# Spread of avian influenza in The Netherlands: identifying areas at high risk

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#### Summary

A risk map of the between-farm spread of avian influenza (AI) in The Netherlands was constructed during the Dutch AI outbreak as a tool to support decision-making for control strategies. The risk map was based on an estimated distance-dependent probability of transmission of AI from an infectious farm to a susceptible farm. The estimated probability function was used to derive a threshold value for the local density of farms. In areas with local farm density above this threshold ('high risk'), transmission could lead to major outbreaks by local spread alone. In belowthreshold areas ('low risk'), local spread alone will not cause a propagating epidemic. Distance-dependent probability was estimated from the data available at the start of the 2003 AI epidemic in The Netherlands. The resulting map predicted that two areas were at high risk. This approach might be applicable for other livestock infections and to other countries.

#### Keywords

Avian influenza, Control, Disease, Epidemiology, Geographic information system, Risk map, Spatial kernel, Spatial spread, The Netherlands.

# Diffusione dell'influenza aviaria nei Paesi Bassi: identificazione di aree ad alto rischio

#### Riassunto

Una mappa della diffusione dell'influenza aviaria tra aziende nei Paesi Bassi è stata disegnata nel corso del focolaio olandese di influenza aviaria come strumento per supportare decisioni di strategie di controllo. La mappa del rischio è stata basata sulla probabilità stimata distanza-dipendente di trasmissione di influenza aviaria da un'azienda infetta ad un'azienda suscettibile di infezione. La funzione di probabilità stimata è stata utilizzata per ottenere un valore di soglia per la densità locale delle aziende. Nelle aree con densità locale di aziende al di sopra di questa soglia ("alto rischio"), la trasmissione può portare a più estesi focolai unicamente attraverso diffusione locale. Secondo questo modello nelle aree con un valore di densità delle aziende al di sotto della soglia ("basso rischio") la sola diffusione causerebbe una propagazione locale non dell'epidemia. La probabilità distanza-dipendente è stata stimata a partire dai dati disponibili all'inizio del focolaio di influenza aviaria verificatosi nei Paesi Bassi nel 2003. La mappa risultante dall'analisi di questi dati ha identificato due aree ad alto rischio. Tale approccio può essere applicato ad altre patologie animali ed in altri paesi.

#### Parole chiave

Controllo, Diffusione spaziale, Epidemiologia, Influenza aviaria, Malattia, Mappe del rischio,

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Sistema informativo geografico, *Spatial kernel*, Paesi Bassi.

## Introduction

Outbreaks of highly contagious animal infections such as avian influenza (AI) are inflict significant losses in production animals. Contact infections are an important cause of spread of infectious diseases between farms. To suppress this type of transmission during an outbreak, a standstill of animal movement for several days is ordered by European regulation. Despite such standstills, some transmission may occur via 'neighbourhood Geographic infections' (5). information systems (GIS) provide a powerful tool to visualise disease risk (indicated by the density of farms) on a map (4). An incursion of infectious disease in high-risk areas, visualised with such a map, could lead to a major disease outbreak even during a standstill order. We applied this procedure to produce a risk map, based on 'neighbourhood infections' (2), at the beginning of the AI-epidemics in The Netherlands in 2003 (6).

## Materials and methods

## Mathematical method

To produce an AI risk map, we used a simple mathematical method to locate the high-risk areas (2). In this framework the neighbourhood infections are described by a spatial kernel  $p(r_{ij})$ , which is the distance dependent probability of transmission between herd *i* and *j* separated by a distance  $r_{ij}$ . With this spatial kernel a kernel density is calculated as follows:

$$R_i = \frac{1}{f_c} \sum_{j \neq i} p(r_{ij}), \qquad [1]$$

in which the summation was over all the neighbour flocks j. This kernel density represents the average number of j flocks infected by an infectious flock at position i. In epidemiology, this is the definition of the reproduction ratio (3). As expected,  $R_i$  corresponds to a threshold behaviour. In an area with a high kernel density ( $R_i > 1$ ), major outbreaks could occur, while in an area with a low kernel density ( $R_i < 1$ ), only minor outbreaks would occur. The factor  $f_c$  corrects

for the effect that during an outbreak some of the flocks neighbouring an infectious flock are already infected. A phenomenological description of  $f_c$  in terms of the first few spatial moments of the spatial kernel is possible by writing  $f_c = 1 + f(g_1, g_2...)$ . Here, the correction fis a function of dimensionless parameters  $g_1$ ,  $g_2$ , ..., because  $f_c$  itself is also dimensionless. Based on dimension n of the first three moments  $m^{(n)}$ , we constructed the two simplest dimensionless parameters leading to an expression for the factor  $f_c$  (2):

$$f_{\epsilon} = 1 + \left(\frac{(m^{(2)})^2}{m^{(3)}m^{(1)}}\right)^{1.7} \left(\frac{(m^{(1)})^2}{m^{(2)}}\right)^{0.6}$$
[2]

with the moments of  $p(r) m^{(n)}$ 

$$m^{(1)} = \int_{0}^{\infty} p(r)dr \quad m^{(2)} = \int_{0}^{\infty} p(r)rdr \quad m^{(3)} = \int_{0}^{\infty} p(r)\frac{1}{2}r^{2}dr \qquad [3]$$

in which the scaling factors 1.7 and 0.6 resulted from the analysis of simulations of transmission on a network of randomly distributed nodes (2). We were able to use this method to produce a risk map, because essential data was accessible.

#### **Outbreak data**

First, we estimated the spatial kernel for the spread of AI in The Netherlands. At the start of the AI epidemics in 2003, data was available for the first detected infectious poultry flocks (day of detection, estimated day of infection and the infectious period of each case) (6). We used the following method to estimate the spatial kernel from these data. As sources of infection, we selected the first 19 cases that were presumed to be infectious before the intervention measures came into force. We assigned an infected flock to an infectious flock, when the infection day of the first matched with the infectious period of the latter. We considered the infectious farm with the shortest distance to the infected farm as the most probable source of infection. We counted the number of secondary cases and the total number of poultry flocks in concentric rings of 1-km width around the 19 cases. The probability of transmission per ring was estimated by means of generalised linear model (GLM), using a binomial distribution and a log link function.

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### Location data

Second, to estimate the spatial kernel (equation 1) we needed to have location data of all the poultry farms in The Netherlands. We had access to the geographic coordinates of all poultry farms in The Netherlands from the Animal Health Service Ltd.

Outbreak and location data were used as input for the mathematical method to produce a risk map with high-risk areas ( $R \ge 1$ ) and low-risk areas ( $R \le 1$ ).

## Results

The spatial kernel estimated at the start of the epidemic (Fig. 1) had the following parameters:

$p(r) = \langle$	0.060	$0 < r < 1 \mathrm{km}$
	0.020	$1 \le r < 2 \text{ km}$
	0.0039	$2 \le r < 3 \text{ km}$
	0.0024	$3 \le r < 4 \text{ km}$
	0.00066	$4 \le r < 5$ km
	0	$r \ge 5 \text{ km}$

The probability of between-farm transmission for AI is given for each ring. Using this spatial kernel, the factor  $f_c$  was estimated to be 1.29, according to equations 2 and 3. The high-risk areas in The Netherlands for transmission of AI are shown in Figure 2.

## **Discussion and conclusions**

The spatial kernel decreases as a function of between-farm distance (Fig. 1), assuming that the nearest neighbour infectious farm is the most probable source of infection. We used this approach because it could be applied readily and rapidly during the outbreak. However, the spatial kernel probability at local distances could be overestimated and, as a consequence, the probability at intermediate (e.g. transmission via humans) and longer (e.g. transmission via transport of animals) distances could be underestimated. To overcome this bias, we performed a more elaborate kernel estimation using the total dataset of the AI outbreak in The Netherlands (1). Although the shape of kernel changed considerably, it has very little effect on the size and location of the two high-risk areas in The Netherlands. Thus, our results appeared to be robust under different assumptions for kernel estimation.



Figure 1 Spatial kernel p(r) for the transmission of avian influenza infection in The Netherlands, estimated from the 2003 epidemics

The factor  $f_c$  can vary between 1 (no local depletion of susceptible farms) and about 4 (local spread of the infection) (2). In the present study,  $f_c$  was estimated to equal 1.29, so that the spread of AI infection cannot be described as purely local. This is consistent with non-zero probability of transmission up to and including intermediate distances in the spatial kernel. In reality, the non-local transmission could be even more pronounced because our method of kernel estimation may have overestimated local transmission.

During the outbreak, we only had the dataset of the first 19 cases to estimate the spatial kernel. We used those cases only to estimate transmission, without considering the effect of preventive slaughter. However, during this first period, standstill of animal movements to reduce transmission came into force. To be conservative, we used this spatial kernel to represent the standstill situation. As a consequence, this spatial kernel corresponds to the worst case scenario in which measures like standstill are not effective.

As we knew the limits of the kernel estimation, we tested the sensitivity of the size of the highrisk areas for uncertainties in the threshold density. We lowered the cut-off value for  $R_i$ from  $1/f_c$  to  $0.75/f_c$ . We observed that the size of



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#### Figure 2

An estimate of the high-risk area for spatial spread of avian influenza in The Netherlands The red points are the high-risk flocks ( $R_i>1$ ), the amber points ( $0.8<R_i<1$ ) and the green points ( $0.6<R_i<0.8$ ) are added to check the sensitivity of the high-risk areas

high-risk areas did not change considerably. We concluded that the size of the high-risk areas is not sensitive to the uncertainties in the kernel estimation, leading to a robust risk map for transmission of AI in The Netherlands. Two main areas at high risk of AI are apparent in the risk map produced (Fig. 2). At the time we produced this map, infection was only spreading in the northern high-risk area. Only minor outbreaks were observed outside this high-risk area. The risk map predicted that infection could also spread in the southern high-risk area. Subsequently, incursion of the infection in the southern high-risk increased confidence in the validity of our risk map.

We conclude that the procedure outlined produces an easily understandable visualisation of high-risk areas for AI spread in The Netherlands. Such a risk map is a useful tool in the development of accurate, regiondependent surveillance and control strategies. A risk map can even be produced during an outbreak with available preliminary data, to assist optimisation of disease control measures. This approach might be applicable to other infections in other countries, provided that an accurate data set of the geographic locations of livestock herds or flocks is available and that the spatial kernel of that specific infection can be estimated.

## Acknowledgements

We would like to thank Annemarie Bouma for providing the initial data of the AI outbreak in The Netherlands and André Luppen (Animal Health Service Ltd) for technical support.

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