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Effectiveness of control measures on the transmission of avian influenza virus (H7N7) between flocks

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Abstract

On 28 February 2003 an epidemic of fowl plague started in The Netherlands, caused by a highly pathogenic avian influenza virus (HPAIV) of type H7N7. The epidemic started in the 'Gelderse Vallei', spread to adjacent areas and to the province of Limburg. During the epidemic, 255 flocks were diagnosed as infected. The epidemic was combated by stamping out infected flocks and pre-emptive culling of flocks within a 1-km radius. Moreover, screening and tracing activities were implemented to enhance the detection of infected flocks. In addition, a transportation ban was enforced. In a further stage of the epidemic, poultry-free buffer zones were created, contacts between different parts of the country were reduced by compartmentalization and large areas were depopulated of all poultry. In all, 1,000 commercial flocks were pre-emptively culled, in addition to over 17,000 flocks of smallholders.

In this study we quantified the transmission of HPAIV between flocks during different phases of the epidemic. To stop an epidemic, infected flocks should be detected and depopulated before they have infected on average more than one other flock. This average number of secondary infections caused by one infectious flock is called the reproduction ratio (R_h). Upon the implementation of the control measures in the Gelderse Vallei, R_h dropped from 5.0 (95% confidence interval (CI): 2.9-8.6) to 0.91 (95%CI: 0.39-2.13). Moreover, in Limburg, R_h dropped from 2.5 to 0.86 (95%CI: 0.28-2.68) after the control measures came into force. Apparently, the measures significantly reduced the transmission of the virus. However, because the 95% confidence intervals of R_h after the implementation of control measures include one, it is uncertain whether the implemented measures are really sufficient to eliminate the virus in an area with a high poultry density. Consequently, additional control measures should be considered.

Key words: avian influenza; fowl plague; transmission; control measures

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Introduction

On 28 February 2003 a suspicion of fowl plague or highly pathogenic avian influenza (HPAI) was notified to the Dutch Veterinary authorities. In a layer flock, comprising 7,150 animals, the hens had refused food and water since 22 February. Shortly afterwards, mortality increased and by 28 February approximately 90% of the hens had died. This presumed index flock appeared to be the onset of a huge epidemic, caused by a highly pathogenic avian influenza virus (HPAIV) of type H7N7.

Already on the same day four other herds were reported as fowl-plague-suspect. The epidemic was combated by movement restrictions, stamping out infected flocks and pre-emptive culling of flocks in the neighbourhood of infected flocks. Nevertheless, 1,255 commercial flocks and 17,421 flocks of smallholders had to be depopulated. The total number of animals killed mounted up to 25.6 million. In addition, the virus was also transmitted to a considerable number of humans that had been in close contact with infected poultry. Sadly, one of these persons died.

Obviously, the Dutch veterinary authorities want to reduce the probability that an un hoped-for new introduction of HPAIV will develop in an epidemic of similar size in the future. Consequently, it is important to have quantitative knowledge of the effectiveness of the control measures that were implemented during this epidemic. To stop an epidemic, infected flocks should be detected and depopulated before they infect on average more than one other flock. The average number of secondary infections caused by one infectious flock is called the reproduction ratio (R_h). The value of R_h depends on the infectivity of infected flocks, the susceptibility of non-infected flocks and the contact structure between flocks. Control measures intervene at one or more of these items.

In this study we quantified the transmission of HPAIV between flocks during different phases of the 2003 epidemic of fowl plague in The Netherlands.

Materials and methods

Outbreaks

During the epidemic 255 outbreaks of fowl plague were diagnosed. In 241 of these outbreaks clinical disease was present and H7N7-HPAIV was detected by virus isolation, PCR or both. On the basis of data collected from the outbreaks, the time of virus introduction was estimated for each of the infected flocks. The data comprised the contacts of the flocks with previous outbreaks and the history of the disease in the flock. Most farmers registered the mortality within their flocks over time. In transmission experiments, Van der Goot et al. (2003) observed that contact-infected chicken died 4-8 days after the exposure to HPAIV. By use of this period the time of virus introduction could be estimated from the moment the mortality in a flock rose above the base line. The remaining 14 flocks were detected by serological screening. No clinical disease was present, but one or more sera were positive in the H7 Haemagglutination Inhibition Assay. Estimation of the time of virus introduction is not possible in this situation.

Control measures

Several measures were implemented in order to stop the virus circulation. To start with, infected flocks were depopulated. In addition, flocks within a radius of 1 km of an outbreak were culled pre-emptively. In that situation the goal was to establish

culling within 48 hours after notification of the outbreak. Furthermore, upon detection of an outbreak, official veterinarians performed forward and backward tracing. Moreover, a transport ban was implemented; a protection zone and a surveillance zone were established around an infected flock; and the flocks in these areas were examined for clinical disease symptoms. As the epidemic proceeded, more measures were implemented such as the establishment of buffer zones, compartmentalization of The Netherlands into separate units and the culling of all poultry in large areas.

Analysis of data

The data were analysed by a model that has previously been used to quantify the transmission of Classical Swine Fever virus between pig farms (Stegeman et al. 1999) and the transmission of foot-and-mouth disease virus between cattle farms (Bouma et al. 2003). In short, this model assumes that the number of newly infected flocks (C) in a time interval dt can be described as

$$C = \beta * I \quad (1)$$

with β , the infection rate parameter (the average number of new infections per infectious flock per time unit) and I , the number of infectious flocks present in time interval dt . Consequently, if we have for each time unit the number of newly infected flocks and the number of infectious flocks, β can be established by a Generalized Linear Model (GLM) with a Poisson distribution and a log-link function. In this model C is the dependent variable and the natural logarithm of I is included as an offset variable. Moreover, we included different periods of the epidemic as explanatory variables. These periods were: 1) period until detection of an outbreak in a previously unaffected area; 2) first two weeks after detection of the first case in an area (assuming that it would take some time before measures were fully implemented); 3) remaining time until the end of the epidemic in the region. Finally, the established β s were transformed into R_h s, using the equation

$$R_h = \beta * T \quad (2)$$

with T = the duration of the infectious period. We assumed that a flock was not infectious for other flocks during the first two days upon virus introduction.

Results

Descriptive epidemiology

The epidemic started in the middle of The Netherlands, in a region called the 'Gelderse Vallei'. This region has a very high density of poultry flocks. Figure 1 shows the course of the number of outbreaks throughout the epidemic. Figure 2 shows the distribution of the infected flocks over the Netherlands.

The number of diagnosed outbreaks increased during the first week of March 2003. Subsequently, the number of outbreaks per day fluctuated between 2 and 11 until the end of March, without a clear trend up or down. During that period, outbreaks were only detected in the Gelderse Vallei. By the beginning of April, however, the number of outbreaks per day dropped markedly. The reason was that almost all flocks in the Gelderse Vallei had been culled at that time and consequently, the number of susceptible flocks became restricted. However, after that drop, the number of outbreaks fluctuated throughout most of April between 0 and 5 outbreaks per day. The reason was that by the end of March the virus had escaped from the Gelderse Vallei to the Southern part of The Netherlands. Here the virus also continued to spread in the province of Limburg (Figure 2). Again, until 15 April no clear trend up or down is visible in the epidemic curve and the total number of outbreaks in Limburg mounted

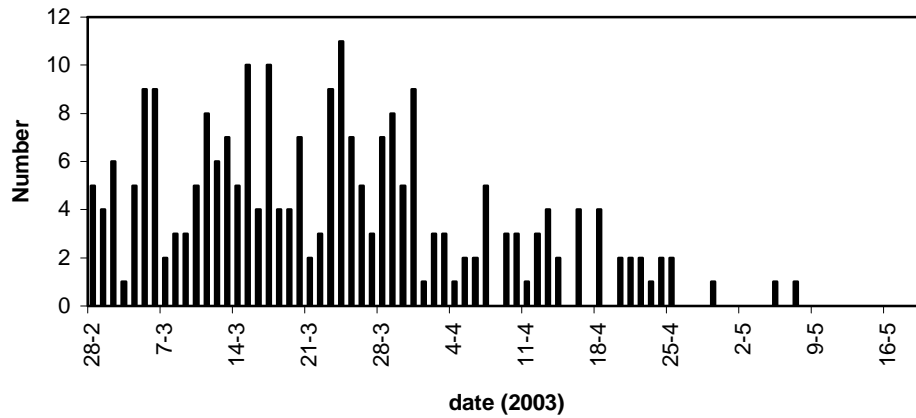


Figure 1. Course of the number of outbreaks (based on virus isolation or positive PCR) detected per day during the 2003 epidemic of fowl plague in The Netherlands

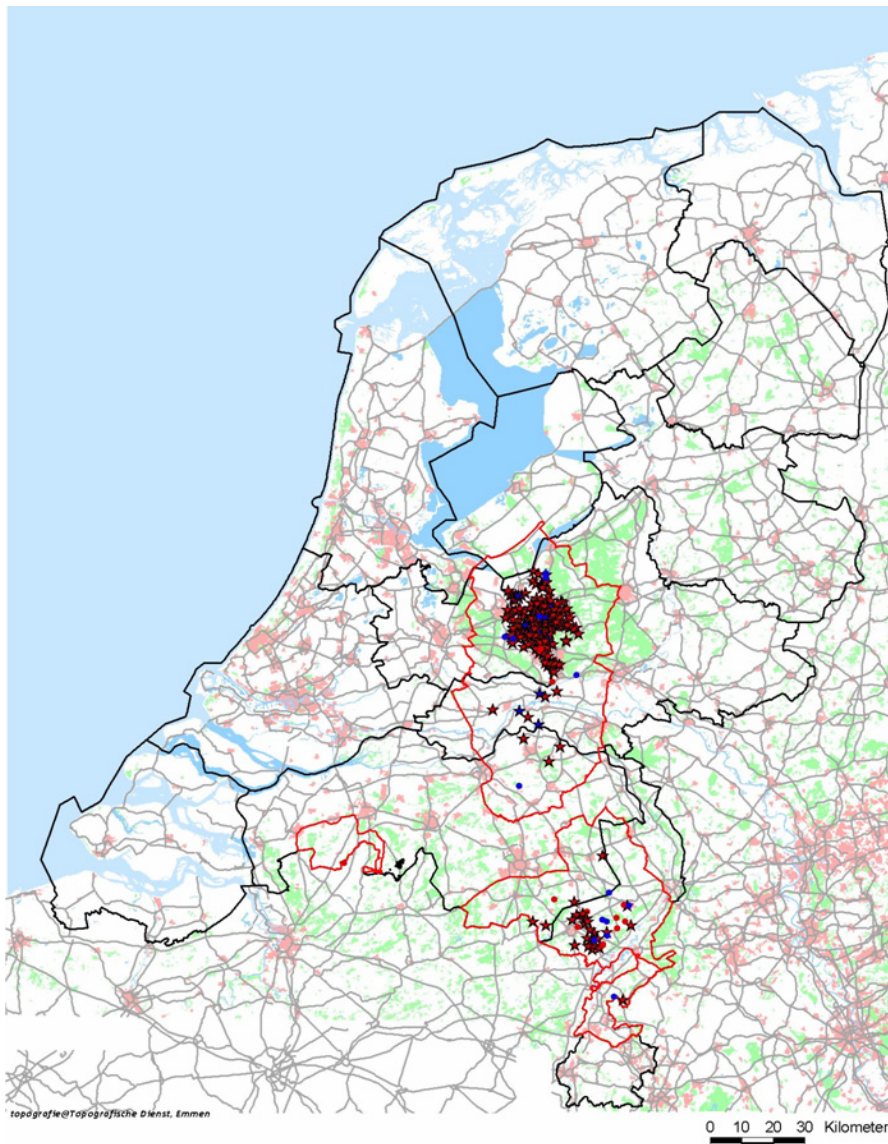


Figure 2. Localization of the flocks infected during the 2003 epidemic of fowl plague in The Netherlands. Infected flocks are represented as stars; suspected flocks, not confirmed at that time, are represented as dots

up to 43. Next, however, the epidemic faded out, with only a few outbreaks in May. By then, in the Southern part of The Netherlands large areas had been emptied of all commercial poultry.

The distribution of the infected and culled flocks over the various types of poultry is shown in Table 1. If we assume that the total number of flocks culled per poultry type represents the flocks at risk for infection, laying flocks had a much higher probability of getting fowl plague than broiler flocks (Relative Risk (RR) = 10.5 [95% Confidence Interval (95%CI): 2.7-41.5]), duck flocks (RR = 5.7 [95%CI: 1.5-22.4]), and hobby flocks (RR = 334 [99%CI: 191-585]). However, the probability of turkey flocks and breeder flocks to become infected was comparable to the probability of laying flocks.

Type of poultry	Number of infected flocks (%)	Number of culled flocks
Layers	168 (25%)	673
Turkeys	18 (29%)	62
Breeders	34 (31%)	110
Broilers	2 (2.4%)	84
Ducks	2 (4.3%)	46
Pets	13 (0.07%)	17,421
Others	4 (1.4%)	280

Table 1. Distribution of the number of infected flocks (based on virus isolation or positive PCR) and culled flocks over the various types of poultry

Between-flock transmission

The transmission was analysed separately for the Gelderse Vallei and adjacent areas and Limburg in the Southern part of The Netherlands. In both regions, there was no significant difference in β for the first two weeks after the first outbreak had been detected in the region and the period after those first two weeks. Therefore, in each of the two regions only two periods were distinguished, 1) before detection of the first outbreak and 2) after detection of the first outbreak. The results of the analysis are shown in Table 2.

	Before implementation of control measures		After implementation of control measures	
	β^a	R_h^b	β	R_h
Gelderse Vallei	0.42 (0.27-2.41)	5.0 (2.9-8.6)	0.17 (0.11-0.28)	0.91 (0.39-2.13)
Limburg	0.42 (0.17-3.65)	2.9 (no CI)	0.18 (0.08-0.46)	0.86 (0.28-2.68)

^a β , infection-rate parameter, average number of new infections per infectious flock per day

^b R_h , reproduction ratio, average number of new infections per infected flock 95% confidence intervals between brackets.

Table 2. Infection-rate parameter (β) and reproduction ratio (R_h) in the Gelderse Vallei and Limburg, before and after the implementation of measures to eliminate HPAIV

The control measures caused a significant ($p=0.0002$) reduction of the transmission of HPAIV between flocks in the Gelderse Vallei. In Limburg a similar reduction of β was observed, although in this region the difference between the period before detection of the first outbreak and after that detection was not significant ($p=0.07$).

However, the total number of outbreaks in this area, and thus the power of the comparison, was limited in comparison to the Gelderse Vallei. Moreover, the between-flock transmission in both areas shows a remarkable similarity, in the period before detection of the first outbreak as well as in the period afterwards.

In the Gelderse Vallei, the average infectious period decreased from 11.8 days (95% confidence interval (CI) 10.1-13.4) of the 5 herds that were notified as fowl-plague-suspect on the first day of the epidemic to 6.0 (95% CI 5.5-6.5) days in the first week and 5.2 (95% CI 4.9-5.5) during the rest of the epidemic. In Limburg, the estimated infectious period of the flock first affected was 7 days. In the subsequent period of the epidemic the infectious period was 4.8 (95% CI 4.3-5.3) days.

Although the between-flock transmission decreased upon implementation of the control measures, the accompanying R_h was only slightly less than 1 in both regions. The latter implies that, even after implementation of the control measures, we cannot falsify the hypothesis $R_h > 1$. Moreover, the reduction in the infectious period after the first week in the Gelderse Vallei did not result in a significant reduction in the value of R_h .

Discussion

In this study we quantified the transmission of HPAIV-H7N7 between poultry flocks during different phases of the 2003 epidemic of fowl plague in The Netherlands. In the Gelderse Vallei, the region first affected, control measures markedly reduced the between-flock transmission of HPAIV. Unfortunately, we are unable to establish the contribution of each of the individual measures to the reduction of the virus transmission. Nevertheless, it is clear that the stamping-out policy markedly contributed to this reduction, because it halved the infectious period and thus also halved R_h . Moreover, pre-emptive culling may also have caused some of the reduction of β , if infected flocks have been culled in a very early stage of the infection when it was still impossible to detect HPAIV. However, measures like the movement ban, restricted admittance of persons to farms and other hygienic measures probably also contributed to the reduction of the transmission.

Remarkably, in Limburg the values of β before and after the implementation of control measures were almost the same as in the Gelderse Vallei. Consequently, the awareness of HPAIV being in the country did not result in a lower infection rate. However, this awareness probably caused a shorter infectious period of the flock first infected in Limburg as compared to the flocks first infected in the Gelderse Vallei, and thus in a lower value of R_h . As a result, the number of infected flocks was much smaller at the start of the epidemic in Limburg than in the Gelderse Vallei.

In the Gelderse Vallei as well as in Limburg the transmission rate was not significantly reduced further during later phases of the epidemic. This raises questions as to the effectiveness of control measures implemented in these later phases, such as compartmentalization, creation of poultry-free buffer zones and the culling of all poultry in large areas. These questions are raised even more, because it is likely that the between-flock transmission towards the end of the epidemic was underestimated, because of the strong reduction in the number of susceptible flocks in the affected areas.

Upon the implementation of the control measures, in both regions the value of R_h was only slightly below one. Consequently, a considerable number of flocks still became infected during the epidemic. Moreover, the 95% CIs of R_h include one, indicating that it is uncertain whether the applied set of control measures is really

capable of eliminating the virus. Also here we should bear in mind that the transmission was probably underestimated due to the reduction of the number of susceptible flocks. Consequently, new or additional measures should be considered in future epidemics. Further reduction of the infectious period seems difficult. Consequently, we should focus on measures to reduce β , such as further restriction of the contacts between flocks or vaccination.

In conclusion, we found that a package of control measures including stamping out infected herds, pre-emptive culling of surrounding flocks, movement bans, screening and tracing and hygienic measures markedly reduced the transmission of HPAIV H7N7. However, it is uncertain whether this reduction is really sufficient to eliminate the virus in an area with a high poultry density.

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