

Stochastic scenario-tree modelling of the cost-effectiveness of bovine brucellosis surveillance in a disease-free country: implications for improving system efficiency

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Abstract

Surveillance systems of exotic infectious diseases aim to identify any introductions and support the disease-free status. In a context of decreasing resources, evaluation of surveillance efficiency is essential to help stakeholders make relevant decisions about prioritisation of control measures and funding allocation. This study evaluated the efficiency of the French bovine brucellosis surveillance system using stochastic scenario tree models. Cattle herds were categorised into three risk groups based on the annual number of bovine purchases. The cost-effectiveness (calculated as the ratio of the mean cost to the mean sensitivity) of the current surveillance system, which includes abortion surveillance, programmed testing and controls of bovines at introduction in a herd, were compared to alternative surveillance scenarios. With a predicted 93%-sensitivity at a design prevalence of 0.02% and a yearly cost of 15.1 million €, the cost-effectiveness of the current system was estimated to be about 164 k€ per 1% of sensitivity. Yet, alternative scenarios including serological screening in either randomly or high-risk selected herds and surveillance of abortion series were predicted to be more efficient. Such changes would align with the European specifications for disease-free status and would reduce annual surveillance cost by 43-54%. This work may be used as decision support to improve brucellosis surveillance and make a more efficient use of resources.

Keywords: *Bovine brucellosis, cost-effectiveness, disease freedom, scenario tree modelling, surveillance system.*

Introduction

Surveillance systems of exotic infectious diseases aim to support disease-free status and to identify any introductions to allow rapid response, hence limiting public health impact and control measures costs. However, in a context of decreasing resources, evaluation of performances and costs of surveillance systems is required to optimise resource allocation.

France is officially brucellosis-free (OBF) in cattle since 2005. Bovine brucellosis, due to *Brucella abortus* or *B. melitensis*, is a major zoonosis responsible for late abortions in cattle. Surveillance and control were implemented in France in 1965 and enabled the eradication of the disease. However, the risk of reintroduction is not null as demonstrated by the occurrence of two outbreaks in 2012. The current surveillance system consists in clinical surveillance of abortions (CLIN), annual

programmed serological testing (PROG) and controls of animals at introduction (i.e. purchase) into a herd (INTRO). Several studies evaluated the effectiveness of this system (1,2), the performances of abortion surveillance (3,4), and the global cost of brucellosis surveillance (5). However, the efficiency of the system (i.e. sensitivity in regards to the costs) has never been evaluated.

The goal of this study was to evaluate the efficiency of the current French bovine brucellosis surveillance system using stochastic scenario-tree modelling (6). Alternative scenarios were compared to the current system, by relating the performance of surveillance components (sensitivity) to their cost, to identify the most efficient surveillance system(s).

Materials and methods

Risk stratification of the cattle population

Trading of live cattle has been widely considered as the main pathway for brucellosis introduction into free cattle herds (7-10). Cattle farms were divided into three risk groups, depending on the number of bovine purchases: no-trade, low-trade and high-trade groups, using data from the French national cattle register database for 2010-2014. Beef and dairy production types, which represent about 60 and 40% of farms, respectively, were assumed to be equally distributed among risk groups. For each risk group, the probability of disease entry into a herd corresponded to the probability that at least one purchased bovine is infected (which depends on the annual number of purchases and the prevalence of infection in the herd(s) of origin) (11). The relative risks (RR) were calculated as the ratio between the probabilities of disease entry in the risk group to the reference group (i.e. the no-trade group) and then weighted according to the proportion of farms in each group to obtain average adjusted risks (AR) (6).

Surveillance system components (SSC)

The current CLIN surveillance (CLIN1) relies on the mandatory notification and investigation of all abortions. Critical steps of this SSC include the occurrence of abortion in infected females, the detection of abortions by farmers, the notification of abortions to the vet, and the tests for brucellosis. The current PROG surveillance (PROG1) consists in annual serological testing in all cattle herds. In most dairy herds, testing is conducted on bulk milk. In beef herds and in dairy herds producing raw milk products, testing is conducted

on blood samples from 20% of cattle over 24-month-old. Controls at introduction into a herd (INTRO1) are required for purchased animals, aged two years or over, originating from holdings presenting a particular risk or if the transfer between departure and arrival herds exceeds six days.

Scenario tree analysis

Calculation of the annual sensitivity of the surveillance system is based on the assumption that disease is hypothetically present at a specific between-herd prevalence (denoted design prevalence, P_H^*). The sensitivity of the brucellosis surveillance system was calculated for $P_H^*=0.02\%$ over a one-year period. It was assumed that the specificity of the surveillance system was 100%. For each SSC, the scenario tree characterised all possible pathways from the occurrence of an infection to the detection of the case, as a set of events with specified probabilities. Herd-level sensitivity (CSeU) and component sensitivity (CSe) were calculated as described in (6,12,13) using binomial, hypergeometric or exact distribution depending on the size of the sample relative to population. Briefly, for each risk group, the probability (CSeU) that any randomly drawn farm would give a positive outcome was calculated considering the within-herd prevalence for PROG and CLIN or the probability of infection in purchased animals for INTRO (P_U^*) and the probabilities for the different steps in the detection process. The sensitivity of each SSC (CSe), corresponding to the probability of detecting at least one brucellosis-positive herd given the presence of brucellosis at P_H^* , was calculated considering the proportion of farms falling into each specified risk group and the corresponding effective probability of infection ($AR \times P_H^*$). Assuming that all SSCs are independent, the overall sensitivity of the surveillance system (SSe) was calculated as $\prod_{i=1}^n CSe_i$, where n is the number of SSCs. Input parameter values, with uncertainty (error) or variability (randomness), were derived from the literature and modelled with PERT distributions. SSe was estimated using a Monte-Carlo approach with 1,000 simulations in R (14).

Surveillance costs for each SSC

Veterinary fees for farm visit, commuting time and blood sampling were extracted from the regulations for animal health or from agreements between veterinarians' and farmers' organisations for 2013. A survey was conducted among veterinary laboratories and inter-professional milk-testing laboratories to obtain the costs of brucellosis-screening analyses for 2013 (5).

Alternative surveillance systems

Several alternatives to the current SSCs were tested. For CLIN, we considered a SSC in which notification would be required after a series of two abortions (CLIN2); the probability of detecting abortion series was assumed to be one (15). For PROG, alternatives included: (i) testing of all bovines in a random sample of 20% of beef herds and testing of 100% of dairy herds (PROG2), (ii) testing of all bovines in a random sample of 20% of beef herds and testing of 20% of dairy herds (PROG3), (iii) testing of all bovines in

a sample of 20% of (dairy and beef) herds from the high-risk group (PROG4), and iv) testing of 20% of bovines in a sample of 20% of herds (dairy and beef) from the high-risk group (PROG5). INTRO1 was considered or not in scenarios. In total, 20 scenarios (including the current system) were considered.

Identification of the most efficient system(s)

Cost-effectiveness of each combination of CLIN, PROG and/or INTRO SSCs was calculated as the ratio of the mean cost to SSe (in %) (12). This ratio provides a valuable measure of efficiency (i.e. cost per 1% sensitivity) by which to compare alternative scenarios; a high value represents poor cost-effectiveness.

Influence of input parameters

A sensitivity analysis, using Latin hypercube sampling, was conducted to identify the most influential parameters. Linear correlation coefficients (LCC) were used to measure the correlation between each model parameter value and both CSe and costs of the current surveillance system at $P_H^*=0.02\%$. A Bonferroni-corrected p-value below 0.05% was considered significant.

Results

During the period 2010-2014, 45% of herds did not introduce any animals and constituted the no-trade group. The remaining part of the population was equally divided between the low- and high-trade groups. The relative risks (RR) were estimated to be two for the low-trade group and 15 for the high-trade group.

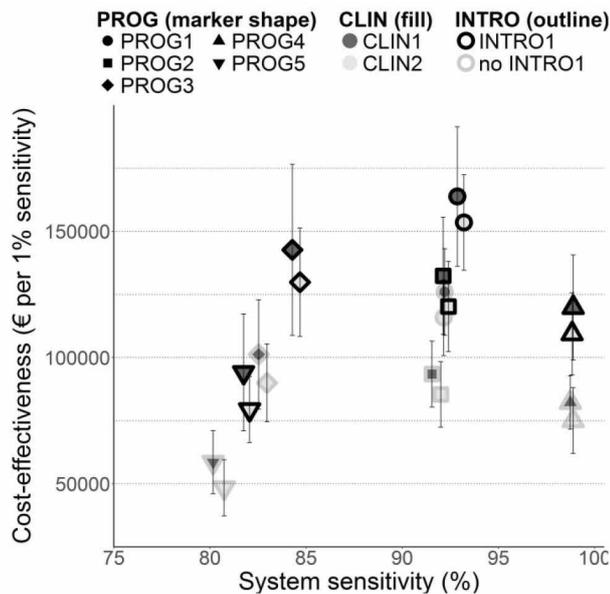
The sensitivity of the current system (CLIN1+PROG1+INTRO1) was estimated to be $93\pm 6\%$ (mean \pm SE) at $P_H^*=0.02\%$, as a result of the high sensitivity of PROG1 ($92\pm 7\%$) in comparison to CLIN1 ($4\pm 3\%$) and INTRO1 ($11\pm 4\%$). The cost of the surveillance system was predicted to be 15.1 ± 2.3 million € (M€), including 3.2 ± 1.5 M€ for CLIN1, 8.6 ± 1.1 M€ for PROG1 and 3.4 ± 0.6 M€ for INTRO1. The cost-effectiveness ratio of the current system was 164 ± 28 K€ per 1% of sensitivity.

All alternative scenarios were predicted to be more efficient than the current surveillance system, but not necessarily as effective (Figure 1). Among scenarios with a mean sensitivity above 90% at $P_H^*=0.02\%$, scenarios CLIN1+PROG2, CLIN2+PROG2, CLIN1+PROG4 and CLIN2+PROG4 (all with no-INTRO1) were the most efficient, with a cost per 1% of sensitivity ranging from 75 ± 13 K€ to 93 ± 13 K€. It would correspond to a reduction by 43-54% of surveillance costs in comparison with the current system.

For CLIN1, we found an influence of the within-herd prevalence (LCC=0.48) on CSe and of the proportion of farmers notifying abortions on both CSe (LCC=0.71) and cost (LCC=0.93). For PROG1, the within-herd prevalence (LCC=0.76) and the sensitivity of the confirmatory test (LCC = 0.44) influenced CSe; the costs of the vets' visit (LCC=0.59)

and blood serology analysis (LCC=0.58) influenced its cost. For INTRO1, both the annual number of purchases in high-risk herds and the proportion of herds with introduction controls influenced CSe (LCC=0.64 and LCC=0.44, respectively) and cost (LCC=0.40 and LCC=0.65, respectively).

Figure 1. Relationship between surveillance system sensitivity and cost-effectiveness for bovine brucellosis in France at $P_H^*=0.02\%$. Each scenario included programmed serological testing (PROG), clinical surveillance of abortions (CLIN), and/or testing at introduction (INTRO). See text for a description of alternative SSCs.



Discussion

With a predicted sensitivity of 93%, our study showed that the current surveillance system is able to meet its objective of detecting at least one case in a year at $P_H^*=0.02\%$. This P_H^* value is ten-times lower than the threshold prevalence fixed by the European regulations for maintaining the OBF status but it corresponds to about 40 infected herds which would imply a control cost of several M€ (e.g. 1.7 M€ were spent in 2012 for two outbreaks).

The estimated surveillance cost of the current system (15.1 M€) matches a previous data-based evaluation of 17.4 M€ (5), which included 11.7 M€ (76%) paid by the private sector for PROG1 and INTRO1 and 3.7 M€ covered by public funds for CLIN1. Operating costs have never been estimated and were not included in the analysis but are assumed to be more or less constant whatever the scenario.

Our findings indicated that several alternative scenarios would be more efficient than the current system. The range of suitable surveillance scenarios depends on both the choice of the minimum expected sensitivity (for a given P_H^*) decided by animal health authorities. For a minimum expected sensitivity of 90% at $P_H^*=0.02\%$, the most efficient scenarios included serological screening of all animals (over two years-old) in

a random (PROG2) or risk-based (PROG4) sample of cattle herds and clinical surveillance with the notification of series of two abortions (CLIN2). These changes in surveillance would meet the European specifications for country disease-free status and align with farmers' perceptions on brucellosis risk and surveillance. In particular, revising the definition of a suspect case (shift from one abortion to a series of two abortions within one month) would make the clinical surveillance more acceptable for farmers and veterinarians, who are anticipated to be more likely to report abortions if several cows are concerned (4).

The 50% saving in annual costs expected from these changes in the surveillance system could be reallocated to enhance risk communication, develop differential diagnosis of abortions and revise the surveillance procedures to improve clinical surveillance; these improvements being anticipated in the frame of the French Platform for Animal Health Surveillance.

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