Assessment of the effectiveness of bluetongue surveillance in Belgium and Switzerland

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Abstract

The objective of the project was to compare the surveillance for demonstrating freedom from Bluetongue (BT) infection between seven European countries. The surveillance was considered as in place in 2011 and 2012. Information describing the BT virus surveillance activities were collected from relevant veterinary services or institutes by a comprehensive questionnaire. The sensitivity of the surveillance systems of Belgium and Switzerland were investigated more in depth using scenario tree modeling. The effectiveness of individual and combined surveillance system components regarding demonstration of freedom from infection was quantified by simulating the sensitivity of individual components as well as the combined sensitivity of all components together. Analysis of the questionnaires confirmed that Belgium and Switzerland conducted active and passive surveillance according to the European Commission regulation 1266/2007, last amended in May 2012. For active surveillance of BT, both countries had implemented a risk-based approach: in 2012, Belgium sampled non-vaccinated dairy cattle, and Switzerland, in 2011, sampled non-vaccinated cattle in high-risk areas. The overall sensitivity of both surveillance systems was calculated to be approximately 100%. In both countries, a main contributor to the high sensitivity was passive surveillance, i.e. case detection by farmers and veterinarians. The main reason for the high value is seen in the very large population under observation and the relatively long observation time of one year. Our results demonstrated that for demonstrating disease freedom, investment in keeping disease awareness at a high level may be more effective than expensive active data collection.

Keywords: Surveillance, Bluetongue, Scenario tree modeling, Belgium, Switzerland

1. Introduction

In 2006, Bluetongue virus (BTV) serotype 8 (BTV-8), which was previously reported in the sub-Sahara region, Asia, South America and Spain emerged unexpectedly in northern Europe, in a region including Belgium, France, Germany, Luxembourg and the Netherlands (Mehlhorn et al., 2007; Toussaint et al., 2006). In the following years, the virus spread rapidly throughout Europe. In Belgium, the first BTV-8 cases occurred in August 2006. From September to November 2006 the disease spread over the entire country. After the vector-free season during the winter, BT re-emerged in July 2007 and within two weeks, the whole of Belgium was affected (Alliance, 2006). In 2008, vaccination against BTV-8 was mandatory in Belgium. Switzerland had an early warning system for BT in place since 2003, in the southern part of the country. After the unexpected outbreak in 2006 in the northern neighboring countries, the surveillance system was adapted to the new epidemic situation. The first BTV-8 cases in Switzerland were diagnosed in October 2007 (Schorer & Schwermer, 2012), four cases in cattle and one case in sheep. Vaccination against BTV-8 was mandatory in Switzerland in 2008, 2009 and 2010, which prevented further spread of the disease.

This incursion caused substantial economic losses due to mortality and reduced production in cattle and sheep. Further, restrictions on trade of animals and animal products between BTV infected and non-infected areas (Maclachlan & Osburn, 2006) had economic consequences. Due to the rapid spread and economic significance, the European Union passed a regulation on the surveillance of BT (European Commission, 2007a). The countries in northern Europe implemented a range of surveillance strategies from 2006 onwards with the aim to detect and control the spread of BTV as

well as to prove freedom from disease after implementation of the control measures. The performance (sensitivity) of a surveillance system to establish freedom from disease at a defined design prevalence can be assessed as its capacity to detect at least one infected animal given that the disease is present. A surveillance system consist one or more surveillance system components (SSC). The components may be passive (clinical observations) or active (e.g. cross-sectional serological survey)(Doherr & Audigé, 2001). Scenario tree modelling, a method to estimate the sensitivity of surveillance systems was first described by Martin at al. (Martin, Cameron, & Greiner, 2007). In summary, those models compute the sensitivity of a complete surveillance system and its components based on a bifurcation chart (Fig. 1) describing the demography of the reference population, its risk distribution and the diagnostic protocols. All SSCs are considered to be independent and a specificity of each SSC is assumed to be 100%. This approach accounts for the fact that not all animals in a population have the same probability of being infected or detected. The method has been widely used for designing and evaluating risk-based surveillance (Frössling, Agren, Eliasson-Selling, & Lewerin, 2009; Hadorn, Racloz, Schwermer, & Stärk, 2009; Knight-Jones, Hauser, Matthes, & Stärk, 2010).

In the present study, the objective was to describe and compare the implemented surveillance activities to demonstrate freedom from BTV infection in different European countries in 2011 and 2012. The analysis focused particularly on Belgium and Switzerland, because comprehensive data were available from both countries. Both countries used passive and active surveillance according to the European Commission regulation 1266/2007, and followed a risk-based approach for latter: Belgium sampled non-vaccinated dairy cattle, Switzerland sampled non-vaccinated cattle in geographical areas which were considered high risk.

2. Material and Methods

2.1. Data collection

A comprehensive questionnaire was developed to collect all existing data about the past and ongoing surveillance activities to demonstrate freedom from BTV infection in Belgium, Switzerland, Germany, the Netherlands, Denmark, Sweden and Norway from 2006 to 2012. The questionnaire was completed during a telephone or face-to-face interview and supplemented by e-mail correspondence. It was structured into the following parts:

General context: Aim of BT surveillance, motivation and legal basis.

Population data: General data about the cattle and sheep population.

Surveillance design: Random sample or risk-based, risk factors for BT in the country considered and the probabilities for each risk factor, distribution of the population within the country, i.e. distribution of the population into different subpopulation according to the identified risk factors. *Surveillance system components:* Seven possible components of a BT surveillance system were identified by literature review (Hadorn et al., 2009; Vandenbussche et al., 2008), and were included in the questionnaire: a) Blood serology in cattle, b) Blood serology in sheep, c) Bulk milk serology, d) Direct pathogen detection in blood samples of cattle (means detection of virus antigen), e) Vector monitoring (VM), f) Reporting of clinical signs in cattle and g) Reporting of clinical signs in sheep. For each component, we collected details such as the target population, the sample size (n_{Animals}), the number of herds included in the survey (n_{Herd}), the number of animals sampled per herd (n_{inHerd}), the frequency of sampling and if it was a simple random sample or risk-based sampling. Finally, respondents had to specify the diagnostic test used to analyze the samples and its sensitivity and specificity.

2.2. The scenario tree model

A generic scenario tree model was designed for the passive and active BT surveillance and adapted to the situation of Belgium and Switzerland, respectively. The surveillance period was one year. The generic scenario tree consisted a sequence of nodes, with branches dividing the reference population into subpopulations homogeneous with regard to the probabilities of infection and detection of BT. According to Martin et al. (2007) nodes were categorized as infection, detection or risk nodes. The infection nodes specify the infection status of a unit, detection nodes define all events that must take place for the detection of the infection, and risk nodes represent those factors that affected the probability of a unit being infected or detected. Figure 1 shows the generic tree for the active SSC. The scenario tree model for passive SSCs had the same structure, but between the nodes "animal status" and "test" additional detection nodes were implemented, in the following order: "morbidity", "disease awareness of the farmer" and "disease awareness of the veterinarian".

2.2.1. The model settings and assumptions

All calculations were conducted according to Martin et al. (Martin et al., 2007). In a first step we calculated the herd level sensitivity (SeH), means the probability to detect an infected herd, i.e. sampling was modelled using a hypergeometric distribution, because a large proportion of the herds in Switzerland were small. We defined the following five risk category nodes: species (cattle vs. sheep), geographical risk (high risk areas vs. low risk areas), production type (dairy vs. meat), husbandry type (outdoor access vs. indoor husbandry), vaccination status (non-vaccinated vs. vaccinated). Each of these risk nodes had two possible outcomes, resulting in a total of 32 population strata each with different risks of BTV infection. The contribution of a given risk node to the overall probability of infection (or detection) depends on the relative risk of its branches and the proportion of animals exposed to it. To further combine the risks of successive branches they need to be "adjusted" for the proportion exposed to them according to formula 1. The effective probability of infection in a herd is then computed by multiplying the herd-level design prevalence and the "adjusted risks" of the contributing branches along a limb in the scenario tree (formula 3). As described for scenario tree models (Martin et al., 2007) the relative risk of infection in a high risk category (RR_{HR}) compared to a low risk category (RR_{LR}) was included in the model as adjusted risks (AR_{HR} and AR_{LR}). These adjusted risks considered both the relative risk and the proportion of herds (PrPop_{HR} and PrPop_{LR}) within the different categories by using the formulae:

$$AR_{LR} = \frac{1}{RR_{HR} x PrPop_{HR} + PrPop_{LR}}$$
(1)

and

$$AR_{HR} = RR_{HR} x AR_{LR} \tag{2}$$

For each stratum defined by the risk categories, the design prevalence and the product of adjusted risks on herd level were used to calculate the effective probability of a herd being infected (EPIH):

$$EPIH = P_H^* \times \prod_{j=1}^{J} AR_j$$
(3)

where *J* denotes scenario tree strarum within the population. In this way the total probability of infection (i.e. design prevalence) is shifted at each bifurcation to the stratum with higher risk. Because no data were available from literature, relative risks (RR) were estimated based on, expert opinion. The combined estimates of the four experts from different European countries are shown in table 1. The probability to detect an infected herd, was computed using the following formula:

$$SeH = 1 - \left(1 - TestSe \ x \ \frac{n_{inHerd}}{N_{inHerd}}\right)^{(N_{inHerd} \times P_A^*)}$$
(4)

where *TestSe* is the sensitivity of the diagnostic test, n_{inHerd} is the number of animals sampled in a herd N_{inHerd} is the number of animals in a herd, and P_A^* is the within-herd design prevalence. Finally, the sensitivity of a SSC (CSe), is composed of the probabilities to detect at least one case in any of the stratum of the scenario tree, according to formula 5:

$$CSe = 1 - \prod \left[(1 - SeH \, x \frac{n_{RS}}{N_{RS}})^{(N_{RS} \, x \, EPIH_{RS})} \right]$$
(5)

where n_{RS} is the number of herds sampled in the risk stratum RS and N_{RS} is the total number of herds in risk stratum RS, and *EPIH_{RS}* is the effective probability of a herd being infected in the risk stratum RS. For the passive SSC the detection process is additionally influenced by morbidity and disease awareness resulting in the following formulae:

$$SeH = 1 - \left(1 - DA_{farmer} \ x \ DA_{vet} \ x \ TestSe \ x \ 1\right)^{(N_{inHerd} \ x \ P_A^* \ x \ morbidity)}$$
(6)

and

$$CSe = 1 - \prod \left[(1 - SeH \ x \ 1)^{(N_{RS} \ x \ EPIH_{RS})} \right]$$
(7)

where DA_{farmer} is the disease awareness of the farmer and DA_{vet} is the disease awareness of the veterinarian, and the other variables as described before. The product of P_A^* and *morbidity* describes the probability of one animal susceptible of showing clinical sings at the set design prevalence, by multiplying with N_{inHerd} we achieve the total number of clinically diseased animals. $N_{RS} \times EPIH_{RS} \times$ *morbidity* is the number of diseased herds in the risk stratum.

The sensitivity aggregated at risk stratum level, means the probability to detect one case in a particular risk stratum, can be calculated in active and passive SSC by the formula:

$$SeRS = 1 - (1 - SeH)^{(N_{RS} \times EPIH_{RS})}$$
 (8)

For the clinical component, it was assumed that all non-vaccinated animals were susceptible to be infected and show clinical signs, thus the sample size was set equal to the total number of animals and herds in population. If more than one SSC is used within the surveillance system, the overall system sensitivity SSe is calculated with the following formulae:

$$SSe = 1 - \prod (1 - CSe_j) \tag{9}$$

where *j* denotes the jth SSC. The SSe is the probability that one or more SSC will yield a positive result if the population is infected at the design prevalence.

The model was implemented using Excel (Office Excel 2010, Microsoft Corporation, Redmond, WA,

USA) and @RISK 6.1.2 Industrial Edition (Palisade). 10,000 iterations were performed.



Fig. 1. Scenario tree illustrating active SSC to demonstrate freedom from BTV infection. Dashed lines indicate that a branch is identical to the other branch for that particular node and that for simplification it has been excluded from the illustration.

2.2.2. Input parameters

The model was executed using parameters derived from the surveillance data of Belgium 2012 and Switzerland 2011. Switzerland did not perform BT surveillance in 2012, therefore the data from 2011 had to be used. All parameters are listed in Tables 1 and 2.The herd-level design prevalence (P*_H) was set at 2% (according to EC 1266/2007). To account for within-herd correlation (Faes et al., 2011) we used a P*_A of 10%. DA_{farmer} included the probability that the farmer sees the clinical signs given the animal is infected and shows clinical signs and the probability that the farmer calls the veterinarian. DA_{vet} is the probability that the veterinarian takes a sample and sends it to the laboratory. Because BT has not the same pathology and clinical manifestation in cattle as in sheep we made a difference in DA_{farmer} and DA_{vet} regarding these two species. We used mortality values for BTV-8 from Elbers et al. (A. R. W. Elbers et al., 2008) as the lower margin for the DA of farmers and veterinarians; because we assumed that dead animals would trigger further investigation. For the upper margin of DA_{farmer} and DA_{vet}, i.e. the maximal sensitivity we used the estimated sensitivity of expert examination reported by Elbers et al. (a R. W. Elbers, Backx, Ekker, van der Spek, & van Rijn, 2008). We assumed the veterinarians to be more aware of BT than the farmers, therefore we defined the most likely values at 1/5 of the range for the farmers and 4/5 for the veterinarians.

| | | Minimum | Most | Maximum | Source |
|-------------------|--------------|---------|--------|-------------|-----------------------------------|
| | | value | likely | value | |
| | | | value | | |
| NinHerd | Belgium | | | | |
| | Cattle dairy | 1 | 70 | 1542 | |
| | Cattle meat | 1 | 70 | 1542 | |
| | Sheep | - | 7 | - | CODA-CERVA, Brussels ¹ |
| | Switzerland | | | | |
| | Cattle dairy | 1 | 20 | 600 | |
| | Cattle meat | 1 | 60 | 600 | FVO, Berne ² |
| | Sheep | 1 | 35 | 2500 | |
| | | | | | |
| $n_{inHerd}{}^3$ | Belgium | 2 | 15 | 17 | CODA-CERVA, Brussels |
| | Switzerland | - | 10 | - | FVO, Berne |
| N _{Herd} | Belgium | | | See table 2 | CODA-CERVA, Brussels |
| | Switzerland | | | | FVO, Berne |
| N _{Herd} | Belgium | - | 300 | - | CODA-CERVA, Brussels |
| | Switzerland | - | 300 | - | FVO, Berne |
| Morbidity | Cattle | - | 0.025 | - | (A. R. W. Elbers et al., |
| | Sheep | - | 0.077 | - | 2008) |

Table 1: Summary of the inputs for the scenario tree model, developed to estimate the sensitivity of the SSC as well as the overall sensitivity of the surveillance systems of Belgium and Switzerland to demonstrate freedom from BTV infection for the years 2012 and 2011, respectively.

| DA _{farmer} | Cattle | 0.0022 | 0.15 | 0.67 | (a R. W. Elbers et al., |
|----------------------|---------------------------------------|--------|--------|--------|--------------------------|
| | Sheep | 0.044 | 0.2 | 0.76 | 2008; A. R. W. Elbers et |
| | | | | | al., 2008) |
| DA _{vet} | Cattle | 0.0022 | 0.55 | 0.67 | (a R. W. Elbers et al., |
| | Sheep | 0.044 | 0.6 | 0.76 | 2008; A. R. W. Elbers et |
| | | | | | al., 2008) |
| TestSE | RT-qPCR | | | | |
| | Cattle | 0.9902 | 0.995 | 0.997 | (Vandenbussche et al., |
| | Sheep | 0.9903 | 0.9955 | 0.9998 | 2008) |
| | cELISA | | | | |
| | Cattle | 0.8528 | 0.8865 | 0.9229 | |
| Relative | | | | | |
| Risks | RR _{Species} ⁴ | 0.5 | 1 | 1.6 | Expert opinion |
| | RR _{Geo} ⁵ | 1 | 2 | 50 | Expert opinion |
| | RR _{Production} ⁶ | 0.5 | 1 | 2 | Expert opinion |
| | RRoutdoor ⁷ | 0.05 | 1 | 3 | Expert opinion |
| | RRvaccination ⁸ | 1 | 10 | 100 | Expert opinion |

¹ CODA-CERVA=Veterinary and Agrochemical Research Centre, ² FVO=Federal Veterinary Office, ³ n_{inHerd} is the number of animals sampled per herd,⁴ is the risk of being infected with BTV in cattle compared to sheep, ⁵ is the risk of being infected with BTV in geographical high risk areas compared to geographical low risk areas, ⁶ is the risk of being infected with BTV in dairy production compared to meat production, ⁷ is the risk of being infected with BTV in herds with outdoor access compared to indoor husbandry, ⁸ is the risk of being infected with BTV in non-vaccinated herds compared to vaccinated herds.

2.2.3. Performance and sensitivity analysis

The risk-based sampling as described in the questionnaire was compared to random sampling without considering risks. The model was validated by setting some critical parameters to zero. To identify further parameters of the model with potentially high influence on the outcome, sensitivity analysis was performed by using a built-in sensitivity analysis function of @RISK using systematic changes in selected inputs, i.e. it perturbs the values within the range that is given in the PERT distribution, while the other parameters are kept constant. We did not consider the RR values in the sensitivity analysis because they did not have a big impact on the outcome (data not shown) and we were more interested in the influence of the other parameters. We chose tornado charts to display the ranking of the influential input parameters of the scenario tree model. We conducted the analysis for the active and passive SSC separately.

3. Results

3.1. BT surveillance in participating European countries

All partner countries conducted passive and active surveillance as well as vector monitoring based on

EC regulation 1266/2007 (European Commission, 2007b). The proportions of the target populations

and the structure into population risk strata are summarized in Table 2.

| Switzerland the data are from 2011, because Switzerland did no BT surveillance in 2012. | | | | | | | |
|---|------------------|------------------|--------------------|-------------|-----------|-----------|-----------|
| | Belgium | Switzerland | Germany | The | Denmark | Sweden | Norway |
| | | | | Netherlands | | | |
| Number of cattle | 2,670,292 | 1,427,584 | 12,477,389 | 3,885,000 | 1,613,276 | 1,511,846 | 860,965 |
| Number of cattle herds | 28,172 | 41,027 | 162,867 | 31,752 | 24,886 | 20,503 | 15,511 |
| Number of sheep | 220,561 | 469,034 | 1,641,000 | 1,088,000 | 179,995 | 622,711 | 2,214,985 |
| Number of sheep herds | 31,523 | 13,620 | 10,600 | 12,528 | 9,571 | 9,499 | 14,423 |
| Proportions of cattle regard | ling the distrib | oution within th | e different risk s | strata: | | | |
| Geographical risk | | | | | | | |
| high | 0.36 | 0.30 | - | - | 0.10 | - | 0.30 |
| low | 0.64 | 0.70 | - | - | 0.90 | - | 0.70 |
| Dairy production | | 0.64 | 0.62 | 0.67 | | 0.25 | |
| in high risk | 0.45 | - | - | - | 0.34 | - | 0.56 |
| in low risk | 0.38 | - | - | - | 0.21 | - | 0.68 |
| Meat production | | 0.33 | 0.38 | 0.33 | | 0.75 | |
| in high risk | 0.55 | - | - | - | 0.66 | - | 0.44 |
| in low risk | 0.62 | - | - | - | 0.79 | - | 0.32 |
| Husbandry type | | | | | | | |
| outdoor | 0.74 | 1.00 | - | 0.8 | - | 1.00 | 1.00 |
| indoor | 0.26 | 0.00 | - | 0.2 | - | 0.00 | 0.00 |
| Vaccination status | | | | | | | |
| No vaccination | 0.21 | 0.38 | - | - | 0.76 | 0.35 | 1.00 |
| Vaccination | 0.79 | 0.62 | - | - | 0.24 | 0.65 | 0.00 |

Table 2: Summary of the data describing the implemented surveillance systems to demonstrate freedom from BTV infection in participating European countries, obtained from the questionnaire. All data are from 2012 except for Switzerland the data are from 2011, because Switzerland did no BT surveillance in 2012.

In Table 3, the active SSCs of each country are described. In addition, VM had been conducted in

each country over several years, with the aim to determine the vector active period. No details of VM

are provided here.

Table 3: Details about the implementation of active surveillance strategies to demonstrate freedom from bluetongue infection are shown. The presented data are from 2012 except those for Switzerland are from 2011, because Switzerland did no BT surveillance in 2012.

| Country | Performed SSC's | Target | Risk based | | Sample size | | Test |
|--------------------|--|--------------|------------------------------|-------------|----------------------|--------------------|---------------------------|
| | | ροριιατιστι | Geographical localization | Vaccination | n _{Animals} | n _{Herds} | |
| Belgium | Blood serology in sentinel cattle and direct pathogen detection | Dairy cattle | - | + | 4,500 | 300 | cELISA, PCR (parallel) |
| Switzerland | Direct pathogen detection | Cattle | + | + | 3,000 | 300 | PCR |
| Germany | Direct pathogen detection | Cattle | - | - | 43,939 | - | PCR |
| The Netherlands | Blood serology in cattle | Dairy cattle | - | + | 378 | 290 | cELISA |
| Denmark | Blood serology in cattle | Cattle | - | - | 600 | 60 | cELISA |

| Sweden | Direct pathogen detection | Cattle | + | + | 55,834 | 2,405 | PCR |
|--------|------------------------------|--------------|---|---|--------|-------|-----------------------|
| Norway | Bulk milk serology | Dairy cattle | + | - | 134 | 259 | ELISA on bulk milk |

3.1.1. Additional results for Belgium and Switzerland

Belgium sampled a total of 4,500 non-vaccinated dairy cattle from 300 sentinel herds.

Switzerland sampled 3,000 non-vaccinated cattle in geographical high risk areas (Racloz, 2008) from 300 herds. In addition, both countries conducted passive clinical surveillance.

3.2. Estimation of surveillance sensitivities in Belgium and Switzerland

The estimated median of CSe and SSe as well as some SeRS are presented in Table 4. For active surveillance, Belgium implemented sampling of non-vaccinated dairy cattle, and tested with RT-qPCR and cELISA parallel. Switzerland sampled non-vaccinated cattle in geographical high risk areas, and samples were analyzed with RT-qPCR.

Table 4: Output of the scenario tree model, designed to estimate the sensitivity of BT surveillance in Belgium (2012) and Switzerland (2011). Results for the overall sensitivity of the surveillance system (SSe), the sensitivity of SSC's (CSe) and the sensitivity aggregated at risk stratum level (SeRS) are shown.

| | Median | 95% confidence interval |
|---------------------------|--------|-------------------------|
| Belgium | | |
| SSe | 1 | 1-1 |
| CSe_active | 1 | 0.9999-1 |
| SeRS_Cattle | 1 | 0.9999-1 |
| SeRS_HighRisk | 1 | 0.9998-1 |
| SeRS_LowRisk | 0.9842 | 0.7282-0.9999 |
| SeRS_Indoor | 0.9974 | 0.9155-0.9999 |
| SeRS_Outdoor | 1 | 0.9998-1 |
| CSe_passive | 0.9998 | 0.9372-1 |
| SeRS_Cattle | 1 | 1-1 |
| SeRS_HighRisk | 1 | 0.9999-1 |
| SeRS_LowRisk | 0.9999 | 0.9282-1 |
| SeRS_Dairy | 1 | 0.9995-1 |
| SeRS_Meat | 1 | 0.9999-1 |
| SeRS_Indoor | 1 | 0.9784-1 |
| SeRS_Outdoor | 1 | 0.9999-1 |
| Switzerland | | |
| SSe | 1 | 1-1 |
| CSe_active | 1 | 0.9999-1 |
| SeRS_Cattle | 0.9999 | 0.9999-1 |
| SeRS_HighRisk | 0.9999 | 0.9999-1 |
| SeRS_LowRisk ¹ | 0 | 0 |
| SeRS_Indoor ² | 0 | 0 |
| SeRS_Outdoor | 0.9999 | 0.9999-1 |
| CSe_passive | 1 | 1-1 |
| SeRS_Cattle | 0.9998 | 1-1 |
| SeRS_HighRisk | 0.9995 | 0.9999-1 |
| SeRS_LowRisk | 0.9905 | 0.9611-1 |

| SeRS_Dairy | 0.9995 | 0.9999-1 |
|--------------------------|--------|----------|
| SeRS_Meat | 0.9976 | 0.9982-1 |
| SeRS_Indoor ² | 0 | 0 |
| SeRS Outdoor | 0.9998 | 1-1 |

¹ the result is 0 because Switzerland did no active sampling in the low risk area, ² the result is 0 because Switzerland has no animals in the indoor stratum.

As the charts for Belgium and Switzerland look very similar, we only show the Belgian tornado chart

of the active SSC (Fig. 2) and the tornado chart of the passive SSC from Switzerland (Fig. 3).



Figure 2: Tornado chart of all input parameter for the active SSC in Belgium 2012. The chart shows the influence of the model inputs on the median sensitivity (CSe) of the active SSC.

The sensitivity analysis for the active SSC identified the number of tested herds (n_{Herd}) and the design prevalence (P^*_{Herd}) to be the most influential inputs in Belgium as well as in Switzerland. The effect is the same for both inputs: If n_{Herd} and P^*_{Herd} decrease, the component sensitivity decreases too. Because the component sensitivity is 1 for the baseline scenario, it remains constant when n_{Herd} and P^*_{Herd} increase. However, the magnitude of the impact of n_{Herd} as well as P^*_{Herd} is largely negligible even for a substantial decrease. For the active components of both countries, the sensitivity was re-estimated in a scenario ignoring differential risk of infection in all risk nodes. The result of this simulation was a drop of the median sensitivity of 1% for Belgium and 2% for Switzerland.



Figure 3: Tornado chart of all input parameter for the passive SSC in Switzerland 2011. The chart shows the influence of the model inputs on the median sensitivity (CSe) of the passive SSC.

For the passive SSC, the sensitivity analysis identified DA_{farmer} in cattle and in sheep to be the most influential inputs both in Belgium and in Switzerland. The CSe decreases if the DA decreases. The absolute drop was only 0.01 which is practically irrelevant as sensitivities higher than 99% are not targeted, for illustration see Figure 4.

In the scenario where the DA_{farmer} in cattle and in sheep was defined to be zero the output was as expected zero.



Figure 4: The disease awareness of the farmer in cattle and in sheep was identified to be the most influential input for the passive SSC in the scenario tree model to demonstrate freedom from BTV infection. In the left figure the influence of the disease awareness of the farmer in cattle and sheep on sensitivity of the passive SSC of the surveillance system from Belgium, 2012, is shown. In the right figure the influence of the disease awareness of the farmer in cattle and sheep on sensitivity of the passive SSC of the surveillance system from sensitivity of the passive SSC of the surveillance system from Switzerland, 2011, is shown. ¹The base values for DA_{farmer} in cattle and sheep are 15% and 20%, respectively.

The sensitivity analysis indicated that a change in N_{inHerd} had no effect on the sensitivity to detect at least one infected animal, given that the disease is present, within the SSC (data not shown). Fig. 5 illustrate the influence of N_{Herd} on the CSe in the passive SSC, N_{Herd} has to decrease massively to produce a decrease in the CSe.



Figure 5: Shows the influence of the input parameter N_{Herd}, i.e. all cattle and sheep herds in the country, on the median CSe in the passive SSC of the scenario tree model, developed to demonstrate freedom from BTV infection. Data are from Belgium 2012.

4. Discussion

The aim of this study was to evaluate the performance of current surveillance practices to demonstrate freedom from BTV infection in a number of European countries. The surveillance systems of Belgium and Switzerland were investigated in-depth using scenario tree modeling. The passive surveillance yielded an extremely high median sensitivity of 99.98% in both countries, with a 95% CI of 0.93 to 1 in Belgium and 0.89 to 1 in Switzerland. In the study of Welby et al. 2013 comparable results with sensitivity values of 98% and 99% for the passive surveillance in Belgium 2007 (Welby et al., 2013) were shown. We concluded that this outcome was largely related to the combination of the very large population and the low values we used for P*_A and P*_H. But as shown with the sensitivity analysis, the sample size (N_{Herd}) in the passive SSC had only a limited influence, as the median CSe remained 80% after a decrease of the sample size of 79%. As we assumed that all animals were to be "sampled" and seen by the farmer every day in the passive SSC, it follows that the

sensitivity is accumulating over the time of the surveillance period and can reach such high values. The efficiency of the passive SSC is very much dependent on the DA of farmers and veterinarians. The sensitivity analysis confirmed the DA of farmers and veterinarians to be the most influential input. In other studies, the DA of farmers and veterinarians were identified to be influential on the sensitivity of passive surveillance too (Doherr & Audigé, 2001; Hadorn et al., 2009). In a situation where vaccination is applied or when natural immunity has been established, clinical signs may no longer be distinct which may result in a decreased disease awareness. Regarding passive surveillance, an issue that should be discussed is the risk of underreporting. The motivation of farmers and veterinarians to report cases is difficult to assess, but fewer reports of cases finally result in a lower value for the DA. Because we defined the DA of farmers and veterinarians with a wide distribution we consider underreporting to be covered.

Although Belgium and Switzerland had different strategies for active surveillance of BT, both reached a median CSe of 100% by risk-based sampling of non-vaccinated dairy cattle, and non-vaccinated cattle in geographical high risk areas, respectively. The number of sampled animals within each herd was shown to be high enough in both countries to reach a high herd sensitivity level (2 to 17, most likely 13 samples per herd in Belgium and 10 samples per herd in Switzerland). With a sample size of 300 herds out of 3,228 located in the targeted risk stratum in Belgium and 4,756 in Switzerland, respectively, both countries also used a large sample size at herd level. The results of the sensitivity analysis for the active SCC showed, that n_{Herd} and P^*_{Herd} were the most influential inputs on the CSe. This finding can be explained with the mathematics behind the scenario trees: both values are part of the last step within the calculation of CSe, furthermore P^*_{Herd} is in the exponent of the formula and n_{Herd} is in the numerator of the division. That means that both values are highly influential in the calculation.

The results of the questionnaire showed that all partner countries focused their active BT surveillance on cattle and neglected more or less sheep. This is probably due to the fact that most of the diagnostic tests for BT are validated for cattle only. Further, field observations in 2006 to 2007

showed that cattle seems to be more susceptible for BTV8 than sheep (Méroc et al., 2008). This could be a potential risk, especially if a large proportion of cattle are vaccinated.

Five of the seven countries used a risked-based approach in their sampling. That demonstrated the interest in this method, probably indicating a wish to increase the efficiency of existing surveillance programs. The vector monitoring was done with the objective to determine the vector active period. This information can affect the design of active surveillance, mainly the time point of sampling. However, we did not consider the data about the vector active period within our scenario tree model, because we calculated the sensitivity over the whole year.

The output of stochastic scenario tree models will only be as good as the quality of the input data. To ensure data consistency and quality the questionnaires were filled in during a telephone interview or a face-to –face meeting. The RR values we used were based on expert opinion. Due to the fact that all four experts gave comparable values independent of each other, we assumed the values to be robust. Furthermore, stochastic simulation allows the inclusion of uncertainty and variability of inputs in the model.

The scenario tree methodology has proven to be a useful tool to quantify the sensitivity of a country's surveillance system (Frössling et al., 2012; Hadorn et al., 2009; Knight-Jones et al., 2010; Stärk et al., 2006). Alternatively, disease spread modelling could have been used. However, due to the common application and validation of scenario trees in the context of surveillance evaluation, we considered this approach to be accepted and standardized. Our scenario tree models had three key assumptions: The first assumption was that the specificity of the surveillance system to be 100%. If the specificity was imperfect, false positive results would be possible. In the situation of demonstrating freedom from disease each SSC should be seen to encompass all follow-up testing to resolve potential false positive outcomes. Other authors took a similar approach (Cannon, 2002; Martin et al., 2007). Second, we considered all SSC to be independent. This does not completely reflect reality, because there is an overlapping coverage of the population between SSC.

assumption is related to the way of calculation. Compared to the binomial, the hypergeometric approximation includes the herd size in the calculation. Because of the fact that we have small herds and a low P*_A, the hypergeometrical approximation is more suitable for our model. We defined all variables with uncertainties by using a pert distribution. The reason for this proceeding was the fact that we did not have enough information to use other distributions. Although the model was developed for the evaluation of BT in Belgium and Switzerland, it is not specific to Belgium and Switzerland. The design prevalence, the input parameters and the sensitivities of the diagnostic tests may be easy adapted to other population. The risk factors we defined and the RR values we used are specific for BT. The adaption of the model to another vector-borne disease is possible, but the risk factors and the RR must be adapted as well.

The estimated sensitivities of BT surveillance in Belgium and Switzerland were comparable despite different designs. This confirms that outcome-based surveillance targets provide flexibility in the design of components, taking into account local situation, feasibility and risk factors, and yet yield similar guarantees towards freedom status, as required by the international standards. On the other hand, one might conclude that the surveillance programs were too effective in the sense that both countries invested too much resource to demonstrate freedom from BT infection. Similar surveillance performance could have been achieved with less effort, i.e. mainly by using a smaller sample size. The preferred approach would be to decrease the number of animals within a herd rather than sampling fewer herds. In the light of these results, decision makers may re-consider legislation and continue to promote output-based standards (Cameron, 2012). This is especially significant regarding the financial effort of the applied surveillance strategies. In this context we suggest further studies regarding the costs of different SSC for BT surveillance. In general, formal evaluation of surveillance activities should be more systematically applied to assure that technical and economic targets are met as well as legal obligations.

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