the four figures. Centres without any abortion cases are shown with triangles while those that have cases are represented by circles which increase in size as the number of submissions increases.

Figure 6.16 shows the situation in January. Large areas of the lower North Island meet the stock and climatic conditions that would allow vector survival. However, for the first quarter of 2002 there were no submissions of abortion cases to laboratories from these areas. Any surveillance required to be carried out at this time would need to be by an alternative method, for example serology, and may therefore encompass non-breeding animals.

In Figure 6.17 it can be seen that in April there are only coastal areas that meet the required conditions and there are small numbers of abortion case submissions. The highest number of abortions occur in the spring quarter (Figure 6.18) but the conditions in July are not suitable for vectors. In October (Figure 6.19) abortion cases are still being submitted but there is only a very small area where environmental conditions are

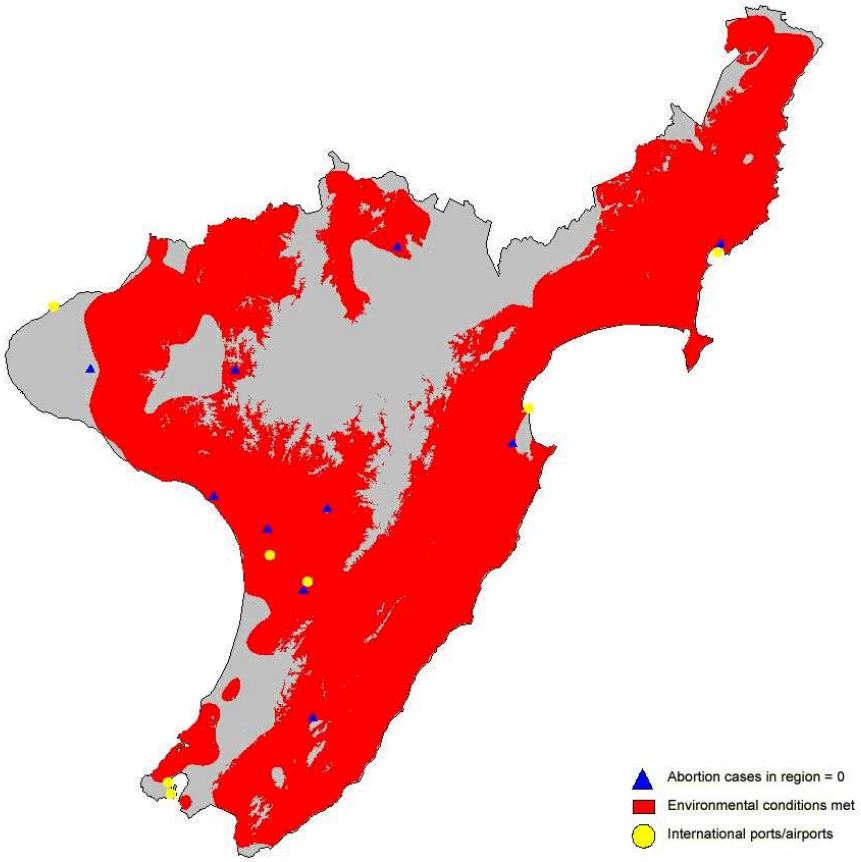

Figure 6.16: Areas where disease conditions were met (red shading) in January and number of abortion case submissions for the summer quarter.

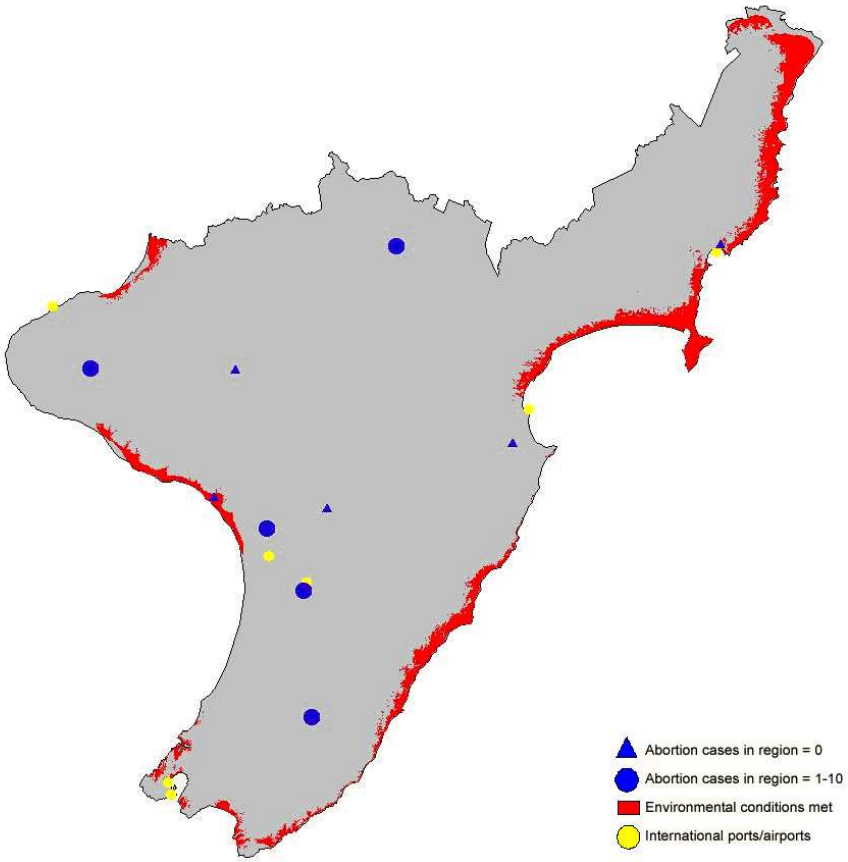

Figure 6.17: Areas where disease conditions were met (red shading) in April and number of abortion case submissions for the autumn quarter.

met (Mahia peninsula; shading is not obvious in the figure due to the small area size).

6.4.7 Incursion zone surveillance

Use of a risk-based surveillance system is illustrated using a hypothetical example of an incursion of bluetongue vector *Culicoides* at Whangarei port. *Culicoides* are active (i.e. capable of oviposition, feeding and flight) within a temperature range of 10^0C to 35^0C and able to adapt to a range of moisture conditions (Walton and Osburn 1992). Whangarei Port received 5,444,743 tonnes of international cargo in the year ending June 2003 (this represents 33.8% of international cargo unloaded at New Zealand ports in that year) in 673 vessel arrivals (Statistics New Zealand). This region has summer

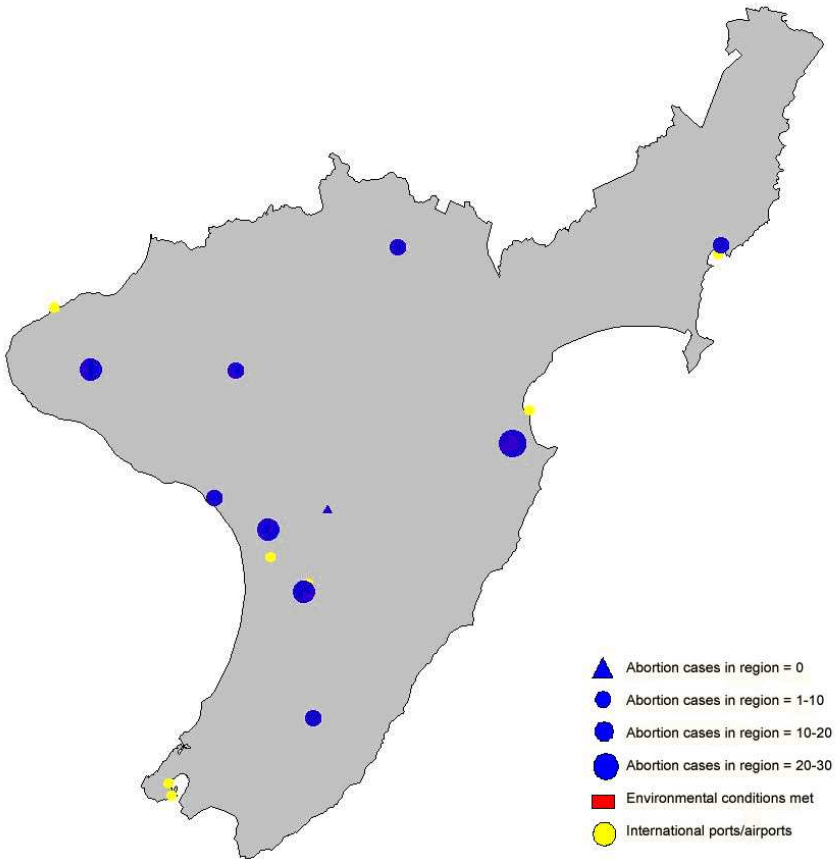

Figure 6.18: Areas where disease conditions were met (red shading) in July and number of abortion case submissions for the spring quarter.

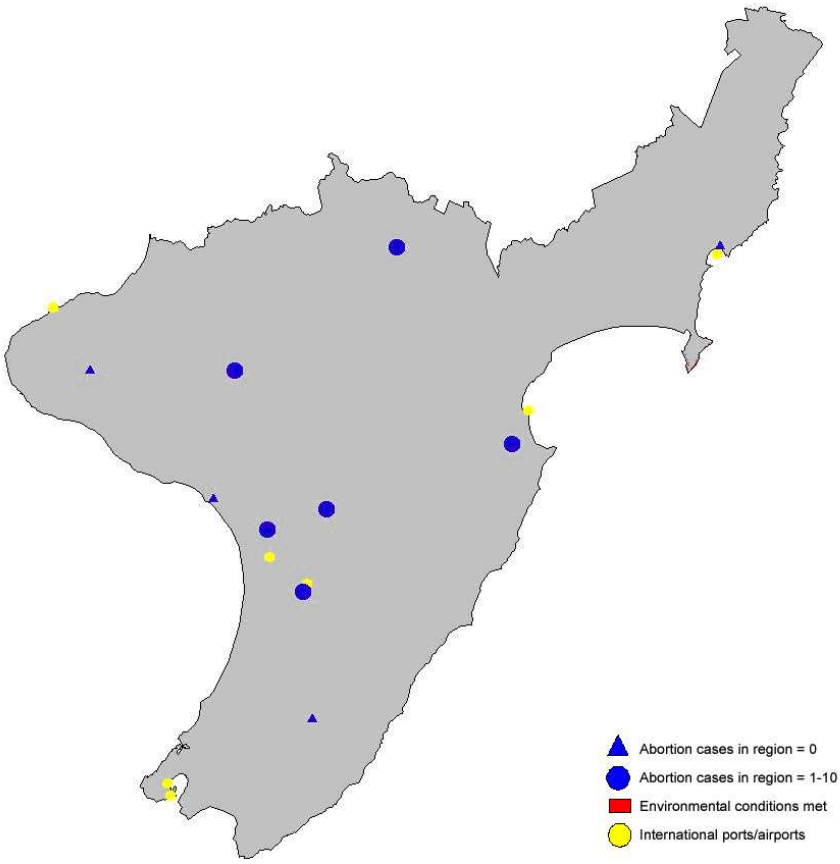

Figure 6.19: Areas where disease conditions were met (red shading) in October and number of abortion case submissions for the summer quarter.

maximum air temperatures ranging from 22^0C to 26^0C, very occasionally exceeding 30^0C, and winter maximum temperatures ranging from 12^0C to 17^0C. Conditions would therefore be suitable for *Culicoides* survival and replication for much of the year.

Using a geographic information system it can be determined that there are 27 properties grazing sheep or goats within a five kilometre radius of Whangarei Port (five kilometres being considered the maximum unassisted vector flight range), with a total of around 500 breeding ewes and a small number of goats at risk. The stock density of breeding ewes in this incursion zone is 6.9/km^2 and total stock density of 11.9 animals/km^2. Abortions occurring in this population would thus be a potential primary target for testing, although serology would be an alternative outside of the traditional months during which ewes are pregnant. The number of individual animals to test solely within the incursion zone would be 55, with $\alpha = 0.05$ and a design prevalence of 0.05. On a flock basis, 24 of the 27 flocks would need to be tested.

6.5 Discussion

A target for the number of ovine and caprine abortion surveillance cases to be tested annually has previously been set according to the number of cases processed by laboratories in 1999. This does not provide a scientific basis for the number of tests that are required to be carried out in order to either detect disease or attest freedom from disease, and is one of the reasons for the current study. Stratification by region is desirable to allow for differences in management practices and climatic factors that result in variation of risk of disease occurrence and submission of abortion cases.

Agribase is a comprehensive database of domestic animal populations in New Zealand. It is continually updated and because of this, reported stock numbers may fluctuate widely throughout the year. It can be difficult to get updates on a regular basis from all farmers and some records are outdated (R. Sanson, pers. comm.). Lifestyle blocks are considered to be under-represented due to the challenge of locating the increasing number of newly subdivided properties in recent years. In the event of disease incursion the latest data would be used to calculate testing requirements and locate flocks of interest, but work would be required to ensure all properties were identified and included in the sampling frame. Compulsory registration and regular updating of information would be very beneficial for use in all types of disease outbreaks.

Following discussion with laboratory staff it has been assumed in this study that one outbreak of abortion results in one case submission to the laboratory, although samples from multiple animals may be included (commonly five to six animals). The number of multiple outbreaks in the same flock in one year are not identifiable in the provided datasets, but this is expected to be an unusual occurrence. Detection of exotic causes of abortion relies on a chain of observations from farmers, veterinarians and laboratory

staff followed by appropriate testing. Once a case arrives at the laboratory it is defined as a surveillance case if the previously stated description is met. Exotic diseases are then ruled out on the basis of clinical or epidemiological history, pathology or testing. For a disease such as leptospirosis the situation is complicated by the presence of some abortion-causing serovars in New Zealand. The testing procedure may diagnose these but exotic serovars could potentially be overlooked unless specific reagents were used, which are not routinely held in all laboratories. The reasons for the large number of cases (309; 47% of 2003 submissions) unable to be considered as surveillance cases is unknown but should be considered so that efforts to increase the quality of submissions can be made. This would allow an increased sample size to be obtained from within current submissions, with a resulting increase in likelihood of detecting exotic diseases if present and higher confidence in declaring freedom from disease. Surveillance cases also have a lower proportion of undiagnosed cases (12% in 2002-2003) than do non-surveillance cases (50% in 2002-2003).

Abortions in New Zealand flocks result in large numbers of lamb losses annually. However there have been few studies on within- and between-flock abortion rates, which makes estimating the appropriate parameters challenging. Abortion must firstly be defined so as to distinguish these losses from embryonic, intra-parturient and postnatal deaths. Quinlivan and Jopp (1982) recorded a range of 0-16% incidence of abortion between properties in Hawkes Bay, which had various flock sizes, age structures and winter management systems. It was shown that a significantly higher rate of abortion is seen in smaller flocks, which may reflect the comparative ease of observing and recording such losses on smaller and more intensively managed farms. However, calculating the mean flock size on a regional basis and finding the number of submissions per 100 ewes in the average flock for each area with the current data shows that Canterbury and Southland have higher submission rates than do regions with a small average flock size. This is of course generalising information across large areas but does not shed any light on the reasons for higher submissions from the South Island.

The number of animals sick and at-risk of abortion for each case was provided as part of the 2002 laboratory data, but was of little use due to the very small number of records (5 of 793 cases) containing this information. The prevalences in each of these flocks were 2%, 3%, 5%, 8% and 18%. Improved case history on submission forms would provide useful information which should be stored and incorporated into the surveillance system. Over time such information would improve knowledge of the usual patterns of disease effects and provide a baseline for identification of abnormal trends.

In the @Risk simulation model, outputs appeared plausible for within-flock incidence, flock size and the number of abortions per flock in each region. The cutoff value for 'problem' flocks was chosen from Binns' (2002) British study. Farm management

systems are very different in the United Kingdom to those in New Zealand, however it was thought that an abortion incidence of 5% or over would be noticed as above 'normal' by the farmer, and a veterinary investigation initiated. The results of the simulation showed that on average 14.6% of flocks in each region had an incidence risk higher than the cutoff value. In all regions the number of 'problem' flocks was considerably higher than the number of laboratory submissions made from that region in 2003. Of course it is also likely that there would be some submissions from flocks with an abortion rate below cutoff, as for example the number of abortions may be more noticeable in smaller flocks and be of relatively greater economic significance to the farmer yet still be less than 5%. There may also be an inclination to investigate when abortion is occurring in a flock of any size at a level that is estimated to be higher than that of previous years, but still below 5%. Studies on two groups of sentinel farms (30 and 66 farms) in New Zealand have shown that veterinarians were used in 28% and 37% of abortion cases, with laboratory submissions made in 16% of cases in the first group and 100% in the second group (which consisted entirely of government-owned Landcorp farms) (H. Black, personal communication).

On a between-flock basis the number of flocks to be tested to detect disease when the minimum expected prevalence is 2% is between 140 and 147 ($\alpha = 0.05$) (Table 6.13). At 5% prevalence the required number of flocks is 58 in most surveillance zones. Comparing this to the number of cases submitted, it can be seen that in 2003 the required number of cases were submitted in Wellington, Canterbury and Southland areas (Table 6.13). However not all of these cases were able to be evaluated for exotic diseases, and only in Canterbury and Southland were enough surveillance cases assessed to show that flock prevalence was not greater than 5%; Southland could also demonstrate a flock prevalence of less than 2%. This is illustrated in Figure 6.20, where the number of surveillance cases submitted from each region is expressed as a percentage of those required to detect disease at 5% and 2% prevalence levels. A total of 405 surveillance cases would be required to show that between-flock prevalence was less than 5% ($\alpha = 0.05$) if testing was carried out separately in each surveillance region; 1014 flock tests would be necessary at 2% prevalence. Across the 30,826 flocks in the whole of New Zealand, 148 flocks would need to be tested for 2% prevalence. With the current level of testing on a national basis the maximum number of infected flocks would be 264 (0.9%). Each exotic disease would need to be considered on an individual basis and the number of cases ruling out this disease counted to enable an accurate declaration of status. Test sensitivity should also be taken into account, with the definition of test in this case including clinical and epidemiological history along with pathology and laboratory test results.

Lack of abortion incidents (and therefore case submissions) at times and in areas of

Table 6.13: Number of flocks required to be tested to detect disease at 2% and 5% flock prevalence with $\alpha = 0.05$, compared to actual number of submissions and surveillance cases in 2003

Surveillance zone	Number of flocks[a]	Number to test at 2% flock prevalence	Number to test at 5% flock prevalence	Number of cases submitted	Number of surveillance cases
Auckland	3195	145	58	14	6
Waikato	4323	146	58	30	29
Hawkes Bay	2642	144	58	51	41
Wellington	7193	147	58	66	48
Canterbury	6000	146	58	188	70
West Coast	1253	140	57	4	2
Southland	6220	147	58	300	150
New Zealand[b]	30,826	148	58	653	346

[a] Number of flocks of breeding ewes.
[b] Number of flocks to test and number of cases submitted across the whole of New Zealand.

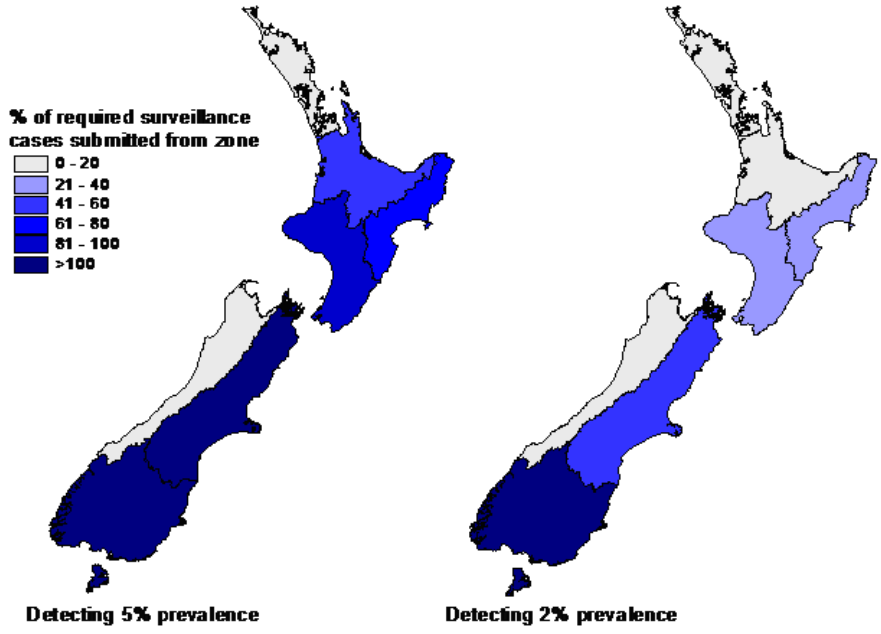

Figure 6.20: The number of cases submitted from each surveillance zone in 2003 expressed as a percentage of the number of cases required to detect disease prevalence at 5% and 2% levels.

high risk for vector-borne disease incursion highlight the need for alternative methods of diagnosis (such as serology) to be included in a surveillance system for exotic diseases causing abortion. If a vector incursion was known to have happened, the environmental requirements of the vector should indicate the appropriate geographical areas to investigate at the time of (and subsequent to) the incursion, then the population at risk would be targeted for testing using the most appropriate procedures. Following an incursion of disease or disease vectors consideration should be given to other factors such as stock movements and patterns of tourist activity throughout the country. Such information could be added to that illustrated above in a GIS so that surveillance can be carried out in all risk areas. The rule-based approach to evaluating data variables that influence the risk of disease occurrence is a straightforward one, and could easily be developed to encompass a greater level of complexity. Performing similar evaluations for each of the surveillance zones and including representation of incursion zones would give a comprehensive coverage of New Zealand. Tests that had already been performed could be also be included as a layer of the risk landscape, with recent tests receiving a higher weighting than older ones. It would be necessary to obtain accurate and higher quality epidemiological and demographic data than is currently acquired, in order to maximise the potential of this method.

Within the larger study of which this report forms part, work is being undertaken to design a suitable framework for surveillance systems that meet specific objectives, for example minimising the cost of demonstrating freedom from a number of diseases, and optimal scheduling of a fixed number of surveillance tests. The framework developed is likely to make use of both statistical and computer modeling methods to demonstrate optimal solutions to various surveillance needs.

6.6 Conclusions

The analysis evaluated current laboratory submissions as an information source for the surveillance of exotic pathogens causing abortions in ewes. While sufficient samples were obtained from some areas, a higher submission rate from other parts of New Zealand would be desirable. Surveillance on a regional basis would be possible providing these additional cases could be obtained. There are a number of gaps in our knowledge of abortion incidence and laboratory submission behaviour that could be remedied by further studies. A risk-based surveillance system would enable greater efficiency in disease detection ability, as illustrated using a vector-borne disease example.

Acknowledgements

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Appendix 1: Risk-based surveillance for causes of ovine and caprine abortion exotic to New Zealand

Table 6.14: Seaports: total number of animals to test to detect disease at a range of design prevalences in each incursion zone when $\alpha = 0.05$. N = number of stock (sheep and goats of all classes) in each zone.

	p	0.01	0.02	0.03	0.04	0.05	0.06	0.08	0.1	0.12
Incursion Zone	N									
Auckland	0	0	0	0	0	0	0	0	0	0
Bluff	4224	288	146	97	73	58	48	36	28	23
Devonport	0	0	0	0	0	0	0	0	0	0
Dunedin	4630	289	146	97	73	58	48	36	28	23
Gisborne	8460	293	147	98	73	58	48	36	28	23
Lyttelton	18,759	296	148	98	73	58	48	36	28	23
Marsden Point	50	50	48	43	38	34	31	26	22	19
Napier	11,272	294	147	98	73	58	48	36	28	23
Onehunga	604	235	131	91	69	56	47	35	28	23
Port Chalmers	30,296	297	148	98	73	58	48	36	28	23
Port Nelson	552	230	130	90	69	55	46	35	28	23
Taranaki	1081	260	139	94	71	57	47	35	28	23
Tauranga	0	0	0	0	0	0	0	0	0	0
Timaru	9497	293	147	98	73	58	48	36	28	23
Wellington	4445	288	146	97	73	58	48	36	28	23
Whangarei	930	255	137	93	71	57	47	35	28	23
All incursion zones	97,050	298	148	98	73	58	48	36	28	23

Table 6.15: Airports: total number of stock to test to detect disease at a range of design prevalences in each incursion zone when $\alpha = 0.05$. N = number of stock (sheep and goats of all classes) in each zone

	p	0.01	0.02	0.03	0.04	0.05	0.06	0.08	0.1	0.12
Incursion zone	N									
Auckland International	29	29	29	28	27	25	24	21	18	16
Christchurch International	24,540	296	148	98	73	58	48	36	28	23
Dunedin	45,169	297	148	98	73	58	48	36	28	23
Hamilton	12,464	295	147	98	73	58	48	36	28	23
Ohakea	40,937	297	148	98	73	58	48	36	28	23
Palmerston North	12,233	294	147	98	73	58	48	36	28	23
Queenstown	18,133	296	148	98	73	58	48	36	28	23
Wellington	7780	292	147	98	73	58	48	36	28	23
Whenuapai	2314	280	144	96	72	58	48	36	28	23
All incursion zones	163,599	298	148	98	73	58	48	36	28	23

Chapter 7

Application of portfolio theory to risk-based allocation of surveillance resources in animal populations

7.1 Abstract

Distribution of finite levels of resources between multiple competing tasks can be a challenging problem. Resources need to be distributed across time periods and geographic locations to increase the probability of detection of a disease incursion or significant change in disease pattern. Efforts should focus primarily on areas and populations where risk factors for a given disease reach relatively high levels. In order to target resources into these areas, the overall risk level can be evaluated periodically across locations to create a dynamic national risk landscape. Methods are described to integrate the levels of various risk factors into an overall risk score for each area, to account for the certainty or variability around those measures and then to allocate surveillance resources across this risk landscape. In addition to targeting resources into high risk areas, surveillance continues in lower risk areas where there is a small yet positive chance of disease occurrence. In this paper we describe the application of portfolio theory concepts, routinely used in finance, to design surveillance portfolios for a series of examples. The appropriate level of resource investment is chosen for each disease or geographical area and time period given the degree of disease risk and uncertainty present.

Prattley, D., Morris, R.S., Stevenson, M.A. and Thornton, R. 2007. Application of portfolio theory to risk-based allocation of surveillance resources in animal populations. Preventive Veterinary Medicine 81 56-59.

7.2 Introduction

'... it is the part of wise men to preserve themselves to-day for to-morrow, and not risk all in one day ...'

Miguel de Cervantes(1605) in Don Quixote, translated by John Ormsby, London 1885.

Modern portfolio theory embraces concepts that have long been familiar to society, with people often warned against putting all their eggs in one basket. For decades prior to formalisation of the underlying theory, financial institutions also applied this principle by diversifying investments into multiple assets for their clients. However, it was the groundbreaking work of Markowitz (1952) and Roy (1952) that defined portfolio theory, developed portfolio selection and assessment methods, and determined the effects of investing in assets with correlated risks.

A portfolio of assets can be simply described as a collection of items owned by an individual or group. Such items may include tangible objects, for example a house or car, or less palpable assets such as financial investments or shares. There may be very practical reasons for investing in certain assets, such as property, but if the decision has been made to invest in financial markets the investor is faced with choosing between many possible combinations of assets (alternative portfolios), with differing levels of expected return and likelihood of obtaining that return. Portfolio theory was thus developed as an aid to the process of decision-making under risky circumstances, to help simplify the selection of assets for inclusion in a portfolio that is acceptable to the investor.

Both Markowitz (1952) and Roy (1952) undertook portfolio selection by considering the expected return and the variance of the expected return on a portfolio. Markowitz's mean-variance model can be developed from Roy's safety first method (Elton et al. 2003). One of the main differences between the two analyses was the recommendation of a particular portfolio by Roy, compared to the construction of an 'efficient frontier', a set of efficient portfolios defined by Markowitz (1999).

Surveillance resources may take the form of, for example, a monetary budget, an available number of laboratory tests or an available number of human-resource hours to carry out inspections. The need to vary the amount of resource invested in each subset of the population arises because the level of risk of disease incursion and subsequent establishment (hereafter referred to as 'disease risk' for simplicity) varies both spatially by region, as well as temporally within regions. In order to increase the probability of detecting disease should it occur, logic dictates the direction of more resources towards the areas at greatest risk and fewer resources to regions where disease is less likely to occur. Furthermore, consideration is given to the amount of uncertainty surrounding the identified level of disease risk.

This paper describes three examples of application of the safety first model and mean-variance portfolio theory to the allocation of a fixed amount of resource to different surveillance scenarios. Firstly, the safety first model is used to allocate resources proportionately between exotic diseases that have been evaluated for risk of occurring in New Zealand, using semi-quantitative risk assessment. Secondly, safety first is used in a two-stage approach to illustrate distribution of a fixed annual number of laboratory tests, with a requirement to allocate tests by month and region for detection of exotic causes of abortion in sheep flocks in New Zealand. Finally, the single index model (a technique used to simplify the inputs and application of mean-variance theory) is used to provide a conceptual comparison with safety first, using the same dataset as the previous example.

7.3 Methods

7.3.1 Characteristics of a portfolio - expected return and standard deviation of return

It is assumed that all available resources should be utilised, and that the portfolio should consist of more than one asset. The expected return on a portfolio is a weighted average of the returns expected on the individual assets (Elton et al. 2003):

$$R_P = \sum_{i=1}^{N} X_i R_i \tag{7.1}$$

where:

R_P = expected return on the portfolio

X_i = the amount of each asset i held. $\sum X_i$ is fixed, equal to the total amount of resource available.

R_i = the expected return from each asset i.

The standard deviation of the return on a portfolio (a measure of the risk of a portfolio) is equal to (Elton et al. 2003):

$$\sigma_P = \left[\sum_{i=1}^{N} (X_i^2 \sigma_i^2) + \sum_{i=1}^{N} \sum_{\substack{j=1 \\ j \neq i}}^{N} (X_i X_j \sigma_i \sigma_j \rho_{ij}) \right]^{1/2} \tag{7.2}$$

where:

X_i = the amount of each asset i held

σ_i = the standard deviation of the return on asset i

ρ_{ij} = correlation coefficient on returns between assets i and j.

The second term in this equation can be removed when returns from all assets are independent, i.e. there is no covariance between assets. The standard deviation is then

equal to:

$$\sigma_P = \left[\sum_{i=1}^{N}(X_i^2\sigma_i^2)\right]^{1/2} \tag{7.3}$$

In selection of financial portfolios, investors tend to be risk-averse and prefer a higher to a lower return. That is, investing in an asset with high return and high risk would be less desirable than selecting an asset that had an equal or higher return but lower risk. One strength of the portfolio approach appears when it is considered that investment in a combination of assets can reduce the overall risk of the portfolio compared to the risk of the individual assets. The subset of all possible portfolios which meet the investor's return and risk criteria is known as the efficient frontier, which can be visualised by plotting the return against the standard deviation (risk).

7.3.2 Portfolio allocation

7.3.2.1 The safety first model

In financial calculations using a constant correlation model (a model which assumes that the correlation between all pairs of assets is the same), the excess return is measured against the return on a riskless asset (Elton et al. 2003), which may for example be an investment in government bonds. Roy's (1952) safety first model used a critical value, or cutoff level, in place of the riskless return, with individual assets allocated points according to:

$$pts = \frac{(R_i - C)}{\sigma_i} \tag{7.4}$$

where C is the chosen cutoff value. The critical value is the value below which the return should not fall. The amount of each asset to be held is found by determining the proportion of the sum of the points that were contributed by each asset. The optimal portfolio minimises the probability of receiving a return below the specified cutoff.

7.3.2.2 The single index model

The single index model (SIM) was developed to simplify the input data and calculations required to implement mean-variance portfolio theory. If assets are correlated, a correlation coefficient must be estimated for each pair of assets under consideration, which can result in very large numbers of estimations being required. To avoid this, the SIM assumes that co-movement between assets is due to common movement with the market rather than any direct relationship between the assets themselves. The value of β is used to measure the amount of change in the return of an asset given the change in return of the overall market, and can be estimated using values of return on assets and return on the market over multiple time periods (Elton et al. 2003):

$$\beta_i = \frac{\sum_{t=1}^{n}[(R_{it} - \bar{R}_{it})(R_{mt} - \bar{R}_{mt})]^2}{\sum_{t=1}^{n}(R_{mt} - \bar{R}_{mt})} \tag{7.5}$$

where, for time periods 1 to n:
β_i = the value of beta for asset i
R_{it} = the return on asset i at time t
R_{mt} = the return on the market at time t.

The 'excess return' is the difference between the expected return of an asset and the return on a riskless asset. Assets are ranked from highest to lowest according to the ratio of excess return to β. Inclusion of assets in the portfolio is determined by a cutoff level (C^*), so that all assets with an excess return to β ratio above cutoff are selected. To determine C^*, a series of potential cutoff levels are calculated (C_i) by including increasing numbers of the assets (in the ranked order) in the potential portfolio (Elton et al. 2003):

$$C_i = \frac{\sigma_m^2 \sum_{j=1}^{i} \frac{(\bar{R}_j - R_F)\beta_j}{\sigma_{ej}^2}}{1 + \sigma_m^2 \sum_{j=1}^{i} \left(\frac{\beta_j^2}{\sigma_{ej}^2} \right)} \tag{7.6}$$

where:
C_i = the potential cutoff level
σ_m^2 = the variance of the return on the market
$\bar{R}_j$ = the expected return on asset j
R_F = the return on a riskless asset
σ_{ej}^2 = the variance of the random element of the return on asset j. The return on the asset has two components, one part being dependent on the market and one part being independent of the market. The independent component can then be subdivided into an expected value and a random element. σ_{ej}^2 is the variance of this random part, also termed the unsystematic risk.

The first C_i is calculated including only the highest ranked asset, then a second C_i is calculated including the first and second ranked assets, and so on. C_i is equal to C^* when all of the assets included in calculating C_i have an excess return to β that is greater than C_i. The proportion of each asset (X_i) to include in the portfolio is found by:

$$X_i = \frac{Z_i}{\sum_{included} Z_j} \text{where } Z_i = \frac{\beta_i}{\sigma_{ei}^2} \left(\frac{\bar{R}_i - R_F}{\beta_i} - C^* \right) \tag{7.7}$$

7.3.3 The surveillance portfolio

7.3.3.1 Safety first: allocating surveillance resources between multiple exotic diseases

A semi-quantitative risk assessment was carried out by the Ministry of Agriculture and Forestry in 1994, including 51 diseases exotic to New Zealand. Each disease was scored on a scale of one to three (1 = low, 3 = high) for each of seven variables: risk of disease entering New Zealand, risk of disease establishing, likely time to detection (1 =

weeks, 2 = months, 3 = years), morbidity, mortality, cost to production and likelihood of eradication (dichotomous variable, 1 = possible, 3 = impossible). In this example equal weighting was given to all seven parameters. The challenge was to distribute a fixed amount of surveillance resource between the diseases.

Financial assets have the attributes of an expected level of return at the end of a chosen time period, and a measure of uncertainty (standard deviation) around that return. To apply the portfolio theory concept in this example, each disease was viewed as an asset into which resources would be invested. The median risk score of the seven risk variables was conceptually equated to a measure of return and the semi-interquartile range used as a measure of variability. A cutoff value of one was chosen, so that diseases with a median risk score of one were not included in the portfolio. In this example not all diseases were required to be allocated resources, although it is recognised that in reality it may be desirable to do so and adding a minimum level of investment for each disease could be simply done.

7.3.3.2 Safety first: regional and temporal allocation of laboratory tests for exotic causes of ovine abortion

In the following example, allocation of a fixed amount of surveillance resource was required on a temporal and regional basis according to the disease risk in each region. Therefore each time period and geographical region (referred to as a surveillance area, SA) was regarded as an entity in which it was possible to invest resources, i.e. each SA could be regarded as an asset. Each time period (month) within the year was allocated an expected maximum score for disease risk, with an associated degree of uncertainty around that risk score, and each SA was allocated an expected maximum score and level of uncertainty for the disease risk for a coming time period. Semi-quantitative risk assessment is an appropriate method of determining the required risk score values.

Two or more SA's may have a similar mean risk score but very different levels of uncertainty around the risk score. Rather than invest more resources in areas of less uncertainty around the level of disease risk (as is the norm with the equivalent process in the financial world), it may be more appropriate within the surveillance context to increase the direction of surveillance resources towards areas where the risk level is less certain. Thus, Equation 7.8 may be used:

$$pts = (R_i - C)\sigma_i \tag{7.8}$$

The requirement was for regional allocation of laboratory tests for exotic arboviral causes of abortion in ewe flocks in New Zealand. A complete set of risk factors is not described as it is considered that these would be identified and evaluated using risk analysis procedures. However, a simple rule-based evaluation of four potential risk factors (minimum monthly temperature, average monthly rainfall, number of international

vessel arrivals at sea/air ports and flock density) was used as a basis for simulating risk scores for each SA (@Risk, Palisade Corporation, 2004). It was assumed that the risk scores were independent. Although there may be very low risk of disease in some areas at particular times of the year, zero risk cannot be guaranteed. Therefore all SAs were required to be included in the surveillance testing portfolio. This was effected by adding a constraint so that one point was awarded if the points calculated for a SA would otherwise be less than one. The cutoff value C was chosen as a critical risk score below which minimal investment of resources in a SA was desired (if no lower constraint was added, there may be regions to which no resources were allocated).

A two-tier approach was used to accommodate both temporal and regional fluctuations in the risk score. Risk scores for each region were simulated for each month using random number generation, with multipliers to introduce seasonality. The total risk score and standard deviation of the total risk score were calculated for the whole country using Equations 7.1 and 7.3. This was, in effect, calculating the return and risk on the portfolio of SA risk scores. The total number of surveillance tests to be carried out each month was then allocated according to the risk score and associated uncertainty for the whole country for that month using Equation 7.8. The number of tests allotted to each month was distributed regionally according to the expected maximum risk score and associated uncertainty for each SA for that month, also using Equation 7.8.

The results for the example shown use simulated data for seven SAs within New Zealand using monthly time periods. When considering temporal changes in risk score, multipliers were added to the simulation process to produce a seasonal pattern. Critical risk scores C were 6.0 for allocation of resources to each month for New Zealand and 3.0 for each SA by month.

7.3.3.3 SIM: regional allocation of laboratory tests for exotic causes of ovine abortion

The same dataset was used as generated for the previous example. SAs were regarded as assets and were ranked using the ratio of excess return to β. The excess return was calculated using the risk score of the SA in relation to having a SA with a risk score of zero. β was calculated using the simulated temporal risk score data described in the previous example. In finding β, the return on each asset was found by subtracting the risk score for each month from the average risk score across all months for each SA. For the market return values, calculations were carried out on a monthly basis, with the average risk score across all SAs and all months subtracted from the average risk score for all SAs for each month. The excess return to β ratio is equivalent to the ratio of the amount of risk in a SA to the change in risk that occurs in that SA given the

change in risk across the whole country. This process resulted in resource allocation to each of the SAs for the period of the whole year, rather than on a monthly basis.

The calculated cutoff level determines which SAs should be included in the optimal portfolio, which in this example originally included all SAs except Waikato. However, as it was desirable to include all SAs in the portfolio, the cutoff level was manually set at a level below the calculated C^*.

7.3.4 Evaluation of resource allocation methods

The allocation of laboratory tests using both the safety first and SIM models was evaluated by calculating the maximum number of diseased ewe flocks that might remain undetected in the population if all surveillance tests allocated to each region returned negative results. Comparison was made between allocation of tests using portfolio theory and according to the proportion of New Zealand ewe flocks in each SA.

7.4 Results

7.4.1 Safety first: allocating surveillance resources between multiple exotic diseases

Figure 7.1 shows the median risk score and the interquartile range of the risk scores for each of the diseases evaluated. The proportion of resources allocated to each disease is plotted on the secondary y axis. Thirteen diseases were allocated no resources, as they had a median risk score of one. For diseases with equal median scores but different semi-interquartile ranges, more resources were allocated to those diseases with less variation in the risk score.

7.4.2 Safety first: regional and temporal allocation of laboratory tests for exotic causes of ovine abortion

The number of ewe flocks (data obtained from Agribase, Agriquality New Zealand) per SA and the number of laboratory tests required to detect disease in each region with a flock prevalence of 5% and $\alpha = 0.05$ are stated in Table 7.1. A total of 405 tests was required across the whole country. However, this assumes random, representative sampling occurs within each region. The 405 tests were therefore allocated to the different regions using the safety first model.

Table 7.2 shows the generated mean and standard deviation of the risk score for each SA by month. The values for New Zealand for each month were calculated using the equations for finding the expected return (Equation 7.1) and standard deviation of the expected return (Equation 7.3) of a portfolio.

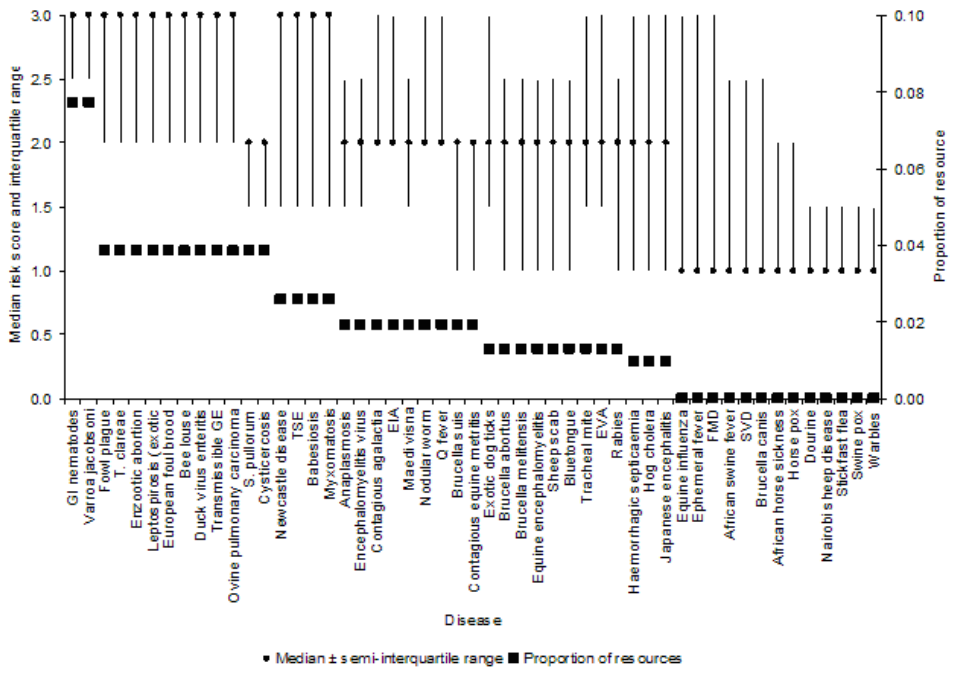

Figure 7.1: Median risk score and interquartile range of risk scores for each disease considered, and the proportion of resources allocated to each disease. Diseases are ordered according to the proportion of resources.

Table 7.1: The number of ewe flocks present in each surveillance area (SA) and the number of surveillance tests required in each SA to detect at least one positive flock when disease prevalence is 5% and $\alpha = 0.05$ (assuming perfect test sensitivity and specificity).

SA	Number of flocks	Number of tests
Auckland	3195	58
Waikato	4323	58
Hawkes Bay	2642	58
Wellington	7193	58
Canterbury	6000	58
West Coast	1253	57
Southland	6220	58
New Zealand total	30,826	405

Table 7.2: The simulated mean (standard deviation) risk score for each surveillance area (SA) by month. This data would ideally be obtained using risk assessment procedures and would be used to allocate resources to each SA over time.

SA	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Auckland	6.0 (1.23)	4.8 (1.22)	4.5 (1.23)	5.1 (1.26)	7.1 (1.25)	4.9 (1.23)	6.7 (1.26)	7.0 (1.20)	9.3 (1.24)	6.2 (1.24)	4.8 (1.24)	7.0 (1.20)
Waikato	4.7 (1.31)	5.3 (1.26)	4.7 (1.26)	7.2 (1.27)	5.7 (1.28)	6.3 (1.30)	7.0 (1.24)	10.7 (1.32)	9.6 (1.27)	5.4 (1.29)	7.8 (1.28)	6.0 (1.27)
Hawkes Bay	6.2 (0.97)	4.7 (0.97)	6.1 (1.00)	3.4 (0.95)	4.2 (0.98)	4.4 (0.97)	6.1 (1.00)	7.6 (0.98)	5.8 (1.00)	3.7 (0.94)	4.0 (0.97)	4.4 (0.98)
Wellington	7.8 (1.17)	5.9 (1.17)	7.6 (1.18)	7.4 (1.17)	6.2 (1.17)	5.8 (1.17)	6.9 (1.16)	7.6 (1.18)	5.1 (1.17)	5.3 (1.16)	4.9 (1.17)	6.2 (1.17)
Canterbury	4.4 (1.26)	6.6 (1.25)	4.7 (1.29)	6.4 (1.25)	4.7 (1.32)	6.8 (1.31)	8.2 (1.28)	9.4 (1.30)	5.8 (1.29)	8.3 (1.30)	4.5 (1.25)	5.1 (1.28)
West Coast	3.4 (0.95)	3.9 (0.96)	5.4 (0.97)	4.4 (0.93)	5.9 (0.97)	4.9 (0.96)	4.3 (0.96)	8.1 (0.96)	4.5 (0.99)	4.7 (0.94)	4.3 (0.97)	6.5 (0.98)
Southland	6.6 (1.30)	8.3 (1.29)	5.6 (1.32)	6.3 (1.26)	7.2 (1.29)	8.3 (1.29)	7.2 (1.30)	10.7 (1.32)	6.9 (1.29)	6.5 (1.27)	8.0 (1.28)	6.1 (1.25)
New Zealand[a]	5.9 (0.46)	6.0 (0.47)	5.6 (0.45)	6.2 (0.47)	6.3 (0.46)	6.5 (0.47)	7.9 (0.46)	13.6 (0.47)	8.3 (0.48)	6.2 (0.47)	5.8 (0.48)	6.2 (0.45)

[a] Values calculated using data shown for all surveillance areas for each month and Equations 7.1 and 7.3

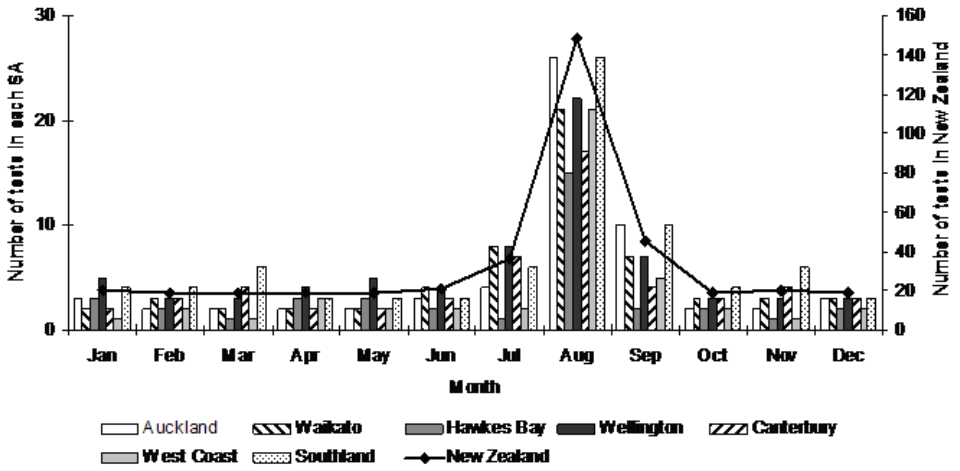

Figure 7.2: Number of surveillance tests to be carried out in each SA by month, and the total number of tests per month across the whole of New Zealand. A total of 405 tests were available for the year.

The number of points per SA were calculated using Equation 7.7. Resources were allocated by finding the number of points held by each SA as a proportion of the total number of points across all SAs.

The number of surveillance tests to be carried out in each SA in each month is shown in Figure 7.2. There is a seasonal peak of testing required in the spring months, coinciding with the increased disease risk at that time. Fifty-seven per cent of resources were used from July to September. During each month resources were allocated according to regional disease risk, with regions at higher risk levels and with greater uncertainty around the risk level receiving more input. Each SA received between 10% and 19% of resources during the year.

7.4.3 SIM: regional allocation of laboratory tests for exotic causes of ovine abortion

The number of laboratory tests allocated to each SA using the SIM method is shown in Figure 7.3. Most resources are expended on the Hawkes Bay region, followed by Southland. Comparison is made to allocation using the safety first model and also using proportional allocation, where tests were allotted to the region in proportion to the number of ewe flocks. The number of tests allocated to Southland is fairly similar for each method, with greater variation between methods shown in other SAs.

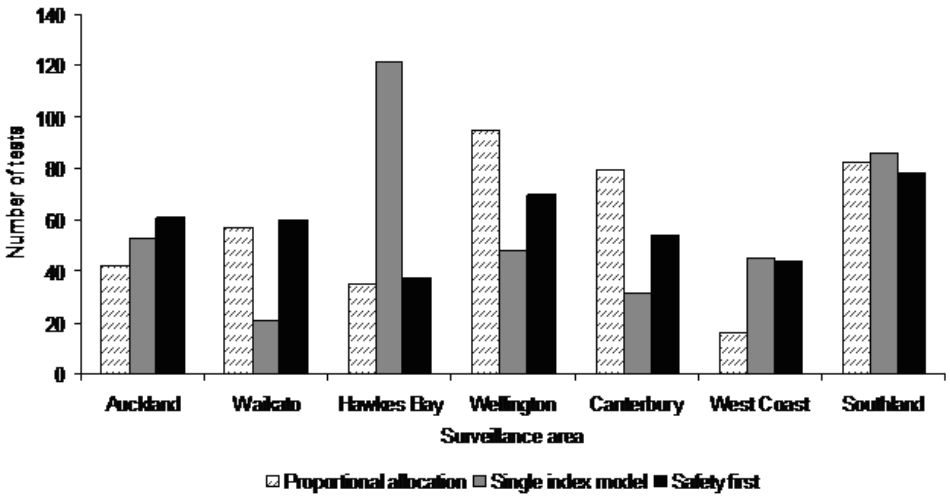

Figure 7.3: The number of tests allocated to each SA using proportional allocation, the single index model and the safety first method.

7.4.4 Evaluation of resource allocation methods

Figure 7.4 shows the maximum flock prevalence for each SA if all surveillance tests carried out during the year were negative ($\alpha = 0.05$). Results are given for allocation using the described SIM and safety first approaches, along with the results of distribution according to the proportion of ewe flocks per region. It can be seen that the maximum prevalence of diseased flocks is more evenly distributed across the SAs using the safety first method, with the highest maximum prevalence occurring in the West Coast region when proportional allocation was used.

7.5 Discussion

When managing complex issues or situations, decision makers need to choose the best course of action from a set of competing alternatives. The portfolio approach simplifies this process to an extent, by quantifying alternatives using two measures - expected outcome and uncertainty (or variability) around that outcome. The examples given were designed to illustrate the concepts of portfolio theory and various elements of the application of this theory to surveillance resource allocation. As pointed out by Galligan and Marsh (1988), inefficient allocation of funds can occur when the risk of returns is not considered. Galligan has given examples of the application of portfolio theory to dairy herd health management (Galligan and Marsh 1988; Galligan et al. 1991) where the economic consequences of various interventions were evaluated. However, as illustrated in this paper, it is possible to develop slightly more abstract applications of

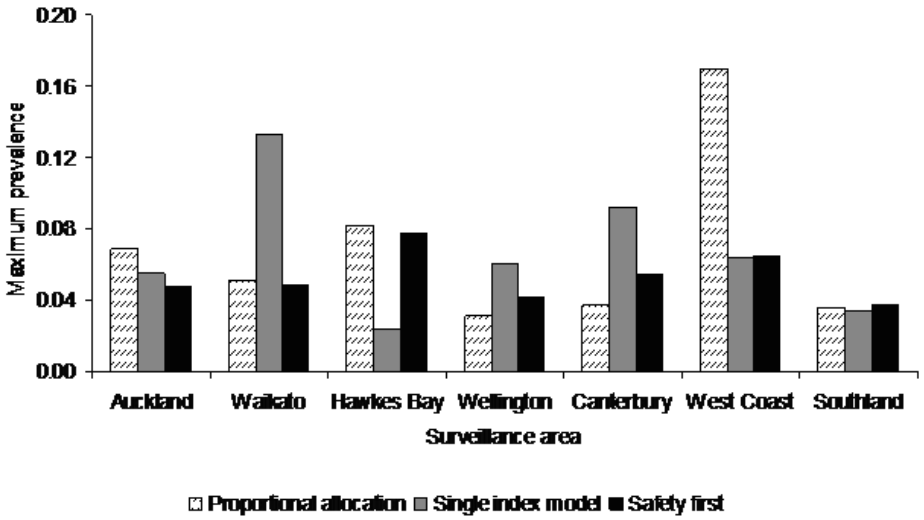

Figure 7.4: The maximum prevalence (proportion) of diseased ewe flocks in each surveillance area to be missed ($\alpha = 0.05$) using proportional allocation, the single index model and the safety first method .

portfolio theory in animal health and to make use of semi-quantitative data, which is often the type of information that is available.

Estimates of disease risk can be obtained from modelling factors that affect the probability of disease occurrence. Examples of risk mapping models range from simple rule-based analyses (Meentmeyer et al. 2004) to multivariable applications, and cover local through to national, continental and global scales (see Haine et al. 2004, Pfeiffer et al. 1997 and French and Morgan 1996 as examples; see also Ostfeld et al. 2005, Graham et al. 2004 and Kitron 2000 for overviews). The appropriate risk factors to consider would of course vary by disease, but may for example include climatic factors such minimum or maximum temperature (affecting vector or disease agent survival), the number of livestock sales and volume of animals traded per sale (affecting the spread of an infectious disease) or presence of intermediate host species. Weighting of risk factors could also be considered, as each risk factor may not be equally important. If there is a requirement to allocate resources to a range of diseases where different tests are used for detection, it may be necessary to include consideration of the relative values of those tests in terms of test sensitivity per dollar.

The approach taken to determining the temporal pattern of risk levels may depend on available data. The simulation process used in this research could be replaced by firstly completing a risk assessment for the whole country, for the period of a year divided into chosen time segments (for example, by month or season), to enable temporal allocation

of resources. Secondly, risk analyses would be completed for the first time period for each SA, and the resources available for that time period distributed accordingly. For each subsequent time slot, the SA risk assessment would be updated using the most recently available information, and resources again allocated. Both historical data and expert opinion may be incorporated into the risk assessments, and with the progression of time accrued data should be added to previous knowledge in order to predict values for coming time periods. A dynamic risk landscape could be constructed, mapping the risk of disease as it changes over time across the area of concern.

The demarcation of SA boundaries in this example has been according to geopolitical boundaries. The appropriate size of a SA should be such that the risk score would be appropriate to the whole area. For example, this may be an incursion zone around an international port or airport, where there is an increased risk of vector incursion. Such a zone could have a radius of the maximum flight distance of the vector of concern. The standard calculation used to find the number of samples required per SA assumes a homogenous population at risk, which is not likely to be the case even in small SAs, and random selection of samples is not always possible. However the distribution of tests according to disease risk should be more effective in terms of disease detection.

The lower constraint imposed on the number of points allocated to each asset in the safety first model is easily adjusted to alter the minimum level of resources allotted to the regions of least concern. Similarly, choice of an appropriate cutoff value C can be determined by evaluating various portfolios and accepting one with a satisfactory level of disease detection across the country. It should also be remembered that the measures used to describe risk and return can be varied and there will be consequences to the results and interpretation of the outcome. The appropriate measures should be chosen after consideration of the types of data available and the aims of the project. Assets with mixed levels of risk characteristics (those that receive a high score for some risk factors but a low score for others) might be excluded from a portfolio unless a weighting system is used in conjunction with an appropriate cutoff value.

The safety first and SIM approaches resulted in a lower maximum disease prevalence in ewe flocks than proportional allocation. The differences between the two portfolio theory methods were due to the different underlying assumptions. The SIM used a risk-averse attitude, where for a given expected risk score, more resources were directed towards areas with less uncertainty around the score. The equivalent safety first example used a risk-favourable attitude, with more resources allocated to areas with greater uncertainty around the risk score. The standpoint on risk that would be used in practice would depend on the surveillance objectives and the way in which risk assessment was carried out. Both methods were included in order to illustrate the concepts.

The described approaches to distribution of resources between competing interests illustrate application at different levels. For example, there may be a fixed surveillance

budget to cover monitoring of diseases in different animal species, geographic locations or production sectors. If it were necessary to choose between multiple diseases, it may be possible to group conditions into epitypes, where diseases within an epitype would have similar epidemiological characteristics. Diseases of particular concern could remain ungrouped, and resource allocation would be between the individual diseases and identified epitypes. Risk assessment can provide measures of the probability of disease incursion, establishment and impact on affected populations, and the budget allocated to each sector accordingly. Such processes could also be applied to public health programmes.

Sound decision-making requires that all options be identified and selection criteria defined so that an acceptable solution to a problem can be more easily arrived at. With a large array of disease threats to human and animal populations imposing increasing pressure on finite resources, it can become difficult to decide how to divide attention between competing concerns. Becoming overly focussed on a single disease, geographical location or time period may result in early signs of other significant problems being overlooked. The portfolio theory approach, used in conjunction with established risk assessment methods, provides a means of dividing surveillance resources between maintaining a scanning surveillance of the whole population of concern, while simultaneously targeting subgroups at higher risk of disease. Further evaluation of this approach will be made in order to validate it's use.

7.6 Conclusions

'... Behold the fool saith, 'Put not all thine eggs in the one basket' — which is but a manner of saying, 'Scatter your money and your attention;' but the wise man saith, 'Put all your eggs in the one basket and WATCH THAT BASKET.'

Mark Twain, in Puddn'head Wilson, 1894

Although Mark Twain disagreed with the tenets of portfolio theory, the concept has been known to society for a considerable period, and implemented (often informally) by many. In current times, with increasing drives towards efficiency and accountability, a portfolio theory approach to prioritisation of animal health issues and allocation of surveillance resources may enable a more structured, defined and balanced approach towards the implementation of risk-based surveillance. This is achieved, in part, by considering not only measurements of risk, but also the certainty or variability around those measures.

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Chapter 8

General Discussion

The main goals of this thesis were to develop methods to enhance the design and analysis of risk-based surveillance activities, and to apply financial resource allocation techniques to veterinary surveillance problems. Novel approaches to some of the issues surrounding risk-based animal health surveillance were constructed, and their versatility demonstrated by applying the methods to different diseases.

8.1 A review of the studies in this thesis

In Chapter 3, a method of estimating the prevalence of BSE in a national cattle population was developed. The model inputs utilised population demographic data and inherently biased post-mortem surveillance data. As with any epidemiological study, data availability and quality can have a profound impact on the ability to apply analytical methods. Over twenty countries participated in workshops explaining the use of the BSurvE model (Prattley et al. 2007a; Prattley et al. 2007b). Participants were asked to bring their national BSE surveillance data to the workshops, and it was soon revealed that there was a high level of variability in the quality and quantity of input data that different countries had available. Some nations with good demographic and surveillance records asked for modifications to be made to earlier versions of the model, to allow them to make maximal use of their data. These modifications included expansion of the age range for demographic data and an increase in the number of years of surveillance data the model would accept. Other countries were guided in the adaptation of limited data for use in BSurvE (e.g. how to expand grouped age data), and were advised of the consequences to the model's results. Ways in which the required data could be gathered were discussed, including the use of surveys and the collection of additional data from current surveillance activities. For some countries there was little infrastructure to support the acquisition of accurate and complete demographic or surveillance data. Other countries were challenged by geographic features that limited surveillance activities. For example, collection of fallen stock from remote

mountainous regions was likely to be compromised, meaning that this group would be under-represented in surveillance data and these animals would be unavailable to contribute to targeted surveillance activities without considerable expenditure. One of the major challenges of the BSurvE model was to develop a tool that could be used by multiple countries, each with different levels of BSE infection and data availability, yet allow some comparison of the results between nations. National results of the BSurvE model were generally in agreement with known events that influenced BSE infection within the country (e.g. the importation of animals from infected countries or the implementation of control measures). The method used in BSurvE was adapted by the OIE, who implemented a simplified point-based approach in their requirements for BSE surveillance (OIE 2008).

In the BSurvE model the calculation of various probabilities was based on input data that was largely country-specific. The age distribution of a cohort was held constant for each birth year, which would not apply in circumstances where the population was severely disrupted. Although likely to be rare, this would for example have applied to the sheep and cattle populations in the UK as a consequence of the foot-and-mouth disease outbreak in 2001. Another example where dramatic changes in national cattle populations occurred was in some European countries where national borders were altered. Interpretation of the model results for these years required more caution. Repeated runs of the model using input data representing specific time periods would mitigate this issue. Development of a model that could take different age distributions for different years would be possible, but would add a significant amount of complexity and would only be useful if the required demographic data were available.

The first stage of the BSurvE method is a series of probability calculations. These could be represented using a scenario tree structure (Martin et al. 2007a), and stochasticity introduced to allow for uncertainty and variability in the input values. However, the large number of age/stream combinations required in the BSurvE model might be unwieldy to represent under a scenario tree structure. The scenario tree methodology in its current format also ceases to apply once a case of disease is detected, rendering it ineffective for countries who already know they have disease. In contrast, the BSurvE approach can be used by both infected and uninfected countries. Detecting cases of disease substantially increases the point target, but does not negate the use of the model. If demonstration of disease freedom fails (i.e. a case is detected) the BSurvE model includes this information in estimating prevalence. Initial versions of BSurvE included a Bayesian component for the estimation of BSE prevalence, but this approach was not favoured under peer-review and was replaced by the described methodology.

Passive surveillance is considered to have low detection sensitivity, with under-reporting being one of the major flaws of the approach. Utilisation of the benefits of passive surveillance (such as increased coverage of the animal population) can be

enhanced by combining compulsory notification programmes with other techniques. Chapter 4 describes how the BSurvE model offers a way to quantify the effects of varying the level of clinical suspect reporting and the patterns of active surveillance of other sub-populations of cattle. Input data can be constructed to represent a country's desired pattern of surveillance activities, and the model run so that it can be seen how that pattern would alter the number of points obtained, the confidence of being below the required design prevalence and the costs of the surveillance programme. Further work could look towards designing an optimisation tool that would enable countries to input the numbers of animals available for each age and stream, the costs of testing animals in each category, and (depending on the required outcome) the desired design prevalence and confidence level, the time until this was achieved or a maximum cost. The optimisation programme could then output the optimal number of animals of each age/stream category that should be tested in order to achieve the required outcome. Techniques such as portfolio theory could also be used to divide resources between passive and active or scanning and targeted surveillance activities, providing each of these were quantifiable in some way.

Temporal discounting of points earned by testing was suggested in earlier documentation, but was not formally implemented as part of the BSurvE model. The OIE did, however, impose a seven-year life span of points gained under their current guidelines for BSE surveillance (OIE 2008).

A spreadsheet containing analytic and simulation tools was constructed to: (1) simulate the way cohorts leave the national cattle population and the subsequent sampling process for BSE; (2) evaluate the accuracy of the prevalence estimation method used in the BSurvE model; and (3) allow assessment of the effects of uncertainty in BSurvE's input parameters on the prevalence estimation. The results suggested that the method used by BSurvE was adequate, that the estimates were (on average) close to the correct values, and that the 95% confidence limits did cover the true value 95% of the time for the high levels of prevalence and generally over 90% of the times for lower prevalence values.[1]

The BSurvE method allows biased post-mortem data to be utilised to estimate population parameters. This was applied to both BSE and trichinellosis, resulting in greater use of data that were already being gathered and providing essential information to aid planning of further disease surveillance and control strategies. Chapter 5 describes how the BSurvE approach was, in some respects, simplified in its application to trichinellosis. Because there was no differentiation between animals that were infected or uninfected in terms of the way in which they left the population, the probability calculations were more straightforward. The age of the animal leaving the population was also not

[1] A paper describing this work is in the final stages of preparation for submission.

considered for all species in developing the *Trichinella* model, due to both a lack of appropriate data and the different epidemiology of the disease in comparison to BSE (infection by *Trichinella* can occur at any age, so a birth-cohort approach was inappropriate). On the other hand, older animals have had a greater time at risk of exposure to *Trichinella* and could be more likely to be infected than younger animals. A negative test from an older animal would therefore be of greater surveillance value than one from a juvenile - a consideration that was included in the trichinellosis model for the grower and breeder pig sub-populations. In order to apply a similar consideration to the fox and horse populations, the aging of foxes would need to be more accurately done (limited data were provided that broadly classified foxes as juvenile or adult, usually on the basis of size and dentition), and more data would need to be collected about slaughtered horses. However, it may not be possible to accurately age all animals. The relative surveillance value of testing animals of different ages would need to be determined and justified.

Risk-based surveillance systems generate datasets that are not representative of the entire population at risk. In some circumstances, even though a surveillance programme may not have been designed on the basis of risk, the only available data may be biased with respect to the population about which measurements are required to be made. The analysis of BSE and *Trichinella* data fall into the latter category, but in either case the methods applied to these diseases could equally be applied to biased data from deliberately targeted systems. If disease detection is the sole objective, gathering biased data is not an issue providing alternative strategies are used to estimate any required population parameters after disease was found.

Chapter 6 described and evaluated surveillance for exotic causes of sheep and goat abortion in New Zealand. A rule-based method of assessing risk on a seasonal basis across the lower North Island was developed to demonstrate the basis for designing a risk-based surveillance programme. A small number of easily quantifiable risk factors were used for illustrative purposes. The concept is simple and has been implemented in other circumstances (see Meentmeyer et al. 2004 for an example of the approach applied to a plant pathogen killing oak trees in California). Many surveillance questions would require a far more comprehensive assessment of risk, both in terms of risk factor identification and measurement, which would need to be obtained by other studies.

Under-reporting would also affect the samples received by laboratories for cases of sheep and goat abortion in New Zealand. Due the identified lack of knowledge surrounding farmer and veterinary practitioner behaviour in submitting samples, the degree of under-reporting is difficult to quantify. Further studies are indicated to investigate ewe flock size, estimated number and timing of abortions, reasons that trigger calling the veterinarian and their reasons for sample submission.

The rule-based approach described in Chapter 6 facilitates rare disease detection,

and was used in this example to demonstrate a way in which risk-based surveillance can be implemented. Geographical and temporal risks were considered, although both of these categories have their challenges. The geographical boundaries used were based on political divisions and are unlikely to be respected by pathogens. Natural boundaries such as rivers or mountain ranges could be more effective when considering the likely transmission of disease, although these too would be ineffective if transportation of animals was a factor in disease spread. Clustering of animals could be considered on local as well as national scales when designing a surveillance programme. Temporal boundaries may be no less challenging, as the measurement of risk factors over time needs to be done at a suitable frequency, i.e. one that allows adequate informative data to be gathered without the excessive use of resources to obtain them. Rainfall and temperature data are commonly collected as point-source information. If measurements are taken from multiple point sources within a reasonable proximity, valid estimates can be made for the values between points. However, it is unlikely that sufficient country-wide coverage would be available to make detailed measurements, and micro-climates could easily be overlooked. These might be niches suitable for habitation by disease vectors. Climatic conditions may also be cumulative over time in terms of the development of suitable vector habitats, so it might be necessary to assess climate data at both short and longer intervals.

Laboratory testing for exotic causes of abortion in ewes in New Zealand is targeted towards submissions where the history is incompatible with one of a case of endemic disease, or routine tests for endemic diseases are inconclusive. Such cases are not necessarily at higher risk of being due to exotic disease, but could, for example, be a result of a poor history being provided by the submitting veterinarian, or the provision of inadequate samples. They are also part of a passive system in that cases are only obtained by the laboratory if farmers and their veterinarians consider it is beneficial do so (i.e. it is deemed necessary to try and establish a definitive cause of abortion).

The laboratory case submission data were also assessed using scenario tree methodology (Prattley 2006). Using this analytical approach the sensitivity of the surveillance system was estimated to be low, although the probability of freedom from disease was greater than 0.90 when a low prior probability of disease presence was taken into account.

Chapter 7 demonstrates how portfolio theory techniques can be applied to surveillance problems at different levels — from dividing resources between diseases at a national level, to allocating diagnostic tests across time and space for a particular disease syndrome. While the resources allocated in the latter example were laboratory tests, this technique could easily be applied to the apportioning of human resource hours or surveillance funding dollars. In order to allocate resources on the basis of risk, risks need to be identified and quantified. Allocation using the portfolio theory techniques

applied in this thesis required measurements of central tendency (mean, median) and variation (standard deviation, semi-interquartile range) of expected risk scores. Thus portfolio theory was able to be applied to both semi-quantitative and quantitative data, demonstrating the versatility of the method. Further quantification would be possible in terms of weighting values for risk factors. No individual weighting factors were used in Chapter 7, but these would give a degree of influence over the results, and the values used would depend on the perceived relative importance of risk factors. The relative importance, and indeed perhaps the values attributed to risk factors, might be able to be accurately quantified; alternatively techniques such as Delphi conferencing could be used to elicit expert opinion for the determination of appropriate inputs. The safety first approach is relatively simple, as distributions are represented using only two parameters. The method can be used with multiple data types and could therefore potentially be applied to many different problems.

Safety first methods (Bigman 1996; Roy 1952) seek to minimise the risk of failing to meet a specified minimum target. Adjustment of the cutoff value allows varying amounts of resource to be allocated to targeted versus scanning surveillance. The optimum division could be assessed using modelling techniques. Possibly the value of the cutoff would change according to the relative degree of risk in high- versus low-risk areas. Further investigation could also be carried out into the characteristics of failing to meet the target profit. Bigman (1996) points out that probability measures of risk fail to measure the 'depth' of a failure, quantifying only the likelihood of simply failing. Were safety first methods to be applied in a veterinary surveillance programme, how bad might be the consequences of choosing at threshold that turns out to be sub-optimal? How big might the effects of uncertainty in risk measurements be? Another facet of further work could investigate continuous time modelling of optimal portfolio management.

No similar examples of the application of portfolio theory to veterinary surveillance were located in the literature, although Galligan (1991; 1988) demonstrated the use of portfolio theory in deciding between reproductive interventions within a dairy herd. Other financial techniques such as cost-benefit analysis have been used to evaluate various options for surveillance in particular diseases (Prime and Nimmo-Bell 2002); however, these were used to assess proposed surveillance activities rather than to aid their design.

Several methods of combining data sources have been utilised in the different chapters of this thesis. In Chapter 3, data representing sub-populations of cattle of different ages and exit categories were mathematically combined to produce an estimate of the number of animals per birth cohort that were infected with BSE. Chapter 5 combines data from different species as well as from sub-populations within species. This was possible because the relative prevalences of trichinellosis in the different species and

sub-populations were known, and the data could be weighted accordingly. In Chapter 6, spatial and temporal data were utilised in a geographic information system to develop a disease-risk landscape for exotic causes of abortion in ewes and does. Portfolio theory techniques were applied to semi-quantitative data describing the risks of various diseases occurring in New Zealand. The semi-quantitative data represented a method of quantifying expert opinion, in that the occurrence of a particular variable (such as morbidity or cost to production) was measured as high, medium or low and accordingly given a numerical score.

Hurwicz (1973), in a paper discussing the design of resource allocation mechanisms, considered the difficulties for a single agency trying to obtain all of the information necessary to perform the required calculations. Information was considered to be dispersed throughout the economy and each 'economic unit' knew only about themselves. For example, consumers would know what their own preferences were and producers knew about the technology they used. The obstacles inhibiting the gathering of this information to a central body included monetary costs, loss of data accuracy and loss of data volume. Decentralised techniques aimed to allow economic units to perform their own calculations so as to decrease the amount of information that needed to be transferred. Animal health surveillance suffers from similar issues in obtaining data from discrete entities such as slaughterhouses, farms and laboratories. Organisations such as those that gather climate data can also contribute important information. Suggested surveillance networks are described in Stevenson et al. (2007); the approach was to form a 'data warehouse'. Increased use of computer and communication technologies would facilitate this approach, in contrast to the logistical difficulties faced by Hurwicz (1973).

8.2 Future research

This thesis has developed techniques that can be applied to risk-based surveillance problems at both the design and analytical levels. However, many challenges and opportunities remain.

Donnelly et al. (1997) evaluated culling programmes for BSE in terms of their effectiveness (the prevention of future cases), efficiency (the number of cases of BSE prevented per animal culled), and scale (the number of cattle culled in each proposed strategy). Similar measures can be applied to the evaluation of surveillance strategies. Although proposed surveillance strategies should be, and often are, evaluated prior to implementation (see Chapter 2), this is not always a comprehensive process. In surveillance the terms effectiveness, efficiency and scale could be defined as: (1) the ability to detect cases when present; (2) the number of cases detected for the number of tests carried out; and (3) the number of tests required to detect disease. Effectiveness

relates largely to system sensitivity. These measures would be appropriate if the aim was early disease detection (either finding highly infectious disease at the early stages of an outbreak or finding cases of a disease with low prevalence) but are only all possible by modelling outbreaks if a disease is not actually present in a country. The BSurvE model included a component that evaluated the cost of the surveillance strategy in simple terms — the actual cost of performing the test, plus the cost of animal collection in the case of fallen stock. Other methods such as cost-benefit analysis or expected return (as discussed in Chapter 2) could be used to evaluate the surveillance system in monetary terms.

Exit strategies for surveillance are a developing area where risk-based surveillance is likely to be applied (Willeberg 2006). As the incidence of a disease such as BSE declines in an infected country where control measures have been successful, a point will be reached at which the costs of extensive surveillance could be argued to outweigh the benefits. This might happen before the conditions of disease 'freedom', as determined by the OIE, have been met (OIE 2008). Targeting high-risk sub-populations of animals would help to maintain an acceptable degree of surveillance while decreasing the costs of more comprehensive surveillance strategies.

Resource allocation is a topic that has not benefited from substantial formal consideration in animal health surveillance. As described in Chapter 2 there are a number of concepts and methodologies available, each with their own advantages and disadvantages. The lack of uptake of these ideas may be due to their satellite position relative to traditional veterinary fields, along with limited exposure, training and understanding of the concepts and techniques by veterinarians and policy makers. There are many opportunities for further exploration of both risk-based surveillance and resource allocation techniques, some of which were suggested in Chapter 2. In addition to those previously described, a study of the missile allocation problem (Matlin 1970) brings to mind further ways in which concepts from other fields could be applied to veterinary surveillance. Target sharing and redundancy could be applied by examining current and ongoing surveillance exercises to see whether or not samples taken in one programme could be appropriately used for multiple surveillance purposes. Hohzaki and Nagashima (2009) described a possible application of a two-person game theory where a target (player one) hid in cell i with probability p, while the second player could search in any cell at any time point with a known cost for each looking. The detection probability of the target depended on the time of looking and whether or not the target was present in the cell at that time. An optimal search plan, taking into account time factors and a fixed budget, was the desired outcome. This concept could be applied to animal health surveillance, with a pathogen or disease taking the role of the first player and those interested in detecting disease representing player two.

8.3 Conclusions

Implementation of risk-based surveillance and resource allocation techniques can occur at all levels, from herd or flock through to national strategies. Continued development of risk-based surveillance programmes and methods of data analysis and resource allocation will further facilitate efficient yet effective use of resources while achieving surveillance objectives. This thesis has been produced during the infancy of risk-based surveillance and has developed a number of novel approaches to disparate problems. Avenues for further work have been described and have the potential to explore the variety of tools available.

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'But I don't want to go among mad people,' Alice remarked.
'Oh, you can't help that,' said the Cat. 'We're all mad here. I'm mad. You're mad.'
'How do you know I'm mad?' said Alice.
'You must be," said the Cat. 'or you wouldn't have come here.'
Lewis Carroll