

Scenario tree modelling of the Danish diagnostic system to demonstrate freedom from highly pathogenic avian influenza

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### **Summary**

Scenario tree modelling is the basis of a new method for analysis of surveillance data (including non-random data) from various sources, to calculate the probability that a country is free from a disease of livestock. We use this method to estimate the sensitivity of the Danish diagnostic system for detection of highly pathogenic avian influenza (HPAI) if it were present in 1% of domestic poultry flocks, with the result of a mean sensitivity of 71% for a 50 day surveillance period. This results in a probability that Denmark is free from HPAI of 99%, given a prior estimate of 95%.

### **Introduction**

The SPS agreement of the WTO requires that, in international trade, measures taken to protect animal health should be based on scientific principles and not maintained without 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, representative surveys, which are generally difficult, expensive, and ephemeral in their applicability. 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.

### **Objectives**

To present a method for quantitative analysis of general and targeted surveillance data for disease freedom, and its application to the Danish poultry diagnostic surveillance system to calculate the sensitivity of the surveillance system and the probability that Denmark is free from highly pathogenic avian influenza (HPAI).

### **Materials and methods**

Danish poultry flocks may be categorised into four industry sectors: broilers, layers, breeders and backyard birds. For this analysis the unit of interest was the batch of broilers, the house of layers or breeders, and the flock of backyard birds. The diagnostic system, incorporating all stages of disease diagnosis, from farmer observation to laboratory diagnosis, has comprehensive coverage of the population: all units in the population are covered by the surveillance system.

A stochastic scenario tree model was used to analyse the Danish diagnostic system. Analysis of the tree is aimed at answering the question “What is the probability that disease will be detected if it is present?” This probability is the sensitivity of the surveillance system, and can only be calculated when the level of disease present is specified. This is done using threshold prevalences ( $P^*$ ), commonly among-herd

prevalence ( $P_H^*$ ) and within-herd prevalence ( $P_U^*$ ). In this case  $P_H^*$  is the proportion of farms infected and  $P_U^*$  is the proportion of units that is infected on an infected farm (assumed to be one per farm). For each industry sector  $P_U^*$  was the reciprocal of the average number of units per farm: 0.445, 0.714, 0.714 and 1.0 for broilers, layers, breeders and backyard respectively. System sensitivity was estimated for  $P_H^* = 0.01$ .

A scenario tree was developed in which each node represents a factor influencing the probability that a unit will give a positive outcome of the surveillance process (i.e. the detection of HPAI virus), given that the country is infected at the specified  $P^*$ s. Nodes in the tree and their branches are shown in the table. Each branch has an associated probability. Nodes 3 – 11 are repeated for each industry sector. In surveillance for exotic disease, all positive findings will inevitably be followed up to determine whether disease is truly present; so this model assumes perfect specificity, and all positive outcomes represent the presence of HPAI. All actual surveillance outcomes are negative; if there are positive outcomes the analysis is not needed.

Nod e	Name	Outcome	Next nod e	Nod e	Name	Outcome	Next nod e
1	Country infected	infected	2	6	Farmer seeks diagnosis	Veterinarian	7
		uninfected	end			Direct to lab.	8
2	Industry sector	Broilers	3			No vet. investigation	end
		Layers	3			7	Vet. sends samples to lab. (HM*)
		Breeders	3	no samples	end		
		Backyard	3	8	Lab. diagnoses HPAI (HM*)	Positive	end
3	Farm infection status	infected	4			Negative	end
		uninfected	end	9	PMs conducted (reasons other than HM*)	Veterinarian	10
4	House / batch infection status	infected	5			Direct to lab.	11
		uninfected	end	no PMs	end		
5	High mortality	High	6	10	Vet. sends samples to lab. (no HM*)	Samples	11
		not high	9			no samples	end
11	Lab. diagnoses HPAI (no HM*)	Positive	end	11	Lab. diagnoses HPAI (no HM*)	Positive	end
		Negative	end			Negative	end

\* HM: High Mortality

For each limb of the tree the conditional probabilities associated with each node branch along the limb are multiplied together to give the overall probability of the limb's outcome; these are summed for all limbs with positive outcomes to give the probability that the whole surveillance system will have a positive outcome for a randomly chosen unit, given that infection is present in the country (the system unit sensitivity,  $SUS_e$ ). For calculation of surveillance system sensitivity  $SS_e$ , in which all units are included, clustering of units and disease within farms, and farms within industry sector are taken into account as described below.

For an infected broiler unit the sensitivity of detection is  $Se_U$ , derived as above from all limbs emanating from the infected branch of the batch infection status node. The farm-level sensitivity  $Se_H$  is then calculated as  $Se_{H_i} = 1 - (1 - P_U^* \times Se_U)^n$  where  $n$  is the number of units on the farm. This is repeated for all  $m$  broiler farms, and the sensitivity of the broiler diagnostic system  $ISe_{Broiler}$  is then calculated:

$$ISe_{Broiler} = 1 - \prod_{i=1}^m (1 - P_H^* \times Se_{H_i}) \quad SSe \text{ is then } SSe = 1 - \prod_{j=Broiler}^{Backyard} (1 - ISe_j) \text{ where levels}$$

of  $j$  represent the four industry sectors. The probability that the country is free of HPAI given the negative surveillance findings ( $pFreePost$ ) may then be estimated using Bayesian inference:  $pFreePost = 1 - \frac{CpPrior \times (1 - SSe)}{1 - CpPrior \times SSe}$  where  $CpPrior$  is the prior (pre-surveillance) estimate of  $\Pr(\text{country is infected with HPAI at } \geq P^*)$ .

Excellent data sets are available in Denmark which allow direct estimation of many branch probabilities for this model. Comprehensive broiler production records, veterinary prescription records, poultry clinic disease investigation records, laboratory records, and the central husbandry register were used to estimate values for key variables for both low and high mortality scenarios, including:  $\Pr(\text{farmer seeks diagnosis})$ ;  $\Pr(\text{farmer consults veterinarian} \mid \text{seeking diagnosis})$ ;  $\Pr(\text{vet sends samples to lab})$ ;  $\Pr(\text{lab attempts viral culture})$ . Weekly mortality rates are available for all batches of broilers in Denmark, and high mortality was deemed to have occurred in a batch when the farm- and production week-specific 99<sup>th</sup> mortality rate percentile was exceeded. Estimates of branch probabilities for layers and breeders were derived from broiler estimates and expert opinion, while estimates for backyard flocks were derived from expert opinion.

## Results

Sensitivity of the diagnostic process applied to a single infected broiler house is 0.09 (0.07, 0.12) (mean (90% CI)). Applying the process to one rotation of broilers through each house in the country (663 batches),  $ISe_{Broiler}$  with  $P_H^*$  of 1% is 0.23 (0.18, 0.28). The  $SUSse$  for  $P_H^*$  of 1% was 0.00002 (0.00002, 0.00003); applied to all 51,000 chicken flocks in Denmark, the probability that one or more will test positive ( $SSe$ ) is 0.71 (0.64, 0.78). Sensitivity analysis shows that  $SSe$  is most sensitive to  $\Pr(\text{lab will diagnose AI} \mid \text{infected samples submitted})$ , and then to  $\Pr(\text{vet sends samples to lab})$ .

If HPAI had been present undetected in Denmark during the many years that the diagnostic system has been in place, the prevalence would certainly have risen to a substantial proportion of domestic flocks. Now  $SSe$  for  $P_H^*$  of 5% is >99%, so we can be almost certain that historically Denmark has been free of HPAI. It is therefore reasonable to use a high prior estimate for  $\Pr(\text{Denmark free of HPAI})$ : using 95% we estimate  $pFreePost$  to be 99% for  $P_H^*$  of 1%.

## Discussion

Further work is required to establish a method to incorporate into this methodology the differential valuation of historical surveillance data, and how best to determine a prior estimate of the probability that the country is free of disease.

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