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Editorial

Using scenario tree modelling to evaluate the probability of freedom from Enzootic bovine leukosis (EBL) in Italy and Slovenia

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Abstract

Documented freedom from disease is paramount for international free trade of animals and animal products. This study describes a scenario tree analysis to estimate the probability of freedom from Enzootic bovine leukosis (EBL) in Italy and Slovenia using information gathered via the data collection tool developed in the COST action project SOUND-control. Data on EBL control programmes (CPs) from 2018 to 2021 were used to build the models. Since animals are only sampled on the farm, one surveillance system component (SSC) was considered. The posterior probability of freedom (*PostPfree*) was estimated in time steps of one year, from 2018 to 2021. After each year, the calculated from the previous year, combined with the probability of introduction, was used as a prior probability for the next year. The herd level design prevalence was set to 0.2% in accordance with the Council Directive 64/432/EEC and the within herd design prevalence was set to 15%. As Slovenia implemented a risk-based surveillance, targeting the herds importing cattle, in its model the design herd prevalence was combined with an average adjusted risk to calculate the effective probability of a herd importing cattle being infected. The models were run for 10,000 iterations. Over the study period the mean estimates were: i) for Italy both the surveillance system sensitivity (*SSe*) and *PostPFree* 100%, with no differences between simulations and years, ii) for Slovenia the*SSe* was 50.5% while the *PostPFree* was 81.6%.

Keywords

Scenario tree model, Freedom from disease, Enzootic bovine leukosis, Italy, Slovenia

Introduction

Enzootic bovine leukosis (EBL) is the most common neoplastic disease of cattle caused by the bovine leukaemia virus (BLV) (Moratorio et al., 2013). The majority of the infected cattle remain asymptomatic while roughly 30% of them present with persistent lymphocytosis associated with non-malignant polyclonal expansion of B-cells, and less than 10% develop malignant lymphoma (Ghysdael et al., 1984). BLV is primarily transmitted horizontally through contact with body fluids. Iatrogenic procedures (e.g., use of infected needles) are the most common sources of infection. Vertical transmission may occur in utero or through the ingestion of infected colostrum or milk (Ruiz et al., 2018). *Hematophagus* flies are also suspected to contribute to the disease spread (Kuczewski et al., 2021).

EBL leads to a direct economic loss, due to clinical lymphosarcoma and loss of income from condemned carcasses. Additionally, BLV infection hinders the immune system, increasing the susceptibility of cattle to other opportunistic pathogens which, in turn, may lead to decreased milk production, reduced fertility, and increased heifer replacement costs. Lastly, the disease causes a significant economic impact, due to restrictions on the international trade of animal and animal products (Bartlett et al., 2020).

In the EU Animal Health Law Regulation (EU) 2016/429, EBL is listed in category C, which includes diseases for which an official free-status can be requested. The output-based nature of the regulations for EBL allows every country to implement its own control programme (CP), resulting in countries developing CPs that best suit the national industry (Hodnik et al., 2021). Therefore, output-based methods are required to compare the EBL status between countries and ensure a safe intracommunity trade (Costa et al., 2020).

Among others, Italy and Slovenia were recognized free from EBL. In 2017, Italy was declared free from EBL by the European Commission (European Commission, 2017), despite the presence of some limited endemic areas, so called "clusters". In Italy, the EBL control programme is heterogeneous because stricter control measures are applied in the clusters. Specifically, in the free territories cattle over 24 months old should be tested serologically with an ELISA screening on either individual samples or pooled samples (sera or bulk milk) based on a five-year plan (for instance, 20% of bovine and buffalo herds are controlled each year). Conversely, in the clusters all herds are monitored twice a year by individual serological screening of animals older than 6 months (Ordinanza Ministero della Salute, 2015). In both free-areas and clusters, if a sample tests positive in the screening test, the Italian Reference Laboratory for the Study of Ruminant Retroviral Infectious Diseases (CEREL) must confirm the diagnosis obtained in the first instance by using a confirmatory ELISA and AGID test. With regard to Slovenia, it obtained EBL-free status in 2005. Since then, it has maintained this status in accordance with Directive 64/432/EEC. However, in 2016 EBL was detected in three imported animals. Therefore, targeted risk-based monitoring has been carried out since 2017. Every year, in herds that have imported animals from EBL risk areas in the past two years, all animals older than 12 months are tested with an ELISA test on individual serum. If positive animals are detected, two samples are taken: one serum sample for antibody detection with ELISA and one blood sample with EDTA for antigen detection (PCR).

Scenario tree modelling is the reference statistical method used to demonstrate freedom from disease. This is an objective quantitative analysis which enables the comparison of the output of different CPs. Scenario tree modelling combines multiple sources of data to support claims of freedom from animal diseases. One of the assumptions of the method is that there is no evidence that the disease is present in the country or zone (Martin et al., 2007).

The COST Action (CA17110) SOUND control promoted and supported the use of output-based methods, such as scenario tree modelling, with the view of substantiating the confidence of freedom and cost-effectiveness in current CPs for endemic infectious cattle diseases, such as EBL (SOUND control - COST Action CA17110 Website, 2022).

The aim of this study was to estimate the probability of freedom from EBL in Italy and Slovenia, using scenario tree analysis.

Materials and Methods

The information gathered through a SOUND control data protocol (previously designed by Rapaliute et al. (Rapaliute et al., 2021), improved and embedded in a Google form later on) was used to build a stochastic scenario tree model and produce estimates of probability of EBL freedom in Italy and Slovenia. For each country, a representative provided data on the EBL CP. The representatives were government veterinary officers or researchers. Information on active surveillance is summarized hereunder. Additional surveillance components, namely passive clinical surveillance and abattoir inspection were not considered as no detailed information was submitted by the data providers.

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Data on EBL active surveillance

Number of herds and animals tested for EBL in Italy

Table I shows the number of herds and animals tested in the EBL-free areas of Italy during the study period.

Year	Number of herds tested	Number of animals tested
2018	24,459	685,230
2019	20,219	519,504
2020	16,796	381,269
2021	20,406	1,007,358

Table I. Italy: number of herds and animals tested for EBL in the free areas from 2018 to 2021.

Number of herds and animals tested for EBL in Slovenia

In Slovenia, the yearly number of tested herds (Table II) represents approximately 1% of the herds in the whole country.

Year	Number of herds tested	Number of animals tested
2018	204	4,493
2019	287	5,538
2020	301	4,639
2021	98	1,127

Table II. Slovenia: number of herds and animals tested for EBL from 2018 to 2021.

The number of imports in 2021 was very low and therefore the number of cattle sampled in that year was limited.

Scenario tree modelling

Database creation

Only the total number of animals sampled at the country-level for Slovenia and Italy was available. The minimum number of samples per herd was constrained to include a minimum of 1 sample per herd from Slovenia and 10 samples per herd in Italy. The remaining samples were taken from a multinomial hypergeometric distribution with a maximum of 23 samples per herd for Slovenia and 100 for Italy.

Surveillance system components

Only one surveillance system component (SSC) was considered for Italy (free areas) and Slovenia as cattle were only sampled on the farm. The scenario tree for Slovenia is illustrated in Figure I.

For Italy, the first branch dividing the proportion of herds tested in the free areas from those in the clusters is not considered in the calculation (Figures II and III). Moreover, given the lack of information on the number of herds and cattle tested with each testing strategy, the structure of the tree was simplified considering only two diagnostic nodes and the most common method of screening (ELISA on individual sera). In both models, the specificity of the surveillance systems was assumed to be 1.

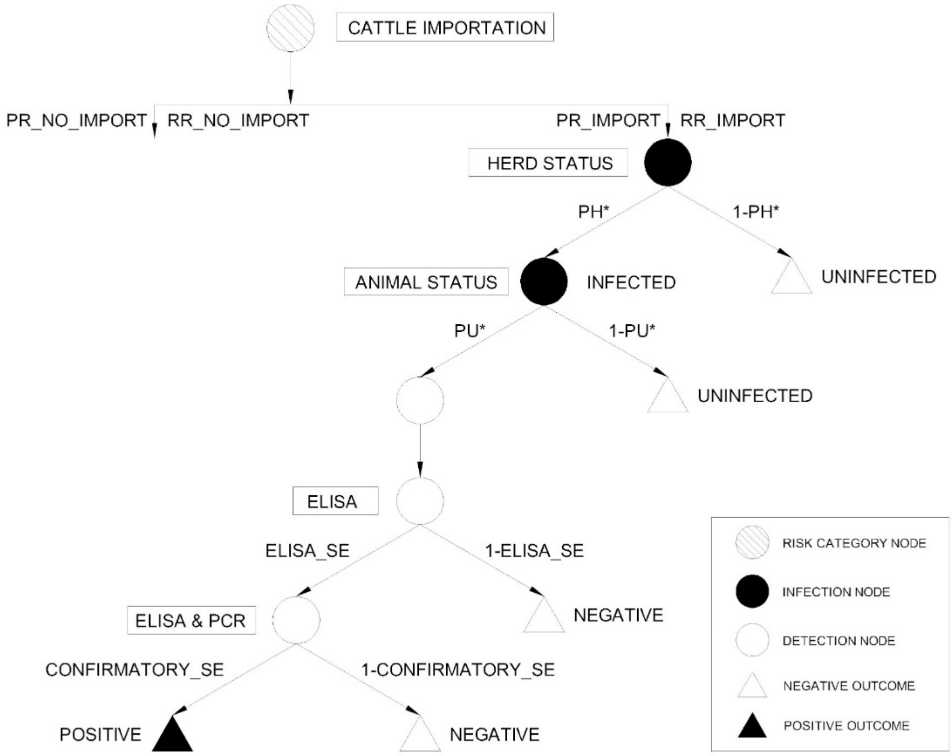

Figure 1. Scenario tree model illustrating the active surveillance system for EBL in Slovenia (2018-2021). Herd level design prevalence: PH*, within herd prevalence PU*, sensitivity: SE.

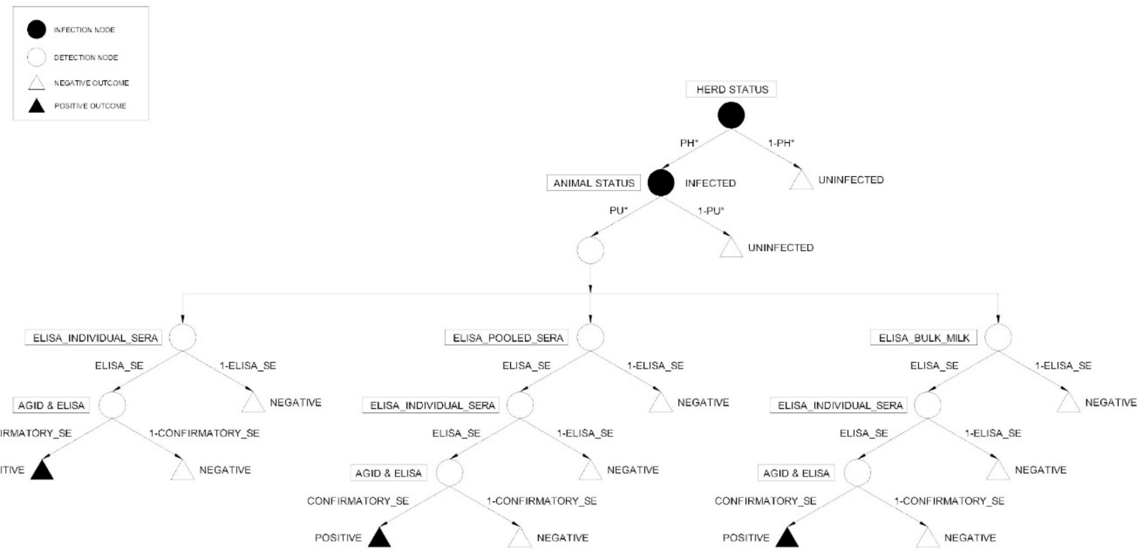

Figure 2. Scenario tree model illustrating the active surveillance system for EBL in Italy -free areas (2018-2021). Herd level design prevalence: PH*, within herd prevalence PU*, sensitivity: SE.

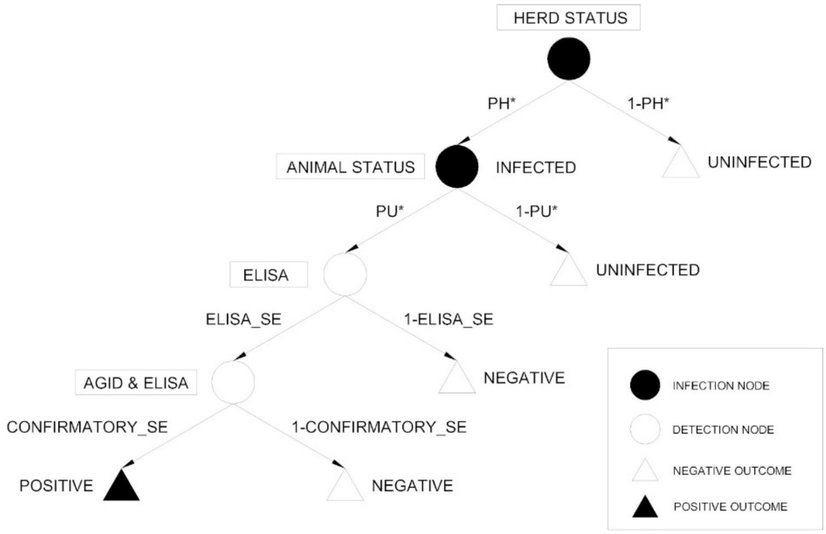

Figure 3. Simplified scenario tree model illustrating the active surveillance system for EBL in Italy -free areas (2018-2021). Herd level design prevalence: PH*, within herd prevalence PU*, sensitivity: SE. Please note that for Italy, given the heterogeneous sampling framework, the tree was simplified.

Design prevalences

Design prevalences define the level at which the sensitivity of the system is valid (the probability that the SSC would detect infection if it was present at the design prevalences) (Martin et al., 2007). In this study the herd level design prevalence (P^*_H) was set to 0.2% in accordance with the Council Directive 64/432/EEC (European Commission, 1964)1, and the within herd prevalence (P^*_U) was set to 15% (SVA, 2020) (Table III).

Parameter	Source of information	Input value
P_H^*	(European Commission, 1964)	0.2%
P_U^*	(SVA, 2020)	15%
$RR_{importing}$	Data provider	2
$ELISA_{Se}$	(Monti *et al.*, 2005; Sakhawat *et al.*, 2021; Trono *et al.*, 2001)	(26.57,0.38)[a] (26.04,0.34)[a] (13.73,0.68)[a]
$CONFIRMATORY\ TESTS_{Se}$ (AGID&ELISA)	(Monti *et al.*, 2005; Rusenova *et al.*, 2022; Sakhawat *et al.*, 2021; Trono *et al.*, 2001)	(0.58,0.75,0.83)[b]
PCR_{Se}	(Eaves *et al.*, 1994; Rusenova *et al.*, 2022)	(6.36,1.29)[a] (3.19,0.26)[a]

Table III. Input values used in the scenario tree models to estimate the probability of freedom from EBL in Italy (free areas), and Slovenia. a Input value described by a beta distribution. Values shown are the parameters shape1 and shape2. b Input value described by a Pert distribution. Values shown are the minimum, mode and maximum of the distribution.

Adjusted relative risks of infection (Slovenia)

In Slovenia, the herds importing cattle from other countries were regarded as having a risk two times higher of EBL infection (relative risk-RR).

Thus, the design herd prevalence (P^*_H) was combined with an (weighted) average adjusted risk *(AR)* to calculate the effective probability of a herd being infected $(EPIH_\gamma)$

$$EPIH_{import} = P_H^* \times AR_{import}$$

The *AR* was calculated according to Martin et al. (Martin et al., 2007):

$$AR_{import} = AR_{no\ import} \times RR_{import}$$

where $AR_{noimport}$ is the *AR* for the low-risk population (herds that do not import cattle), RR_{import}, the *RR* for the high risk population (herds importing cattle), and $PrP_{no\ import}$ and PrP_{import}refer to the whole population, and they are the proportions of herds importing and not importing cattle respectively.

Unit, herd and surveillance system sensitivities

The probability that the infected unit (animal) was detected was considered equal to the sensitivity of the diagnostic tests (*SeU*). This was done as no factors (category nodes) affecting the probability of detection at unit level were included. Given the lack of information on the sensitivity of the tests used in the EBL country-specific control programme, the beta distribution of the sensitivity of several ELISA tests retrieved from literature (Monti et al., 2005; Sakhawat et al., 2021; Trono et al., 2001) was simulated using 1,000 iterations. Afterwards, we randomly sampled from the set of simulated distributions (with equal weight) to create the ELISA curve. The same approach was implemented to create the confirmatory PCR sensitivity curve used in Slovenia (Eaves et al., 1994; Rusenova et al., 2022). For Italy, the confirmatory tests sensitivity was described as a pert distribution based on the information on AGID and ELISA retrieved from scientific literature (Monti et al., 2005; Rusenova et al., 2022; Sakhawat et al., 2021; Trono et al., 2001).

The overall sensitivity, follow-up tests included, was calculated by multiplying the sensitivities of the screening and confirmatory tests (serial testing).

$$CONFIRMATORY\ TESTS_{Se} = ELISA_{Se} + PCR_{Se} - ELISA_{Se} \times PCR_{Se}$$

Where, for Slovenia, the confirmatory tests sensitivity was considered as the sensitivity of testing positive to at least one of the two confirmatory tests (ELISA or PCR) (parallel testing).

The estimate of the *SeU* was used to calculate the herd sensitivity *(SeH)* according to the binomial formula:

$$SeH_h = 1 - (1 - P_U^* \times SeU)^n$$

Given that only one component was included in the model, the *Sse* equals the *CSe*. This was calculated considering that *SeH* is variable between herds, and the sensitivity in herd h is available for each of the H herd:

$$SSe = 1 - \prod_{h=1}^{H} (1 - SeH_h \times P_H^*)$$

Probability of freedom

The posterior probability of freedom *(PostPFree)* was estimated as:

$$PostPFree = \frac{1 - PriorPInf}{1 - PriorPInf \times SSe}$$

Where *PriorPInf* is the prior probability of infection for which a neutral prior probability of 0.5 was chosen for the initial calculation.

Temporal discounting

Since data were provided for several years, the posterior probability of infection ($PriorPInf_k$) for the previous year k was used to calculate the prior probability of infection of the next year k as:

$$PriorPInf_k = PIntro + PostPInf_{k-1} - PIntro \times PostPInf_{k-1}$$

Sensitivity analysis

A sensitivity analysis was performed in order to assess the variation of *SSe* and *PostPFree* considering different estimates of *PIntro*, which was the most uncertain parameter. Separate runs of the models were performed assuming worst-case scenarios compared with the original level of *PIntro*. In this analysis, it was set to 70% (1 introduction in 4.28 months) and 80% (1 introduction in 3.75 months) for Italy, and 18% (1 introduction in 5.5), and 28% (1 introduction in 3.5 years) for Slovenia.

Software

All the models were run in R software (R Core Team, 2022) using 10000 iterations.

Results

Italy

Both the mean *SSe* and the mean *PostPFree* from EBL from 2018 to 2021 were 100%, with no differences between simulations and years. These estimates did not change when the *PIntro* was set to 70% (1 introduction in 4.28 months) and 80% (1 introduction in 3.5 months).

Slovenia

Over the years the *SSe* was 50.5% while the *PostPFree* was 81.6%. The outputs mean, min, max, median, 2.5th and 97.5th percentiles are specified in Table IV and Figure IV. The best estimates were obtained in 2020 when the mean *SSe* and *PostPFree* were 66.1% and 90.1% respectively. In 2021, a decrease was observed because of the low population coverage.

Year	PostPFree min	PostPFree 2.5th	PostPFree mean	PostPFree median	PostPFree max	PostPFree 97.5th
2018	65.8	68.3	68.6	68.7	68.7	68.7
2019	78.1	82.5	83.1	83.2	83.2	83.2
2020	84.7	89.5	90.1	90.2	90.3	90.3
2021	80.8	85.5	86.3	86.4	86.4	86.4
	SSe min	SSe 2.5th	SSe mean	SSe median	SSe max	SSe 97.5th
2018	48	53.6	54.3	54.4	54.5	54.5
2019	58.1	65.1	66.1	66.2	66.3	66.3
2020	55.7	64.6	66.1	66.3	66.4	66.4
2021	20	26.1	27.4	27.6	27.8	27.8

Table IV. Slovenia: SSe and PostPFree from EBL from 2018 to 2021 (values are expressed in percentage).

The increase in *PIntro* caused approximately a 6% and 15% decrease in the *PostPFree* when the *PIntro* was set to 18% (1 introduction in 5.5) and 28% (1 introduction in 3.5 years) respectively (Figure 4).

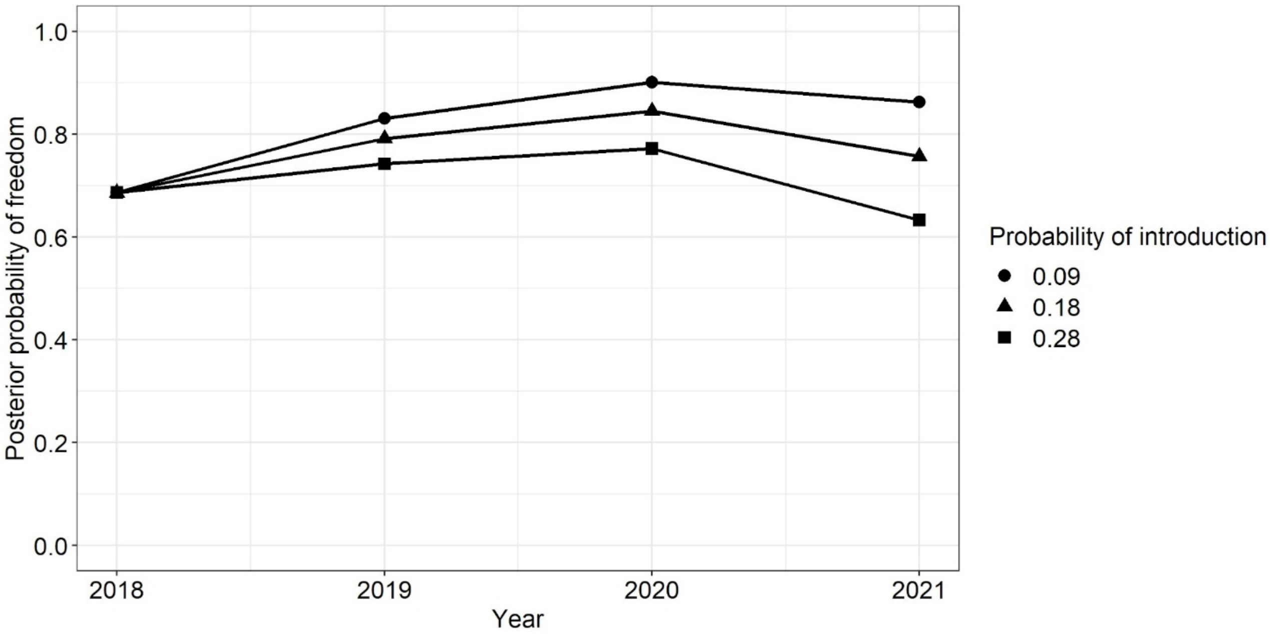

Figure 4. Sensitivity analysis of the PostPFree from EBL in Slovenia. Pintro set to 0.09 (original value), 0.18, and 0.28.

Discussion and conclusions

This paper is the first study estimating the *PostPFree* from EBL in Italy and Slovenia using scenario tree modelling. In line with other studies within the SOUND-Control project (e.g. Madouasse et al., 2022), it represents an attempt to carry out an output-based evaluation of CPs disease. This type of assessment allows for flexibility in inputs, so that it may be tailored to every surveillance system (Cameron, 2012). In this sense, our study was able to capture the heterogeneous activities of EBL CPs in Italy and Slovenia, providing comparable estimates of the *PostPFree* from the disease.

However, it also highlighted some technical limitations of the data collection tool (Rapaliute et al., 2021). For instance, the tool to collect data was more suitable to collect aggregated data on disease CPs rather than detailed information on the animals and herds tested, which is required to build a detailed scenario tree model. Indeed, although the data provided by Italy and Slovenia were of high-quality in terms of description of the EBL active surveillance system, no detail on the number of animals tested within each herd was available. Thus, some assumptions were made to build and run the models as more than one animal was tested within each herd.

It is worth mentioning that the quality of the information on CPs varied depending on the disease under investigation and requirements of national CPs. For EBL, Slovenia applied a risk-based surveillance during the timeframe considered. Results of this model highlight the benefits of this type of surveillance as the strategy of targeting only the holdings importing cattle resulted in lower costs for the country at a high confidence of freedom from EBL.

Conversely, Italy tested a sizeable number of herds and animals from 2018 to 2021, hence the *PostPFree* was 100% with no variation between years. The*SSe* remained high even when the risk of introduction was increased. This is due to the fact that the population coverage was high over several years, thus increasing the confidence of freedom from EBL over time. It is important to highlight that in case of the examination of a high proportion of the population, the *SSe* increases, but also the cost and the resources needed to undertake the surveillance. The sample size for both herds and animals can be optimized to minimize the overall costs of surveillance when the purpose of surveillance is to demonstrate freedom from disease (Ausvet 2022). However, in the case of Italy, the great effort invested in the EBL surveillance was considered to be justified by the fact that some endemic areas persist in the country, and that one of the objectives of the Italian surveillance system is the early detection of positive cases.

One of the drawbacks of this study is the uncertainty in the estimates of the diagnostic tests. The models were constructed by combining data from scientific literature and they were run under a stochastic framework, which incorporates the uncertainty related to the inputs. Moreover, a sensitivity analysis was performed to assess quantitatively the response of the models to change in the *PIntro*. Estimating the risk of introduction can be very challenging. Results of this analysis showed that the increase of *PIntro* into the Slovenian cattle population could cause a decrease in the *PostPFree*. However, the risk of introduction is kept low by the current risk-based strategy of testing imported cattle, which allows for early detection of imported infected cattle.

To date the scenario tree models described in literature incorporate differential risks (e.g. 2 3. These are paramount to improve the estimation of the *PostPFree* (Martin et al., 2007). In this study, only one risk node was considered in the model of Slovenia. Relevant risk factors associated with cattle diseases are communal grazing, shared transport, artificial insemination etc. These should be recorded during surveillance activities and be included in scenario trees. Information on herd-level risk factors is not collected for the EBL CPs in the included countries, thus there is an opportunity to improve the *PostPFree* based on the models from this study, by collecting and including information on differences in risk and risk categories.

Another limitation of this study is related to the sequence of repeated tests that are performed once a test is positive in both Italy and Slovenia's CPs. Indeed, the formula used to calculate the overall diagnostic sensitivity requires that the tests are independent. This assumption can be tenuous in case the tests used have the same biological basis (e.g. two tests that detect antibodies) (Georgiadis et al., 2003). Thus, the estimate of *SSe* are not great as they could have been in case of conditional independence. Moreover, for Slovenia we choose for simplicity to use the same sensitivity values for the primary test and the repeated ELISA test.

In this paper, we adopted an output-based approach considering the information derived from the EBL active surveillance activities. Nevertheless, a surveillance system for EBL includes other components, namely clinical surveillance at farm level and abattoir. Passive surveillance can be effective to detect diseased animals, however, its effectiveness is difficult to estimate since it depends on several factors, such as the probability of infected animals having lesions, the disease awareness of both farmers and veterinarians, and their willingness to report it. Given this difficulty, the inclusion of behavioural effect might result into a bias in the *PostPFree.* It would be of particular interest to run the models adding this information with the aim of estimating how much the results vary. This can pave the way for initiatives aimed at enhancing the participation of farmers and clinical veterinarians in the surveillance strategy, which in turn, would contribute to an improvement of the quality of data collected, and thus refining the estimates of output-based surveillance.

Ethical statement

Ethical approval was not required for this study. This research does not contain any studies with animals or humans performed by any of the authors.

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References

Ausvet. 2022. Epitools. https://epitools.ausvet.com.au/samplesize.

Bartlett P.C., Ruggiero V.J., Hutchinson H.C., Droscha C.J., Norby B., Sporer K.R.B., et al. 2020. Current Developments in the Epidemiology and Control of Enzootic Bovine Leukosis as Caused by Bovine Leukemia Virus. Pathogens, 9, 1058.

Cameron A.R. 2012. The consequences of risk-based surveillance: Developing output-based standards for surveillance to demonstrate freedom from disease. Prev Vet Med, 105, 280–286.

Costa L., Duarte E.L., Knific T., Hodnik J.J., van Roon A., Fourichon C., et al. 2020. Standardizing output-based surveillance to control non-regulated cattle diseases: Aspiring for a single general regulatory framework in the European Union. Prev Vet Med, 183, 105130.

Eaves F.W., Molloy J.B., Dimmock C.K. & Eaves L.E. 1994. A field evaluation of the polymerase chain reaction procedure for the detection of bovine leukaemia virus proviral DNA in cattle. Vet Microbiol, 39, 313–321.

European Commission. 2017. Commission Implementing Decision (EU) 2017/1910 of 17 October 2017 amending Decision 93/52/EEC as regards the brucellosis (B. melitensis)-free status of certain regions of Spain, Decision 2003/467/EC as regards the official bovine brucellosis-free status of Cyprus and of certain regions of Spain, and as regards the official enzootic-bovine-leucosis-free status of Italy, and Decision 2005/779/EC as regards the swine vesicular disease-free status of the region of Campania of Italy (notified under document C(2017) 6891) (Text with EEA relevance.). (https://eur-lex.europa.eu/eli/dec_impl/2017/1910/oj accessed on 21 May 2022).

European Commission. 1964. Council Directive 64/432/EEC of 26 June 1964 on animal health problems affecting intra-Community trade in bovine animals and swine.

Frössling J., Agren E.C.C., Eliasson-Selling L. & Lewerin Sternberg S. 2009. Probability of freedom from disease after the first detection and eradication of PRRS in Sweden: Scenario-tree modelling of the surveillance system. Prev Vet Med, 91, 137–145.

Georgiadis M.P., Johnson W.O., Gardner I.A. & Singh R. 2003. Correlation-adjusted estimation of sensitivity and specificity of two diagnostic tests. J R Stat Soc Ser C Appl Stat, 52, 63–76.

Ghysdael J., Bruck C., Kettmann R. & Burny A. 1984. Bovine Leukemia Virus. In Retroviruses 3 (P. K. Vogt & H. Koprowski, eds). Springer, Berlin, Heidelberg, 1–19.

Hodnik J.J., Acinger-Rogić Ž., Alishani M., Autio T., Balseiro A., Berezowski J., et al. 2021. Overview of Cattle Diseases Listed Under Category C, D or E in the Animal Health Law for Which Control Programmes Are in Place Within Europe. Front Vet Sci, 8, 688078.

Kuczewski A., Orsel K., Barkema H.W., Mason S., Erskine R. & van der Meer F. 2021. Bovine leukemia virus—Transmission, control, and eradication. J Dairy Sci, 104, 6358–6375.

Madouasse A., Mercat M., van Roon A., Graham D., Guelbenzu M., Santman Berends I., et al. 2022. A modelling framework for the prediction of the herd-level probability of infection from longitudinal data. Peer Community J, 2, e4.

Martin P.A.J., Cameron A.R. & Greiner M. 2007. Demonstrating freedom from disease using multiple complex data sources. Prev Vet Med, 79, 71–97.

Monti G.E., Frankena K., Engel B., Buist W., Tarabla H.D. & de Jong M.C.M. 2005. Evaluation of a New Antibody-Based Enzyme-Linked Immunosorbent Assay for the Detection of Bovine Leukemia Virus Infection in Dairy Cattle. J Vet Diagn Invest, 17, 451–457.

Moratorio G., Fischer S., Bianchi S., Tomé L., Rama G., Obal G., et al. 2013. A detailed molecular analysis of complete Bovine Leukemia Virus genomes isolated from B-cell lymphosarcomas. Vet Res, 44, 19.

Norström M., Jonsson M.E., Åkerstedt J., Whist A.C., Kristoffersen A.B., Sviland S., et al. 2014. Estimation of the probability of freedom from Bovine virus diarrhoea virus in Norway using scenario tree modelling. Prev Vet Med, 116, 37–46.

Ordinanza Ministero della Salute. 2015. Misure Straordinarie di Polizia Veterinaria in Materia di Tubercolosi, Brucellosi Bovina e Bufalina, Brucellosi Ovi-Caprina, Leucosi Bovina Enzootica. Gazzetta Ufficiale Serie Generale n.144, 24/06/2015. (https://www.gazzettaufficiale.it/eli/id/2015/06/24/15A04879/sg accessed on 20 May 2022).

R Core Team. 2022. R: A Language and Environment for Statistical Computing , Vienna, Austria. , 2022.

Rapaliute E., van Roon A., van Schaik G., Santman-Berends I., Koleci X., Mincu M., et al. 2021. Existence and Quality of Data on Control Programs for EU Non-regulated Cattle Diseases: Consequences for Estimation and Comparison of the Probability of Freedom From Infection. Front Vet Sci, 8.

Ruiz V., Porta N.G., Lomónaco M., Trono K. & Alvarez I. 2018. Bovine Leukemia Virus Infection in Neonatal Calves. Risk Factors and Control Measures. Front Vet Sci, 5, 267.

Rusenova N., Chervenkov M. & Sirakov I. 2022. Comparison Between Four Laboratory Tests for Routine Diagnosis of

Enzootic Bovine Leukosis. Kafkas Univ Vet Fak Derg. , 2022. , 10.9775/kvfd.2021.26505.

Sakhawat A., Rola-Luszczak M., Osinski Z., Bibi N. & Kuzmak J. 2021. Bayesian Estimation of the True Seroprevalence and Risk Factor Analysis of Bovine Leukemia Virus Infection in Pakistan. Anim Open Access J MDPI, 11, 1404.

SOUND control - COST Action CA17110 Website. 2022. (https://sound-control.eu/ accessed on 3 July 2022).

SVA. 2020. Surveillance of infectious diseases in animals and humans in Sweden 2020.

Trono K.G., PeArez-Filgueira D.M., Duffy S., Borca M.V. & Carrillo C. 2001. Seroprevalence of bovine leukemia virus in dairy cattle in Argentina: comparison of sensitivity and specificity of different detection methods. Vet Microbiol, 14.