Demonstrating freedom from disease using multiple complex data sources
A proposed standardised methodology and case study

Angus Cameron¹, Kristen Barford², Tony Martin³, Matthias Greiner⁴,
Evan Sergeant⁵ and other members of the International EpiLab research team
on Disease Freedom

Scientific Summary

The Agreement on Sanitary and Phytosanitary Measures (SPS agreement) of the World Trade Organisiation requires that, in international trade, measures taken to protect animal, plant or human health should be based on scientific principles and not maintained in the absence of sufficient evidence. Countries support such measures by using science-based risk analysis, which in turn demands science-based assessment of the disease status (free or infected) of each of the trading partners. Traditionally, national disease status has been determined using structured cross-sectional surveys, which are generally difficult and expensive to implement. On-going surveillance may also be assessed by expert panels, but there are no accepted methods for quantifying either confidence in the surveillance process, or the probability of national disease freedom demonstrated thereby. This report presents a proposed framework and detailed methods for quantitative assessment of complex surveillance data from multiple sources, and an illustrative case study using evidence from three surveillance systems to demonstrate Denmark’s freedom from classical swine fever.

¹ Cameron, Angus Robert, BVSc (Hons II) MVS PhD MACVSc; AusVet Animal Health Services Pty Ltd, 140 Falls Road, Wentworth Falls, NSW 2782, Australia; Tel. +61 2 4757 2770, angus@ausvet.com.au
² Barfod, Kristen, DVM; Danish Bacon and Meat Council, Axeltorv 3, DK-1609 Copenhagen V, Denmark; Tel. +45 33 11 60 50, KRB@danishmeat.dk
³ Martin, Tony, BA VetMB MPVM; Department of Agriculture Western Australia, PO Box 1231, Bunbury, WA 6231, Australia; Tel. +61 8 9780 6278, TMartin@agric.wa.gov.au
⁴ Greiner, Matthias, DVM Dr med vet MSc Dipl ECVPH; International EpiLab, Danish Veterinary Institute, Bülowsvej 27, DK-1790 Copenhagen V, Denmark; Tel. +45 35 30 01 40, mgr@vetinst.dk (presenter during the meeting)
⁵ Sergeant, Evan, BVSc (Hons II), MACVSc; AusVet Animal Health Services Pty Ltd, 140 Falls Road, Wentworth Falls, NSW 2782, Australia; Tel. +61 (02) 6362 1598, evan@ausvet.com.au
Note about the case study
This EpiLab project focussed on classical swine fever. Nevertheless, the authors believe that the methodology is not specific to the disease. The materials shown will demonstrate an approach, which -- after necessary modifications -- as also suitable for the surveillance of FMD.

Framework for analysis
The scenario tree is proposed as the modelling format for analysis of surveillance systems under a null hypothesis of the country being infected at a level equal to or greater than specified design prevalences. A scenario tree is developed to represent all known significant factors influencing the probability that a unit in an infected population will be detected as infected. The conditional probabilities associated with each limb of the tree are then multiplied together to give the overall probability of each limb’s outcome, and these are summed for all branches with positive outcomes to give the probability that the whole surveillance process will have a positive outcome for a randomly chosen population unit, given that infection is present in the country (the system unit sensitivity).

Independence and clustering models are described for analysis. Under the independence model, overall system sensitivity of detection is derived directly from system unit sensitivity, as the probability that one or more of the independent units processed would have positive surveillance outcomes, given an infected country. Under the clustering model, animals (and disease) are assumed to cluster in groups, and surveillance system sensitivity is calculated taking this into account, by stepwise aggregation of sensitivity at each grouping level in the tree.

Surveillance processes give either complete or incomplete coverage of the population, and the sensitivity of a process with incomplete coverage must be adjusted for its representativeness of the population. This is achieved through calculation and use of a sensitivity ratio for the process; the ratio of its sensitivity to that of a truly representative surveillance process.

The surveillance process’s sensitivity, \( P(³1\text{ positive unit} \mid \text{country infected}) \), is the confidence level for the statistical test of the null hypothesis. If one has a prior estimate of \( P(\text{country is free of disease}) \), one can then use Bayesian inference to calculate a posterior estimate of this probability, given the negative surveillance results.

Where multiple surveillance systems are available, the results of the analysis of each (whether they be survey-based or the result of scenario tree analysis) may be combined to produce an overall estimate of the confidence of the combined surveillance system.

While this research has developed the framework for a practical methodology to analyse complex surveillance data sources, it has also identified a number of areas of further research which would enhance the methodology. These include 1) standardised, transparent and acceptable methods for eliciting expert opinion, 2) methods to adjust the value of information based on the time of collection, and 3) methods to account for the lack of independence between surveillance systems when calculating the combined confidence that surveillance systems provide.
Case study

The methodology described above was used to analyse three different surveillance systems that provide evidence of Danish freedom from classical swine fever. The surveillance systems examined were:

1) A structured CSF sero-surveillance system, based on the collection of blood samples at abattoirs. Sampling was targeted at adult animals, with differential sampling pressures for boars compared to sows, and for South Jutland compared to the rest of the country;
2) Abattoir inspections (ante-mortem and post-mortem) routinely carried out at all abattoirs, primarily for food safety purposes; and
3) Clinical surveillance based on farmer observation, and routine visits by veterinarians to farms.

Each surveillance system was modelled using separate scenario trees, and estimates of the system confidence generated using stochastic modelling. Data sources used in the analysis included the Central Husbandry Register database, results of serological analysis of blood samples, abattoir slaughter records, and the VetStat drug prescription database (used as a proxy for veterinary visits). A number of parameters in each model were provided either by an expert informant, or through educated guesses.

Analyses were performed using a number of different design prevalence combinations, to examine the impact of the assumptions under the null hypothesis. In addition, for each surveillance system, a parallel analysis was conducted based on a hypothetical fully representative system using the same surveillance approach. For instance, in the case of sero-surveillance, this involved conceptually sampling from the farm population (rather than targeted sampling from the abattoir population). For meat inspections, it was based on the theoretical examination of animals selected from the farm population.

The results of analysis indicated that (not surprisingly) the estimated system sensitivity (or equivalently, confidence in the surveillance system) was very sensitive to the design prevalence assumptions under the null hypothesis. When reduced to a common period of one month’s worth of surveillance, and based on those values used in the study, the sensitivity of the sero-surveillance system was estimated as 26.37% with a 5th to 95th percentile range of 23.44% to 27.87%. The sensitivity for the meat inspection system was 67.80% (39.46% to 90.34%) and for the clinical surveillance system was 93.80% (90.77% to 96.43%).

The sensitivity ratio is the ratio of the sensitivity of the actual system, to the sensitivity of a theoretical fully representative system. It indicates the effect of targeting the system, and indicates if a system is more or less effective than random selection. The sensitivity ratio for the sero-surveillance system was 3.73, for the meat inspection system was 0.998 and for the clinical surveillance system was 0.991. This indicates that the sero-surveillance system was very well targeted and much more efficient that simple population sampling. The other two systems were essentially equivalent to representative population sampling.
The combined sensitivity of the three surveillance systems was calculated providing a monthly confidence of 98.53%. If surveillance data over the period of one year were considered, the confidence would increase to essentially 100% (1 – (1´10−22)).

The strength of evidence for freedom from CSF is undeniable, and sensitivity analysis shows that even if the confidence in one or more systems is greatly overestimated, the annual confidence in the combined surveillance system well exceeds international requirements. Nevertheless, it is recommended that further research be undertaken in this area, including the use of more formal methods to generate estimates from expert opinion, and the application of a proposed methodology to account for the lack of independence between surveillance systems.

Acknowledgement

The research was funded as a project of the International EpiLab (F03-0065) and done at the International EpiLab in Denmark. The contribution of Dr. Mo Salman and Dr. Mariann Chriél, also members of EpiLab's research group on disease freedom, is acknowledged.