

EXTERNAL SCIENTIFIC REPORT**Model for the evaluation of different options for the monitoring of Transmissible Spongiform Encephalopathies in cattle in the European Union (C-TSEMM)¹****Amie Adkin, Robin Simons and Mark Arnold**

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ABSTRACT

The Cattle TSE Monitoring Model (C-TSEMM) has been developed to evaluate different Transmissible Spongiform Encephalopathy (TSE) monitoring regimes in cattle by estimating the trend of the current BSE epidemic within European Member States (MSs). The model has been developed to investigate various sampling scenarios, including the current system of systematically sampling cattle at certain ages and other options such as random sampling of healthy cattle. The model estimates the minimum underlying prevalence in the adult bovine population for each MS which the monitoring regime would be able to detect, together with the sample size from the healthy slaughter stream required for the monitoring regime to detect a specific underlying prevalence of BSE in the adult population (known as the 'design prevalence'). The model can also be used to assess the ability of those schemes to detect either the re-emergence of an existing TSE or emergence of a new TSE disease in cattle. It is assumed that any new disease can be detected by current testing assays. Given an alternative monitoring scenario, estimates can be made for the number of years taken for a monitoring regime to detect a significant increase in cases due to the re-emergence/emergence of a TSE disease in cattle and the number of detectable cases and infected animals that would occur in this time. Results in this report are produced for the baseline and alternative scenarios for the EU25 based on individual MS BSE test positives data, the number of animals tested between 2001 and 2011, and the standing population. When developing the generic model to cover all EU25 MSs, a number of assumptions were made which need to be highlighted, including selected distributions within the calculations and the use of average prevalences for those countries who have reported no, or few, cases post 2001.

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KEY WORDS

cattle, BSE, TSE, model, monitoring

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* Changes were made to the summary, main body of the text and conclusions as a consequence of a correction made in the initial number of samples that was taken as data input in the model considered for the EU in 2002.

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SUMMARY

This is the final report for project CFT/EFSA/BIOHAZ/2011/02: Provision of a model for the evaluation of different options for the monitoring of Transmissible Spongiform Encephalopathies (TSEs) in cattle in the European Union (EU25). This final report presents the model framework and calculations together with the input data required and key assumptions made. Results are provided for each Member State (MS) in the EU25 and merged results for the EU25.

The Cattle TSE Monitoring Model (C-TSEMM) has been developed, supported by a user-friendly interface, to evaluate different Bovine Spongiform Encephalopathy (BSE) monitoring regimes in cattle and the ability of those schemes to detect either the re-emergence of an existing TSE or emergence of a new TSE disease in cattle, by estimating the trend of the current BSE epidemic within Member States (MSs). The C-TSEMM uses individual MS BSE test positives data and the number of animals tested between 2001 and the current time (for the results presented in this report this is 2011, but the model will automatically adjust to the most recent year in the input datasets), divided into four exit streams (healthy slaughtered animals, emergency slaughtered animals, fallen stock and clinical suspects). The model provides different methods to evaluate both the current 'baseline' monitoring regime and alternative hypothetical monitoring scenarios by estimating

1. The minimum underlying prevalence of BSE in the adult bovine population which the monitoring regime would be able to detect.
2. The sample size of adult bovine animals from the healthy slaughter stream required for the monitoring regime to detect a specific underlying prevalence of BSE in the adult population (known as the 'design prevalence').
3. The number of cases that would be missed by an alternative monitoring scenario, compared to the current baseline regime.
4. The number of years taken for a monitoring regime to detect a significant increase in cases due to the re-emergence of an existing TSE or emergence of a new TSE disease in cattle and the number of detectable cases and infected animals that would occur in this time. Results are produced for the baseline and alternative scenario's, calculating any difference in the years to detection, and the number of additional cases and infected animals that would occur during this time.

In this report the baseline regime is defined as the testing of all healthy slaughter animals >72 months, emergency slaughter (ES) and fallen stock (FS) animals >48 months and all clinical suspect (CS) animals, while the theoretical monitoring scenario assumes the same testing for the ES, FS and CS streams but no healthy slaughter animals are tested. The interface provided enables the user to choose alternative values for input parameters including the start and end testing ages for the monitoring regime, the proportion of animals tested, the MS (to be run separately or as a merged epidemiological unit), strain type or merged strain grouping, and the values for the age at onset and test sensitivity.

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BACKGROUND AS PROVIDED BY EFSA

The data collected in the framework of the European Union (EU) Bovine Spongiform Encephalopathy (BSE) monitoring system permits the trend of the disease to be followed and thus, it is a fundamental tool for the risk manager to assess the efficacy of the risk management measures taken against BSE. The objectives of this monitoring are:

- To monitor the declining trend of the current BSE epidemic;
- To detect a hypothetical re-emergence of the BSE epidemic;
- To detect a hypothetical new TSE disease in cattle.

Currently, BSE monitoring in cattle in the EU is undertaken through both active and passive surveillance in different testing groups². Active surveillance is based on the systematic post-mortem testing of the healthy slaughtered cattle after animals reach certain age, and of “at risk cattle”, which include: (i) animals showing any clinical abnormality during ante-mortem inspection prior slaughter, (ii) emergency slaughtered animals and (iii) fallen stock. Passive surveillance is carried out by testing all animals that are clinically suspect of BSE. Another testing group includes some cohort associated animals with a BSE case occurring in a farm.

EFSA has issued five Scientific Opinions on the basis of a model developed by EFSA Experts in the context of the revision of the BSE monitoring regime in some EU MSs (EFSA, 2008a, 2008b, 2009, 2010, 2011)³. These Opinions follow requests made by the European Commission for the revision of the BSE monitoring regime, in view of the declining epidemic of the Classical BSE in cattle in the EU. These Opinions provided scientific basis for the increase of the age at testing based on the estimation of the number of BSE cases expected by birth cohort. This estimation relied on detailed cohort based data on BSE cases collected in the EU.

The aforementioned model developed by EFSA Experts is tailored in order to reply to specific questions, and is not designed for evaluating EU TSE monitoring options in cattle that may be considered in the future by the European Commission (EC), keeping in mind the objectives of the monitoring system as previously described. These options may include, for example, a monitoring system whereby a random sample of the healthy cattle population would be tested for TSEs rather than the systematic testing of cattle in particular age groups, as it is currently performed. However, the capacity of the TSE monitoring system in cattle in the EU to monitor the evolution of known TSEs and the hypothetical emergence of a new type of TSE in the bovine population should be maintained. This is in line with the strategic Commission paper “TSE Roadmap 2”⁴.

The revision of the TSE monitoring regime in cattle in the EU may require consultation within EFSA

² The testing groups are: Clinical suspects of BSE, healthy slaughtered cattle, fallen stock, emergency slaughtered cattle, animals showing abnormalities during *ante-mortem* inspection, and animals slaughtered in the frame of eradication measures.

³ EFSA Panel on Biological Hazards (BIOHAZ), 2008a. Risk for Human and Animal Health related to the revision of the BSE Monitoring regime in some Member States. The EFSA Journal, 762, 1 – 47; EFSA Panel on Biological Hazards (BIOHAZ), 2008b. Further considerations of age-related parameters on the Risk for Human and Animal Health related to the revision of the BSE Monitoring regime in some Member States. The EFSA Journal, 763, 1-8; EFSA Panel on Biological Hazards (BIOHAZ), 2009. Updated risk for human and animal health related to the revision of the BSE monitoring regime in some Member States. The EFSA Journal, 1059, 1-40; EFSA Panel on Biological Hazards (BIOHAZ), 2010. Opinion of the Scientific Panel on Biological Hazards on a second update on the risk for human and animal health related to the revision of the BSE monitoring regime in some Member States. The EFSA Journal, 8(12), 1946; EFSA Panel on Biological Hazards (BIOHAZ), 2011. Scientific Opinion on the review on the risk for human and animal health related to the revision of the BSE monitoring regime in three EU Member States. EFSA Journal 2011;9(4):2142. [4 pp.]

⁴ TSE Roadmap 2 available at: http://ec.europa.eu/food/food/biosafety/tse_bse/docs/roadmap_2_en.pdf

and in particular with the Scientific Panel on Biological Hazards (BIOHAZ). The availability in EFSA of a model to assess epidemiological aspects of different TSE monitoring options in cattle should provide a robust tool for supporting scientific outputs of the BIOHAZ Panel.

TERMS OF REFERENCE AS PROVIDED BY EFSA

Based on the contract/grant number: CFT/EFSA/BIOHAZ/2011/02, the specific objectives of the contract resulting from the procurement tender are as follows:

- To develop a flexible and transparent model supported by a “user-friendly” interface capable of evaluating different TSE monitoring options in cattle employing EU BSE monitoring and cattle population data as well as the performance characteristics of different TSE tests (e.g. sensitivity and specificity, probability of negative, probability of positive, time of first detection during the incubation period):
- To provide results of the evaluation of some possible TSE monitoring options as agreed with EFSA and based on different epidemiological scenarios. These results should be based on scenario analysis done over an initial baseline model that would evaluate the performance of the current BSE monitoring regime.
- To provide EFSA with two draft reports and a final report.
- To develop a user manual.
- To deliver a training session to EFSA staff and other potential users.
- To work closely with EFSA and with relevant experts and to participate in at least four physical meetings with EFSA (in which at least one might be in Parma).
- To provide corrective maintenance: to produce updated versions during the period after delivery of the program until the end of the contract where necessary.

This report addresses in detail the first two specific objectives, while the other ones are tackled through different outputs, namely:

- An independent user manual.
- Physical training session to EFSA staff and other potential users.
- Regular meetings with EFSA and relevant EFSA Experts.
- Provision of a maintenance period for a period as agreed in the contract.

This contract was awarded by EFSA to:

Contractor: Animal Health and Veterinary Laboratories Agency (AHVLA)

Contract title: Provision of a model for the evaluation of different options for the monitoring of Transmissible Spongiform Encephalopathies in cattle in the European Union.

Contract number: CT/EFSA/BIOHAZ/2011/03

INTRODUCTION AND OBJECTIVES

Transmissible Spongiform Encephalopathies (TSEs) are a group of serious conditions that affect the brain and nervous system of various animals including cattle. Regulation in Europe⁵ to control the disease in cattle currently involves extensive testing and removal of high risk bovine tissues from the food and animal by-products chain, together with the ban on the use of proteins of animal origin in feed for farmed animals (with certain exemptions). This is complemented by surveillance in order to monitor the impact of control measures. In view of the continuing steady decline in the number of Bovine Spongiform Encephalopathy (BSE) infected cattle and the lack of emergence of BSE in sheep, it is therefore useful to re-evaluate the level of intervention required to achieve acceptable levels of risk reduction taking into account the needs of surveillance systems to monitor the declining trends of the disease.

In order to quantitatively and systematically evaluate the current monitoring regime within EU25 MSs, and theoretical systems which may be employed, the Animal Health and Veterinary Laboratories Agency (AHVLA) were commissioned by EFSA to develop a mathematical model which would be able to evaluate the effectiveness of different BSE monitoring regimes in cattle and the ability of those schemes to detect either the re-emergence of an existing TSE or emergence of a new TSE disease in cattle. The mathematical model developed by AHVLA is based on a modified back-calculation model (Arnold and Wilesmith, 2003).

Previous research suggests that the prevalence of BSE in cattle is strongly dependent on the year of birth. For example, the incidence is highest among animals born in 1987-1989 for UK cases of BSE. Therefore, when considering whether an animal will test positive at the current time, it is important to consider the year it was born (known as the 'birth cohort'). The C-TSEMM uses historical, MS specific data to estimate the BSE trend using an exponential distribution over birth cohorts and testing periods. This trend is then used to estimate the number of detectable cases and infected animals divided into the four exit streams (healthy slaughter (HS), emergency slaughter (ES), fallen stock (FS), or clinical suspects (CS)).

C-TSEMM has been developed to be a transparent and flexible software package in R, with a bespoke user-interface in VBA for users to input parameter estimates and alternative monitoring scenarios. Therefore, the model is capable of investigating various theoretical monitoring scenarios and includes the current regime of sampling all cattle above certain ages. Other potential options such as random sampling of the healthy cattle population can also be modelled. The model can be run using all available case data. However, where available, strain differentiated data can be used to model classical and unknown type separately from the atypical strains L and H types.

For the purposes of the results presented in this report, the *baseline* monitoring regime simulates current EU25 testing, defined as the testing of all healthy slaughter animals >72 months, emergency slaughter and fallen stock animals >48 months and all clinical suspect animals (as listed in Appendix A), with the alternative theoretical monitoring scenario defined as testing the same in the ES, FS and CS stream, but removes the testing in the HS stream.

To estimate the results, there are three underlying prevalence estimates used:

- **Detectable prevalence in test population:** Period prevalence in a given year of detectable infected animals in the test population. Calculated by the model's predicted number of adult

⁵ Regulation (EC) No 999/2001 of the European Parliament and of the Council of 22 May 2001 laying down rules for the prevention, control and eradication of certain transmissible spongiform encephalopathies. *Official Journal* L 147, 31.5.2001, p. 1-40

animals (>24 months), in the population of animals tested, that would test positive by a diagnostic test, divided by the total number of animals tested in one year.

- **Infection prevalence in test population:** Period prevalence in a given year of infected animals in the test population. Calculated by the model's predicted number of adult animals (>24 months), in the population of animals tested, that are actually infected (i.e. animals that may or may not test positive or be showing clinical symptoms) divided by the total number of animals tested in year.
- **Detectable prevalence in standing population:** Period prevalence in a given year of detectable infected animals in the standing population. Calculated by the model's predicted number of adult animals (>24 months), in the standing population, that would test positive by a diagnostic test, divided by the total number of adult animals in the standing population.

The model provides different methods to evaluate both the baseline monitoring regime and alternative monitoring scenarios. Given the model prediction of the underlying trend in BSE prevalence in the population, each monitoring regime can be assessed according to the following estimates:

1. The underlying prevalence of BSE in the population (1 in X) which the monitoring scenario would be able to detect.
2. The sample size of animals to be tested from an individual stream, for example, healthy slaughter, required to detect a specific underlying prevalence of BSE in the population (known as the 'design prevalence') at a defined confidence level, given the testing in the remaining three streams.

In addition, there are analyses developed to estimate the overall sensitivity of a monitoring system, in terms of the number of test positive animals the monitoring regime is able to detect and the time taken for the system to detect a theoretical increase in a bovine TSE.

3. Comparison of the estimated number of animals detected over one year between monitoring baseline and scenario, for example, number of test positives animals missed if there is a reduction in the number of healthy slaughter animals tested:
 - a. Difference in the number of detected animals (those animals which if tested would test positive) in one year between regimes.
 - b. Total number of infected animals slaughtered/dead per year.
4. Comparison of the estimated number of years taken to detect a hypothetical increase in a bovine TSE between baseline and scenario:
 - a. Number of years taken to cross upper confidence limit.
 - b. Difference in the number of test positive animals detected by baseline and scenario during the time interval between initiation of hypothetical increase and detection.
 - c. Difference in the total number of infected animals slaughtered/dead during the time interval between initiation of hypothetical increase and detection.

The model can consider the impact of either the re-emergence of an existing TSE or emergence of a new TSE disease in cattle given that the disease can be detected by current testing assays. Users can insert different parameters to estimate the age at onset, test sensitivity, and use strain differentiated test positive data to model different strains or a hypothetical strain.

MATERIALS AND METHODS

The materials and methods section of the report provides an overview of the model elements together with discussion on the model inputs and key assumptions made where data gaps exist. The precise formula and calculations used in the model with a summary of input parameters described in Appendix Table B1.

1. Model Overview

Central to the outputs of the model is the estimated underlying trend in the detectable prevalence (test positive cases) and the prevalence of infection for each MS or groups of MSs. The model estimates the detectable prevalence in defined exit streams from historical testing and case data and user defined inputs using a back calculation model (Arnold and Wilesmith, 2003). Briefly, if estimates are available for the age at onset, test sensitivity and the probability of survival to a given age, then an estimate of the fraction of infections that result per year in detectable cases can be made.

The estimated underlying trend in the detectable prevalence and prevalence of infection can then be used to estimate the sample size required to detect a prevalence of at least 1 case per 100,000 adult cattle to a desired confidence level. Alternatively, the prevalence trend and knowledge of the actual number of animals sampled within a monitoring scheme can be solved to estimate the relative prevalence of BSE in the population which a defined monitoring regime would be able to detect.

1.1. Estimating the true prevalence

Available input data by age interval in months and testing year (year of sampling) are converted into birth cohort and testing year. It is assumed that cases from the combined streams of clinical suspect and fallen stock (CSFS) streams are identified at the end of the incubation period, whereas healthy slaughter and emergency slaughter (HSES) stream animals may be within a period of time before clinical onset depending on the distribution of the age at onset and test sensitivity. Maximum likelihood methods are used to estimate two parameters for the best fitting exponential distribution (estimating the trend in prevalence) and one parameter, defined as the differential slaughter parameter, determines the division in prevalence between the combined CSFS exit streams and HSES exit streams. The equations for estimating the true prevalence of infection by birth cohort are provided in Appendix B.1. This generic model for estimating the prevalence trend, probability of detecting a test positive, and probability of an infected animal by birth cohort by testing year is applied to all MS data. While other distributions could be fitted, analysis of alternative distributions has indicated that an exponential decay of prevalence over time is appropriate for the majority of European data.

For MSs with no, or few, BSE cases post 2001 an alternative estimate of prevalence is required. This has been estimated for those MSs based on the average prevalence of the group of MSs with BSE cases under which they were placed in the previous EFSA Opinion (EU17 or the EU8 group)⁶ and are listed in Appendix C.

To indicate a measure of the level of uncertainty about the model results, 95% Poisson confidence intervals are fitted about the model estimates of test positive animals.

The determined values for the exponential curve for the detectable prevalence and the differential slaughter parameter are subsequently used to estimate the number of test positive animals in the combined exit streams. Using these estimated parameters, the probability of an animal at testing year y and cohort c testing positive in the CSFS streams can be estimated and the probability of testing

⁶ EU17: Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Slovenia, Spain, Sweden and United Kingdom;

EU8: Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland and Slovakia

positive in the HSES streams.

These probabilities are then used to estimate the probability of infection by cohort by year. The key assumption that animals testing positive in the CSFS stream are considered to be at the end of the age at onset when tested for BSE impacts the number of infected animals within these streams. The number of infected animals within these streams is estimated as the number detected and those not detected due to test sensitivity. For the CSFS stream it is assumed that all animals are detectable, and therefore the difference between the number of test positive animals and the number of infected animals is small and equal to the test sensitivity at clinical onset (0.99). In estimating the probability of infection for HSES stream, an estimate is included of those animals infected which would not test positive due to the distribution in the age at onset. Therefore, the estimated number of infected but not detectable animals in the HSES streams is relatively higher than for number estimated in the CSFS streams.

Case data by strain, where available, can be used in separate analyses. The baseline scenario includes all strain data. Other possible combinations, which the user may define, are listed as type H, type L, classical and unknown, and type H and L. It is assumed that all cases of BSE are typed by strain such that the number tested for classical and unknown strains is the same number as that tested for atypical H and L type. This is not the case for all MSs. Although separate analyses can be conducted using L and H data, there are currently insufficient case data for the majority of MSs to permit separate country analyses. France is one exception where a significant number of atypical cases have been differentiated.

1.2. Estimating the number of animals testing positive and infected animals by exit stream

Given the totals for the estimated number of infected animals and cases in the CSFS and HSES combined streams, the proportion of test positives from birth cohort c at testing year y , are divided into the individual streams, according to the proportion of test positive animals observed in those streams. The equations for apportioning animals by stream are provided in Appendix B.2.1.

There are many MSs datasets where there are no test positives by exit stream, by birth cohort by year. Analysis of the data suggests that the proportion of test positives by exit stream varies by MS, over both age and testing period, so a universal average value would not be appropriate. Cases from early testing periods were more frequently observed in the ES than the HS exit streams. However, the total number of animals tested in the ES has changed significantly for many MSs in recent years. Therefore, where there are no test positives, it is assumed that the number of animals tested from birth cohort c at testing year y is an appropriate proxy.

1.3. Design prevalence calculations

The estimated underlying trend in the detectable prevalence and prevalence of infection are used to estimate the sample size required to detect a prevalence of at least 1 case per X adult cattle (those >24 months) in (i) the tested population, and (ii) the standing population. The equations for estimating the design prevalence are provided in Appendix B.3.

In order to estimate the number of animals to sample at the specified design prevalence, it is important to account for the relative prevalence in each surveillance stream; the apparent prevalence in each stream varies between MSs and this will influence, for example, the number of healthy slaughter animals that need to be sampled in each MS, i.e. if a relatively high proportion of infected animals end up in a stream with a high prevalence, such as fallen stock, then fewer healthy slaughter animals will need to be sampled in the MS in order for the design prevalence to be detected.

The steps in the calculation for the number to sample for a specified detectable prevalence are as follows:

1. Using the back calculation model, we estimate the detectable prevalence in each surveillance stream and in the standing population (estimated in section 1.1. and apportioned by stream in section 1.2).
2. We scale the estimated prevalence to be 1 in 100,000 for the detectable prevalence in either (i) the tested population, or (ii) the standing population, depending on which specification of design prevalence is being considered. This provides us with the detectable prevalence in each surveillance stream at the specified design prevalence.
3. We calculate the number of healthy slaughter animals required to be sampled, given the number tested in other streams remains unchanged. To do this we use binomial probabilities and calculate the number to be sampled so that there is a 95% probability of detecting at least one positive animal.

The calculation for a given infection prevalence follows the same aforementioned steps, with the use of “infection prevalence” instead of “detectable prevalence”.

Given disease within a MS, the prevalence in the clinical suspect stream is assumed to be independent of the prevalence in the standing population as this stream is specifically established for BSE in cattle. The prevalence in this stream is determined by the correct recognition of BSE infected animals displaying clinical signs which varies between MSs. Therefore, the number of animals tested is scaled rather than the prevalence. This is due to the fact that changes in the underlying prevalence within a MS would directly change the number of clinical suspects tested rather than altering the proportion of animals that test positive. For example, if the baseline prevalence in the total population is 10%, the number of clinical suspects tested 10, and the number testing positive 1, then the prevalence in the clinical suspect stream is 0.1 (1/10). If we assume that the underlying prevalence increases to 20% and the prevalence in the clinical suspect stream was scaled accordingly, then the prevalence would equal 0.2 with 2 test positives out of 10 clinical suspects tested. However, if the underlying TSE prevalence increases it is more biologically reasonable to assume that this would result in an increase in the number of clinical suspects tested, rather than an increase in the stream prevalence.

Given the relative prevalence in each stream, number tested in each stream and a desired confidence interval, the equation for design prevalence can be rearranged to estimate the ‘design prevalence’ that a given monitoring system is achieving. The equations for estimating the detectable prevalence of a specified monitoring regime are provided in Appendix B.3.1. The analysis is implemented by solving for the value of the design prevalence at which the estimated number of animals to be tested in each stream is equal to the actual number of animal tested.

1.4. Sensitivity of the monitoring system: number missed

To investigate the effects of changing the baseline monitoring regime, an alternative scenario with different testing requirement can be compared as detailed in Appendix B.4. In this report, results are shown comparing the baseline and the alternative monitoring scenario defined as the same as the baseline except that no healthy slaughter animals are tested. To calculate the number missed between monitoring regimes the most recent testing data is used to estimate the number of test positives detected by each scheme.

1.5. Sensitivity of the monitoring system: detecting (re) emergence

Changes to monitoring systems may affect the ability to detect long term trends in prevalence of TSEs in cattle, for example, a re-emergence due to a novel exposure route, or the emergence of a

hypothetical strain of TSE that is detectable via current test assays.

Increasing the age when cattle are tested would prevent the detection of any possible emergence of TSEs with similar characteristics to BSE, that is, predilection for infection in young cohorts and long incubation periods to clinical onset.

To evaluate a change in the current declining prevalence of cattle BSE to a theoretical emergence, the number of cases is increased, assuming a percentage increase per year. The percentage increase per year can be defined by the user, with options of 3%, 10%, and 20%. A value of 10% has been used for results presented in this report. The model predicted trend is used to estimate the year when an increasing trend in TSE prevalence will be detected, which is defined as the year in which the number of test positives will exceed the upper confidence limit estimate for the number of test positives in the current testing year. The formula for the calculation is provided in Appendix B.5.

It should be noted that using the upper confidence limit by year does not consider the increase in prevalence by birth cohort and thus may underestimate the time taken for a theoretical form of TSE where young animals are more likely to become infected from exposure than the general population. Prevalence increases applied by birth cohort are likely to increase more slowly. Forecasting methods by birth cohort were trialled and although viable models were developed for certain MSs, a simple, generic model applicable across all MSs, could not be developed in the time available.

2. Input data

In order to estimate the trend of the current BSE epidemic for individual MSs, country specific data on the historical number of cattle tested and test results are required. Disease specific parameters are required as inputs for the probable age at onset and the sensitivity of the diagnostic test. This section of the report details the input data required for the model, data gaps and assumptions made to fill those gaps. A summary table of input parameter is provided in Appendix Table B.1.

2.1. Member State data

The model requires annual historical information on the standing population, slaughter/death of animals in each exit stream and of those animals which have been tested, the test results by strain type if available. These data are required for each MS, where individual country estimates are not available an EU average is used. A questionnaire was sent by EFSA and data gathered up to 2010, to supplement European Commission data up to 2011 and data on standing population from Eurostat. The territories listed within the model and data used to estimate prevalence are presented in Appendix C, however only those MSs within the EU25 are characterised and results detailed in this report. Users will be able to input new data as required once formatted as necessary (refer to the User Manual).

BSE (classical (C), unknown (U), H and L type) case data and the number of animals tested in each exit stream have been provided from 2002 to 2011. Data from 2001, the initial year of testing in Europe, is not properly structured in order to infer age-stratification. Whilst the case data are cohort based, the testing data are provided by surveillance year and age at testing. These data are transformed into cohort based testing data from 2002 assuming an equal probability per month of birth and death.

2.1.1. Standing population

Data for the standing bovine population by MS for the age intervals 0-11 months and 12-23 months was obtained from Eurostat up to 2011. Data for those animals greater than 24 months old in 12 month intervals to 155 months was gathered by EFSA through a questionnaire up to 2010. Data for 2011 was obtained for Czech Republic, Estonia, Slovenia and Netherlands. In the absence of available data for all other MSs for 2011, the standing population recorded for 2010 is used. For some MSs the data between 24 months and 155 months was not available in 12 monthly intervals with only the total

number in the standing population (Czech Republic, Estonia, France, Germany, Ireland and Netherlands). For these MSs the average EU proportion (average of all other MSs which recorded the data) for each age intervals was multiplied by the country total.

Whilst the total number of EU25 animals in the standing population > 155 months is available, there are little data to estimate the age of these older animals in 12 monthly intervals. Data were available for Austria and the UK up to 204 months. For remaining MSs, the average AT/UK proportion (shown in Table 1) for each age interval was multiplied by the country total.

Table 1: Proportion of animals in standing population by age interval >155 months (average of Austrian and UK data)

Age (months)	Proportion of total > 155 m
156-167	0.346
168-179	0.239
180-191	0.166
192-203	0.118
>204	0.130

2.1.2. Number tested and test positive by exit stream

Testing data are available for the following exit streams: healthy slaughtered animals, clinical signs at ante mortem inspection (not related to BSE), emergency slaughter, eradication measures, fallen stock, and clinical suspects of BSE subject to laboratory examination.

Whilst the healthy slaughter, fallen stock and clinical suspects of BSE seem to be populated to a similar degree within European countries; clinical signs at Ante Mortem (AM) and emergency slaughter do not seem to be uniformly applied. Countries such as France and the Netherlands do not use the clinical signs at AM stream with 0 animals slaughtered in 2011, whilst MSs such as Ireland in 2011 slaughtered 94% of risk animals (excluding healthy slaughtered and fallen stock) in clinical signs at AM stream (1050 clinical signs at AM and 64 in emergency slaughter). When considering the definition of the clinical signs at AM and emergency slaughter streams there appears little to distinguish between them. Therefore it has been agreed that the clinical signs at AM stream can be merged into the emergency slaughtered stream (2nd EFSA WG Meeting, 16 March 2012).

Those animals culled under the eradication measures are traditionally difficult to include in modelling work as for most countries there are insufficient test positive data to estimate prevalence on a cohort basis. In the EU25 there have been 48 test positives in this stream, 10 of which were from the UK. It is difficult to characterise the increased risk associated with animals belonging to the cohort of a case that have been culled. Therefore it has been agreed to merge such animals into the fallen stock (2nd EFSA WG Meeting, 16 March 2012). The impact of this assumption has been investigated in the sensitivity analysis.

The aforementioned assumptions lead to the following exit streams being included in the model:

- Healthy slaughtered animals (HS)
- Emergency slaughter (ES) incorporating clinical signs at AM
- Fallen stock (FS) incorporating eradication measures

- Clinical suspects of BSE subject to laboratory examination (CS)

The quality of the data received from each MS varied, with certain countries only able to provide totals for some age categories and/or streams and/or years. The master dataset “Consolidated DDMMYY” lists each data table per MS and footnotes where assumptions have been required to transform the data. There are three key assumptions which have been required across the MSs data as shown in sections 2.1.3, 2.1.4 and 2.1.5.

2.1.3. Number tested data 2002 and 2003

The proportion of animals in the ES and FS streams were merged as one total for a number of MSs (Austria, Belgium, Cyprus, Czech Republic, Germany, Denmark, Estonia, Greece, Spain, Finland, Ireland, Italy, Luxembourg, Malta, Netherlands, Poland, Sweden, Slovenia, and the UK). The assumption was made that the proportion of this total slaughtered/dead by age interval could be represented by that MSs data in subsequent years, most commonly 2004 and 2005.

2.1.4. Young animals slaughtered/dead and not tested <29 months

In order to estimate the number of animals that may be tested in theoretical monitoring schemes, the number of animals in cohorts younger than current testing ages is required, for example, 0-23 months and 24-29 months. European Commission data are not available for these animals, therefore, a questionnaire was sent to each MS by EFSA and data gathered up to 2010 to supplement test data.

Of the data received a large number of MSs did not separately record the age and number of animals slaughtered/dead for the HS and ES animals before 29 months old, with a single total number per year (Austria, Cyprus, Germany, Denmark, Spain, Finland, France, Hungary, Ireland, Italy, Latvia, Poland, Sweden, Slovakia, and the UK). The assumption is made that the proportion of the total accounting for healthy slaughtered animals at these younger ages is the same in that MS as the older animals where the split between the streams is available. Most commonly, the data not available was for those animals less than 30 months with the data used from the age group 30-35 months used averaged between the years 2002 to 2008 where available.

2.1.5. Old animals slaughtered/dead > 155 months

The total number of EU25 animals tested of age > 155 months is available. However, there are little data to estimate the age of these animals in 12 monthly intervals. Figure 1 displays the age at sampling of test positive animals from the fallen stock and clinical suspects exit streams for the EU25. It can be seen that there are a significant number of animals testing positive aged over 13 years. Further analysis of these data indicates that a number of these animals tested positive in 2011, the most recent testing period.

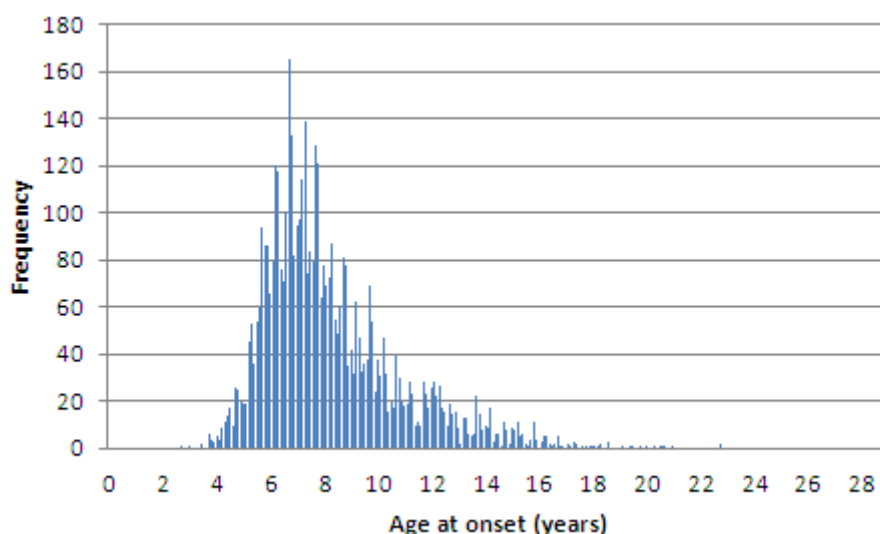


Figure 1: Age at sampling for all EU25 test positives in the fallen stock (FS) and clinical suspect (CS) streams

In order to include animals >155 months in the HS, ES and FS exit streams, it is assumed that a percentage of animals are slaughtered/dead for each 12 month age interval up to >204 months. The proportions for each exit stream are known for the UK data as shown in Table 2.

Table 2: Proportion of animals dead by age interval >155 months (average of UK data 2008 to 2010)

Age at death (months)	HS	ES	FS
156-167	88.0%	71.7%	35.7%
168-179	9.7%	3.4%	25.7%
180-191	2.1%	1.4%	16.6%
192-203	0.1%	0.7%	9.1%
>204	0.1%	22.8%	12.8%

With no further data available, these data are used for HS, ES and FS exit streams and the impact of this assumption has been investigated in the sensitivity analysis.

For clinical suspects > 155 months, in the first instance, test positive data was used to allocate animals to the correct age intervals. If there were any additional animals which tested negative, these animals were assumed to have an equal probability of each remaining age interval. For example, there were a total of two animals tested in the UK CS stream > 155 months in 2008. One animal tested positive aged 156-167 months and was therefore assigned to that age category. The second animal tested negative, so the age interval was not known. Therefore it is assumed that there is equal probability of being in any of the remaining age intervals. In rare cases, the number of animals tested and the test positive data did not match exactly, i.e. there were more test positive animals than those tested. In these cases, the number tested was amended to equal the number test positive with a footnote provided to the table.

2.2. Age at onset distribution

The age at onset distribution represents the age when an animals is infected added to the incubation period of disease to clinical onset. Using European wide data for the clinical suspect and fallen stock

stream, it was determined that a lognormal distribution was appropriate to fit classical and unknown BSE case data.

It was determined early in the project that the age at onset distribution has a significant impact on model outputs (refer to section 4.4). As part of the project a hypothesis test was performed on the EU24 dataset (excluding the UK) and UK case data with the result that the difference is highly significant (results not shown here). In addition, atypical case data of L and H type was shown to be significantly different from classical and unknown age at onset. There was insufficient data to analyse the atypical types separately. The age at onset values fitted to the EU25 data are shown in Table 3.

Table 3: Age at onset parameters for the log normal distribution in R, $\lnorm(\alpha_{ln} \beta_{ln})$ ⁷, by MS grouping and strain type (95th confidence intervals)

Member state and strain type	α_{ln}	β_{ln}
EU25 Classical, L, H and Unknown	2.0703 (2.0621 , 2.0785)	0.2904 (0.2847,0.2963)
EU25 Classical and Unknown	2.0662 (2.058 , 2.0743)	0.2873 (0.2816, 0.2931)
EU25 L and H type	2.561 (2.4832 , 2.6388)	0.2433 (0.1993,0.3124)
EU24 Classical, L, H and Unknown	2.0062 (1.9953 , 2.017)	0.2816 (0.2742, 0.2896)
EU24 Classical and Unknown	1.9996 (1.9889 , 2.0103)	0.276 (0.2686, 0.2837)
UK Classical, L, H and Unknown	2.1439 (2.1322 , 2.1556)	0.2828 (0.2747,0.2913)
UK Classical and Unknown	2.1419 (2.1303 , 2.1536)	0.2811 (0.2731,0.2896)

The age of onset distribution for each strain grouping by age is used for each birth cohorts in the model. The model allows for a user defined option in the form of alternative log normal distribution parameters. The model is not able to perform alternative statistical distributions automatically, but the model code in R can be altered by a technical expert if necessary.

2.3. Test sensitivity

The probability that the diagnostic test detected infection at time t before clinical onset $\psi(t)$, is dependent on the time period prior to clinical onset of the animal. The timing of detectable disease specific prion protein (PrP) relative to clinical onset in the medulla-obex has been experimentally assessed for cattle dosed orally with 100g or 1g of BSE infected brain and killed sequentially throughout the disease course (Arnold, et al., 2007). The sensitivity of BSE testing of healthy slaughtered cattle is assumed to equal the timing of detectable disease specific PrP relative to clinical onset in the medulla-obex for 1g dosed cattle found in Arnold et al. (2007).

$$\psi(t) = \frac{\exp(v + w * t)}{1 + \exp(v + w * t)},$$

where v and w refer to BSE test sensitivity values for the 1 g group which is considered the most likely dose in the field. A user defined estimation of v and w is also currently provided. Parameter estimation determined that $v=5.94$ and $w=-40.8$, with the upper and lower confidence interval values for v determined to be 0.68 and 13.6.

⁷ R documentation on *lnorm* function : <http://127.0.0.1:27947/library/stats/html/Lognormal.html>

3. Modelling assumptions

When developing the model for the different calculations and transforming the various data to feed into those methods, assumptions have been made in order to implement the model for each and every MS. These assumptions need to be considered when evaluating the outputs from the model.

3.1. Transforming input data

Whilst the healthy slaughter, emergency slaughter, fallen stock and clinical suspects of BSE seem to be populated to a similar degree within European countries, clinical signs at ante mortem (AM) does not seem to be uniformly applied. When considering the definition of the emergency slaughter category there appears little to distinguish between the categories and therefore it has been agreed that the clinical signs at AM stream can be merged into the emergency slaughtered stream.

Animals culled under the eradication measures are traditionally difficult to include in modelling work as for most countries there are insufficient test positive data to estimate prevalence on a cohort basis. These were incorporated into the fallen stock category with the impact of this assumption investigated in section 5.1.

For MSs with no, or few, BSE cases post 2001 an alternative estimate of prevalence is required. This has been estimated for those MSs based on the average prevalence of the group of MSs with BSE cases under which they were placed in the previous EFSA Opinion (EU17 or the EU8 group)⁸ and are listed in Appendix C. This results in an overestimate of prevalence for countries with no recorded cases as they are assumed to be a merged epidemiological unit with countries where cases are observed.

The proportion of animals > 155 months in the (i) slaughtered/dead, and (ii) standing population, by 12 month intervals to 204 months (17 years) is not known for most MSs. Therefore, the assumption was made that the proportions by 12 monthly intervals could be approximated by that recorded in (i) the UK slaughtered/dead population between 2008 and 2010, and (ii) an average of that recorded in Austria and the UK standing population in 2010. Assumption (i) has been tested in the sensitivity analysis and could be replaced by assuming equal proportions by 12 monthly intervals without impacting results (refer to section 5.2).

Data are absent for the standing population for most MSs in 2011, It is assumed that the data for 2010 can be used as a proxy.

Age data are transformed into cohort based testing data assuming an equal probability per month of birth and death.

There are little experimental data to assess the sensitivity of the BSE test in cattle. It is assumed that we can use data based on 1g experimentally dosed cattle as detailed in Arnold et al. (2007) to approximate the sensitivity of the test for field cases.

3.2. Model assumptions

Underpinning the estimate of true prevalence it is assumed that the use of an exponential distribution to model the true prevalence. While other distributions could be fitted, analysis of alternative distributions has indicated that an exponential decay of prevalence over time is appropriate for the majority of European data (section 5.3).

⁸ EU17: Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Slovenia, Spain, Sweden and United Kingdom;
EU8: Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland and Slovakia

Cases from the clinical suspect (CS) stream and fallen stock (FS) stream are assumed to be identified at the end of the incubation period, that is, death is as a result of the disease. Whereas healthy slaughter (HS) and emergency slaughter (ES) animals may be within a period of time before clinical onset depending on the distribution of the age at onset and test sensitivity. This assumption impacts the number of infected animals within these streams.

Prevalence estimated for the combined streams (clinical suspects and fallen stock, healthy slaughter and emergency slaughter) can be divided into the individual exit streams according to the proportion of test positive animals observed in those streams. Where there are no test positives, it is assumed that the number of animals tested by birth cohort and testing year is an appropriate proxy.

It is assumed that all cases of BSE are typed by strain such that the number tested for classical and unknown strains is the same number as that tested for atypical H and L type. This is not the case for all MSs and therefore only simulations from MSs where strain differentiation is routinely conducted will be valid.

The design prevalence calculation is based on an infinite population (sampling with replacement) which is based on the binomial distribution. This method is straightforward to implement, however, for MSs with small slaughter populations, the use of the hypergeometric distribution produces lower estimates for the number to test to achieve a desired design prevalence. This has been investigated in the sensitivity analysis (section 5.4). The conclusion is that for those countries with a small slaughter population, the number of animals needed to be tested is still greater than the number that are actually tested with the exception of Finland which has a marginal reduction in the number to test using the hypergeometric equation. For all other MSs that are not achieving a sufficient design prevalence to reduce current levels of testing, conclusions are not affected whether the hypergeometric or binomial based sample size formula is used.

In estimating either the re-emergence of an existing TSE, or emergence of a new TSE disease in cattle, it is assumed that the disease can be detected by current testing assays.

For simulating the EU25 as a whole, it is assumed that it can be merged as an unique epidemiological unit or territory.

RESULTS AND DISCUSSION

4. Introduction to results and discussion

This section of the report presents the comparison of the observed cases from 2002 to 2011 and the model predicted cases using the estimated trend for the detectable prevalence. This is a validation step for the model results.

Tables of results highlighting the key outputs are provided with discussion for: (1) the minimum underlying prevalence of BSE in the population which the monitoring regime would be able to detect, (2) the sample size of animals from the healthy slaughter exit stream required for the monitoring regime to detect a specific underlying prevalence of BSE in the population, (3) the number of cases that would be missed by an alternative monitoring scenario, compared to the current baseline regime, and (4) the sensitivity of the monitoring regime for the number of years to detect a yearly increase in cases due to emergence of a new strain of TSE and how many detectable cases and infected animals would occur in this time.

4.1 Comparison of observed and model predicted cases

The model predicted cases by testing period can be compared to the observed cases during those years to evaluate how well the generic exponential model fits each individual MS and the merged EU25 data. Figure 2 provides the total number of observed test positives for a number of EU25 countries where available (pink), the baseline model prediction (green), the lower 5th confidence interval (blue) and the upper 95th confidence interval (red). When considering the graphs in Figure 2, the number of animals testing positive on the y-axis is on a log scale, such that 1 denotes 10 cases, 2 denotes 100 cases, etc. Various validation graphs such as those presented in Figure 2 can be automatically produced by C-TSEMM as described in the User Manual for the model.

MSs initiated testing for BSE in cattle in different phases. For the EU15⁹, testing data of sufficient quality are available from 2002. For all other MSs, with the exception of Hungary, testing data are available from 2003. For Hungary the data set starts from 2004. In the graphs for Czech Republic and Poland it can be seen that the estimate of prevalence is estimated from 2003 rather than 2002 for the other countries depicted.

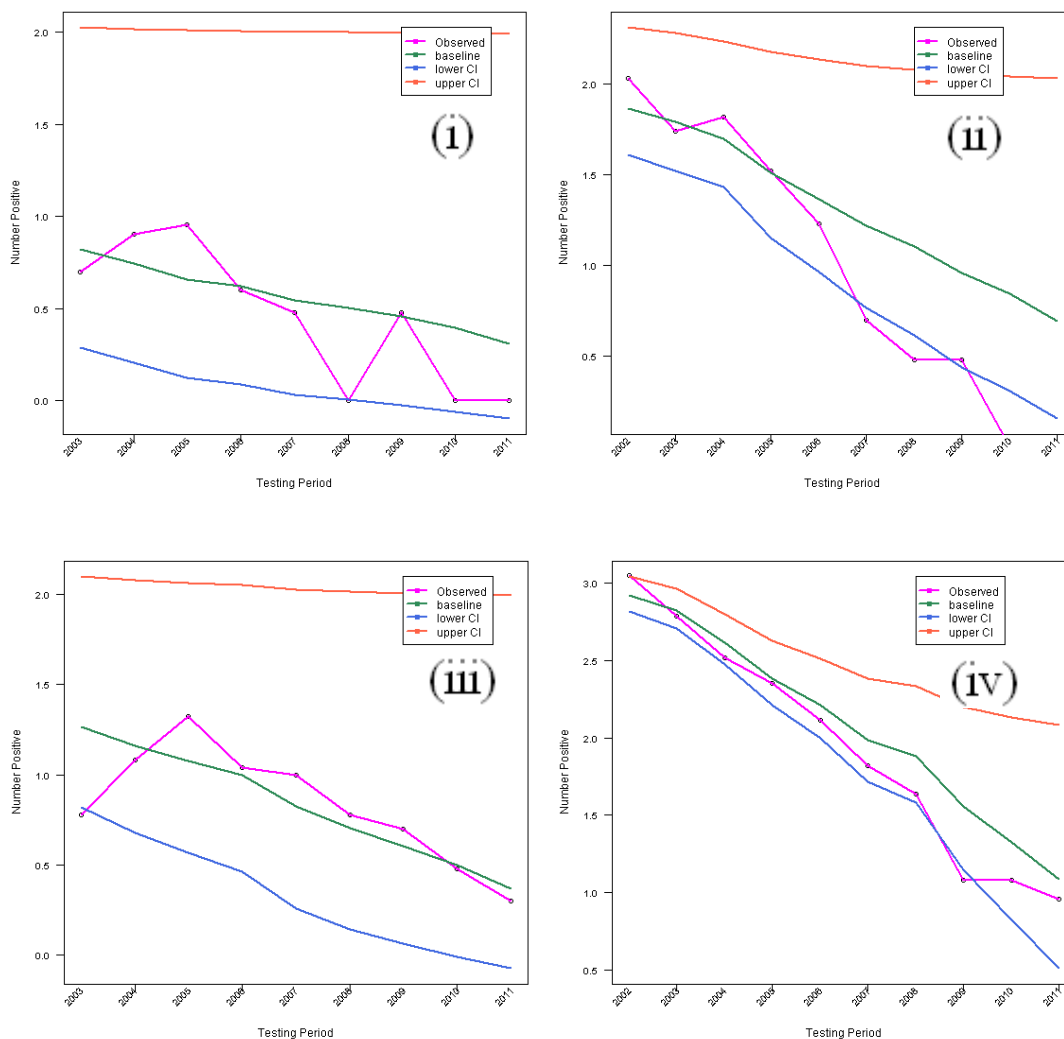
From reference to the upper and lower confidence intervals provided in Table 6 for the baseline regime, it can be seen that using the exponential model, observed values for 2011 for all MSs are between the upper and lower values from using 95% Poisson confidence intervals about the model predictions for the most recent year of data (2011). However, from the graphs in Figure 2 it can be seen that when comparing model estimations for historical testing periods from 2002 to 2011, observed values have for certain MSs fallen below the lower 5th confidence interval. This is most likely to occur at the lower values of observed test positives when numbers fall below 10 per year with increasing between year variability as shown by graph (i) Czech Republic in Figure 2.

There are instances of small peaks occurring against the background of decline in the number of observed cases (Czech Republic 2005 and 2009; Germany 2004; Poland 2005 and 2007; and UK in 2008). The model prediction is the best fit through those data points.

It is important to remember that the model fit is estimated for the CSFS and HSES combined streams. The model, by design, must assume a similar trend in all streams (albeit weighted by the differential slaughter parameter). However, the trends in the individual exit streams observed may differ. This can

⁹ EU15: Austria, Belgium, Germany, Denmark, Greece, Spain, Finland, France, Ireland, Italy, Luxembourg, Netherlands, Portugal, Sweden and the UK.

lead to the model fit overestimating the trend in one of the streams, which may impact the overall trend. This can be seen for Spain where the overall model prediction indicates an increase in the period 2007-2009 for all streams, when there is a decrease in the total observed data. This is due to an increase in healthy slaughter cases during this time which the model fits well (as can be seen in the HS validation graph not shown in this report). However, the model estimates a similar increase in the CSFS combined streams with the resulting graph for all streams shown in Figure 2 graph (v). The selection of the exponential over the Weibull distribution, which in the case of Spain may provide a better fit, is further discussed in section 4.5 of this report.



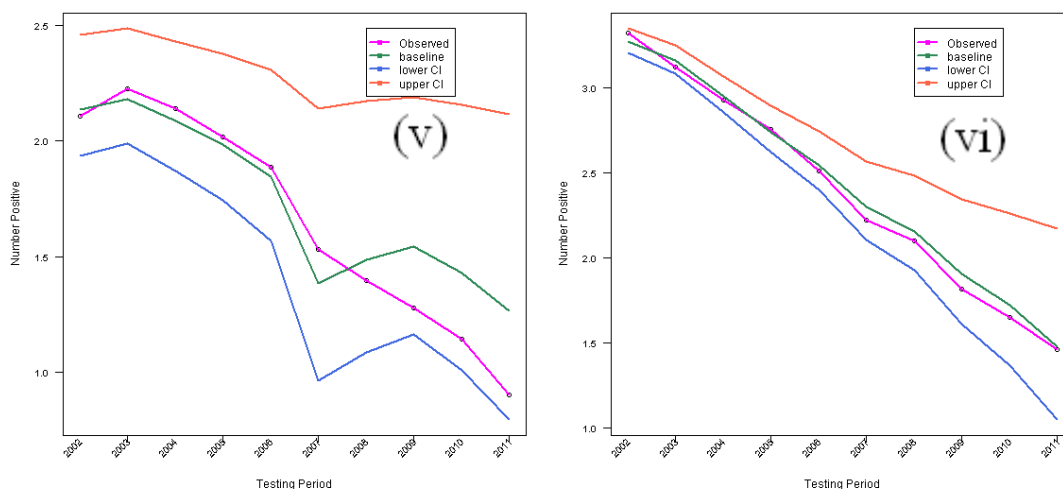


Figure 2: Comparison of log10 observed (pink) and model predicted (green) total BSE classical, unknown, H and L cases for (i) Czech Republic, (ii) Germany, (iii) Poland, (iv) United Kingdom, (v) Spain and (vi) EU25. Results are also shown for the 2.5th (blue) and 97.5th (red) Poisson confidence interval values on the model predictions.

4.2 Estimated design prevalence of baseline monitoring system (all strains)

Output name	Baseline design prevalence
Unit	1 in X
Member State	EU25 and MSs
TSE strain	C, L and H and unknown
Monitoring baseline	HS>72, ES+FS>48, All CS

Table 4 shows the results for different design prevalence calculations that would be detected by the baseline monitoring regime in place by MS with $\tau\%$ confidence. Results are provided based on the detectable prevalence (prevalence of cases) for the adult standing population and adult tested population, together with results based on the infection prevalence (prevalence of infected animals) for the adult tested population. The baseline monitoring regime is the testing of healthy slaughter animals > 72 months, emergency slaughter and fallen stock > 48 months and the testing of all clinical suspect animals. Results are expressed as 1 in X, so a result of 100,000 indicates that we would expect the current system to detect a prevalence in adult cattle >24 months of 1 in 100,000. For the main results $\tau=0.95$, to show the uncertainty surrounding these estimates we also present results for $\tau=0.925$ and $\tau=0.975$. Design prevalence results are shaded where the estimated prevalence detected is greater than the threshold of 100,000. As the level of confidence is increased from $\tau=0.925$ to $\tau=0.975$, it can be seen from the table that the estimated design prevalence reduces in sensitivity.

Table 4: Estimated design prevalence of baseline monitoring system for all strains, using detectable prevalence in the tested population and standing population, and infection prevalence in the tested population to a confidence of 95% (lower 92.5% and upper 97.5% confidence)

MS	Estimated 'design prevalence' of baseline monitoring system: all strains								
	Detectable prevalence in standing population (1 in X)			Detectable prevalence in tested population (1 in X)			Infection prevalence in tested population (1 in X)		
	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$
EU25	7,349,693	6,354,930	5,160,828	2,304,889	1,992,928	1,618,454	706,953	611,268	496,410
AT	142,490	123,205	100,056	55,885	48,321	39,242	14,318	12,380	10,054
BE	323,067	279,342	226,854	74,519	64,433	52,326	20,168	17,438	14,162
CY	6,136	5,306	4,310	N/A	N/A	N/A	461	N/A	N/A
CZ	60,099	51,965	42,201	31,586	27,311	22,181	5,766	4,985	4,049
DE	899,533	777,784	631,638	323,633	279,831	227,250	81,585	70,542	57,287
DK	N/A	N/A	N/A	44,659	N/A	31,359	15,408	13,323	10,819

MS	Estimated 'design prevalence' of baseline monitoring system: all strains								
	Detectable prevalence in standing population (1 in X)			Detectable prevalence in tested population (1 in X)			Infection prevalence in tested population (1 in X)		
	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$
DK*	274,347	237,147	192,626	44,662	38,612	31,357	15,414	13,333	10,825
EE	16,443	14,220	11,548	6,239	5,395	4,381	1,319	1,140	N/A
EL	N/A	N/A	N/A	8,076	6,983	5,672	2,668	2,307	N/A
ES	294,174	254,359	206,565	141,902	122,696	99,624	43,943	37,995	30,856
FI	108,035	90,365	74,692	N/A	17,661	14,343	6,219	5,378	4,367
FR	2,005,412	1,733,985	1,408,168	603,303	521,647	423,629	236,882	204,821	166,335
HU	37,393	32,332	26,257	19,805	17,124	13,907	3,800	3,286	2,669
IE	527,100	455,760	370,123	127,587	110,318	89,590	56,919	49,215	39,968
IT	319,226	276,020	224,155	139,500	120,619	97,937	24,298	21,010	17,062
LT	28,060	N/A	19,703	21,459	18,555	15,069	3,301	N/A	2,318
LU	14,896	12,881	10,461	2,926	2,530	2,055	1,273	1,101	894
LV	18,833	16,284	13,224	11,155	9,646	7,833	1,689	1,460	1,186
MT	N/A	N/A	545	N/A	N/A	N/A	115	100	N/A
NL	336,577	290,828	236,340	110,685	94,162	77,722	29,881	25,836	N/A
PL	210,665	182,152	147,926	166,199	143,704	116,702	28,646	24,769	20,115
PT	73,615	63,652	51,692	N/A	N/A	N/A	9,720	8,405	6,825
SE	116,259	101,010	81,484	29,845	25,805	20,957	7,675	6,636	5,389
SI	17,683	15,290	12,417	8,115	7,017	5,699	2,355	2,036	1,654
SK	16,423	14,200	11,532	8,884	7,682	6,239	1,842	1,592	1,293
UK	785,476	679,164	551,548	246,037	212,736	172,763	62,482	54,025	43,874

N/A signifies that the model has failed to find a viable value

*Values for Denmark using alternative solver routine

From Table 4 it can be seen that the calculation using the detectable prevalence in the standing population produces the highest estimates for the design prevalence the baseline monitoring system is able to detect. Twelve MSs (Austria, Belgium, Denmark, Germany, Spain, France, Ireland, Italy, Netherlands, Poland, Sweden and the UK) have a design prevalence of at least 1 in 100 000 using the estimated detectable prevalence to a confidence level of 0.95.

Using the estimated detectable prevalence, to a confidence level of 0.95, the baseline monitoring regimes in seven MSs (Germany, Spain, France, Ireland, Italy, Poland and UK) have a design prevalence of at least 1 in 100 000. Additionally, France has a design prevalence greater than 1 in 100,000 estimated using the prevalence of infection. The EU25 'design prevalence' is higher than for individual MSs as far more animals are tested, with an estimated design prevalence of 1 in 1,992,928 using the detectable prevalence and 1 in 611,268 using the prevalence of infection. The assumption is made that the EU25 can be estimated as a merged epidemiological unit or territory.

N/A in Table 4 indicates that model has failed to converge. This is due to the use of a solver to calculate the estimated 'design prevalence' a monitoring system is able to detect by the rearrangement of the design prevalence equation (Eq. 2 in Appendix B), where the 'design prevalence' value is solved for a specified number of animals tested. The generic solver routine has been optimised to produce results for the majority of MSs. When considering the detectable prevalence in the standing population, a viable value has not been found at the 95th confidence value for Greece, Lithuania, and Malta. Based on other confidence values and the estimated number to test values provided in Table 5, the design prevalence of these countries is not meeting the 1 in 100,000 threshold. However, for Denmark it is likely that at the 95th confidence value, the monitoring system is detecting greater than 1 in 100,000. To investigate that value for Denmark, the generic solver routine was adapted specifically for Denmark. Results using the specific solver routine for Denmark are denoted in the table with an asterisk.

4.3 Estimated number to test in healthy slaughter stream to achieve design prevalence (all strains)

Output name	Number to test
Unit	animals
Member State	EU25 and MSs
TSE strain	C, L and H and unknown
Monitoring baseline	ES+FS>48, All CS

Table 5 shows the number of healthy slaughter animals that would need to be tested, given the number of animals currently being tested in the other exit streams remains the number tested in those streams in 2011, in order to be $\tau\%$ confident of detecting a positive animal if the overall prevalence in animals >24 months is 1 in 100,000. Results are provided based on the detectable prevalence (prevalence of cases) for the adult standing population and adult tested population, together with results based on the infection prevalence (prevalence of infected animals) for the adult tested population. For the main results $\tau=0.95$, to show the uncertainty surrounding these estimates we also present results for $\tau=0.925$ and $\tau=0.975$. Results for the number of healthy slaughter animals to be tested are shaded where the estimated number is less than current testing in this exit stream.

Table 5: Estimated number of health slaughtered animals required to be tested for all strains, given testing of emergency slaughter, fallen stock and clinical suspect animals, to achieve a design prevalence of 1 in 100,000 using detectable prevalence in the tested population and standing population, and infection prevalence in the tested population to a confidence 95% (lower 90% and upper 97.5% confidence)

MS	Number to test in healthy slaughter to detect prevalence of 1 in 100,000: all strains									
	Actual number tested in HS >72 m (2011)	Detectable prevalence in standing population			Detectable prevalence in tested population			Infection prevalence in tested population		
		$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$
EU25	3,730,778	0	0	0	0	0	0	0	0	0
AT	104,147	40,014	63,640	104,029	273,920	334,160	437,140	1,391,111	1,626,229	2,028,165
BE	112,059	0	0	0	206,255	264,120	363,041	1,202,488	1,416,297	1,781,805
CY	2,140	86,023	100,011	123,925	317,062	367,215	452,954	1,187,398	1,373,789	1,692,427
CZ	42,984	89,981	108,418	139,936	196,307	231,387	291,358	1,199,928	1,392,110	1,720,646
DE	513,746	0	0	0	0	0	0	786,379	1,018,122	1,414,290
DK	55,260	0	0	0	304,008	374,366	494,643	1,157,284	1,361,209	1,709,820
EE	7,739	80,328	93,927	117,189	222,438	258,282	319,557	1,076,700	1,246,265	1,536,138
EL	12,428	175,599	207,618	262,356	483,513	563,732	700,865	1,522,610	1,765,482	2,180,675
ES	255,669	0	0	0	13,615	104,038	258,615	1,301,366	1,593,365	2,092,539

MS	Number to test in healthy slaughter to detect prevalence of 1 in 100,000: all strains									
	Actual number tested in HS >72 m (2011)	Detectable prevalence in standing population			Detectable prevalence in tested population			Infection prevalence in tested population		
		$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$	$\tau=0.925$	$\tau=0.95$	$\tau=0.975$
FI	27,041	22,168	34,146	54,623	344,146	406,524	513,161	1,254,421	1,459,289	1,809,512
FR	1,013,355	0	0	0	0	0	0	0	0	0
HU	24,700	94,256	111,647	141,376	192,920	225,755	281,887	1,076,287	1,247,399	1,539,917
IE	241,637	0	0	0	0	132,508	377,213	1,124,731	1,445,597	1,994,120
IT	255,135	28,898	45,052	72,667	161,855	198,821	262,014	1,281,486	1,493,712	1,856,516
LT	41,066	159,684	185,494	229,616	210,401	244,149	301,843	1,396,379	1,615,774	1,990,832
LU	3,738	107,523	126,612	159,243	606,397	703,576	869,704	1,412,466	1,635,822	2,017,652
LV	21,766	125,166	145,106	179,195	212,838	246,502	304,051	1,418,127	1,640,460	2,020,541
MT	416	95,368	110,347	135,954	115,067	133,130	164,008	647,505	748,912	922,270
NL	165,855	0	0	0	125,683	184,533	285,137	1,142,364	1,360,358	1,733,022
PL	310,559	103,168	132,503	182,651	153,308	190,491	254,057	1,293,962	1,509,697	1,878,497
PT	43,450	96,547	128,047	181,897	384,982	461,632	592,667	1,419,381	1,657,950	2,065,786
SE	45,963	31,314	45,417	69,525	292,182	347,119	441,035	1,305,964	1,519,593	1,884,793
SI	10,595	159,945	188,345	236,895	373,843	435,725	541,514	1,340,888	1,554,145	1,918,712
SK	9,721	114,198	133,766	167,217	220,263	256,433	318,266	1,103,870	1,278,355	1,576,639
UK	409,609	0	0	0	0	0	82,639	875,767	1,070,258	1,402,744

From Table 5 we can see that when the EU25 is merged into one epidemiological unit, the area already tests sufficient animals in the ES, FS and CS streams such that they do not need to test any healthy slaughter animals (represented in the table by a value of 0). Thus, the C-TSEMM model estimates that, with the current BSE monitoring regime but excluding the testing of healthy slaughter cattle, the system is able to detect in the standing population one BSE case in 4,021,940 adult cattle with a confidence level of 0.95.

Using the estimated detectable prevalence in the standing population, at a confidence level of 0.95, eight MSs (Belgium, Germany, Denmark, Spain, France, Ireland, Netherlands, and the UK) do not require the testing of any healthy slaughter animals to meet a 1 in 100,000 design prevalence. The estimate of the numbers of animals needing to be sampled in order to detect a prevalence of 1 in 100,000 is lower (and thus the power of the surveillance in Table 4 is higher) when considering the standing population than when considering the test population. This is because the prevalence of BSE in the standing population is lower than the prevalence in the test population. As such, assuming a design prevalence of 1 in 100,000 in the standing population, as opposed to in the test population, will lead to higher stream prevalences in the test population after the appropriate scaling. In other words, a design prevalence of 1 in 100,000 in

the standing population will lead to a greater than 1 in 100,000 prevalence in the test population (the design prevalence used when considering the test population). Therefore, the standing population prevalence calculations are effectively performed at a higher overall BSE prevalence than the test population calculations, leading to smaller sample sizes.

Using the estimated detectable prevalence in the tested population, At a confidence level of 0.95, three MSs (Germany, France, and the UK) do not require to test any healthy slaughter animals to meet 1 in 100,000 design prevalence given the other exit streams are tested. Italy (IT), for example, with a confidence level of 0.95, is required to test 198,821 HS animals. As Italy (IT) currently tests 255,135 there is a reduction in the animals required to be tested to achieve the desired design prevalence. Luxembourg (LU) is required to test 703,576 HS animals, but only test 3,738 so that MS will not achieve the design prevalence.

When using the estimated infection prevalence only France and the EU25 as a whole achieve the required confidence with no testing of healthy slaughter animals required.

The differences in the results between MSs are based on the estimated ratio of the prevalence in each of the four testing streams and how many animals are tested per year in those streams by MS. France, for example, has a relatively high prevalence in FS and CS testing streams and tests a large number of animals within these streams. Therefore, for France the design prevalence is met without the requirement for testing in the healthy slaughter stream with any measure of design prevalence (detectable or infected prevalence).

4.4 Estimated number to animals missed due to reduction of animals tested by the monitoring system (all strains)

Output name	Number missed
Unit	animals
Member State	EU25 and MSs
TSE strain	C, L and H and unknown
Monitoring baseline	HS>72, ES+FS>48, All CS
Monitoring scenario	No HS, ES+FS>48, All CS

Table 6 displays the estimated number of cases detected by the monitoring baseline and scenario and the total number of infected animals slaughtered/dead over one year. The baseline monitoring regime is the testing of healthy slaughter animals > 72 months, emergency slaughter and fallen stock > 48 months and the testing of all clinical suspect animals. The scenario regime only affects the healthy slaughter stream in that no healthy slaughtered animals are tested. The mean values are presented, together with the 95% confidence intervals in brackets. For comparison purposes, the actual number of test positives for 2011 are shown in the second column by exit stream. The final column on the right hand side displays the total number of infected animals slaughtered/dead (for all four streams including all age groups) irrespective the testing scheme applied.

Table 6: Estimated mean number of cases missed and infected animals of all strains given a change in the monitoring regime from the baseline to a scenario where no healthy slaughter animals are tested with 95% confidence intervals (CI*)

MS	Actual cases in 2011 {HS,ES,FS,CS}	Number of animals missed between monitoring baseline and scenario in one year: all strains			
		Baseline detected [CI*]	Scenario detected [CI*]	Number detected missed [CI*] (baseline - scenario)	Number infected animals dead [CI*] (all streams, all age groups)
EU25	28 { 9 0 19 0 }	28 [11 , 148]	18 [5.6 , 132]	10 [5.2 , 16]	100 [59 , 247]
AT	0 { 0 0 0 0 }	0.53 [0.74 , 101]	0.27 [0.71 , 100]	0.25 [0.03 , 0.52]	2.4 [1.1 , 104]
BE	0 { 0 0 0 0 }	0.22 [0.71 , 100]	0.13 [0.7 , 100]	0.09 [0.01 , 0.19]	0.99 [0.81 , 102]
CY	0 { 0 0 0 0 }	0.03 [0.66 , 96]	0.02 [0.66 , 96]	0.01 [0.001 , 0.02]	0.12 [0.67 , 96]
CZ	0 { 0 0 0 0 }	0.86 [0.77 , 98]	0.34 [0.7 , 97]	0.52 [0.07 , 1.05]	7.5 [2.6 , 110]
DE	0 { 0 0 0 0 }	3.6 [1.3 , 107]	2 [0.98 , 104]	1.5 [0.36 , 2.79]	20 [7.9 , 132]
DK	0 { 0 0 0 0 }	0.01 [0.69 , 100]	0.01 [0.68 , 100]	0.004 [0.0004 , 0.01]	0.05 [0.69 , 100]
EE	0 { 0 0 0 0 }	0.07 [0.67 , 96]	0.03 [0.66 , 96]	0.04 [0.004 , 0.08]	0.52 [0.72 , 97]
EL	0 { 0 0 0 0 }	0.09 [0.69 , 100]	0.06 [0.69 , 100]	0.03 [0.003 , 0.06]	0.30 [0.72 , 100]
ES	7 { 4 0 3 0 }	16 [5.7 , 128]	11 [3.4 , 120]	5 [2.3 , 7.92]	60 [32 , 190]
FI	0 { 0 0 0 0 }	0.23 [0.71 , 100]	0.16 [0.7 , 100]	0.08 [0.009 , 0.16]	0.98 [0.81 , 102]

MS	Actual cases in 2011 {HS,ES,FS,CS}	Number of animals missed between monitoring baseline and scenario in one year: all strains			
		Baseline detected [CI*]	Scenario detected [CI*]	Number detected missed [CI*] (baseline - scenario)	Number infected animals dead [CI*] (all streams, all age groups)
FR	3 { 0 0 3 0 }	2.9 [1.1 , 105]	2.2 [0.98 , 104]	0.69 [0.14 , 1.32]	8.2 [2.6 , 115]
HU	0 { 0 0 0 0 }	0.26 [0.66 , 93]	0.11 [0.64 , 92]	0.15 [0.018 , 0.32]	2 [0.94 , 96]
IE	3 { 0 0 3 0 }	3.9 [1.3 , 107]	3.1 [1.1 , 106]	0.81 [0.18 , 1.51]	9.5 [3 , 117]
IT	1 { 1 0 0 0 }	0.31 [0.72 , 100]	0.07 [0.69 , 100]	0.24 [0.027 , 0.50]	2.2 [1 , 104]
LT	0 { 0 0 0 0 }	0.2 [0.68 , 96]	0.02 [0.66 , 96]	0.17 [0.019 , 0.36]	1.7 [0.89 , 99]
LU	0 { 0 0 0 0 }	0.04 [0.69 , 100]	0.03 [0.69 , 100]	0.009 [0.001 , 0.02]	0.11 [0.7 , 100]
LV	0 { 0 0 0 0 }	0.11 [0.67 , 96]	0.01 [0.66 , 96]	0.098 [0.011 , 0.21]	0.95 [0.78 , 98]
MT	0 { 0 0 0 0 }	0.004 [0.66 , 96]	0.002 [0.66 , 96]	0.0025 [0.00026 , 0.01]	0.043 [0.66 , 96]
NL	0 { 0 0 0 0 }	0.4 [0.73 , 100]	0.24 [0.71 , 100]	0.16 [0.019 , 0.33]	1.8 [0.95 , 103]
PL	1 { 1 0 0 0 }	1.2 [0.82 , 98]	0.26 [0.69 , 96]	0.96 [0.14 , 1.93]	8.9 [3 , 112]
PT	5 { 3 0 2 0 }	3.1 [1.1 , 106]	2.2 [0.97 , 104]	0.91 [0.17 , 1.74]	11 [3.5 , 119]
SE	0 { 0 0 0 0 }	0.31 [0.72 , 100]	0.18 [0.7 , 100]	0.13 [0.02 , 0.26]	1.5 [0.89 , 103]
SI	0 { 0 0 0 0 }	0.39 [0.7 , 97]	0.26 [0.69 , 96]	0.13 [0.016 , 0.27]	1.9 [0.94 , 100]
SK	0 { 0 0 0 0 }	0.56 [0.73 , 97]	0.3 [0.69 , 97]	0.27 [0.034 , 0.54]	4.6 [1.6 , 105]
UK	8 { 0 0 8 0 }	11 [3.2 , 120]	5.2 [1.5 , 110]	5.8 [1.7 , 10.29]	44 [20 , 171]

*Confidence intervals are results from using upper and lower 95% Poisson confidence interval values about the model predictions

If testing in the healthy slaughter stream were to cease, an estimated mean 10 cases (5.2, 16) across the EU25 (when the EU25 is merged into one epidemiological unit) would be missed in 2011. The estimated number missed can be compared against the background estimated number of 100 infected animals slaughtered/dead which includes those animals which, if tested, would test negative.

4.5 Estimated number of years to detect a change in the prevalence of disease (classical and unknown)

Output name	Emergence
Unit	years, animals
Member State	EU25 and MSs
TSE strain	C and unknown
Monitoring baseline	HS>72, ES+FS>48, All CS
Monitoring scenario	No HS, ES+FS>48, All CS

Table 7 displays the model predictions of the estimated number of years taken to detect a hypothetical 10% increase in cases (classical and unknown strains) observed per year given an emergence initiated in 2011. The assumption is made that detection will occur when the number of model predicted cases exceeds the upper confidence interval prediction of number of cases for 2011 (upper confidence interval prediction is calculated in the baseline model using the upper 95% Poisson confidence interval values for the input test positive data). Results for the number of cases (detectable) and the number of infected animals between 2011 and the year of detection are provided, based on an annual 10% increase in the number of test positive animals.

Table 7: Estimated number of years to detect a hypothetical increase in prevalence of 10% per year with classical and unknown strains starting in 2011, together with estimates of the number of detectable cases and infected animals missed during that time interval between the scenario and baseline model

Number of years to detect an annual 10% increase in prevalence and estimated number of positives missed – C&U strains							
Member State	Current number test positives (baseline, scenario)	Upper CI limit ⁺ (0.975)	Years to detection (i.e. cross upper CI limit) (baseline, scenario)	Total test positives at detection (baseline, scenario)	Number of extra cases under scenario before detection (scenario-baseline)	Total infected animals at detection (baseline, scenario)	Number of extra infected animals dead under scenario before detection (scenario-baseline)
EU25	26.85, 16.98	40.34	6, 11	207.14, 314.70	107.56	694.87, 1,668.93	974.06
AT*	0.49, 0.25	0.73	6, 13	3.79, 6.21	2.41	15.47, 49.15	33.69
BE	0.20, 0.12	0.62	13, 19	5.03, 6.22	1.2	19.85, 41.41	21.56
CY*	0.03, 0.02	0.04	6, 11	0.19, 0.28	0.09	0.79, 1.90	1.11
CZ	0.85, 0.33	4.07	18, 28	38.81, 44.84	6.04	254.63, 749.45	494.82
DE	3.64, 2.11	10.9	13, 19	89.31, 108.02	18.72	385.01, 803.20	418.19
DK	0.03, 0.02	0.24	25, 29	2.68, 2.76	0.07	9.57, 14.47	4.89
EE**	0.09, 0.04	0.46	19, 27	4.55, 5.07	0.52	24.32, 57.57	33.25
EL*	0.08, 0.06	0.12	5, 9	0.51, 0.79	0.28	1.67, 3.70	2.04
ES	15.37, 10.57	27.2	7, 11	145.77, 195.88	50.11	510.50, 997.16	486.66

Number of years to detect an annual 10% increase in prevalence and estimated number of positives missed – C&U strains							
Member State	Current number test positives (baseline, scenario)	Upper CI limit ⁺ (0.975)	Years to detection (i.e. cross upper CI limit) (baseline, scenario)	Total test positives at detection (baseline, scenario)	Number of extra cases under scenario before detection (scenario-baseline)	Total infected animals at detection (baseline, scenario)	Number of extra infected animals dead under scenario before detection (scenario-baseline)
FI*	0.22, 0.15	0.33	6, 10	1.71, 2.36	0.65	5.97, 12.33	6.36
FR	2.64, 1.99	6.65	11, 14	48.87, 55.71	6.84	129.50, 195.49	65.99
HU**	0.29, 0.12	1.5	19, 28	14.94, 16.16	1.22	93.81, 246.11	152.29
IE	3.54, 2.81	6.7	8, 11	40.50, 52.05	11.55	92.02, 149.12	57.09
IT	0.32, 0.07	1.26	16, 32	11.41, 13.56	2.15	73.05, 408.69	335.64
LT**	0.22, 0.02	1.07	18, 41	10.12, 11.97	1.85	78.38, 838.52	760.14
LU*	0.04, 0.03	0.06	5, 8	0.25, 0.37	0.12	0.59, 1.10	0.51
LV**	0.12, 0.01	0.6	18, 43	5.70, 7.12	1.43	43.75, 568.36	524.62
MT**	0.01, 0.00	0.03	19, 27	0.27, 0.29	0.02	1.94, 4.58	2.65
NL	0.46, 0.28	2.76	20, 26	26.31, 30.18	3.87	106.48, 202.98	96.5
PL	1.51, 0.31	10.33	22, 38	107.91, 112.65	4.74	727.28, 3,707.99	2,980.72
PT	2.82, 2.00	6.38	10, 14	44.90, 55.87	10.98	143.20, 251.36	108.16
SE*	0.27, 0.15	0.4	6, 12	2.10, 3.26	1.16	8.80, 24.38	15.58
SI	0.39, 0.26	3.59	25, 29	38.38, 38.88	0.5	144.29, 218.06	73.77
SK	0.56, 0.29	3.82	22, 28	39.78, 39.38	-0.4	227.80, 428.17	200.38
UK	10.61, 5.00	21.13	9, 17	144.05, 202.55	58.5	571.95, 1,707.70	1,135.75

*Uses EU17 test positive data. **Uses EU8 test positive data, ⁺Using model fit on 95th Poisson CI input values

From Table 7 it can be seen that across the EU25 (when the EU25 is merged into one epidemiological unit) detection of the emergence would take an estimated 6 years for the baseline monitoring system and 11 years for the scenario monitoring regime. In this intervening five years an additional estimated 108 test positives would be required for the number of cases to be greater than the threshold, and an estimated extra 974 infected animals would be slaughtered/die.

It has been noted that the countries that use the EU17 test positive data, as a proxy, in the absence of cases between 2002-2011, have a fairly short time to detection (i.e. until the model predicted number of cases is greater than the upper threshold value). This early detection is based on the relatively low level of uncertainty associated with the EU17 data and thus the upper CI limit is relatively close to the current number tested. The real level of uncertainty in the

individual MSs is higher, due to a smaller sample size. Therefore the model underestimates the time to detection for these countries. A similar scenario exists for the countries using the EU8 test positive data, but to a lesser degree as it is a smaller sample size than the EU17. Therefore, the results for countries denoted with asterisk(s) in Table 7 could be considered to represent the combined MSs of the EU8 and EU17 rather than individual country time to detection.

For the remaining MSs, it can be seen that Spain has the shortest estimated time to detection of 7 years under the baseline monitoring regime, while both Spain and Ireland have the joint shortest estimated time to detection of 11 years under the scenario monitoring regime. The monitoring system of France and Ireland are estimated to be least affected by the lifting of testing from healthy slaughtered animals, with only three additional years to detect the significant increase. Italy and Poland's monitoring regimes are estimated to be the most affected, with a difference of 16 years between the baseline and monitoring regimes.

The Upper CI limit for the current testing year (2011) in each MS was selected as a means to determine when a MS will 'detect' that there has been a significant increase in the annual number of cases. This approach may not be a realistic method that would be implemented to detect an emergence within the EU25, however, it provides a simple, comparative measure that can be generically applied across all MSs, strains and monitoring regimes without additional assumptions. The upper CI limit for the Slovakia (SK) in 2011 was 3.82, indicating that a significant increase in the number of cases would be detected when a year with greater than 3.82 cases occurs. For SK, the estimated number of cases, when considering a 10% from the current testing year, was greater than 3.79 at 22 years for the baseline regime, and 28 years after under the scenario regime. Over these time periods (22 and 28 years) the model estimates a total of approximately 39.78 observed cases under the baseline regime and 39.38 cases under the scenario regime. The negative results for SK for the number of additional cases are not intuitive, in that there is an estimated additional six years for detection for the scenario regime but this accounts for less cases in total. This is due to the lack of testing of HS animals in the scenario regime, for most other MS's estimates the scenario regime takes sufficiently longer to detect the increase that more cases are detected overall. It is useful to compare the difference in the number of cases with the difference in the number of infected animals dead/slaughtered between monitoring regimes. For SK it can be seen from the table that although the scenario regime detects the theoretical increase with less observed cases, due to the additional year of testing required, an additional 200 infected animals would be slaughtered/die when comparing the regimes.

Whilst Table 7 provides the time to detection for the baseline monitoring system and the scenario of no testing of healthy slaughtered animals, Table 8 provides the results for the scenario where testing could be reduced by certain MSs to achieve a 1 in 100,000 design prevalence. For those countries shaded in Table 5, the testing of healthy slaughtered animals could be reduced to achieve a design prevalence of 1 in 100,000 at the 95% confidence value, using the detectable prevalence in the standing population. Given the estimated number of healthy slaughter animals to test, Table 8 shows the results for the number of years to detect for those countries with reduced testing. The first column on the left hand side of Table 8 refers to the percentage reduction calculated from the number to test for that MS divided by the total number of healthy slaughter animals tested. For example, the results from Table 5 suggest that Austria is required to test 63,640 HS animals to achieve a design prevalence of 1 in 100,000. Austria currently tests 104,147 HS animals, which suggests that they only need test 61% of their HS animals ($63,640/104,147 \times 100$).

Table 8: Estimated number of years to detect a hypothetical increase in prevalence of 10% per year with classical and unknown strains starting in 2011, together with estimates of the number of detectable cases and infected animals missed during that time interval between the scenario and baseline model, where the scenario is testing the proportion of HS slaughter suggested by the results in Table 5 for the standing population with $\tau=0.95$

Member State	Number of years to detect an annual 10% increase in prevalence and estimated number of positives missed – C&U strains							
	Proportion HS >72 months tested	Current number test positives (baseline, scenario)	Upper CI limit ⁺ (0.975)	Years to detection (i.e. cross upper CI limit) (baseline, scenario)	Total test positives at detection (baseline, scenario)	Number of extra cases under scenario before detection (scenario-baseline)	Total infected animals at detection (baseline, scenario)	Number of extra infected animals dead under scenario before detection (scenario-baseline)
EU25	0	26.85 , 16.98	40.34	6 , 11	207.14 , 314.70	107.56	694.87 , 1,668.93	974.06
AT*	0.61	0.49 , 0.40	0.73	6 , 8	3.79 , 4.56	0.76	15.47 , 22.92	7.46
BE	0	0.20 , 0.12	0.62	13 , 19	5.03 , 6.22	1.2	19.85 , 41.41	21.56
DE	0	3.64 , 2.11	10.9	13 , 19	89.31 , 108.02	18.72	385.01 , 803.20	418.19
DK	0	0.03 , 0.02	0.24	25 , 29	2.68 , 2.76	0.07	9.57 , 14.47	4.89
ES	0	15.37 , 10.57	27.2	7 , 11	145.77 , 195.88	50.11	510.50 , 997.16	486.66
FR	0	2.64 , 1.99	6.65	11 , 14	48.87 , 55.71	6.84	129.50 , 195.49	65.99
IE	0	3.54 , 2.81	6.7	8 , 11	40.50 , 52.05	11.55	92.02 , 149.12	57.09
IT	0.18	0.32 , 0.11	1.26	16 , 27	11.41 , 13.51	2.1	73.05 , 246.06	173.01
NL	0	0.46 , 0.28	2.76	20 , 26	26.31 , 30.18	3.87	106.48 , 202.98	96.5
PL	0.43	1.51 , 0.82	10.33	22 , 28	107.91 , 110.35	2.44	727.28 , 1,367.01	639.73
SE*	0.99	0.27 , 0.27	0.4	6 , 6	2.10 , 2.09	-0.01	8.80 , 8.80	0
UK	0	10.61 , 5.00	21.13	9 , 17	144.05 , 202.55	58.5	571.95 , 1,707.70	1,135.75

*Uses EU17 test positive data. ⁺Using model fit on 95th Poisson CI input values

From Table 8 it can be seen that for those MS where no healthy slaughter animals are required to be tested to achieve a 1 in 100,000 design prevalence in the standing population (i.e. those MSs with a 0 in the first column: EU25, BE, DE, DK, ES, FR, IE, NL and UK) the number of years to detect an increase in prevalence is the same between Table 7 and Table 8 where the scenario is no healthy slaughter testing. For those MSs where partial testing achieves the level of confidence required, results are between the baseline (100% testing of healthy slaughter > 72 months) and the scenario of no healthy slaughter testing results given in Table 7. For example, for Austria, under the scenario of no healthy slaughter testing, the number of years to cross the upper confidence interval is achieved at 13 years (Table 7), whereas with the random sampling of 61% of healthy slaughtered animals > 72 months, thus achieving an estimated 1 in 100,000 design prevalence, detection is achieved at 8 years (Table 8).

4.6 Estimated number of animals missed due to reduction of animals tested by the monitoring system (comparison with atypical L and H type)

Output name	Number missed
Unit	animals
Member State	France
TSE strain	L and H type; C, L and H and unknown
Monitoring baseline	HS>72, ES+FS>48, All CS
Monitoring scenario	No HS, ES+FS>48, All CS

Table 9 displays a comparison of the estimated number of atypical cases detected by the baseline and scenario regimes and, as a comparison, the estimated number of infected animals slaughtered/dead for the case study France and the EU25. France was selected as an individual MS case study as the country has the highest number of L and H type strain typed within EU25 MS datasets. The baseline monitoring regime is the testing of healthy slaughter animals > 72 months, emergency slaughter and fallen stock > 48 months and the testing of all clinical suspect animals. The scenario regime only affects the healthy slaughter stream in that no healthy slaughtered animals are tested. The mean values are presented, together with the 95% confidence intervals in brackets.

Table 9: Estimated mean number of cases missed and infected animals missed comparing separate calculation of atypical L and H type with all strains given a change in the monitoring regime from the baseline to a scenario where no healthy slaughter animals are tested with 95% confidence intervals (CI*)

Member State	Actual cases 2011 {HS,ES,FS,CS}	Number of animals missed between monitoring baseline and scenario: L & H strains			
		Baseline detected [CI*]	Scenario detected[CI*]	Number detected missed (baseline - scenario)	Number infected animals dead [CI*] (all streams, all age groups)
FR-L&H	0 { 0 0 0 0 }	1.3 [0.84 , 102.20]	0.94 [0.8 , 101.55]	0.32 [0.045 , 0.64]	3.4 [1.2 , 106.44]
FR-All	3 { 0 0 3 0 }	2.9 [1.1 , 105.30]	2.2 [0.98 , 103.98]	0.69 [0.14 , 1.32]	8.2 [2.6 , 114.81]

*Confidence intervals are results from using upper and lower 95% Poisson confidence interval values about the model predictions

From Table 9 it can be seen that, for France, the estimated number of cases missed between the baseline and scenario monitoring regimes is approximately the same for both strain combinations, that is approximately 24%-25% of the cases currently detected would not be detected under a regime of no healthy slaughter testing.

When analysing results using only the atypical data, it is assumed that all cases of BSE are typed by strain such that the number tested for classical and unknown strains is the same number as that tested for atypical H and L type. This is not the case for all MSs, and therefore only simulations from MSs where strain differentiation is routinely conducted will be valid.

4.7 Estimated number of years to detect a change in the prevalence of disease (comparison with atypical L and H type)

Output name	Emergence
Unit	years, animals
Member State	France
TSE strain	L and H type; C and unknown
Monitoring baseline	HS>72, ES+FS>48, All CS
Monitoring scenario	No HS, ES+FS>48, All CS

Table 10 displays a comparison between the estimated number of years taken to detect a hypothetical 10% increase in French cases between classical and unknown data and atypical L and H type strain types. France was selected as the case study as the country has the highest number of L and H type strain typed within EU25 MS datasets. Results for the number of cases (detectable) and the number of infected animals between 2011 and the year of detection are provided, based on an annual 10% increase in the number of test positive animals. Note, when analysing results using only the atypical data only simulations from MSs where strain differentiation is routinely conducted will be valid.

Table 10: Estimated number of years to detect a hypothetical increase in prevalence of 10% per year in France for different strains starting in 2011, together with estimates of the number of detectable cases and infected animals missed during that time interval for the baseline model

Member State	Number of years to detect an annual 10% increase in prevalence and estimated number of positives missed – C&U strains						
	Current number test positives (baseline, scenario)	Upper CI limit (0.975)	Years to detection (i.e. cross upper CI limit) (baseline, scenario)	Total test positives at detection (baseline, scenario)	Number of extra cases under scenario before detection (scenario-baseline)	Total infected animals at detection (baseline, scenario)	Number of extra infected animals dead under scenario before detection (scenario – baseline)
FR-L&H	1.26, 0.94	10.95	24, 27	111.70, 114.20	2.49	304.88, 417.20	112.32
FR-C&U	2.64, 1.99	6.65	11, 14	48.87, 55.71	6.84	129.50, 195.49	65.99

For France (FR), the upper CI limit in 2011 was an estimated 11 for atypical strains and 6.7 for classical and unknown strains, indicating that a significant increase in the number of cases would be detected when a year with greater than 11 or 6.7 cases occurs. For FR, the estimated number of atypical cases, when considering a 10% increase from the current testing year, was greater than 11 at 24 years for the baseline regime, and 27 years after under the scenario regime. Over these time periods (24 and 27 years) the model estimates a total of approximately 112 observed cases under the baseline regime and 114 cases under the scenario regime. For classical and unknown strains the results are similar, with the estimated number of cases greater than the upper threshold at 11 years for the baseline and 14 years for the scenario monitoring regime. Between these years an estimated 49 cases and 56 cases were observed. The results for France can be compared to those provided in Table 7 for all strains, where the estimated years to cross the upper CI limit were 11 and 14 years for the baseline.

5. Parameter uncertainty and sensitivity analysis

Underpinning the estimate of true prevalence and design prevalence are four key assumptions made in the absence of data or assumptions due to model design: (1) the merging of the eradication measures exit stream with fallen stock; (2) the proportion of animals by age interval > 155 months parameterised by the average of UK data between 2008 and 2010, (3) use of an exponential distribution to model the true prevalence, and (4) the use of the binomial to estimate the design prevalence (sampling without replacement). Additionally, there is uncertainty associated with two estimated parameters; the age at onset and test sensitivity.

5.1 Eradication measures

Those animals culled under the eradication measures have traditionally been difficult to include in modelling work as for most MSs there are insufficient test positive data to estimate prevalence on a cohort basis. To investigate the importance of the merging of the eradication measures stream with fallen stock, those EU25 cases identified in the eradication measures stream were removed from the analysis. There were 39 test positives in the eradication measures exit stream between 2002 and 2011. As shown in Table 11, by removing the eradication measures test positives there is a slight decrease in the estimated mean number of cases in 2011 (0.6 cases).

Table 11: Estimated mean number of EU25 cases detected in fallen stock of all strains with 95% confidence intervals (CI) and observed cases in fallen stock from 2011

Streams	FS cases observed 2011	Number of animals detected under baseline monitoring in one year: all strains
		Baseline detected in fallen stock stream [CI]
Dataset minus eradication measures cases	19	17.2 [5.3 , 130.7]
Dataset including eradication measures cases (baseline)	19+0	17.8 [5.6 , 131.7]

5.2 Age of animals >155 months

The proportion of animals > 155 months slaughtered/dead by 12 month interval up till 204 months (17 years) is not known for most MSs. The total number slaughtered/dead > 155 months by exit stream are known for the majority of EU25 countries. Therefore, the assumption was made that the proportions by 12 monthly intervals were the same as that recorded in the UK between 2008 and 2010 as listed in Table 2. To investigate the impact of this assumption two different scenarios have been used; (a) there is an equal probability of slaughter/death per 12 month interval up to 204 months, and (b) all animals > 155 months are slaughtered/dead by 167 months.

Table 12: Estimated mean number of EU25 cases detected for different age > 155 months assumptions across all streams with all strains with 95% confidence (CI) and observed cases from 2011

% animals >155 m	All Cases observed 2011	Number of animals detected under baseline monitoring in one year: all strains
		Baseline detected from all streams [CI]
UK data (baseline)	28	28.3 [10.9 , 147.5]
(a) Equal probability for each 12 months		28.4 [10.9 , 147.7]
(b) All between 155 and 167 months		26.9 [10.4 , 144.9]

From Table 12 it can be seen that assuming that all animals have an equal probability of slaughter/death for each 12 month interval between 155 and 204 months, or using the UK data from 2008 to 2010, results in a slight increase in the number of cases (0.1 cases per year) with little effect on the confidence intervals at one decimal place. Assuming that all animals are slaughtered in the interval 155 to 167 months decreases the model estimates for the number of test positive animals by a mean of 1.4 cases per year.

From this analysis, it appears there is little requirement for using actual data for the proportion of animals > 155 months slaughtered/dead by 12 month interval up till 204 months which may require considerable resources to collect for each MS, as an equal probability provides similar results. However, separate 12 intervals from 155 months to 204 months does impact results and should therefore be included.

5.3 Selection of model distribution to estimate true prevalence

Historically, using the exponential distribution to model the trend in BSE cases by birth cohort has been an appropriate choice at the tail end of the epidemic. The assumption when using an exponential distribution is that the data described are monotonically decreasing. However, when considering each MS individually, there may be cases where the exponential distribution may not be the best choice of model. Other distributions which could be fitted were investigated and the most likely choice, a Weibull model was elaborated further. The Weibull distribution can be fitted to data that does not monotonically decrease, but data must be non-negative. The Weibull distribution could not be automatically fitted to data for a number of MSs (AT, CY, EE, EL, FI, HU, LT, LU, LV, MT, SE and SI) due to greater instability when compared to the exponential model. For those MSs where the Weibull could be automatically fitted, the resulting estimated number of cases was lower than for that estimated using the exponential distribution.

An important consideration is to compare the model fit over time using the validation graphs. Figure 3 provides the graphs for Spain and France. For Spain, shown in graphs (i) and (ii), the fitting of a Weibull distribution produces a better fit with observed data than the exponential, whereas for France, shown in graphs (iii) and (iv), the exponential yields the better fit for more recent years. From comparing the fit of the Weibull to the exponential for all MSs with cases, only the Weibull fit for Germany is better when compared to the exponential.

Given that the Weibull could not be used in the automated model for systematically modelling all MSs, and was a poorer fit for those countries with recent positive data (excluding Spain and Germany), the exponential was confirmed as the most appropriate distribution for the purposes of this project requiring the fitting of all data for MSs in the EU25 with one distribution.

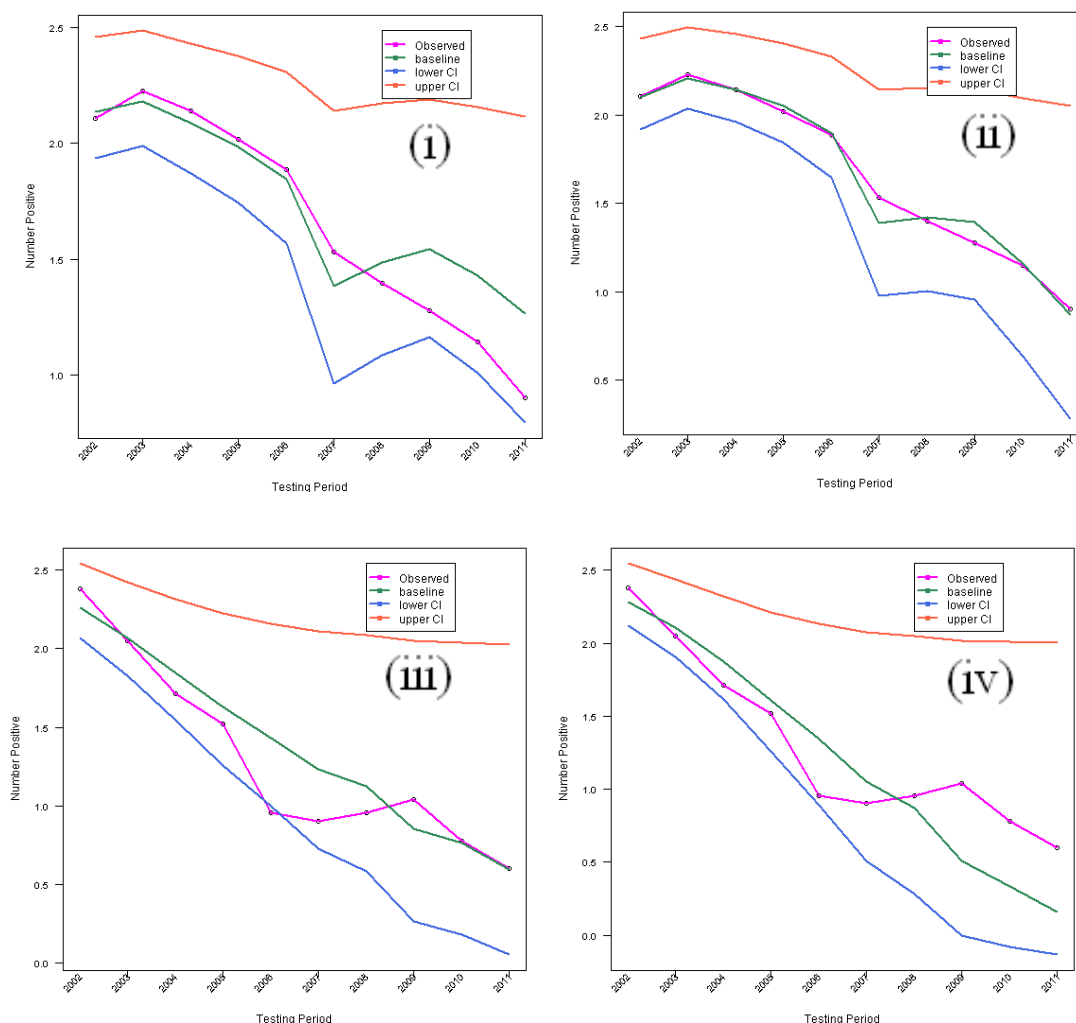


Figure 3: Comparison of log10 predicted number of cases per year with model and member state; (i) Exponential Spain, (ii) Weibull Spain, (iii) Exponential France, and (iv) Weibull France

5.4 Selection of sample size distribution

The sample size calculation was developed assuming an infinite population, that is sampling with replacement. This was achieved using a binomial distribution rather than a hypergeometric distribution for estimation of the probability that at least one animal is detected. Application of the binomial distribution is a straightforward calculation which does not suffer from multiple factorials that are an element of the hypergeometric equation, which can be problematic to calculate. As a rule of thumb, the binomial distribution can be used to approximate the hypergeometric when the sample size is less than 10% of the sampled population. Therefore, for many EU25 countries the binomial approximation is close to the hypergeometric for the countries with larger cattle populations. However, for countries with a small slaughter population, application of the binomial approximation may lead to an overestimation of the required number of animals to be sampled. Therefore, the difference in results achieved when applying the binomial approximation and hypergeometric distribution have been compared.

The impact of the infinite population assumption was tested by developing the equivalent formula for

a finite population size, using the approximation to the hypergeometric adopted in Cannon and Roe (1982). The following equation was derived to estimate the number of healthy slaughter animals required to be tested (where n_{HS} is the total number of animals in the healthy slaughter population in the MS and all other parameters are as defined in Section B3 of Appendix B).

$$\Pi_{HS}(y_0) = \frac{\log(1 - \tau) - \log(1 - \pi_{CS})N_{CS}^*(y_0) - \log(1 - \pi_{ES})N_{ES}(y_0) - \log(1 - \pi_{FS})N_{FS}(y_0)}{\log \left(1 - \frac{\pi_{HS}n_{HS}}{n_{HS} - \frac{\Pi_{HS} - 1}{2}} \right)}$$

It can be seen that if the required sample size, Π_{HS} , is small relative to n_{HS} , then the formula is approximately equal to the sample size formula assuming an infinite population. A key assumption required in order to use this derived hypergeometric distribution is of random sampling. To account for this, the method employed uses the test population, assuming random sampling would occur within this population. Therefore, outputs can be compared to the main detectable prevalence in test population results where an infinite population is assumed. The application of the equation was validated by showing that as $n_{HS} \rightarrow \infty$ the results converged to the values in Table 5.

Implementation of the hypergeometric equation in the model is not straightforward. To produce results comparable with Table 5 required the use of a solver routine, as Π_{HS} appears on both the left and right hand side of the equation. Comparing the hypergeometric results with the results from Table 5 it was observed that:

- Where the model converged, there was little difference in the results for many MSs, mostly those with greater than 50,000 HS animals tested in 2011 (EU8, Belgium, Germany, Denmark, Spain, Finland, Italy, Poland, Portugal, Sweden and the UK).
- There was a noticeable reduction for certain MSs in the number of HS animals predicted to be tested in order to achieve a design prevalence of 1 in 100,000 (Austria, Finland and Sweden). The majority of these MSs test less than 50,000 HS animals. While the number to test was estimated to be smaller this number was still greater than the number of HS animals currently tested by for Austria and Sweden. However, for Finland the number to test using the hypergeometric equation estimates 16,223 as compared to the binomial approximation of 34,146. Finland tests 27,041 animals, and therefore using the hypergeometric equation results would test a sufficient number.
- There were a number of MSs where the solver routine could not ascertain a viable value for the number of healthy slaughter animals to test, these tended to be the MSs which were predicted to have 0 HS to test in Table 4 and included EU25, EU17, France, Ireland, and the Netherlands.
- The hypergeometric equation does not appear to be producing realistic results for MSs where the EU17 is used as a proxy (Austria, Cyprus, Greece, Lithuania, Luxembourg and Sweden).

In conclusion, this analysis suggests that, for those countries which do not test a large number of HS animals, the number of animals needed to be tested are still greater than the number that are actually tested with the exception of Finland. For all other MSs the key conclusion that those MSs are not achieving a sufficient design prevalence to reduce current levels of testing remains whether the hypergeometric or binomial based sample size formula is used.

The use of the hypergeometric equation for the estimation of the number of healthy slaughter animals

to test, to achieve a desired design prevalence, for specific MSs with small population sizes, may be more appropriate than the binomial approximation. However, it cannot be usefully applied across all EU25 MSs as the method employed requires a solver routine which does not work for all MSs.

5.5 Age at onset and test sensitivity

There is uncertainty associated with two estimated parameters; the age at onset and test sensitivity. To investigate the importance of this uncertainty, the EU25 number of test positives was estimated with combinations of the upper and lower confidence interval values and the baseline parameter values for the age of onset parameters α_{ln} β_{ln} (refer to Table 3) and the test sensitivity parameter ν (refer to section 2.3) with results shown in Figure 4. It can be seen from the Figure that the age of onset has a greater influence on the estimated test positives. Values for the upper confidence interval for the age of onset result in a higher estimate of test positives, regardless of the value of the test sensitivity. A similar trend was observed for the majority of individual MSs (results not shown in this report).

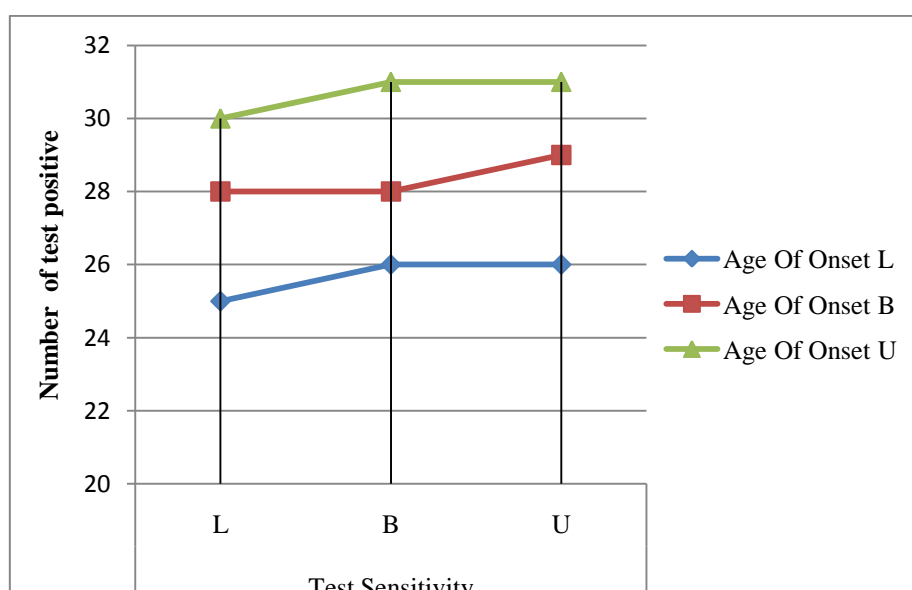


Figure 4: Number of model predicted HS test positive animals from EU25 when model is run with various combination of values for age of onset and test sensitivity: L=Lower confidence interval values, U=upper confidence interval values, B=baseline values

The sensitivity of the model results to the age at onset would appear to justify the approach taken within the model to determine the distribution of the age at onset for different populations rather than the use of one distribution to cover all MSs and any strain differences as shown in Table 3.

CONCLUSIONS

This final report and associated C-TSEMM package provides a model (supported by a user-friendly interface) to evaluate different TSE monitoring options in cattle for their capability in following the trend (declining or increasing) of the current BSE epidemic and to detect a hypothetical new TSE disease in cattle.

The model has been written as a flexible software package, with a bespoke user-interface for users to input parameters and scenarios. The model has been developed to investigate various sampling scenarios, including the current system of systematically sampling cattle at certain ages and other potential options such as random sampling of the healthy cattle population.

Various outputs can be generated based on either the detectable prevalence or infection prevalence. The detectable prevalence is the period prevalence in a given year of detectable infected animals, whereas the infection prevalence is the period prevalence in a given year of infected animals. The detectable prevalence is estimated in the tested population and in the standing population. For the tested population, this is calculated by the model's predicted number of adult tested animals (>24 months) that would test positive by a diagnostic test, divided by the total number of animals tested in one year. For the standing population, this is calculated by the model's predicted number of adult animals (>24 months), in the standing population, that would test positive by a diagnostic test, divided by the total number of adult animals in the standing population.

There are a number of key assumptions in order to implement the model for each member state:

Transforming input data

- The exit streams for cattle in Europe have been rationalised in healthy slaughter, emergency slaughter, fallen stock and clinical suspects. Clinical signs at ante mortem (AM) appears to be indistinct from emergency slaughter and therefore has been merged in that stream. Animals culled under the eradication measures are traditionally difficult to include in modelling work as for most countries there are insufficient test positive data to estimate prevalence on a cohort basis. These were incorporated into the fallen stock category.
- For MSs with no, or very few, BSE cases post 2001 an alternative estimate of prevalence is required. This has been estimated for those MSs based on the average prevalence of the group of MSs with BSE cases under which they were placed in the previous EFSA Opinion (EU17 or the EU8 group) and are listed in Appendix C. This results in an overestimate of prevalence for countries with no recorded cases as they are assumed to be a merged epidemiological unit with countries where cases are observed.

Model assumptions

- The exponential distribution can be used to describe the declining trend in BSE prevalence in the EU25. While other distributions could be fitted, analysis of alternative distributions has indicated that an exponential decay of prevalence over time is appropriate for the majority of European data.
- The binomial distribution is used to calculate the number of animals to test in order to achieve a specific design prevalence. A hypergeometric distribution may produce lower estimates for MSs with small slaughter populations, however, application of the hypergeometric distribution does not alter the conclusion that those MSs are not achieving a sufficient design prevalence to reduce current levels of testing with the exception of Finland which would experience a slight decrease in the number of animals required to be tested.

- Cases from the clinical suspect (CS) stream and fallen stock (FS) stream are identified at the end of the incubation period, that is, death is as a result of the disease. Whereas healthy slaughter (HS) and emergency slaughter (ES) animals may be within a period of time before clinical onset depending on the distribution of the age at onset and test sensitivity. This assumption impacts the number of infected animals within these streams. The number of infected animals within these streams is estimated as the number detected and those not detected due to test sensitivity. For the fallen stock and clinical suspect stream it is assumed that all animals are detectable, and therefore the difference between the number of test positive animals and the number of infected animals is small and equal to the test sensitivity at clinical onset (0.99).
- Prevalence estimated for the combined streams (clinical suspects and fallen stock, healthy slaughter and emergency slaughter) can be divided into the individual exit streams according to the proportion of test positive animals observed in those streams. Where there are no test positives, it is assumed that the number of animals tested by birth cohort and testing year is an appropriate proxy.
- It is assumed that all cases of BSE are typed by strain such that the number tested for classical and unknown strains is the same number as that tested for atypical H and L type. This is not the case for all MSs and therefore only simulations from MSs where strain differentiation is routinely conducted will be valid.
- In estimating either the re-emergence of an existing TSE, or emergence of a new TSE disease in cattle, it is assumed that the disease can be detected by current testing assays.

Results

Results from C-TSEMM are provided for the *detectable prevalence*; the model predicted number of test positive animals (those animals that would test positive if tested) divided by the total population, and the *infection prevalence* defined as the model predicted number of infected animals (including those that would test positive if tested and those that would be false negatives) divided by the total population.

The results from the model indicate that for the EU25 merged into an epidemiological area:

- The baseline monitoring regime in the EU25 has an estimated design prevalence of 1 in 6,354,930 using the detectable prevalence in the standing population to a confidence level of 0.95, and 1 in 1,992,928 in the tested population. When the infection prevalence in the test population is used, a design prevalence of 1 in 611,268 is estimated to a confidence level of 0.95.
- Given that the EU25 baseline estimated design prevalence is sufficiently greater than 1 in 100,000 at the 0.95 confidence level, using either of the prevalences estimated, there is no requirement to test animals in the healthy slaughter stream given that animals are tested > 48 months in the emergency slaughter, fallen stock, and clinical suspect streams.
- For an alternative monitoring scenario, that of no testing of healthy slaughtered animals, an estimated 10 [5.2 , 16] cases would be missed in the first year in the EU25. The reduction in observed cases would impact when a theoretical emergence would be detected by observing the upper confidence interval of current cases in one year. The baseline regime would 'detect' the significant increase in an estimated 6 years, whilst the scenario would detect after 11 years with an additional estimated 108 cases observed. During this three year interval an estimated

974 additional infected animals would be slaughtered/die.

For individual member states:

- Based on the standing population and using the detectable prevalence, twelve MSs (Austria, Belgium, Germany, Denmark, Spain, France, Ireland, Italy, Netherlands, Poland, Sweden and the UK) have a design prevalence of at least 1 in 100 000 using the estimated detectable prevalence to a confidence level of 0.95. Of the twenty five MSs:
 - Eight MSs (i.e. Belgium, Germany, Denmark, Spain, France, Ireland, Netherlands, and the UK) do not require the testing of any healthy slaughter animals to meet a 1 in 100 000 design prevalence.
 - Four MSs (i.e. Austria, Italy, Poland and Sweden) do require testing less healthy slaughtered animals older than 72 months of age than the total number tested in those MSs in 2011 in order to meet a 1 in 100 000 design prevalence.
 - In thirteen MSs (i.e. Cyprus, Czech Republic, Estonia, Finland, Greece, Hungary, Latvia, Lithuania, Luxembourg, Malta, Portugal, Slovenia and Slovakia) the number of healthy slaughtered animals older than 72 months of age that would need to be tested in order to meet a 1 in 100 000 design prevalence is higher than the actual number tested in 2011.
- Based on the tested population, the baseline monitoring regimes in seven MSs (Germany, Spain, France, Ireland, Italy, Poland and UK) have a design prevalence of at least 1 in 100 000 using the estimated detectable prevalence to a confidence level of 0.95. Additionally, France has a design prevalence greater than 1 in 100,000 estimated using the prevalence of infection.
 - Three MSs (Germany, France and the UK) do not require the testing of any healthy slaughter animals to meet a 1 in 100 000 design prevalence based on the test population using the detectable prevalence. Using the prevalence of infection this falls to one MS (France).
 - Four MSs (Spain, Ireland, Italy, and Poland) could reduce testing in the healthy slaughter and still achieve a design prevalence of 1 in 100,000 at the 0.95 confidence level.
- For an alternative monitoring scenario, that of no testing of healthy slaughtered animals, the monitoring system of France and Ireland are estimated to be least affected by the lifting of testing from healthy slaughtered animals, with an additional three years to detect the significant increase. Italy and Poland's monitoring regimes are estimated to be the most affected, with a difference of 16 years between the baseline and monitoring regimes.
- For the combined strains of classical, L type, H type and unknown, there is an estimated 0.7 missed cases in France (case study) when comparing the baseline and scenario monitoring regimes. Considering only atypical strains, there would be an estimated 0.32 cases missed in France. This represented an approximate reduction of 24%-25% of detected cases for France. The time taken for detecting a significant change in the number of cases per year is estimated to be higher for atypical strains than for classical and unknown. The baseline estimates are 24 years for atypical strains and 11 for classical and unknown.

When considering these results, apart from the MS demographic data and case history, there are two

key parameter inputs, namely the age at onset and test sensitivity. Of the two, the age at onset has the greatest impact on the model outputs, yielding estimated EU25 values of 26 to 31 cases for the most recent year using the upper and lower confidence intervals for the age at onset with the mean estimate for test sensitivity.

The results provided in this report are derived from the systematic fitting of an exponential model to MS data and estimation of the design prevalence using the binomial distribution. Sensitivity analysis indicates that in rare cases, the Weibull distribution as opposed to the exponential, for estimating the trend, may be preferable (for Spain and Germany). Whilst, for MSs with small slaughter populations, the binomial distribution may increase the estimated number of animals needed to be tested to achieve a design prevalence as compared to the hypergeometric distribution. However, from an application of the hypergeometric distribution (provided in the sensitivity analysis) the key conclusion that those MSs are not achieving a sufficient design prevalence to reduce current levels of testing remains whether the hypergeometric or binomial based sample size formula is used with the exception of Finland which would experience a slight decrease in the number of animals required to be tested.

In conclusion, the model and results presented in this report permit the systematic comparison of BSE in cattle monitoring systems across EU25 member states for current and scenario monitoring regimes.

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APPENDICES

A. SUMMARY OF THE EU LEGISLATION ON BSE MONITORING IN 2012

	EU 27
Legal provisions	Regulation (EC) No 999/2001 as amended Commission Decision 2007/182/EC as amended Commission Decision 2009/719/EC as amended
Testing categories/streams	
Special emergency slaughter	For EU-25: all > 48 months For BG and RO: all > 24 months
Clinical signs at AM	
Fallen stock	
Animals slaughtered for human consumption	For EU-25: all > 72 months For BG and RO: all > 30 months
BSE suspects	All

B. SUPPLEMENTARY CALCULATIONS

B1 TRUE PREVALENCE OF INFECTION CALCULATIONS

Maximum likelihood methods are used to estimate two parameters for the best fitting exponential distribution (estimating the trend in prevalence) and one parameter determining the division in prevalence between the CS and FS exit streams and the HS and ES exit streams. This generic model for estimating the prevalence trend, probability of detecting a test positive, and probability of an infected animal by birth cohort by testing year is applied to all Member State (MS) data. While other distributions could be fitted, analysis of data suggests that an exponential decay of prevalence over time is appropriate for the majority of European data.

The equation of the curve to be fit is given by

$$r(c) = A_1 e^{A_2 c} \quad (\text{Eq. 1})$$

where r is the estimated proportion of animals infected in birth cohort, c ($c=1$ for the earliest birth cohort in the model calculations set as 1985, as this is the earliest birth cohort from which we are able to determine from the data where MSs have tested animals in the period 2002-2011) and A_1 and A_2 are model parameters which must be estimated together with a differential slaughter parameter, $B=e(b)/(1+e(b))$, by minimising the negative log-likelihood (using the *nlminb*¹⁰ function in R), given initial parameter estimates $\{\hat{A}_1, \hat{A}_2, \hat{B}\}$.

The differential slaughter parameter estimates the probability of an animal being slaughtered in the healthy slaughter or emergency slaughter stream *given* that it is infected (thus $1-B$ is the probability of being in the clinical suspects or fallen stock streams, given that it is infected). Since we are incorporating both active and passive surveillance data into the back-calculation model, the log-likelihood function consists of two parts: the log-likelihood functions of the data for the number of clinical test positives (clinical suspects (CS) and fallen stock (FS)) and pre-clinical test positives (healthy slaughter (HS) and emergency slaughter (ES)) respectively. The testing data for cases in cohort c , at testing year y arises from a binomial distribution. Therefore, ignoring additive constants, the log likelihood function for clinical test positives, L_{CSFS} , is given by

$$L_{CSFS} = \sum_{c=1}^{c_N} \sum_{y=1}^{y_N} (N_{CSFS}(c, y) - D_{CSFS}(c, y)) \ln(1 - \hat{\Lambda}_{CSFS}(c, y)) + D_{CSFS}(c, y) \ln(\hat{\Lambda}_{CSFS}(c, y))$$

Where c_N is the total number of birth cohorts, y_N is the total number of testing periods, N_{CSFS} is the number of animals tested in the CSFS stream, D_{CSFS} is the number of test positives in the CSFS stream and $\hat{\Lambda}_{CSFS}$ is the probability of being detected as a clinical case. This is estimated by the equation

$$\hat{\Lambda}_{CSFS}(c, y) = (1 - \hat{B}) * \psi(0) * O(a) * \hat{r}(c), \quad (\text{Eq. 2})$$

where $\psi(0)$ is the sensitivity of the test at clinical onset (it is assumed that for infected animals in the clinical suspect and fallen stock stream that clinical onset has occurred very recently as death is due to disease), which is assumed to be equal to 0.99 and $O(a)$ is the probability of onset of clinical signs for animals of age $a=y-c$

¹⁰ R documentation on *nlminb* function: <http://127.0.0.1:27947/library/stats/html/nlminb.html>

$$O(a) = \int_{z=a-0.5}^{z=a+0.5} O(z) dz$$

It is assumed that clinical cases arise in the passive surveillance and fallen stock stream, where death is due to disease onset. The log likelihood function for the pre-clinical test positives is given by

$$L_{HSES} = \sum_{c=1}^{c_N} \sum_{y=1}^{y_N} (N_{HSES}(c, y) - D_{HSES}(c, y)) \ln(1 - \hat{\Lambda}_{HSES}(c, y)) + D_{HSES}(c, y) \ln(\hat{\Lambda}_{HSES}(c, y))$$

where N_{HSES} is the number of animals tested in the HS and ES streams, D_{HSES} is the number of test positives in the HS and ES streams and $\hat{\Lambda}_{HSES}$ is the probability of being detected as a case, if culled at age a , which is the product of the probability of being in the HS or ES stream given infection (\hat{B}), the probability of being infected, ($\hat{r}(c)$), and the probability of being detected by the post-mortem test (which depends on the length of time before clinical onset that the animal was slaughtered)

The equation for $\hat{\Lambda}_{HSES}$ is

$$\hat{\Lambda}_{HSES}(c, y) = \hat{B} * \left[\int_{x=t}^{x=\infty} O(x) \psi(x-t) dx \right] * \hat{r}(c). \text{ (Eq. 3)}$$

Note that as $x \rightarrow \infty$, $\psi(x-t) \rightarrow 0$ and thus so does the integral. For all values of t that could be used in the model, evaluation of the integral will be practically indistinguishable from zero for values of $x > t+200$ (i.e. probability of detection through the rapid test will be negligible at two years prior to clinical onset).

$$\int_{x=t+201}^{x=\infty} O(x) \psi(x-t) dx \cong 0.$$

$$\int_{x=t}^{x=\infty} O(x) \psi(x-t) dx = \int_{x=t}^{x=t+200} O(x) \psi(x-t) dx + \int_{x=t+201}^{x=\infty} O(x) \psi(x-t) dx \cong \int_{x=t+200}^{x=\infty} O(x) \psi(x-t) dx$$

Consequently, for ease of numerical computation, in the model we truncate the upper value of the integral at $t+200$.

Therefore the overall negative log-likelihood function that must be minimised to estimate the model parameters, L , is given by

$$L = -\sum_{c=1}^C \sum_{y=1}^Y (L_{CSFS}(c, y) + L_{HSES}(c, y)),$$

The determined value for the exponential curve for the true prevalence, $r(c)$, using estimated values of A_1 , A_2 , and B are subsequently used to estimate the number of test positive animals and infected animals in the four exit streams. Using these estimated parameters, the probability of an animal at testing year y and cohort c testing positive in the CS and FS streams, $\Lambda_{CSFS}(c, y)$, is estimated using Eq. 2 and the probability of testing positive in the HS and ES streams, $\Lambda_{HSES}(c, y)$, is estimated by Eq. 3.

The model also estimates the probability of infection by cohort by year which does not depend on the

sensitivity of the test. The estimate for the probability of infection in the CS and FS streams is given by

$$\tilde{\Lambda}_{CSFS}(c, y) = (1 - B) * O(a) * r(c),$$

while the estimate for the probability of infection in the HS and ES streams is given by

$$\tilde{\Lambda}_{HSES}(c, y) = B * \left(\int_a^{\infty} O(x) dx \right) * r(c)$$

B2 MODEL PREDICTED NUMBER OF TEST POSITIVE AND INFECTED ANIMALS

The model estimates the number of test positives in the combined streams CS and FS, and HS and ES, $\Delta_k(c, y)$ by multiplying the probability of detecting a test positive animal, $\Lambda_k(c, y)$, with the number of animals tested $N_k(c, y)$. The number of infected animals, $\tilde{\Delta}_k(c, y)$ is estimated by multiplying the infection prevalence with the number of animals slaughtered/dead, $S_k(c, y)$, as given by the following equations:

$$\begin{aligned}\Delta_k(c, y) &= \Lambda_k^*(c, y) * N_k(c, y) \\ \tilde{\Delta}_k(c, y) &= \tilde{\Lambda}_k^*(c, y) * S_k(c, y)\end{aligned}$$

Note for the majority of age intervals, the number of animals tested is equal to the number of animals slaughtered/dead. The difference occurs within the young age ranges, where animals are generally not tested in the HS, ES and FS streams. The total number of test positive animals and the total number of infected animals by cohort and testing year are the sums of all streams yielding:

$$\begin{aligned}\Delta(c, y) &= \Delta_{CSFS}(c, y) + \Delta_{HSES}(c, y) \\ \tilde{\Delta}(c, y) &= \tilde{\Delta}_{CSFS}(c, y) + \tilde{\Delta}_{HSES}(c, y).\end{aligned}$$

B2.1 Estimating number infected and cases by exit stream

Given the totals for the number of animals in the CSFS and HSES combined streams, the individual stream results are estimated for the proportion of test positives from birth cohort c at testing year y , that are in the individual streams, according to the proportion of test positive animals observed in those streams. However, there are many MSs datasets where there are no test positives by exit stream, by birth cohort by year. Analysis of the data suggests that the proportion of test positives by exit stream varies over both age and testing period, so a more universal average value would not be appropriate. Cases from early testing periods were more frequently observed in the ES than the HS exit streams. However, the total number of animals in the ES has changed significantly for many MSs in recent years. Therefore, where there are no test positives, it is assumed that the number of animals tested is an appropriate proxy. Therefore, the probability of an animal from cohort c at testing period y being in stream k , $p_k(c, y)$, is given by

$$p_{CS}(c, y) = \begin{cases} D_{CS}(c, y) / D_{CSFS}(c, y) & D_{CSFS}(c, y) \neq 0 \\ N_{CS}(c, y) / N_{CSFS}(c, y) & D_{CSFS}(c, y) = 0 \end{cases}$$

$$p_{FS}(c, y) = 1 - p_{CS}(c, y),$$

$$p_{HS}(c, y) = \begin{cases} D_{HS}(c, y) / D_{HSES}(c, y) & D_{HSES}(c, y) \neq 0 \\ N_{HS}(c, y) / N_{HSES}(c, y) & D_{HSES}(c, y) = 0 \end{cases}$$

$$p_{ES}(c, y) = 1 - p_{HS}(c, y).$$

Therefore, the number of test positives in each stream are estimated by

$$\Delta_{CS}(c, y) = \Delta_{CSFS}(c, y) * p_{CS}(c, y),$$

$$\Delta_{FS}(c, y) = \Delta_{CSFS}(c, y) * p_{FS}(c, y),$$

$$\Delta_{HS}(c, y) = \Delta_{HSES}(c, y) * p_{HS}(c, y),$$

$$\Delta_{ES}(c, y) = \Delta_{HSES}(c, y) * p_{ES}(c, y)$$

and the number of infected animals in each exit stream:

$$\tilde{\Delta}_{CS}(c, y) = \tilde{\Delta}_{CSFS}(c, y) * p_{CS}(c, y),$$

$$\tilde{\Delta}_{FS}(c, y) = \tilde{\Delta}_{CSFS}(c, y) * p_{FS}(c, y),$$

$$\tilde{\Delta}_{HS}(c, y) = \tilde{\Delta}_{HSES}(c, y) * p_{HS}(c, y),$$

$$\tilde{\Delta}_{ES}(c, y) = \tilde{\Delta}_{HSES}(c, y) * p_{ES}(c, y).$$

To show a measure of the level of uncertainty about the model results we also fit the model using the 95% Poisson confidence intervals associated with the model predicted number of test positive animals. The confidence limit values for streams k , $\Delta_k(c, y)$, are given by using the quantile function in R for the gamma distribution, *qgamma*¹¹

$$\Delta_{k, Lower}(c, y) = qgamma(0.025, \Delta_k + 1)$$

$$\Delta_{k, Upper}(c, y) = qgamma(0.975, \Delta_k + 1)$$

¹¹ R documentation on *qgamma* function: <http://127.0.0.1:27538/library/stats/html/GammaDist.html>

B3 ESTIMATING THE DESIGN PREVALENCE

For a given design prevalence, d_p , we want to estimate the number of animals under the given monitoring regime within a given exit stream in the current year that need to be tested in order to achieve a ‘power’ of τ in a given MS.

This method involves scaling the MS outputs, under the assumption that the prevalence in the MS is equal to the design prevalence d_p . For the HS, ES and FS exit streams this entails scaling the estimated prevalence to this value. However, for the clinical suspect stream the number of animals tested is scaled. This is due to the fact that changes in the underlying prevalence within a MS would directly alter the number of clinical suspects tested rather than altering the proportion of animals that test positive.

The model predicted test prevalence for the current year, for stream k , under monitoring regime H , is found by dividing the number of test positives by the number of animals tested

$$\rho_k(y_0) = \sum_{c=1}^{c_N} \frac{\Delta_{k,H}(c, y_0)}{N(c, y_0)}.$$

where c_N is the number of birth cohorts in the dataset and y_0 is the current year. The overall detectable prevalence, δ , is found by dividing the number of test positives by the total number of animals tested

$$\delta(y_0) = \sum_{c=1}^{c_N} \frac{\Delta(c, y_0)}{N(c, y_0)}.$$

Similarly, the overall infection prevalence, $\tilde{\delta}$, is given by

$$\tilde{\delta}(y_0) = \sum_{c=1}^{c_N} \frac{\tilde{\Delta}(c, y_0)}{N(c, y_0)},$$

Next the estimated MS prevalence in the current testing year is scaled, by calculating a ‘design conversion factor’, d_c . Two estimates of d_c are calculated: the number that the overall detectable prevalence is required to be multiplied by in order to equal the design prevalence,

$$d_c = d_p / \delta_H$$

and the number that the overall true prevalence is required to be multiplied by in order to equal the design prevalence

$$\tilde{d}_c = d_p / \tilde{\delta}_H$$

The model also predicts test prevalence for the current year in the standing cattle population, using the standing population prevalence. In this case the overall detectable prevalence is given by

$$\delta = \frac{\sum_c N_s(c) r(c) \int_{a_c}^{a_c + \infty} O(x) \mu(x - a_c) dx}{\sum_c N_s(c)}$$

Where $N_s(c)$ is the number in the standing population in cohort c and $r(c)$ is the prevalence of infection in cohort c (estimated using the original model). The integral represents the proportion of the infected cattle in the standing population that would test positive if sampled by a rapid test. All other calculations proceed as before, using this alternative value of δ .

The scaled test prevalence at time t , for each stream, $\pi_H(y_0)$, is obtained by multiplying the model predicted test prevalence for each stream, $\rho_H(y_0)$, by the design conversion factor

$$\begin{aligned}\pi_H(y_0) &= d_c * \rho_H(y_0) \\ \tilde{\pi}_H(y_0) &= \tilde{d}_c * \rho_H(y_0)\end{aligned}$$

As previously mentioned, for the clinical suspects exit stream the number tested is scaled as opposed to the prevalence.

$$\begin{aligned}N_{CS}^*(y_0) &= d_c(y_0) * N_{CS}(y_0); \pi_{CS}(y_0) = \rho_{CS}(y_0) \\ \tilde{N}_{CS}^*(y_0) &= \tilde{d}_c(y_0) * N_{CS}(y_0); \tilde{\pi}_{CS}(y_0) = \rho_{CS}(y_0)\end{aligned}$$

The number of animals of the healthy slaughter exit stream that need to be tested, in order that at least one animal is detected with a probability of τ , is given by using binomial formulae (as used in Cannon & Roe).

$$\begin{aligned}\Pi_{HS}(y_0) &= \frac{\log(1-\tau) - \log(1-\pi_{CS})N_{CS}^*(y_0) - \log(1-\pi_{ES})N_{ES}(y_0) - \log(1-\pi_{FS})N_{FS}(y_0)}{\log(1-\pi_{HS})} \\ \tilde{\Pi}_{HS}(t_0) &= \frac{\log(1-\tau) - \log(1-\tilde{\pi}_{CS})\tilde{N}_{CS}^*(y_0) - \log(1-\tilde{\pi}_{ES})N_{ES}(y_0) - \log(1-\tilde{\pi}_{FS})N_{FS}(y_0)}{\log(1-\tilde{\pi}_{HS})}\end{aligned}$$

(Eq. 2)

These equations can be rearranged to calculate the number of animals that need to be tested for any of the other streams.

Note that Π_{HS} will be negative if the MS is already testing sufficient animals in the other streams to achieve the desired confidence interval.

B3.1 Current ‘design prevalence’

The design prevalence formula can be rearranged to calculate the ‘design prevalence’ under the monitoring regime, given the number of animals tested in all four exit streams, for the design prevalence and the infection prevalence. This is done by finding the value of d_p at which the estimated number of animals to be tested in each stream, Π_k , is equal to the actual number of animals tested in each stream N_k . For the detectable prevalence, this is done by using the *nlminb* function in R to find the value of the design prevalence, d_p , that minimises the function

$$F(d_p) = (\Pi_{HS}(y_0) - N_{HS}(y_0))^2 + (\Pi_{ES}(y_0) - N_{ES}(y_0))^2 + (\Pi_{FS}(y_0) - N_{FS}(y_0))^2 + (\Pi_{CS}(y_0) - N_{CS}(y_0))^2$$

We do a similar thing for the infection prevalence

$$F(\tilde{d}_p) = (\tilde{\Pi}_{HS}(y_0) - N_{HS}(y_0))^2 + (\tilde{\Pi}_{ES}(y_0) - N_{ES}(y_0))^2 + (\tilde{\Pi}_{FS}(y_0) - N_{FS}(y_0))^2 + (\tilde{\Pi}_{CS}(y_0) - N_{CS}(y_0))^2$$

B4 ESTIMATING THE NUMBER MISSED BETWEEN MONITORING REGIMES

To calculate the number missed between monitoring regimes the most recent testing data is used to estimate the number of test positives under each scheme. The number of test positives missed is estimated for the most recent testing year, $\Delta_M(y_0)$, by subtracting the number of estimated test positives from the Scenario run, $\Delta_S(y_0)$, from the number of test positives from the Baseline run, $\Delta_B(t_0)$

$$\Delta_M(y_0) = \Delta_B(y_0) - \Delta_S(y_0).$$

B5 ESTIMATING THE TIME TO DETECTION BETWEEN MONITORING REGIMES

To simulate a change in the current declining prevalence of cattle BSE to a theoretical emergence, the number of cases is increased from 2011, assuming a $\omega\%$ increase per year. The value of ω is defined by the user, with options of 3%, 10%, and 20%. The model predicted trend is used to estimate the year, Y , when an increasing trend in BSE prevalence will be detected, which we define as the year in which the number of test positives will exceed the upper confidence limit estimate for the number of test positives in the current testing year y_0 , $\Delta_{B,Upper}(y_0)$. To calculate this value we fit the model using the upper 95% Poisson confidence interval values associated with the input number of test positive animals. The confidence limit values for streams k , $D_k(c, y)$, are given by using the quantile function in R for the gamma distribution, *qgamma*¹²

$$D_{k,Upper}(c, y) = qgamma(0.0975, D_k + 1).$$

The model is then run using these values to get the estimate of $\Delta_{B,Upper}(y_0)$. Assuming that there will be a $\omega\%$ increase in prevalence every year, starting in the current testing year y_0 , then Y is given by the formula

¹² R documentation on *qgamma* function: <http://127.0.0.1:27538/library/stats/html/GammaDist.html>

$$Y = \frac{\log(\Delta_{B,Upper}(y_0)) - \log(\Delta_B(y_0))}{\log(1 + \omega/100)},$$

B6 SUMMARY TABLE OF INPUT PARAMETERS

Table B1: Description of input parameters and variables together with the symbols and distribution/value

Description	Parameter	Probability distribution/value	Reference
Test prevalence parameters	$A1, A2$	variable	Model estimate
Age of animal	a	$y-c$	
Differential slaughter parameter	B	variable	Model estimate
Birth cohort	c	1=born in 1985, 2=born in 1986	
Number of test positives for stream(s) k	D_k	variable	European Commission, 2012
Design prevalence	d_p	1/100,000	
Exit streams	k	{HS,ES,FS,CS, HSES,FS,CS }	
Number of animals tested by stream(s)	N_k	Input data	European Commission, 2012
Proportion of test positive animals by stream(s)	\hat{P}_k	variable	Model estimate
Number of animals slaughtered/dead by stream(s)	S_k	variable	European Commission, 2012
Time before onset (months), dependent on the age of animal (a)	t	variable	Model estimate
Test prevalence trend by birth cohort	$r(c)$	$A_1 e^{A_2 c}$	
Testing year (year of sampling)	y	{2001,..., 2011}	European Commission, 2012
Test sensitivity	$\Psi(t)$	$\frac{\exp(\alpha + \beta * t)}{1 + \exp(\alpha + \beta * t)}$	(Arnold and Wilesmith, 2003)
Test sensitivity default parameters	α, β	5.94, -40.8	(Arnold and Wilesmith, 2003)
Probability of clinical onset at age a (by month)	$O(a)$	$O(a) \sim \text{LogNormal}(\mu, \sigma)$	Model estimates
Age of onset default parameters	μ, σ	Refer to Table 3	European Commission, 2012
Design prevalence 'power' (lower, upper values)	$\tau (\tau_L, \tau_U)$	0.95 (0.925, 0.975)	Assumed by author
Probability of detecting a test positive for stream(s) k	Λ_k	variable	Model estimates
Probability of infection for stream(s) k	$\tilde{\Lambda}_k$	variable	Model estimates
Model predicted number of test positive animals for stream(s) k	Δ_k	variable	Model estimates
Model predicted number of infected animals for stream(s) k	$\tilde{\Delta}_k$	variable	Model estimates
Increasing trend rate (for emergence)	ω	10%	European Commission, 2012

C. LIST OF TERRITORIES INCLUDED IN MODEL VERSION AND PREVALENCE ESTIMATION

Acronym	Territory	Data used for prevalence estimate
AT	Austria	Merged EU17
BE	Belgium	Belgium
BG	Bulgaria	Not currently estimated
CY	Cyprus	Merged EU17
CZ	Czech Republic	Czech Republic
DK	Denmark	Denmark
EE	Estonia	Merged EU8
FI	Finland	Merged EU17
FR	France	France
DE	Germany	Germany
EL	Greece	Merged EU17
HU	Hungary	Merged EU8
IE	Ireland	Ireland
IT	Italy	Italy
LV	Latvia	Merged EU8
LT	Lithuania	Merged EU8
LU	Luxembourg	Merged EU17
MT	Malta	Merged EU8
NL	Netherlands	Netherlands
PL	Poland	Poland
PT	Portugal	Portugal
RO	Romania	Not currently estimated
SK	Slovakia	Slovakia
SI	Slovenia	Slovenia
ES	Spain	Spain
SE	Sweden	Merged EU17
UK	United Kingdom	United Kingdom
EU25	EU25	Merged EU25
EU27	EU27	Not currently estimated
NO	Norway	Not currently estimated
CH	Switzerland	Not currently estimated
HR	Croatia	Not currently estimated
MK	Former Yugoslav Republic of Macedonia	Not currently estimated
IS	Iceland	Not currently estimated
TR	Turkey	Not currently estimated
AL	Albania	Not currently estimated
BA	Bosnia and Herzegovina	Not currently estimated
KS	Kosovo under UN Security Council Resolution 1244	Not currently estimated
ME	Montenegro	Not currently estimated
SRB	Serbia	Not currently estimated

GLOSSARY AND ABBREVIATIONS

BSE Bovine Spongiform Encephalopathy

Cases Test positive animal that are tested.

CS Clinical suspects risk category

CSV Comma Separated Values

Detectable prevalence in test population:

Period prevalence in a given year of detectable infected animals in the test population. Calculated by the model's predicted number of adult animals (>24 months), in the population of animals tested, that would test positive by a diagnostic test, divided by the total number of animals tested in one year.

Detectable prevalence in standing population:

Period prevalence in a given year of detectable infected animals in the standing population. Calculated by the model's predicted number of adult animals (>24 months), in the standing population, that would test positive by a diagnostic test, divided by the total number of adult animals in the standing population.

ES Emergency slaughtered risk category

FS Fallen stock risk category

GIF Graphics interchange format

HS Healthy slaughtered risk category

Infected animals Total of animals that would test positive, if tested, and those infected that would test negative.

Infection prevalence in test population:

Period prevalence in a given year of infected animals in the test population. Calculated by the model's predicted number of adult animals (>24 months), in the population of animals tested, that are actually infected (i.e. animals that may or may not test positive or be showing clinical symptoms) divided by the total number of animals tested in year.

MS Member State of the European Community

PNG Portable Network Graphics

Test positive animals Animals that would test positive if tested.

TSE Transmissible Spongiform Encephalopathy

VBA Visual Basic for Applications