Preventive Veterinary Medicine 121 (2015) 21–29

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

Comparison of output-based approaches used to substantiate bovine tuberculosis free status in Danish cattle herds

Alessandro Foddai[a,b,*], Liza Rosenbaum Nielsen[c], Preben Willeberg[b,c], Lis Alban[a]

[a] Risk Analysis Group, Department of Food Safety and Veterinary Issues, Danish Agriculture & Food Council, Axeltorv 3, DK-1609 Copenhagen V, Denmark
[b] Section of Epidemiology, National Veterinary Institute, Technical University of Denmark, Bülowsvej 27, 1870 Frederiksberg C, Denmark
[c] Department of Large Animal Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, 1870 Frederiksberg C, Denmark

ARTICLE INFO

Article history:
Received 5 April 2015
Received in revised form 13 May 2015
Accepted 20 May 2015

Keywords:
Surveillance sensitivity
Freedom from disease
Stochastic Scenario tree
Bovine tuberculosis

ABSTRACT

We compared two published studies based on different output-based surveillance models, which were used for evaluating the performance of two meat inspection systems in cattle and to substantiate freedom from bovine tuberculosis (bTB) in Denmark. The systems were the current meat inspection methods (CMI) vs. the visual-only inspection (VOI). In one study, the surveillance system sensitivity (SSe) was estimated to substantiate the bTB free status. The other study used SSe in the estimation of the probability of freedom (PFree), based on the epidemiological concept of negative predictive value to substantiate the bTB free status. Both studies found that changing from CMI to VOI would markedly decrease the SSe. However, the two studies reported diverging conclusions regarding the effect on the substantiation of Denmark as a bTB free country, if VOI were to be introduced.

The objectives of this work were: (a) to investigate the reasons why conclusions based on the two models differed, and (b) to create a hybrid model based on elements from both studies to evaluate the impact of a change from CMI to VOI. The hybrid model was based on the PFree approach to substantiate freedom from bTB and was parametrized with inputs according to the newest available information. The PFree was updated on an annual basis for each of 42 years of test-negative surveillance data (1995–2037), while assuming a low (<1%) annual probability of introduction of bTB into Danish cattle herds.

The most important reasons for the difference between the study conclusions were: the approach chosen to substantiate the bTB free status (SSe vs. PFree) and the number of years of surveillance data considered.

With the hybrid model, the PFree reached a level >95% after the first year of surveillance and remained ≥96% with both the CMI and VOI systems until the end of the analyzed period. It is appropriate to use the PFree of the surveillance system to substantiate confidence in bTB free status, when test-negative surveillance results can be documented over an extended period of time, while maintaining a low probability of introduction of bTB into the cattle population. For Denmark, the probability of introduction of bTB should be kept <1% on an annual basis to sustain the high confidence in freedom over time. The results could be considered when deciding if the CMI can be replaced by VOI in cattle abattoirs of countries for which bTB freedom can be demonstrated.

1. Introduction

Bovine tuberculosis (bTB[1]) is caused by *Mycobacterium bovis*, which can infect domestic cattle, wild animals, and humans (de la Rua-Domenech, 2006). In Denmark, bTB was considered eradicated from the cattle population in 1952 as a result of a targeted national eradication effort (Anonymous, 1952). In the European Union (EU), Member States can be classified officially free from bTB (OTF), if <0.1% of the cattle herds in the country are confirmed infected with *M. bovis* (Council Directive 64/432/EEC; Council Directive 98/46/EC). Denmark obtained the OTF-status in 1980 (Commission Decision 80/984/EEC; Reviriego Gordejo and Vermeersch, 2006).

In OTF countries, surveillance systems for bTB primarily consist of meat inspection at the abattoir. The current meat inspection (CMI) procedures include palpation and incision of specific organs and lymph nodes to identify affected animals and herds (Regulation (EC) No 854/2004). In Denmark, only selected groups

* Corresponding author at: Risk Analysis Group, Department of Food Safety and Veterinary Issues, Danish Agriculture & Food Council, Axeltorv 3, DK-1609 Copenhagen V, Denmark. Tel.: +45 26243099; fax: +45 33394141.
E-mail address: afo@lf.dk (A. Foddai).

[1] A list of abbreviations is provided in the Appendix.

http://dx.doi.org/10.1016/j.prevetmed.2015.05.005
0167-5877/

of cattle undergo tuberculin skin testing for bTB, e.g., bulls used for insemination and live cattle exported to specific markets (Reviriego Gordejo and Vermeersch, 2006; Danish Veterinary and Food Administration, 2007).

Changes to the CMI procedures for bovines are under discussion in the EU. It has been argued that it might be possible to reduce the cross-contamination with zoonotic hazards, such as *Salmonella* spp., *Campylobacter*, and verocytotoxin-producing *Escherichia coli* by introducing visual-only meat inspection (VOI) (EFSA, 2013a). It has, however, also been estimated, that applying VOI in cattle would decrease the sensitivity of the national surveillance systems (SSe) (Calvo-Artavia et al., 2013; EFSA, 2013b; Hill et al., 2014; Stärk et al., 2014). A decision on introduction of VOI for cattle has not yet (primo-2015) been made by the EU.

The European Food Safety Authority (EFSA) has made an evaluation of the ability of alternative meat inspection procedures (CMI vs. VOI) to validate the bTB status of a country or region (EFSA, 2013b; Zancanaro et al., 2013). SSe of ≥95% was defined to represent the acceptable level of confidence in detecting at least one infected animal with bTB-lesions, should the between-herd prevalence (BHP) be equal to the threshold of 0.1%. Moreover, estimation of SSe based on 1 year of surveillance data corresponds to the confidence in detection, and this was interpreted as the annual confidence in bTB free status in a country. This 'detection approach' is considered 'a first generation surveillance standard' and has been adopted by a range of international standard setting organizations, as described by Cameron (2012). Estimates of SSe have been presented for all EU Member States; for Denmark the annual mean SSe of detecting at least one infected animal (by meat inspection only) would decrease from 99% with the CMI, to 77% with the VOI assuming a threefold lower detection sensitivity of bTB-like lesions for VOI than for CMI, and 59% assuming a fivefold lower detection sensitivity for VOI than that for CMI (EFSA, 2013b).

A different approach was used to estimate the effect on the confidence in freedom from bTB for Denmark, assuming that a change from CMI to VOI would have been introduced in 2013 (Calvo-Artavia et al., 2013). According to this model, freedom from disease can be substantiated by considering one or more years of surveillance data, based on the approach developed by Martin et al. (2007a,b). In this case, the SSe is used in an intermediate step to calculate the probability of freedom (PFree) representing the negative predictive value (NPV) of the surveillance system, to express the confidence in freedom from bTB. The PFree denotes the probability that a country classified as free from bTB by the surveillance system is truly free, according to the assumed design prevalence and given test-negative surveillance results (Martin et al., 2007a). This 'freedom approach' is considered 'a second generation surveillance standard' (Cameron, 2012).

According to Calvo-Artavia et al. (2013), the annual mean SSe of detecting at least one bTB infected animal by meat inspection with follow-up laboratory testing of suspicious lesions, would decrease from 32% to 18% if CMI was replaced by VOI, assuming a twofold decrease in the probability of detection of bTB-lesions. Still, starting out with a very high level of confidence in freedom (>90%) based on test-negative surveillance data from 1995 to 2012, Denmark could substantiate continued high confidence in freedom from bTB (≥94%), even after 24 years with VOI in place (2013–2037), if the annual probability of introduction of bTB (PIntro) could be kept low (<1%).

Hence, the two studies agreed on the fact that introducing VOI would cause a marked decrease in the SSe, while they had diverging conclusions regarding the effect on the substantiation of the bTB free status of Denmark, which is the main concern of relevance for trade of cattle and cattle products.

Therefore, this paper looks closer into the two approaches for substantiating bTB free status of the Danish cattle population. The specific objectives were: (a) to investigate the effects of the different definitions, assumptions, methodologies, and inputs used in the two models, and (b) to develop a hybrid model based on elements from both studies and literature. Thereafter, the hybrid model was used to evaluate the impact of a potential change from CMI to VOI on the SSe and the PFree, as estimators of the confidence in bTB detection and the bTB free status, respectively.

2. Materials and methods

According to our aims, we first synthesized the differences in the terminology (Section 2.1), assumptions (Section 2.2), methodologies (Sections 2.3 and 2.4), and inputs (Section 2.5) used in the two studies (Calvo-Artavia et al., 2013; EFSA, 2013b).

Secondly we carried out an alternative Scenario analysis using the model by Calvo-Artavia et al. (2013) (Section 2.6), to investigate (i) the importance of each single input on the outputs (SSe and NPV), and (ii) the importance of the number of surveillance years used in the two models.

Finally, we developed the hybrid model (Section 2.7) using elements of and information gained from Sections 2.1–2.6. The model was set in an Excel spreadsheet using @Risk-6 (Palisade Corporation®) and simulations were performed with 10,000 iterations.

2.1. Terminology

According to the European legislation, a Member State, or a region of a Member State of the EU can be recognized OTF if 'the percentage of bovine herds confirmed as infected with tuberculosis has not exceeded 0.1% per year of all herds for six consecutive years' (Council Directive 64/432/EEC; Council Directive 98/46/EC). Hence, a low number of infected herds can be tolerated in OTF countries. Currently, most of the EU Member States are recognized, partly or entirely, as OTF (Commission Decision 2003/467/EC). OTF is a risk management concept with other factors included apart from the prevalence. In the remaining part of this paper, we will use the term 'bTB free status', because we are focusing on the epidemiological measures related to the substantiation of freedom from bTB. Both surveillance output standards (SSe and PFree) are assessed using a defined prevalence of infected herds and/or animals called the design prevalence (P^*), which may be determined by international standards, legislation, agreements between trading partners, biological plausibility, resources, or political considerations (Martin et al., 2007a).

In both studies (Calvo-Artavia et al., 2013; EFSA, 2013b), the SSe represented the annual probability of detecting at least one bTB-infected animal, by CMI or VOI, if bTB were present in the Member State at the assumed design prevalence. In the study by EFSA (2013b), the between-herd (BHP) and within-herd (WHP) prevalences were both specified in the model. In contrast, Calvo-Artavia et al. (2013) used an overall animal-level design prevalence (based on multiplication of the BHP and WHP) for the whole country (see Section 2.5).

In the Danish model (Calvo-Artavia et al., 2013), the confidence in freedom from bTB, also known as the probability of freedom (PFree), was estimated for each year over a specified surveillance period of 42 years based on the epidemiological concept NPV. This approach is typically used by countries that have been completely free from a disease for several years and have systems in place aimed at preventing the introduction of disease from abroad.

2.2. Assumptions

In both studies, the surveillance system was used as a 'diagnostic test', to define the bTB status of Denmark, and the probability