



# Risk based surveillance for early detection of low pathogenic avian influenza outbreaks in layer chickens



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## ABSTRACT

Current knowledge does not allow the prediction of when low pathogenic avian influenza virus (LPAIV) of the H5 and H7 subtypes infecting poultry will mutate to their highly pathogenic phenotype (HPAIV). This mutation may already take place in the first infected flock; hence early detection of LPAIV outbreaks will reduce the likelihood of pathogenicity mutations and large epidemics. The objective of this study was the development of a model for the design and evaluation of serological-surveillance programmes, with a particular focus on early detection of LPAIV infections in layer chicken flocks. Early detection is defined as the detection of an infected flock before it infects on average more than one other flock (between-flock reproduction ratio  $R_f < 1$ ), hence a LPAI introduction will be detected when only one or a few other flocks are infected. We used a mathematical model that investigates the required sample size and sampling frequency for early detection by taking into account the LPAIV within- and between-flock infection dynamics as well as the diagnostic performance of the serological test used. Since layer flocks are the target of the surveillance, we also explored whether the use of eggs, is a good alternative to sera, as sample commodity. The model was used to refine the current Dutch serological-surveillance programme. LPAIV transmission-risk maps were constructed and used to target a risk-based surveillance strategy. In conclusion, we present a model that can be used to explore different sampling strategies, which combined with a cost-benefit analysis would enhance surveillance programmes for low pathogenic avian influenza.

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## 1. Introduction

Low pathogenic avian influenza viruses (LPAIV) of the H5 and H7 subtypes can mutate to highly pathogenic avian

influenza virus (HPAIV). Outbreaks caused by these LPAIV are notifiable to the World Organisation for Animal Health (OIE). Therefore, Member States (MS) of the European Union (EU) have implemented surveillance programmes (Gonzales et al., 2010), and in the event of detection of a LPAIV, eradication measures are implemented (European Council, 2005). Nevertheless, mutations from LPAI to HPAI virus have occurred (DEFRA, 2008; San Miguel and Sanchez, 2010). This mutation can take place in the first infected flock (Rojas et al., 2002; DEFRA, 2008; San Miguel and Sanchez, 2010), but also after transmission of the LPAIV

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to several other flocks (Eckroade and Silverman, 1986; Capua and Maragon, 2000). Therefore, implementing active surveillance targeting early detection of LPAIV outbreaks will reduce the probability of virulence mutations and subsequent animal health, welfare, and economic consequences.

Current surveillance programmes for LPAI, in the EU, are designed to serologically detect infected flocks while assuming a design prevalence (Gonzales et al., 2010). It is expected that infection is present at a level equal or greater than this intuitively chosen design prevalence (Cannon, 2002). The current design approach allows the estimation of sample size, and the intuitive selection of the target populations. However, because of both the assumption that prevalence in an infected flock will always exceed the design prevalence and that the rate of virus introduction is unknown, optimal sampling frequency is not obvious. Since new introductions of LPAIV in poultry in the EU occur on regular basis (Gonzales et al., 2010), sampling frequency is an important variable in surveillance. Hence, a method that could estimate the optimal sampling frequency would help to improve current surveillance regulations.

The Dutch surveillance programme aims to detect infections caused by H5 or H7 LPAIV subtypes and to complement the demonstration of a 'free of infection' status. This programme samples all poultry flocks at least once a year. It assumes that outdoor (free range) layer chicken flocks, have a high risk of virus introduction (Thomas et al., 2005; Koch and Elbers, 2006). Therefore outdoor layer flocks have to be sampled 4 times per year (Elbers et al., 2007a). Recently, it has been confirmed that outdoor layer flocks have eleven times higher risk of introduction of LPAIV than indoor layer flocks (Gonzales et al., 2013). As a result, possible changes in the surveillance regulations such as increasing sampling frequency and targeting early detection are being considered (Bijleveld, 2012). Hence, there is a need to develop a method that quantitatively provides estimates for sample size and sampling frequency to improve the current programme.

The objective of this study was to develop a model for the design and evaluation of surveillance programmes for early detection of LPAI infections in layer chicken flocks and to use this model to derive the relations between sample, test, sample size and sampling frequencies, which suffice the minimal control criteria – we established for surveillance design – of a between-flock reproduction ratio ( $R_f$ ) < 1. We developed a model that takes into account the within- and between-flock infection dynamics and the performance of the diagnostic test. As a result, the required combination of sample size and sample frequency to ensure early detection is obtained. We explored the possibility of implementing a programme using sera samples for surveillance, or an alternative programme using egg samples.

## 2. Methods

### 2.1. Within flock infection dynamics

The within-flock infection dynamics were analysed using a deterministic SIR (Susceptible–Infectious–Recovered) model for a flock with 20,000 chickens

(average size of a layer chicken farm in the Netherlands). The differential equations describing the transition rates in this model have been described elsewhere (Keeling and Rohani, 2008). To account for the variation in the within-flock transmission characteristics of various LPAIV strains, the model was parameterised using data from various transmission experiments (van der Goot et al., 2003; Gonzales et al., 2011, 2012a,b) and from outbreaks (Gonzales et al., 2012b) (Table 1). With these data, the dynamics of LPAIV of low and high transmission characteristics were considered in the analysis (Table 1).

### 2.2. Infectiousness of a flock and transmission to other flocks

How capable an infected flock is to transmit infection to other flocks is defined here as infectiousness and it is denoted by  $A(t)$  (Diekmann and Heesterbeek, 2000). This function is a measure of the infectiousness of an infected flock towards susceptible flocks, and is given by:

$$A(t) = \int_0^t I(t)dt \quad (1)$$

where  $I(t)$  is the prevalence of infectious animals at time  $t$ . Hence, the expected overall infectiousness of the farms is obtained from Eq. (1), by integrating over  $t \in [0, \infty]$ . This overall infectiousness multiplied by a constant  $c$  (Diekmann and Heesterbeek, 2000), which combines information about the rate at which this infected farm connects with susceptible farms and the probability of transmission, defines the expected number of secondary infected flocks, induced by a primary infectious flock during its entire infectious period, in a susceptible environment. This expected number is the between-flock reproduction ratio  $R_f$ :

$$R_f = cA(\infty) \quad (2)$$

Our basic principle is to detect an infected flock before it infects on average more than one other flock. In that case, a LPAI infection will be detected when only one or a few other flocks are infected.

We study a situation where the population is initially free from infection and infection is introduced in a single flock. This means that any infectious flock (flocks), if detected, is removed from the population.

### 2.3. Between flock transmission

Transmission between flocks is described by the between-flock reproduction ratio  $R_f$ . We calculated  $R_f$  for all layer flocks in the Netherlands and used this estimates to define the level of transmission risk at an area level. The estimation of  $R_f$  was made according to Boender et al. (2007a,b,c). We first calculated the probability of transmission  $P(x_{ij})$  from flock  $i$  to  $j$ , a distance  $x_{ij}$  apart, using  $P(x_{ij}) = 1 - \exp[-h(x_{ij})T_i]$ , where  $T_i$  is the infectious period of flock  $i$ , and  $h(x_{ij})$  is a transmission kernel (Boender et al., 2007b). The latter describes how the transmission rate scales with distance. We examined different kernel functions (Table 2), and, on the basis of the Akaike's Information

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