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Project identification

1. Defra Project code: SE4303
2. Project title: Development and use of an integrated model to simulate disease occurrence and estimate the economic impacts of surveillance systems in order to improve resource allocation for scanning surveillance
3. Contractor organisation(s): Animal Health and Veterinary Laboratories Agency
4. Total Defra project costs (agreed fixed price): £ 99649.06 (ex VAT)
5. Project: start date .... 1st April 2011
   end date .... 31st March 2012

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Executive Summary

7. The executive summary must not exceed 2 sides in total of A4 and should be understandable to the intelligent non-scientist. It should cover the main objectives, methods and findings of the research, together with any other significant events and options for new work.

Early warning surveillance in Britain enables early detection of new, re-emerging and exotic animal health threats so that prompt action can be taken to reduce their impact.

The aim of the work carried out in this project was to develop and integrate epidemiological and economic models and use these models to simulate the occurrence of an emerging disease and compare the economic impacts of disease occurrence under different surveillance implementation scenarios. The long term aim being to improve resource allocation for early warning surveillance.

Epidemiological and economic models of early warning surveillance in England and Wales were developed, based upon the system of surveillance current in 2012. Outbreaks of a hypothetical disease of cattle were simulated using the epidemiological model and the detection of this disease was modelled using three different surveillance implementation scenarios. These scenarios were: the 2012 model of laboratory-based surveillance in England and Wales assuming the then existing level of submissions and contact with veterinary surgeons; the 2012 model of surveillance with enhanced submission of carcases for post mortem resulting from the implementation of a subsidised carcase collection service; and the 2012 model of surveillance with enhanced contact between veterinary surgeons and laboratories encouraged by the implementation and promotion of a dedicated telephone advice line. Outputs from the epidemiological model were combined with economic data (including market prices, demographic statistics and expert opinion) to provide inputs for a stochastic economic model to conduct cost-effectiveness and cost-benefit analyses of the enhanced surveillance scenarios.

The results of the initial application of these models suggest that implementing a carcase collection service in 2012 would lead to earlier detection of the epidemic and a substantial reduction in the number of holdings and cattle affected by the hypothetical disease. Enhanced telephone contact between private veterinary surgeons and AHVLA regional laboratories is likely to have a more modest impact on epidemic duration and size but is likely to be cheaper to implement. The economic analysis suggested that both enhancements to surveillance would demonstrate a positive net economic benefit in 93% of the simulated epidemics and both would be likely to show an ability to limit the probability of a "worst-case" disease epidemic occurring.

This work has achieved the project aim and demonstrated the usefulness of integrating epidemiological and economic models to inform decision-making concerning the allocation of resources for animal health

surveillance. Further work is required to validate the assumptions and input parameter values before robust conclusions can be drawn regarding the optimal allocation of resources for early warning surveillance.

Suggested future work on the tools developed here includes sensitivity analyses of the epidemiological model inputs and assumptions, updating the model and parameters to reflect changes to the delivery of surveillance in England and Wales and further validation of the method by applying it to a known disease. Once the tools have been finalised and validated a more comprehensive picture of the added value of enhanced surveillance could be obtained by application of the model to several different disease types (with appropriate model modifications), assessing the impact of varying time frames for enhanced surveillance and the impact of different surveillance enhancements. It may also be possible to make an assessment of the value of early warning surveillance by making assumptions about how disease would be detected in the absence of an early warning surveillance system.

Project Report to Defra

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1 Introduction

Early warning surveillance[1] in Britain enables early detection of new, re-emerging and exotic animal health threats so that prompt action can be taken to reduce their impact. Examples from recent years include the early detection of pandemic H1N1 influenza in pigs, four of the 12 notifiable avian disease outbreaks, bovine tuberculosis in non-bovine species, antimicrobial resistance in *Salmonella* and virulent psoroptic mange in cattle. Early warning surveillance cost approximately £10 million in 2009/10. Economic case studies carried out in 2010 (ASSP 2011) suggest the benefits derived from the programme greatly exceeded its costs over recent years, but it is difficult to assess the economic value of surveillance aimed at detecting new animal health threats. The current pressure to reduce the costs of animal health surveillance means that evidence to support the effectiveness of different approaches is required.

Objectives

The aim of the work carried out in this project was to develop an integrated epidemiological-economic model which simulates disease occurrence and compares the economic impacts of disease occurrence using different enhancements to surveillance in order to improve resource allocation for early warning surveillance. Specific objectives include:

1. Simulate the occurrence of a hypothetical disease in the cattle population in Great Britain using the epidemiological model (GEM)
2. Determine the costs of different early warning surveillance approaches assess the effectiveness of these approaches and, where appropriate, the benefits
3. Create an integrated model that links the epidemiological model and the economic model
4. Use the integrated model to compare the cost effectiveness and, where appropriate, cost benefit of the existing and alternative early warning surveillance strategies for a hypothetical emerging disease in cattle.
5. Disseminate the information obtained from this model about the value and effectiveness of different early warning surveillance approaches to the scientific community and decision makers.

The extent to which these objectives have been met

Epidemiological and economic models of early warning surveillance in England and Wales have been developed, based upon the structure of surveillance current in 2012. Outbreaks of a hypothetical disease of cattle have been simulated under three surveillance scenarios (baseline and two enhanced surveillance scenarios). Output from the epidemiological model has been integrated into the economic model to inform cost-effectiveness analyses of the enhanced surveillance scenarios. This work has demonstrated the usefulness of integrated epidemiological and economic modelling to decision-making concerning the allocation of resources for animal health surveillance.

2 Methods

Bovine Wasting Disease (BWD)

Bovine wasting disease (BWD) is a hypothetical chronic disease of cattle characterised by decline in milk production and progressive wasting and weakness leading to recumbency, respiratory distress and eventual death. Some of the epidemiological features of BWD were made similar to BSE to provide a basis for comparison with an emerging disease that was difficult to detect in the early stages of the outbreak.

Infection in the model is associated with exposure to contaminated feed and it assumed that the force of infection experienced by animals increases exponentially over time. As cattle on beef holdings are assumed to receive less concentrate feed, the infection force was reduced to 5% of that on dairy and mixed herds. It was assumed that there was no horizontal or vertical transmission of disease between cattle.

[1] Previously termed 'scanning surveillance' in the UK; the new term was defined during an international workshop attached to the 2011 International Conference on Animal Health Surveillance (Hoinville 2011)

Infected cattle were assumed to experience a prolonged incubation period (ie lognormal distribution with a mean of 5.3 years and so similar to BSE (Arnold and Wilesmith, 2004)) and a die after a clinical episode lasting between 60 and120 days. Cases are typically sporadic in affected herds.

BWD poses a putative risk to public health through the consumption of affected meat and tissues, but not through the consumption of milk or direct contact with infected cows.

Surveillance scenarios

The integrated models developed in this task were used to examine three scenarios of early warning surveillance in cattle: the baseline scenario of the current level and delivery of early warning surveillance; surveillance enhanced by a subsidised carcase collection service; and surveillance enhanced by a dedicated telephone advice line with centralised recording and analysis of telephone call data:

1. Baseline scenario

This scenario simulates the laboratory-based early warning surveillance system used in England and Wales in 2012. It assumes the level of submissions and telephone contact expected in 2012. Detection of the emerging disease is based upon carcase submissions to the regional laboratories, telephone contact between private veterinary surgeons (PVS) and Animal Health and Veterinary Laboratories Agency (AHVLA) regional laboratories (RL) veterinary investigation officers (VIO) or quarterly analysis of undiagnosed (DNR) submissions across the AHVLA network.

2. Baseline surveillance with enhanced submission of carcases through a carcase collection service

In this hypothetical scenario submission of carcases to AHVLA RLs is enhanced through the implementation of a subsidised carcase collection service. All farms are assumed to have the same probability of carcase submission as the current submission levels from those closest to the RL. This results in an increase in overall probability of carcase submission. Mechanisms for detection of the emerging disease are the same as for the baseline scenario.

3. Baseline surveillance with additional data collected from a dedicated telephone advice line

This scenario simulates the baseline surveillance system with additional data collected centrally from all telephone contact between the PVS and the AHVLA. Telephone contact is enhanced through promotion of AHVLA services. In addition to the three detection mechanisms in the baseline scenario a new detection threshold was created to reflect monthly analysis of the data recorded in the telephone database.

Overview of the epidemiological model

The epidemiological model assumes that disease detection occurs as a result of information provided by the laboratory based early warning surveillance system operated by the AHVLA in England and Wales in 2012. The model simulates the spread of BWD in cattle, observation of clinical disease by the farmer and PVS, submission of samples to the AHVLA laboratory network and the generation of surveillance data and the subsequent 'detection' of disease and the implementation of control measures. Further details of the epidemiologic model can be found in Annex 1.

Population and cattle movements

The model population was drawn from Cattle Tracing System (CTS) data for England and Wales: 73,371 unique cattle holdings (19% dairy, 72% beef and 8% mixed/other) are represented in the model. Each holding is assigned to a feed mill and a RL according to its geographical location.

The movement of animals between farms and to slaughter was replayed using historical data from CTS recorded during the period between 01/01/2008 and 31/12/2010. When an infected animal is moved to Scotland it is recorded as a model output and then removed from the model. No disease transmission within Scotland or movements from Scotland to holdings in England and Wales are considered in the model.

The number of herds and herd size is assumed to remain constant during the course of the epidemic. Births and deaths are not explicitly modelled and no age structure is included in the model. Cattle leaving a herd through movement or death from BWD are immediately replaced by a new susceptible.

Model structure
The epidemiological model is a state transition model (Figure 1), live cows occupy one of five states: Susceptible, (latently) Infected, Clinically diseased, Observed by the farmer and Visited by the vet. Transition through the five states is progressive and unidirectional. Transition from susceptible to clinically affected is determined by the biology of the hypothetical disease and transition into the observed and visited groups is determined by the action of the farmer and PVS.

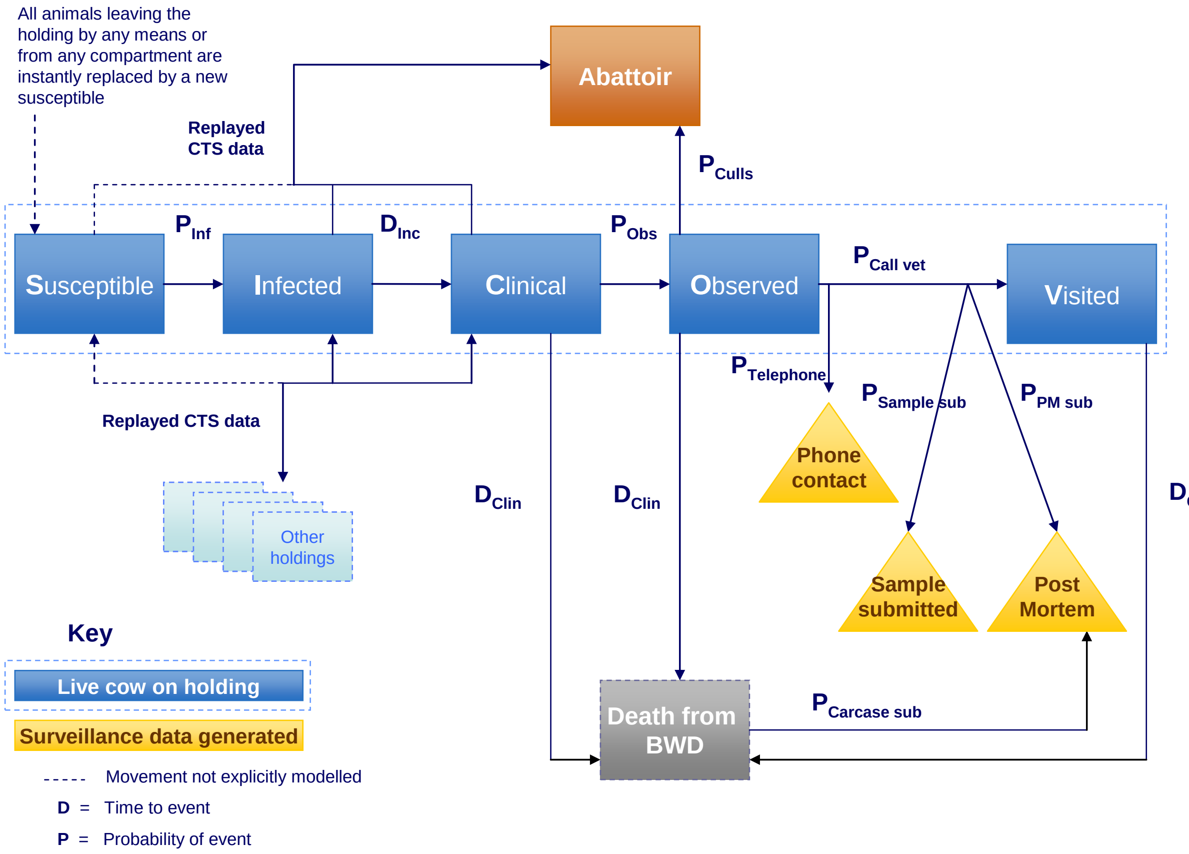

Figure 1 Structure of the epidemiological model of early warning surveillance, including the transition states of cattle, animal movements and death and the production of surveillance data.

Disease transmission and biology
Cattle are assumed to become infected with BWD due to exposure to infected feed originating from contaminated feed mills. There are 165 feed mills supplying the cattle holdings in England and Wales in the model. At the start of each simulation 16 feed mills (~10%) are selected from which the contaminated feed will be distributed. All susceptible cattle on holdings that are supplied by those feed mills are then subject to the force of infection. There is no horizontal or vertical transmission of disease between animals.

All animals that develop clinical signs of BWD die following an illness which lasts between 60 and 120 days, so animals in the 'clinically affected', 'observed' and 'visited' groups move into the death group when their clinical duration is over. A proportion of the animals that die are sent to AHVLA for post-mortem examination.

Farmer and veterinary behaviour and generation of surveillance data
Once the farmer has observed a clinically affected animal (ie the cow moves from C to O), the farmer may choose to (i) send the cow to the abattoir, (ii) call the private veterinary surgeon (PVS) to examine the observed cows or (iii) do nothing.

Once the vet has been called to see an observed animal (and any other observed animals that are on the farm when the vet is called) it is moved, with all other observed animals, into the visited group. At this point, the farmer is reclassified from 'naïve' to 'experienced', modifying their probabilities of observing affected cows and subsequent actions.

Cows in the visited group remain there until death from the hypothetical disease. The visited group is an approximation of all subsequent actions on an affected cow: including attempted treatment by the farmer and repeat examinations by the PVS.

Surveillance data is generated by telephone contact between the PVS and the AHVLA at the point of visiting the farm, submission of a blood/faecal sample and submission of carcases for post-mortem. Animals are submitted for post mortem either following a decision to sacrifice an animal at the visit of the PVS or following the death of the cow on-farm.

Parameter values for farmer and veterinary behaviour were derived from statistical analysis of FarmFile submission data and consultation with VIOs, the AHVLA cattle expert group and PVS. See Annex 1 to this report for further details of the parameter values used in the model.

<u>Detection mechanisms</u>
The detection of the emerging BWD is simulated in the model through one of four detection mechanisms (Table 1). It is assumed that if a number of BWD cases are submitted to a single RL within a specified time period this would stimulate further investigation of these cases and lead to the identification of the new disease. Likewise if several PVS contact a single RL by phone to discuss cases of BWD it is assumed an investigation would be undertaken. The third detection mechanism relies on the routine analysis of the data recorded about submissions across the AHVLA to determine whether the number of undiagnosed (DNR) submissions in different disease syndromes exceeds expectation. The fourth detection mechanism, analysis of the data recorded about telephone calls to all RL, was only applied in the surveillance scenario which included a dedicated telephone advice line (scenario 3). This relied on analysis to determine whether the number of phone calls about animals with diseases in a particular syndrome was in excess of expectation. The threshold values for the carcase submission and telephone contact mechanisms were derived from expert opinion. The threshold values for the DNR and telephone database analyses were derived from statistical analysis of existing and simulated submission data, using outbreak detection algorithms (Stroup et al 1993, Farrington et al 1996, Höhle 2007) with expert opinion used to assess how many BWD cases would be assigned to different syndromes.

Table 1 Construction of the four detection thresholds used in the epidemiological model for each of the three surveillance scenarios

Name of mechanism	Surveillance data examined	Threshold	Time period	Network coverage	Scenarios including thresholds		
					Baseline	Carcass collection service	Telephone advice line
Carcass submission	Carcass submissions	3	6 mo	Each RL	√	√	√
Telephone contact	Phone calls	3	6 mo	Each RL	√	√	√
FarmFile DNR analysis	Carcass and non-carcass submissions	9	3 mo	AHVLA network	√	√	√
Telephone database analysis	Phone calls	17	1 mo	AHVLA network			√

When the number of BWD cases entering a particular data stream exceeds the threshold set in the model it is assumed that an investigation is carried out to identify the cause. It was assumed that this investigation and the subsequent decision process to allow control measures to be introduced takes one year; following which infection via contaminated feed is stopped. The model continues to run until all infected animals have been removed from the system by movements, death or farmer/PVS actions.

Outputs for the economic model
Data on number of animals and holdings affected, time to detection, the number of non-carcase submissions, telephone calls to AHVLA, cow-days spent in each epidemiological compartment and animals sent to slaughter, post-mortem or deaths from BWD in the epidemic period were provided as input to the economic model (table2).

Overview of the economic model

A stochastic spreadsheet model to estimate the economic impact of BWD was devised in Palisade @Risk 5.7 for Excel. The model includes six components (Figure 2), the sum of which provides an estimate of the impact of BWD. These components can be classified as either expenses or losses, as defined by McInerney et al. (1992).

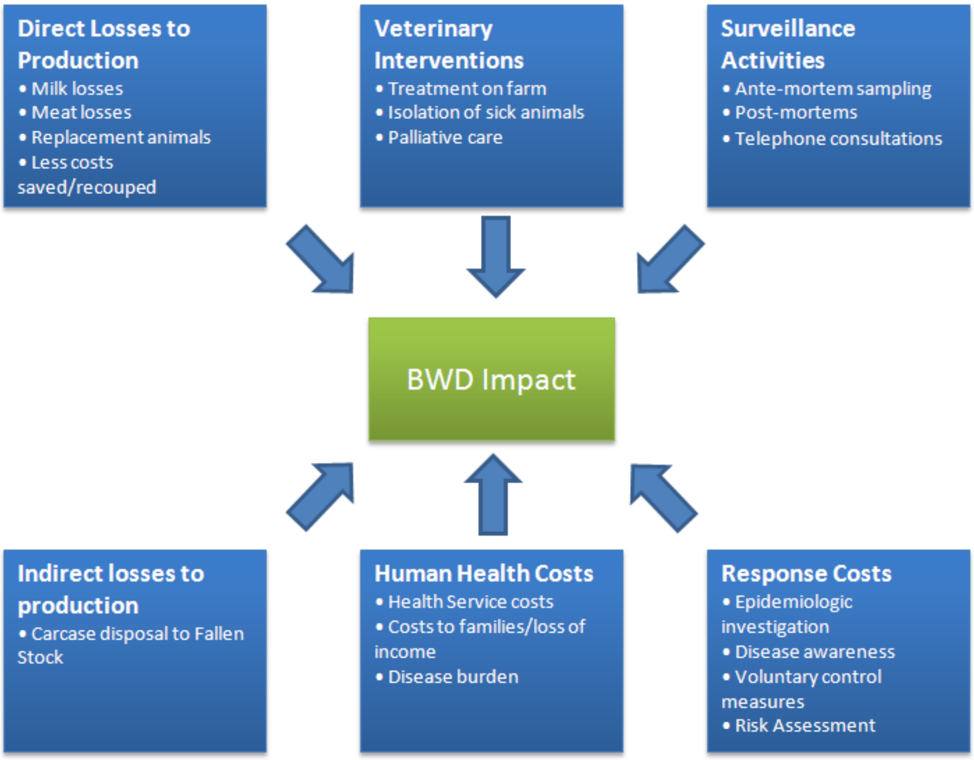

Figure 2 Components included to estimate the economic impact of hypothetical bovine wasting disease. Each component listed generates a cost estimate which is summed to provide an overall estimate of disease impact.

Analysis of component costs within the economic model output allowed the attribution of disease-associated costs between the public and private sectors. Given the clinical similarities between BWD and bovine spongiform encephalopathy (BSE), it was decided to assess the costs to human health of zoonotic transmission of a disease analogous to new variant Creutzfeldt-Jakob disease (nvCJD).

Estimation of costs and input parameters used
Losses were calculated using equations of the form:

$$PL = \sum_{e} \sum_{f} NoA_{e,f} \cdot LPP_{e,f} \cdot p_{e,f}$$

Where $NoA_{e,f}$ is the number of animals of type *e* affected by disease *f*, *LPP* is the loss of production parameter and *p* is the price coefficient for the product produced. Within each component estimates for parameters were derived from literature review and market prices. Where no data were available, contact was initiated with relevant parties to elicit expert opinion. Table 2 lists the input requirements of the economic model in calculating component costs.

Table 2 Input parameters used to estimate outputs in the economic model.

Outputs / Inputs	Losses to production	Veterinary Interventions	Indirect costs to production	Surveillance Activities	Human health Costs	Response costs
Epidemiological parameters	Cow days infected Movements to abattoir, AHVLA and deaths	Total animals transiting states and cow-days spent in each state	Number of animals dying from BWD	Total carcase and non-carcase submissions, telephone calls and distance from farm to lab.	Total movement of infected animals to abattoir	Total cow days in Visited group
Market Prices	Milk price Cull cattle prices Replacement animal prices Feed costs	Cost of veterinary treatment, isolating animals on farm and labour	Cost of carcass disposal and labour	Cost of diagnostic services and telephone consultation. Fuel and labour costs	Cost of treatment, care and loss of income for nvCJD.	Cost of epidemiological investigations, movement restrictions and disease awareness campaign
Production parameters	Milk yield Cattle weights Feed consumption Weight loss Milk yield reduction	Probability of treatment, repeat treatment and isolating animals.	N/A	N/A	Case per infected animal ratio	N/A

Where uncertainty or variation in parameters was found, probability distributions were used to define inputs. Details of parameters and equations used to determine component costs can be found in Annex 2; assumptions surrounding these parameters are also described within Annex 2. Further to this, an additional component, that of impact on trade, was assessed qualitatively but not modelled.

Data on number of animals infected, holdings affected, times of detection, blood and faecal submissions, telephone calls to AHVLA, cow-days spent in each epidemiological compartment and animals sent to slaughter, *post-mortem* or dying from BWD during the epidemic period were provided from the epidemiological simulation. These data were imported into Microsoft Excel, where probability distributions were fitted to each input using the distribution fitting tool in @Risk. Input distributions were selected based on chi-squared analysis, the distribution most likely to produce the epidemiological data being that which was selected.

The models were run with 10,000 iterations and sensitivity analyses were conducted to identify epidemiological input parameters that were most influential. The source data for these key inputs were then assessed for correlation with each other. Where significant correlation was found, relevant correlation coefficients were attached to the equivalent model distributions.

<u>Cost-effectiveness analysis</u>

Cost-effectiveness ratios were calculated by comparing the surveillance costs and effectiveness outputs of scenarios 1 and 2, respectively, to the baseline according to the following equation:

$$Cost - Effectiveness\ Ratio = \frac{Cost\ Surveillance\ Baseline - Cost\ Surveillance\ Scenario}{Effectiveness\ Baseline - Effectiveness\ Scenario}$$

The cost-effectiveness measures used were:

- Cost per animal saved from infection
- Cost per infected animal prevented from entering the food-chain
- Cost per DALY saved (a measure of human disease burden)

- Cost per day to detection saved.

The cost of surveillance under each scenario was taken to be the cost of surveillance until the point of detection calculated using the current annual budget and modified for the scenarios. BWD was assumed to have no effect on future budget allocation i.e. budgets were constant throughout the simulation.

3 Results

Epidemic simulations

The epidemiological model simulated the spread of and response to BWD under all three surveillance scenarios; between 104 and 112 simulations were available for analysis for each scenario (Table 3). In the baseline scenario the BWD epidemic ran for an average 1,932 days (5 years and 3 months) before detection of the emerging disease (Table 3, Figure 3); with the majority of epidemics being detected following the *post-mortem* examination of several carcases in a single RL. An average total of 10,986 unique holdings were affected by BWD over the duration of epidemics, with over 900 animals dying from BWD per month at the epidemic peak. The apparent delay to detection was mostly due to the long incubation period assumed for BWD; this also resulted in a large and lengthy 'overshoot' of the epidemic post detection and intervention (Figure 3). Average holding-level incidence was greater for dairy (21%) and mixed (29%) holdings compared to beef holdings (16%) across all scenarios.

Table 3 Summary statistics of simulations in the epidemiological model for the three surveillance scenarios

	Scenario 1 Baseline surveillance	**Scenario 2 Carcase collection**	**Scenario 3 Telephone advice line**
Number of runs analysed	104	112	110
Size of epidemic			
Mean total no. affected holdings (range)	10 986 (6444,19433)	9 906 (6066, 13344)	10 567 (6167, 18635)
Mean total no. of cattle dying from BWD (range)	32 570 (11022, 93193)	24 460 (10255, 51630)	29 090 (9910, 74822)
Time to detection of epidemic			
Mean number of days to detection (range)	1 932 (1450, 2797)	1 799 (1254, 2400)	1 911 (1460, 2818)
Surveillance data produced			
Mean total no. of PMs performed	845 (224, 1912)	1 075 (439, 2164)	718 (153, 1651)
Mean total no. of non-carcase submissions	941 (258, 2442)	625 (164, 1413)	801 (122,2025)
Mean total no. of phone calls to RLs	1 157 (309, 2895)	767 (174, 1859)	1 467 (212, 3569)
Detection mechanism triggered			
Carcase submission	61%	92%	38%
Telephone contact	39%	8%	62%
FarmFile DNR analysis	0%	0%	0%
Telephone database analysis	-	-	0%

Implementing a carcase collection service (scenario 2) reduced the average time to detection of BWD by 133 days and the total epidemic size by around 10% in terms of affected holdings and 25% of cattle deaths (Table 3, Figure 3). The carcase collection service resulted in a marked increase in the total number of carcase submissions and the proportion of epidemics detected following post-mortem examinations in RLs (Table 3).

Enhancing telephone contact between the PVS and AHVLA (scenario 3) had a more modest impact on the duration and size of BWD epidemics: reducing the average time to detection by just 21 days and the mean total number of affected holdings by 437 (Table 3, Figure 3).

Data driven analyses of submission trends or telephone calls across the AHVLA network did not result in detection of BWD in any scenarios (Table 3).

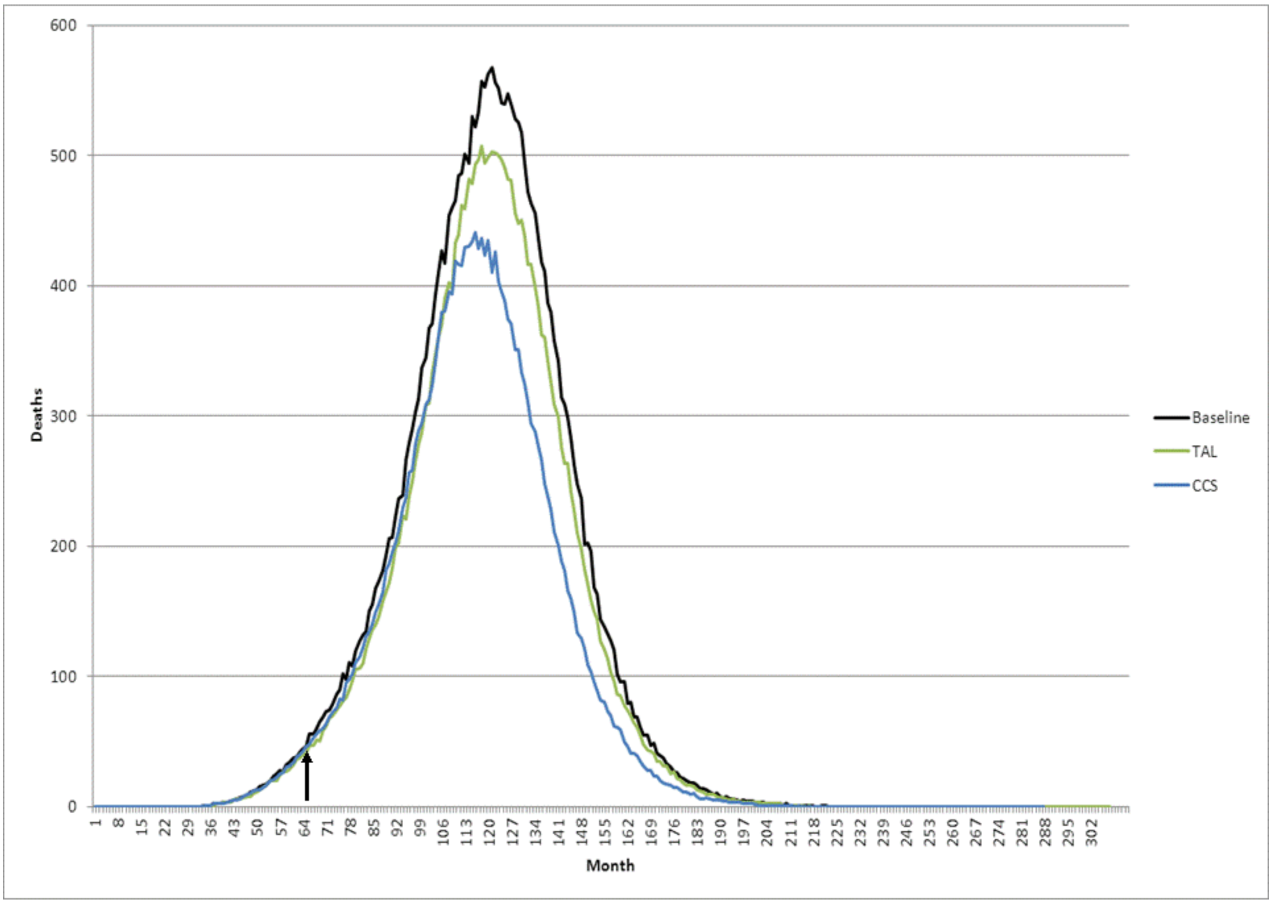

Figure 3 Number of cattle dying each month for the baseline (black), carcase collection service (blue) and telephone advice line (green) scenarios. Time of detection for the baseline epidemic is indicated by the arrow.

Economic analyses

The carcase collection and telephone advice scenarios produced net benefits in terms of reducing the overall economic cost of the BWD outbreak when compared to the baseline. Table 4 gives detailed figures relating to the magnitude and distribution of costs relating to BWD under the baseline and alternative scenarios.

Table 4 Summary of outputs from the economic model. 1 disability adjusted life year (DALY) equals 1 year of life lost due to disease (weighted for age), providing a measure of disease burden on society.

	Scenario 1 Baseline Surveillance	Scenario 2 Carcase collection	Scenario 3 Telephone Advice Line
Annual surveillance budget	**£3,739,283**	**£5,473,598**	**£4,052,933**
Cost of surveillance to point of detection	**£19,817,015**	**£26,984,109**	**£21,311,717**
Difference in surveillance cost at detection		**+£7,167,094**	**+£1,494,702**
Surveillance costs attributable directly to BWD	**£630,397**	**£731,326**	**£557,156**
Of which held by public sector	43.21%	44.39%	44.77%
Of which held by private sector	56.79%	55.61%	55.23%
Median cost of BWD outbreak	**£56,707,971**	**£43,423,914**	**£50,191,593**
5th percentile	£34,321,717	£29,146,319	£31,215,946
95th percentile	£91,496,223	£66,343,880	£81,495,273
Total public costs (median)	£1,627,519	£1,485,098	£1,510,767
Total private costs (median)	£55,080,452	£41,938,816	£48,680,826
Expected DALY cost	**545.04**	**393.64**	**484.48**
Median infected number of animals entering food-chain	**74,084**	**56,292**	**65,823**
5th Percentile	39,515	35,857	38,520
95th percentile	124,608	88,225	109,512
Median total animals infected	**106,209**	**81,030**	**94,397**
5th Percentile	59,185	52,607	56,786
95th percentile	176,416	126,597	156,235
Undiscounted net value (median values)		**£6,116,963**	**£5,021,676**
5th percentile		-£695,170	-£766,221
95th percentile		£12,891,705	£10,861,173

The two alternative scenarios both exhibited lesser degrees of variation around the most likely outbreak size, with the interquartile range being £22.8m for the baseline and £13.9m and £20.0m for the carcase collection and telephone advice line scenarios respectively. The median outbreak cost under the baseline scenario was £56.7m, the probability of having a larger outbreak being 1 in 6.94 in the carcass collection scenario, and 1 in 2.91 in the telephone advice line scenario. Taking the 95th percentile of the distribution of outbreak cost for the baseline as a worst-case scenario, the likely outbreak cost would be £91.4m with a probability of occurrence of 1 in 20 outbreaks. The probability of an outbreak of this magnitude occurring under the alternative scenarios would be 1 in 200 and 1 in 45.5 for the carcase collection and telephone advice line scenarios respectively. This relationship is illustrated in Figure 4.

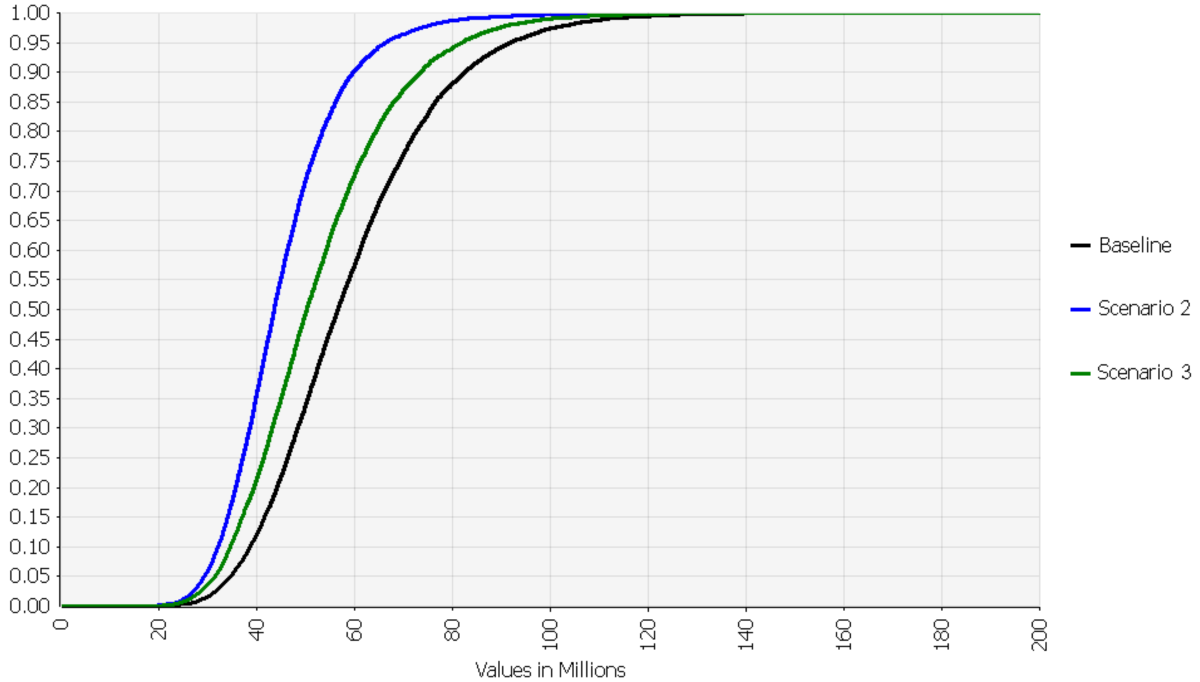

Figure 4 Cumulative probability (y-axis) of outbreak cost for baseline and scenarios 2 (carcass collection) and 3 (telephone database). The steeper curve indicates less variation in likely outbreak costs. The further a curve is to the left indicates a reduction in overall cost

Table 5 illustrates the marginal cost-effectiveness ratios calculated for the carcase collection and telephone advice line scenarios relative to the baseline.

Table 5 Summary of cost-effectiveness measures for surveillance changes under the carcase collection and telephone advice line scenarios using median values. DALY = Disability-adjusted life-year

Cost-effectiveness measures Additional cost per:	Scenario 2 Carcase collection	Scenario 3 Telephone advice line
Animal NOT infected	£285	£127
Infected carcass removed from food chain	£403	£181
DALY saved	£47,339	£24,681
Day to detection saved	£53,096	£99,061

Total outbreak costs (the sum of all modelled components for the duration of the epidemic) were in the main attributed to direct losses to the beef and dairy industries, which accounted for approximately 70% of costs under all scenarios. Figure 5 illustrates the breakdown of costs accrued within each component of the model. Of the total outbreak cost, over 96.5% was held by the private sector under all scenarios. Public costs accrued from surveillance activities and response to the detection of the new disease, that is, epidemiological investigations and raising disease awareness. Of the surveillance costs directly attributable to BWD, i.e. *post-mortem* examinations, *ante-mortem* testing and telephone consultations, approximately 55% of costs were covered by the private sector.

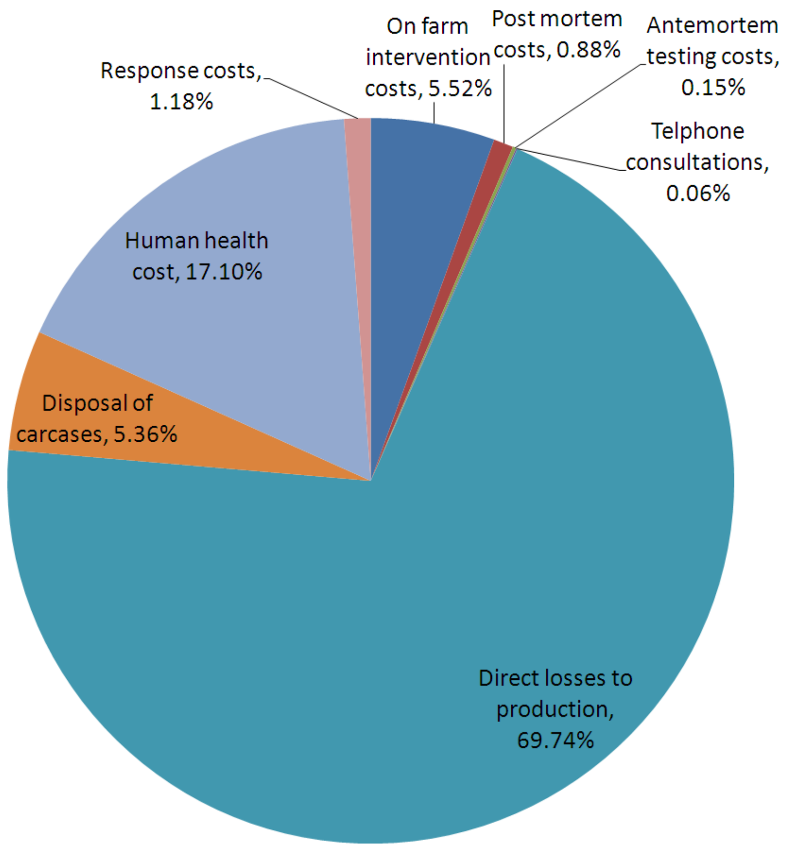

Figure 5 Total outbreak costs for the baseline divided by activity. Cost divisions were similar under both alternative scenarios.

Sensitivity analysis by step-wise linear regression identified the most influential inputs to the economic model as the number of animals dying from BWD (typical R^2 values of 0.45, 0.25 and 0.15 depending on source compartment), the greatest variation being attributed to the number of deaths in animals in the O compartment on dairy farms. Economic inputs identified as influential included the cost of replacement animals (typical R^2 values of 0.12 and 0.11 by production type) and the expected human caseload (typical R^2 value of 0.25).

4 Discussion of the results and their reliability

Results of the initial application of the model

This project illustrates the potential of a modelling approach to assess the value of future changes to the design and implementation of early warning surveillance. The occurrence, detection and control of a hypothetical disease (BWD) was simulated by the epidemiological model; the outputs of this model were integrated into a stochastic economic model to estimate the disease impact and conduct cost-effectiveness analyses of enhancements to early warning surveillance in cattle.

The results of this initial application of the integrated model suggest that both of the proposed additions to surveillance (the carcase collection system and the telephone advice line scenarios) could reduce the average time to detection (Table 3) and so the median total epidemic size and cost (Table 4), assuming the structure of surveillance and level of submissions current in 2012. Additionally, both of the enhancements to surveillance would realise a net economic benefit in 93% of epidemics of BWD and both showed an ability to limit the probability of a "worst-case" disease outbreak developing (Figure 4). The benefit of the carcase collection service was greater than for the telephone advice line.

Another interesting result of these simulations is that neither the DNR analysis nor the telephone database analysis mechanisms lead to detection of BWD in any of the scenarios. All outbreaks were detected by submission of a number of carcasses or discussions by a number of PVS with VIOs at a single RL. This is not inconsistent with the available data about how real outbreaks have been detected and confirms the importance of the existing communication networks between PVS and VIOs. However, different disease types are likely to elicit different responses from farmers, PVS and VIOs and therefore it is possible that different disease types may be detected by different surveillance streams to that simulated in the present study. Sensitivity analyses would allow us to investigate the dependence of these results on the thresholds chosen for different detection mechanisms.

Model parameterisation

The epidemiological model produced disease outbreaks in which the outbreak duration and time to detection were similar to those seen in the BSE epidemic in the UK although the total number of farms and animals affected by BWD was considerably lower than the number affected by BSE. However, further sensitivity analyses of the parameter estimates are required to establish the validity of these results. The focus of this work was on the development of a tool and the demonstration of its utility and although as much data as possible was collected to accurately parameterise the model there is still some uncertainty surrounding the estimates of some parameters.

The parameter estimates that are currently considered to be most uncertain are those describing the probability of farmer actions and the thresholds for detection which were based upon consultation with VIOs and the AHVLA cattle expert group. Parameterisation of the four detection mechanisms is expected to have a considerable impact on the model output in terms of time to detection and epidemic size. In addition, indirect losses to production (costs of veterinary treatment on-farm, interventions and carcass disposal) were shown to account for approximately 11% of total outbreak costs. Further investigation of parameters surrounding farmer and PVS actions would also allow for a more robust estimation of the associated costs.

There was limited data available on which to base the estimates of the likely impact of the enhancements to the surveillance system. The carcase collection service was expected to eliminate the impact of farm-lab distance on the probability of carcase submission. Estimates of the impact of this on submission levels was estimated using available data and this led to a roughly two-fold increase in the probability of carcase submissions. This is consistent with data from the Netherlands where a carcase collection system is in place and the probability of carcase submission from adult cattle dying on farms is estimated to be about three times that in UK (personal communication, Linda van Wuijckhuise). It was not possible to base the estimate of the likely impact of implementing a telephone advice service on available data so this was estimated by VIOs as likely to increase the probability of telephone contact by 50%. The proposed sensitivity analysis would allow further investigation of the likely impact of these assumptions. In addition AHVLA are proposing to conduct pilot studies to investigate the likely impact of changes to early warning surveillance which could provide data for estimating these effects.

The complexity of the data required as inputs for the economic model meant that it was not possible to fully automate the production of outputs from the epidemiological model during the time allowed for this project. Processing the data produced by the epidemiological model is currently very time-consuming and so it was only possible to conduct a relatively small number of simulations for each scenario (from 104 to 112). This limited the value of the epidemiological model output for examining the occurrence of “worst-case” epidemics under each scenario and also prevented formal sensitivity analyses of the parameter inputs. Improving the efficiency of the epidemiological model and conducting sensitivity analyses is a high priority area of future work.

A sensitivity analysis of the economic model was carried out which indicated the output was highly dependent on the inputs provided by the epidemiological model confirming the need for a sensitivity analysis of the epidemiological model. The most influential input to the economic model was the number of deaths in animals in the Observed group on dairy farms (R^2 value 0.45). The only economic inputs identified in the top ten most influential variables were the cost of replacement animals (R^2 values of 0.12 and 0.1), the labour requirement for keeping an animal in isolation (R^2 value of 0.06) and the expected human caseload (R^2 value of 0.25). The two former inputs were drawn from real data: DEFRA compensation prices for TB reactors which are defined as 100% of market value of the animal (November 2010 to October 2011) and from a survey of practices on 6 cattle farms (4 dairy, 2 beef). Expected caseload was based on estimates from literature for the number of infected animals entering the UK food chain with BSE (750,000, Anderson et al., 1996) and the number of human cases of vCJD to date (NCJDRSU, 2012).

Model structure

The long term aim of this work is to build a model that could be used to investigate the performance of early warning surveillance for different types of disease. The first step was to build a model to simulate the occurrence and detection of one example disease which could be adapted in the future to simulate the occurrence of other disease types. The intention in building the model was to provide a sufficiently realistic representation of the occurrence and detection of the chosen disease without including unnecessary complexity.

One of the simplifications used in the epidemiological model is that the cattle population included in the model is static and takes no account of herd age structure. This was sufficient for modelling a sporadic disease of low incidence that affects adult cattle – the baseline scenario saw an average of 2.4 affected cattle per affected holding over 20 years – but would not allow accurate epidemiological/economic modelling of diseases where the population at risk could not be so clearly defined. In the case of BWD, due to the long latency, all clinically affected animals could be modelled as breeding females.

The five states (SICOV) of the within-herd model were sufficient to describe the progression of disease and treatment of affected cattle for the untreatable and progressively fatal BWD. The Visited state prevented repeated PVS visits to individual animals and allowed the costs of isolation, treatment, palliative care visits and production losses to be taken into account. For example cows in the Observed group on dairy farms had a reduction in milk yield due to disease occurrence whilst those in the Visited group experienced 100% milk wastage due to antibiotic withholding.

Movement of cattle between herds was included by replaying the actual movements recorded in CTS which was considered to be a simpler and more realistic approach than generating cattle movements between herds and to slaughter (Vernon and Keeling, 2009). The static nature of the population meant that movements from three years of existing data were replayed in the model on a loop for the duration of the epidemics as the creation and establishment of new herds prevented the use of movement data spanning a longer time period. The impact of this approach to simulating cattle movements may be greater for diseases in which horizontal or vertical transmission of disease between cows occurs: transmission between animals could lead to significantly greater geographical spread of disease through animal movements. The simulation, rather than replaying of movements, would be especially important if the model were to be used to represent pathogen transmission where movement restrictions are placed on affected herds.

In the economic model the number of cases per infected animal entering the food-chain represents a simplification for assessing the true risk of transmission to humans. The true probability of transmission through contaminated flesh is contingent on many factors which would have had to be defined specifically for a hypothetical disease (degree of infectivity at stage of infection, tissues affected, effect of processing on infectivity etc). It was felt that defining such factors would be introducing greater complexity without adding value to the project outcome.

The model currently assesses disease outbreak cost with minimal state intervention in response as this was deemed to be most appropriate in the current political climate by discussion with Defra staff (Gibbens, J., personal communication). Historically response has been a major component of disease cost, for example the total cost of compensation payments for BSE in the UK has been estimated at 2.4 billion USD (Morgan and Prakash, 2006). Such compensation payments have the ability to cause a dramatic shift in the division of costs between the public and private sectors. In the case of BSE 63.5% of the total cost to the UK economy has been estimated to have fallen on the public sector (Morgan and Prakash, 2006). By comparison, the model predicts 96% of BWD outbreaks would fall on the private sector. Further work would enable different response scenarios to be modelled using the framework devised (Figure 4 in Annex 2: *Economic model to assess the value of changes in early warning surveillance in England and Wales).*

The economic model did not explicitly examine the impact of BWD on trade of livestock and livestock products: it was assumed that the impact on public health was realised post-epidemic. Consideration of the impact of animal disease on access to domestic and international markets for the trade of livestock and livestock products and consumer confidence in these products will have a significant impact on the estimates of total economic cost of an epidemic – particularly for an epidemic enduring for many years.

For example, following the announcement of a potential link between BSE and nv-CJD in 1996, UK exports of beef and veal fell from 300,000 tonnes a year to virtually zero. Recovery in export volumes was only seen after the lifting of the EU trade ban on British beef was lifted in 2006; however the UK remains a net importer of beef to this day.

Since the UK is a net importer of beef, it is suggested that a market shock due to a health scare such as BWD would reduce demand for UK produced beef. At retail level, this fall in demand would be likely to be offset by increased imports and movements to alternative products (Morgan and Prakash, 2006). The market power of UK grocery retailers would potentially result in increases in retailer-producer and retailer-wholesaler price spreads (Lloyd et al., 2001, Lloyd et al., 2006). It is suggested therefore that the cost of any reduced trade in British beef would be felt most strongly at producer and wholesale level and in industries with strong links to these levels of the beef supply chain.

The introduction of risk mitigation measures, such as the Over Thirty Months Scheme used during the BSE epidemic removed a significant number of animals from the food-chain, mainly cull cows from the dairy sector. The UK cull cow market slaughtered 448,000 animals in 2010 and 530,000 animals in 2011. The total farmgate value of these animals is estimated at £261m in 2010 and £383m in 2011 (EBLEX, personal communication). If such a scheme were reintroduced in response to an emerging disease threat some proportion of this value would have to be transferred to the public purse in the form of compensation payments. Further, supply of certain cuts of meat would have to be sourced elsewhere, increasing the UK's reliance on beef imports.

Morgan and Prakash (2006) state that historically the impact of disease-related market shocks is thought to be short-lived and markets typically recover within a few years. Yet the data (see Appendix 1) indicate that after 10 years the UK beef market has yet to recover from the emergence of BSE, either in terms of price or volume. Exports from the UK have also not returned to previous levels. The initial shock took place in 1996 and such diseases had long and important impacts on the sector.

5 Main implications of the findings

We have integrated epidemiological and economic models to develop a tool to evaluate the economic performance of early warning surveillance and demonstrated its usefulness. This has involved the successful simulation of a disease outbreak under different surveillance scenarios using real demographic data and assumptions regarding disease reporting behaviour. The outputs from this simulation were used together with market prices, demographic statistics and expert opinion in an economic analysis.

As discussed above the results of this initial implementation of the model are heavily dependent on the assumptions made about parameter estimates, some of which are still subject to a considerable amount of uncertainty. Further sensitivity analysis is required to clarify the impact of this uncertainty. Bearing in mind this uncertainty, the results of our initial application of this tool suggest that the design of early warning surveillance in England and Wales, as implemented in 2012, could be enhanced to allow earlier detection of disease and reduce epidemic costs. Because the costs of enhancement were estimated to be lower than the loss avoidance, both types of enhancements would result in a net benefit over the simulated time period. The results also highlight the importance of enhancing existing communication networks between PVS and VIOs as well as enhancements to the statistical analysis of data sources.

The design and implementation of early warning surveillance in England and Wales is currently undergoing a process of change. The AHVLA's *Surveillance 2014* project is currently engaged in redesigning the delivery of surveillance in England and Wales to accommodate future public budgets and the recommendations made by the Independent Surveillance Advisory Group (SAG 2012). Changes to the design and implementation of surveillance in England and Wales will limit the applicability of the epidemiologic and economic models in their current state but not the method developed by this project; future applications of the combined models will require updates to the structure of the models and parameter values accordingly.

These results have demonstrated that enhancing early warning surveillance may be beneficial for this example disease which is transmitted via feed, has a very low incidence, long incubation period and does not spread between individual animals. This example disease was chosen as one which has some features in common with BSE, a disease type for which detection is likely to be heavily dependent on the efficiency of the early warning surveillance system used. However, early warning surveillance operates to detect changes in the occurrence of numerous endemic, exotic and emerging diseases simultaneously. The efficiency of early warning surveillance will also have an impact on the ability to detect other disease types. So the impact of changes to the design and implementation of early warning surveillance should not be considered solely in the context of a single type of disease (like BWD). The impact of proposed changes would need to be explored in the context of the probability of an outbreak occurring for various disease types and different production sectors. If the enhancements to surveillance would also reduce detection time for other diseases and the related outbreak costs, the net value of surveillance enhancements would be larger and our results can be interpreted as a "conservative" outcome. Hence, inclusion of other diseases and increasing the complexity of the model is expected to add to the assessment of the net value of enhanced surveillance.

Likewise the costs of enhancements to surveillance were modelled as an addition to the budget for early warning surveillance in cattle. In reality these services would be utilised across sectors and therefore potentially add value to surveillance in all species, with the costs split between different budgets.

6 Possible future work

The epidemiological and economic models developed were based upon the design and delivery of early warning surveillance in England and Wales in 2012. A key area of further work will be to take account of changes to early warning surveillance arising from the AHVLA's *Surveillance 2014* project in terms of the structure and parameterisation of the two models.

As discussed above it was not possible to fully automate the production of output data from the epidemiological model during the time frame of this project. This has limited our ability to conduct sensitivity analyses and would limit the ability to apply the model to other disease types. Enhancing the efficiency of the epidemiological model and carrying out a sensitivity analysis to assess the impact of the uncertainty surrounding the input parameters is a priority area for future work.

We also discussed above the need to apply the model to different disease types to provide a full assessment of the benefits of enhancing early warning surveillance systems. The selection process for diseases to be included could be based on a risk assessment that would estimate the probability of emergence or incursion (for exotic diseases) and allow an assessment of the likelihood of occurrence of these diseases.

In addition the work carried out so far has assumed that the enhancements to surveillance were implemented for the duration of the BWD outbreak until detection occurred but in reality surveillance enhancements are likely to continue for a longer time period. Investigation of the benefit of surveillance taking into account the likelihood of disease occurrence and using varying time frames for enhanced surveillance would be useful.

Another consideration in making a full assessment of the value of surveillance is that the model was developed to perform an incremental economic analysis, i.e. two additions to surveillance were compared with the baseline system in place. Such an approach does not allow an assessment of the economic value of the system in place. Adaptation of the epidemiological and economic models would allow investigating this type of question, although this may be difficult as it would require major assumptions to be made about how disease detection might occur in the absence of a formal early warning surveillance system.

The final issue to consider when assessing the benefits of additions to surveillance is that only two enhancements to the existing surveillance system were assessed in this work. It may be necessary to consider other enhancements, including the incorporation of other data steams and combinations of these enhancements to inform decisions about changes to early warning surveillance.

An additional benefit of applying this approach to real diseases would be the ability to validate the model output against real data and help to clarify critical assumptions made. In order to apply these models to different diseases some elements of the model design and parameterisation will need to be adapted. These adaptations could include a review of the parameter estimates and model structure used to simulate farmer and

PVS behaviour, incorporation of age structure into the model, review of the compartments used for the disease transmission dynamics and adaptation of the economic model to incorporate varying responses and trade effects. Each of these possible adaptations is described in more detail below.

Farmer and PVS behaviour regarding treatment of affected animals and use of diagnostic services will be influenced by many factors including the biology of the disease (ie the conspicuousness of signs and impact on productivity), herd-level factors (eg production type and location) and the cost and perceived value of AHVLA diagnostic services. These parameter values would need to be re-defined when applying the model to other diseases.

Changes to the model structure, beside those concerning changes to the future delivery of surveillance, may also need to be considered: The current model structure permitted farmers to cull animals observed to be clinically affected to the abattoir but not sell them to other farms – movement to other farms may be required for diseases with less conspicuous clinical signs and/or milder impacts on productivity. It may also be desirable to incorporate more complexity in PVS behaviour parameters to allow PVS submissions to depend on whether telephone calls was made to AHVLA or whether they have previously seen similar cases on other farms. In addition the model assumes that all practices are similarly likely to contact the AHVLA and use the diagnostic services offered. Analysis of FarmFile submission data suggests around 70% of registered cattle practices in GB submit samples to AHVLA each year; exploring such heterogeneity in coverage might be of value in future applications of the model.

In order to apply the model to another disease which affected animals of all ages and types, adding an age structure to the population would enable the decision-making process to be parameterised separately for different subsets of the population at risk.

The model is currently structured to allow feed borne transmission of infection but could be relatively easily adapted for other modes of transmission. The compartmental structure will need to be reviewed. For example, to allow for situations in which infected cattle may recover and become immune (eg Schmallenburg virus) would require the inclusion of a *Recovered* compartment. The uses of the *Visited* group to accurately model the actions applied to affected animals beyond their initial treatment may also require review.

In addition to these modifications to the epidemiological model some adjustments to the economic model may be required to take account of varying responses and trade effects of different disease types. An important point would be to look at producer and consumer surplus with changes in supply and demand curves and different prices. With inclusion of age structure in the epidemiological model, we could also look at issues related to animal replacements.

In summary the suggested next steps are

- To update the models to accommodate changes in the design and delivery of surveillance in England and Wales.
- To enhance the efficiency and carry out sensitivity analysis of the epidemiological model. This is considered to be high a priority and would be required prior to publication of the model in a peer reviewed journal.
- Validation of the model by applying it to a known disease with appropriate review and modification of the model structure and parameters as described above
- Obtaining a more comprehensive picture of the added value of enhanced surveillance by application of the model to different disease types (with appropriate model modifications as described above), with varying time frames for enhanced surveillance, different surveillance enhancements and if possible an assessment of the value of early warning surveillance

Annex 1 – Documentation of the epidemiological model of early warning surveillance

SE4303 epi annex 25jun2013.doc

Annex 2 – Documentation of the economic model of early warning surveillance

SE4303 - Annex 2

Appendix 1 – Further discussion of trade impacts of Bovine Wasting Disease

SE4303 - Appendix 1

References to published material

9. This section should be used to record links (hypertext links where possible) or references to other published material generated by, or relating to this project.

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