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Controlling highly pathogenic avian influenza outbreaks: An epidemiological and economic model analysis

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ABSTRACT

Outbreaks of highly pathogenic avian influenza (HPAI) can cause large losses for the poultry sector and for animal disease controlling authorities, as well as risks for animal and human welfare. In the current simulation approach epidemiological and economic models are combined to compare different strategies to control highly pathogenic avian influenza in Dutch poultry flocks. Evaluated control strategies are the minimum EU strategy (i.e., culling of infected flocks, transport regulations, tracing and screening of contact flocks, establishment of protection and surveillance zones), and additional control strategies comprising pre-emptive culling of all susceptible poultry flocks in an area around infected flocks (1 km, 3 km and 10 km) and emergency vaccination of all flocks except broilers around infected flocks (3 km).

Simulation results indicate that the EU strategy is not sufficient to eradicate an epidemic in high density poultry areas. From an epidemiological point of view, this strategy is the least effective, while pre-emptive culling in 10 km radius is the most effective of the studied strategies. But these two strategies incur the highest costs due to long duration (EU strategy) and large-scale culling (pre-emptive culling in 10 km radius). Other analysed pre-emptive culling strategies (i.e., in 1 km and 3 km radius) are more effective than the analysed emergency vaccination strategy (in 3 km radius) in terms of duration and size of the epidemics, despite the assumed optimistic vaccination capacity of 20 farms per day. However, the total costs of these strategies differ only marginally. Extending the capacity for culling substantially reduces the duration, size and costs of the epidemic.

This study demonstrates the strength of combining epidemiological and economic model analysis to gain insight in a range of consequences and thus to serve as a decision support tool in the control of HPAI epidemics.

1. Introduction

Avian influenza (AI) is considered a serious threat to both humans and animals, and gained much attention especially since the emergence of highly pathogenic avian influenza (HPAI) H5N1 in South-East Asia in 2003 (Sims et al., 2005). With migratory birds as a possible introduction route (Alexander, 2000; Chen et al., 2005), waterfowl as a possible virus reservoir (Sturm-Ramirez et al., 2005; Gilbert et al., 2006) and the possible transformation from low pathogenic AI (LPAI) to HPAI virus (Capua and Marangon, 2000), commercial poultry flocks are at risk of infection.

HPAI epidemics have a major impact on animal welfare and the poultry industry (Stegeman et al., 2004; Mannelli et al., 2006). For example, in 1999 Italy experienced a HPAI epidemic caused by an H7N1 virus subtype. In total 16 million birds were culled and the estimated loss was about € 507 million, with € 112 million in direct losses and € 395 million in consequential losses (Sartore et al., 2010). The 2005 to 2006HPAI outbreak in Turkey caused a loss for broiler producers of € 28 million (Aral et al., 2010). In the 2003 epidemic of Avian Influenza in the Netherlands, caused by an H7N7 virus, 30 million birds were culled and destructed, i.e., approximately one third of the total poultry population (Stegeman

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et al., 2004). HPAI virus was detected in 241 farms, but in total 1349 commercial farms and 16,490 backyard flocks were depopulated. The poultry industry in the affected areas suffered substantial economic losses and the total direct costs amounted to € 270 million (Anon, 2004).

In HPAI epidemics, such as the 2014 outbreak in the Netherlands (ECDC, 2014), control measures will – as required by the EU – encompass culling of detected farms, zoning, transport regulations, and screening of dangerous contacts (Council Directive 2005/94/EC). When necessary, the most likely additional measure will be pre-emptive culling around infected flocks (Anon, 2007). Massive culling of mostly uninfected animals is increasingly criticized, mainly on ethical grounds (Cohen et al., 2007), but emergency vaccination in the case of HPAI does not seem to be a viable alternative at the moment. Commercially available vaccines need to be individually applied by injection, which would put a great logistical burden on the disease control organization. Also the limited availability of staff and equipment for (pre-emptive) culling will affect the size and duration, and thus costs, of an epidemic. However, the most efficient control strategy from an epidemiological perspective (e.g., smallest number of animals killed) is not necessarily the most economical. These two perspectives can be compared by joining epidemiological and economic models.

Epidemiological models are increasingly recognized as valuable for analysing and developing AI control strategies. Stegeman et al. (2010) emphasize the importance of thorough analysis of past epidemics, such as the estimation of the within-flock (Tiensin et al., 2007; Bos et al., 2009, 2010) or between-farm reproduction ratio (Mannelli et al., 2007; Stegeman et al., 2010). These estimates of the transmission parameters can be used for predictive modeling. For instance, the effectiveness of control strategies has been evaluated for commercial poultry in the UK (Truscott et al., 2007; Sharkey et al., 2008).

The overall objective of this study is to assess the epidemiological and economic impacts of different HPAI control strategies in an integrated model analysis. The control strategy as required by the EU is compared with additional strategies comprising pre-emptive culling of all flocks around infected flocks and emergency vaccination of all flocks except broilers around infected flocks, in three poultry areas of differing farm densities in the Netherlands. In a sensitivity analysis, the simulations are repeated in a low and high setting for between-farm transmission to study the robustness of the outcomes. An alternative strategy of premature slaughter is evaluated, where broiler flocks with broilers younger than 21 days of age are pre-emptively depopulated. Furthermore, the control strategy of pre-emptive culling in a 3 km radius around infected flocks is repeated with unlimited culling capacity (i.e., flocks are instantly culled) to gage the effect of the culling capacity. Finally, the economic comparison not only includes the differences in total costs, but also the distribution of these total costs over specific loss components.

2. Material and methods

2.1. Farm density and control strategies

The epidemic and economic outcomes of an HPAI outbreak depend upon a variety of factors, including poultry farm density in the area in which an outbreak occurs and the chosen control strategy.

The model analysis is applied to the Dutch poultry situation of 2008, involving 2771 commercial poultry farms with in total approximately 109 million chickens, ducks and turkeys. The latter two species comprise less than three percent of the total poultry population. Farms with laying hens (62% of all farms) have a median size of 20 000 birds (5–95% variation of 2000–93 000), while chicken broiler farms (32% of all farms) are much larger at a median size of around 50 000 birds (11 000–132 000) (Longworth et al., 2014a). Location coordinates, farm type (layer, broiler, etc.) and number of birds in each farm are used in the model. As farms are not evenly distributed over the Netherlands (Fig. 1), three classes of farm densities are distinguished: low density poultry areas (LDPA, 0.11 farms/km^2 in a 10 km radius around index farm), medium density poultry areas (MDPA, 0.47 farms/km^2), and high density poultry areas (HDPA, 0.97 farms/km^2). In the simulations HPAI is introduced in one of these areas, and transmission and control is simulated to assess how farm density influences the effectiveness of control strategies.

Five control strategies were evaluated. The EU minimum strategy (EU) (Council Directive 2005/94/EC) consists of culling of infected flocks after detection, a 72 h stand-still, transport regulations, tracing and screening of dangerous contacts and establishment of protection zones (3 km) and surveillance zones (10 km). Pre-emptive culling of all AI susceptible birds was evaluated in a radius of 1 km (Cul1), 3 km (Cul3) and 10 km (Cul10) around infected flocks in addition to the EU strategy. Emergency vaccination of all flocks except broilers was assessed in a vaccination radius of 3 km (Vac3) around infected flocks in addition to the EU strategy. The pre-emptive culling strategy in 3 km radius was repeated with additional targeted pre-emptive culling of broilers younger than 21 days of age in surveillance zones. This premature slaughter reduces the density of farms with susceptible flocks, while retaining the economically more valuable animals that are closer to slaughter age.

During the first five days after the first detection, pre-emptive culling was applied in a radius of 1 km around detected flocks, with a culling capacity of 10 farms/day. From six days onwards the capacity was increased to 20 farms/day, for both culling and vaccination. For culling this is supported by the culling capacity of 750 000 birds/day that was reached in the later stages of the 2003HPAI outbreak in the Netherlands (Stegeman et al., 2004). For vaccination however, this is a very optimistic estimate as the birds need to be vaccinated by individual injection.

2.2. Epidemiological model

In the current analysis a two-level epidemiological model is applied that describes virus transmission within a flock and between farms. The same approach has been previously applied to evaluate control strategies for classical swine fever (Backer et al., 2009) and foot-and-mouth disease (Backer et al., 2012).

The infection from bird to bird within a flock is described by an SEIR compartmental model with frequency-dependent mixing. When a susceptible bird (S) is infected, it will after a latent period (E) become infectious (I) until it either recovers (R) or dies (D). A proportion of the susceptible birds will be immunized by vaccination (V). Data at the animal level, such as the latent and infectious period, as well as the disease mortality and effect of vaccination are taken from literature on transmission experiments (Table 1). Parameter values for turkeys and ducks are assumed to be identical to the parameter values for chickens, as the parameter value variability for different host species and virus strains is comparable. Detection of HPAI by observed mortality in duck flocks is expected to be lower (Van der Goot et al., 2008), but this is counteracted by targeted clinical examination and serological screening during the epidemic (Anon, 2007). So, even though the small numbers of turkey and duck farms can play an important role during the silent spread phase, the numerous chicken farms are thought to drive the epidemic during the control phase of the epidemic.

The transmission parameter of 1.9 day^{-1} was estimated from mortality data of 174 infected flocks in the 2003 HPAI H7N7 epidemic in the Netherlands. Together with the median infectious

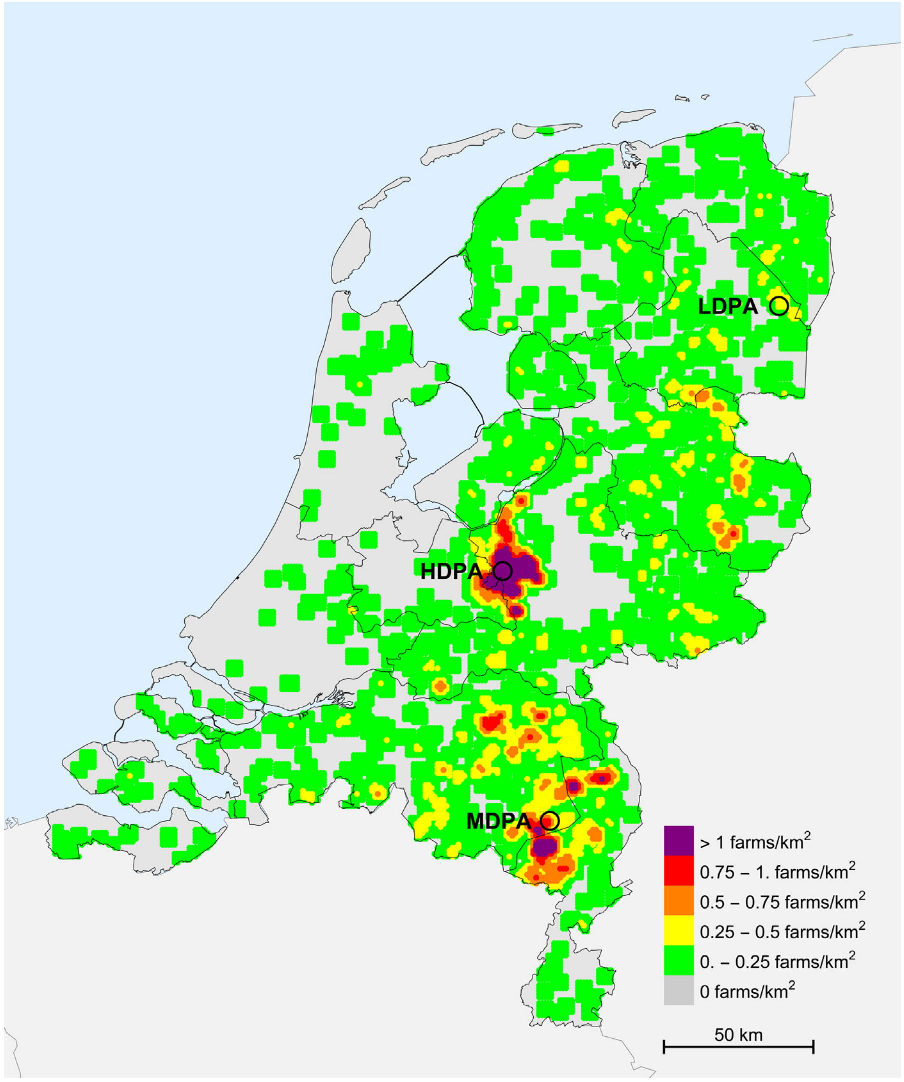

Fig. 1. Density of all poultry farms in the Netherlands and the positions (circles) of the layer farms where the epidemics are seeded in a high (HDPA), medium (MDPA) and low (LDPA) density poultry area.

period of 4 days, this leads to a within-flock reproduction ratio of 7.6. In the model, the detection of an infected flock is determined by the cumulative fraction of dead birds. From the mortality reports of the 2003HPAI epidemic, an empirical distribution was derived with a median value of 0.0061 (i.e., for instance 300 birds in a median sized broiler farm). This value is lower than the current Dutch monitoring threshold that requires AI notification at an observed mortality of 0.005 per day on two consecutive days (Anon, 2005), i.e., a mortality of 0.01 in two days. The reason is that the monitoring rule is designed for an HPAI-free period, while during an epidemic a higher alertness of farmers and veterinarians is expected to lead to earlier detection. Stochastic simulations showed that transmission in flocks that are not vaccinated or vaccinated after infection, is very high but with little variation. Transmission dynamics in such flocks are therefore simulated deterministically by numerically solving a system of ordinary differential equations. Transmission in flocks that are vaccinated prior to infection however, is much lower but with large variation. It is therefore simulated stochastically (using Gillespie's algorithm with tau-leaping, (Keeling and Rohani, 2008) to capture the variation in within-flock dynamics due to vaccination.

The transmission between farms depends on the distance between source and destination farm and the infection pressure generated at the source (i.e., the number of infectious birds at within-flock level). In general, the smaller the distance and the higher the infection pressure, the higher the infection probability will be. The distance dependency is described by three parameters of a transmission kernel, where all possible infection routes are modeled as one probability function. This is a fundamentally different approach than network models (e.g., Longworth et al., 2014a), where each infection route is modeled separately with an assumed probability. The advantage of the kernel approach is that the transmission kernel can be parameterized using outbreak data. For HPAI the kernel parameters have been estimated from the 2003HPAI epidemic in the Netherlands by Boender et al. (2007), and adjusted to the 2008 situation (Table 1). These kernel parameters correspond to the situation where the 2003HPAI epidemic would be an average epidemic. To assess the uncertainty of the transmission kernel, a high-transmission setting (upper bound of the transmission kernel, i.e. the 2003HPAI epidemic was a luckily small realization of what could have happened) and a low-transmission setting (lower bound of transmission kernel, i.e., the 2003HPAI epidemic was an extremely large realization) are compared in a sensitivity analysis. The upper and lower bounds of the transmission kernel (Table 1) were estimated from the 95% confidence area (Boender et al., 2007).

Table 1
Parameters of the epidemiological model: within-flock transmission model (upper part) and between-farm transmission model (lower part).

Within-flock parameters	Median value	5%–95%			Remarks	References
Latent period of bird	1 day	0.05–3.0	Exponential distribution	Van der Goot et al. (2005); Bouma et al. (2009); Poetri et al. (2009)		
Infectious period of bird	4 days	2.5–5.8	Gamma distribution (with number of stages $n = 16$)	Van der Goot et al. (2003); Van der Goot et al. (2005); Bouma et al. (2009)		
Fraction mortality	0.70			Van der Goot et al. (2005); Bouma et al.(2009)		
Vaccination coverage[a]	0.80		Due to non-perfect vaccine response or failed vaccinations			
Start effect vaccination	7 dpv[b]		Linear vaccination effect on susceptibility	Van der Goot et al. (2005)		
Full effect vaccination	14 dpv			Van der Goot et al. (2005); Poetri et al. (2009)		
Transmission parameter	1.9 day^{-1}	0.61–8.1	Estimated from outbreak data 2003, median value used in model	Van der Goot et al. (2003); Bos et al. (2009); Bouma et al. (2009)		
Cumulative fraction of dead birds at detection	0.0061	0.0041–0.034	Estimated from outbreak data 2003, empirical distribution used in model			
Between-farm transmission kernel	**Maximum likelihood estimate (MLE)**	**95% Confidence interval**	**Lower bound kernel[c]**	**Upper bound kernel[c]**	**Remarks**	**References**
Half-kernel distance	1.9 km	1.1–2.9	2.6 km	1.3 km	MLE used as default	Boender et al. (2007)
Kernel shape	2.1	1.8–2.4	2.5	1.8	MLE used as default	Boender et al. (2007)
Kernel height	0.0039 day^{-1}	0.0023–0.0076	0.0023 day^{-1}	0.0074 day^{-1}	MLE used as default, fitted to 2008 situation to reproduce 2003 outbreak	Boender et al. (2007)

[a] Vaccination coverage: fraction of birds within a flock that are (after two weeks) fully protected by vaccination.
[b] Dpv: days post vaccination.
[c] Upper and lower bound kernel parameters used for sensitivity analysis, estimated from 95% confidence area (Boender et al., 2007).

The production cycle of 6 weeks on broiler farms, followed by a downtime period of one week (Borck Høg et al., 2011) is taken into account in two ways. First, broiler farms cannot be infected during their downtime period. And second, when a broiler farm is located in a surveillance zone, it cannot obtain chicks for production and will stay empty at the end of its production cycle until the surveillance zone restrictions are lifted, 40 days after the last detection in that area.

The simulations are initialized using one hundred possible courses of HPAI spread per poultry area up to the moment of the first detection, that were previously simulated by Longworth et al. (2014a). During the high risk period (HRP) between introduction of HPAI in a poultry area and first detection, a network model is more appropriate to model the spread of the pathogen, as the transmission kernel was estimated for the control period following the HRP. At the time of first detection, the simulated number of infected flocks differed largely: in the HDPA a median value of 27 (with a 5–95% interval of 4–70) flocks were infected, in the MDPA 7 (1–22) and in the LDPA 2 (1–6). For each of these infected flocks, the location, infection moment and future detection moment were used to initialize our simulations. Per control strategy and per poultry area, 1000 epidemics were stochastically simulated (i.e., 10 epidemics per HRP initialization), starting at the time of the first detection in the country. For the sensitivity analysis of the transmission kernel 100 epidemics were simulated (i.e., 1 epidemic per HRP initialization) in the HDPA only, as the largest deviations are expected in this area. The epidemiological outcomes were used as input for the economic evaluation.

2.3. Economic model

For the economic analysis, the model of Longworth et al. (2014b) was used to calculate direct costs and direct consequential costs of an outbreak of HPAI for all direct stakeholders involved. The model outcomes were subsequently used in a partial budget model (Dijkhuizen and Morris, 1997), in which all types of costs that did not or only marginally differ between strategies – and thus did not alter the ranking of the strategies – were excluded from further calculations. The main additional costs in the partial budget model are direct costs and consequential losses (Meuwissen et al., 2003; Van Asseldonk et al., 2005). Direct costs that are included in the economic analysis comprise the compensation values for different types of culled poultry (Table 2). These and other economic parameters presented were estimated from the Dutch 2003 epidemic and discounted to reflect current prices. Other direct costs originating from depopulation are labor for culling, cleaning and disinfection, transport and destruction, materials, tracing and screening. In case of a vaccination strategy, additional costs comprise vaccine costs, labor costs for application and preparation, and costs for monitoring and surveillance in the vaccination zone.

Accounted consequential losses related to established restriction zones comprise value losses for slaughtered poultry because of welfare reasons and price effects if eggs are downgraded. Reared

Table 2
Input parameters used for the economic evaluation.

Costing component	Value	Unit
Value culled poultry		
Broiler chickens	0.98	€/bird
Ducks	2.09	€/bird
Turkeys	10.63	€/bird
Inside layers	1.98	€/bird
Outside layers	2.14	€/bird
Ready-to-lay layers	2.00	€/bird
Ready-to-lay breeders	5.84	€/bird
Breeders (parents stock)	7.00	€/bird
Culling, cleaning and disinfection	1.90	€/bird
Transport and destruction	0.66	€/bird
Materials for cleaning, disinfection and others	505.10	€/farm
Tracing	501.68	€/farm
Screening	541.33	€/farm
Vaccination	0.05	€/dose
Labor costs for application	0.28	€/bird
Labor costs for preparation	230.10	€/farm
Monitoring vaccination	152.50	€/farm
Surveillance in vaccination zone	152.50	€/farm
Value slaughtered poultry for welfare reasons		
Broiler chickens	1.50	€/bird
Ducks	3.43	€/bird
Turkeys	12.17	€/bird
Inside layers	1.15	€/bird
Outside layers	1.47	€/bird
Ready-to-lay layers	1.14	€/bird
Ready-to-lay breeders	2.84	€/bird
Breeders (parents stock)	5.42	€/bird
Value of eggs		
Normal egg of inside layers	0.05	€/egg
Industry egg of inside layers	0.03	€/egg
Normal egg of outside layers	0.07	€/egg
Industry egg of outside layers	0.03	€/egg
Normal egg of breeders (parent stock)	0.16	€/egg
Industry egg of breeders (parent stock)	0.03	€/egg
Normal hatching egg (hatchery)	0.27	€/egg
Industry hatching egg (hatchery)	0.03	€/egg

pullets (ready-to-lay) within a movement restriction zone may run into welfare problems if these restrictions last longer than the production cycle. Layer and breeder farms located inside the restriction zone which are not empty are assumed to continue production, but eggs can only be delivered to the egg product industry at a lower price (industrial value), resulting in a loss of revenue (Table 2).

Moreover, business interruption occurs because farm buildings become empty due to stamping-out and welfare slaughter and stay empty until restriction zones are lifted. Poultry farms which are depopulated are assumed to be empty until the end of the epidemic (calculated as day of last detection + 40 days). The loss of idle production factors was derived from the average gross margin for each type of poultry.

3. Results

The epidemiological and economic results of the different control strategies in different areas are combined in Table 3. The key characteristics of a simulated epidemic are the duration, the number of farms detected, culled and vaccinated, and the total costs, expressed as the median or mean value, as well as the 5% and 95% percentiles.

3.1. Comparison of control strategies

The epidemiological results show (Table 3) that in a HDPA the EU strategy will too often result in a lengthy epidemic, and is therefore not likely to be a preferred option for any of the stakeholders. Additional measures are (in HDPA and MDPA) required to bring the epidemic under control. Pre-emptive culling reduces the epidemic duration and the number of infected flocks, but the total number of culled farms increases with expanding culling radius in comparison to the EU strategy. At the largest analysed culling radius of 10 km not much is gained in epidemic duration or number of infected flocks compared to 3 km culling, because of the limiting culling capacity. Emergency vaccination in 3 km around detected flocks in a HDPA yields shorter epidemics than the EU strategy but longer than any culling strategy. However, the total number of culled farms is the lowest of all control strategies analysed.

When simulations are repeated in a high-transmission and a low-transmission setting, the size and duration of the epidemics naturally increase and decrease respectively, but the ranking of the control strategies is unchanged (Table 4). The EU strategy yields the largest and longest epidemics, pre-emptive culling increases in effectiveness with increasing culling radius but not much is gained by expanding the culling radius from 3 km to 10 km, and

Table 3
Epidemiological and economic outcomes for different HPAI control strategies of 1000 simulated epidemics that started in areas of different poultry farm density in the Netherlands, given as medians/means and 5th and 95th percentiles.

Strategy_area[a]	Duration (days)[b]			Number of detected farms			Number of culled farms[c]			Number of vaccinated farms			Total costs (Million €)		
	Median	5%	95%	Median	5%	95%	Median	5%	95%	Median	5%	95%	Mean	5%	95%
EU_HDPA	88	46	203	278	80	491	278	80	491	0	0	0	106	52	281
Cul1_HDPA	47	0	99	84	1	235	297	12	548	0	0	0	62	11	173
Cul3_HDPA	30	0	57	44	1	227	412	12	848	0	0	0	63	12	175
Cul10_HDPA	26	0	48	40	1	225	681	12	1541	0	0	0	106	26	269
Vac3_HDPA	67	0	113	140	1	331	163	12	374	397	0	678	68	10	196
EU_MDPA	91	0	249	131	1	427	131	1	427	0	0	0	105	6	223
Cul1_MDPA	46	0	110	32	1	124	106	6	391	0	0	0	56	2	127
Cul3_MDPA	27	0	55	15	1	73	164	6	519	0	0	0	51	2	115
Cul10_MDPA	18	0	38	8	1	65	374	6	1099	0	0	0	85	2	190
Vac3_MDPA	59	0	115	43	1	168	49	6	185	194	0	580	56	2	121
EU_LDPA	8	0	111	3	1	147	3	1	147	0	0	0	8	1	25
Cul1_LDPA	6	0	56	3	1	30	3	1	102	0	0	0	5	0	21
Cul3_LDPA	6	0	33	3	1	15	5	1	143	0	0	0	5	0	21
Cul10_LDPA	6	0	28	2	1	10	14	1	464	0	0	0	10	0	49
Vac3_LDPA	6	0	67	3	1	39	3	1	39	0	0	198	5	0	23

[a] Strategies: EU measures (EU), pre-emptive culling in 1 km (Cul1), 3 km (Cul3) and 10 km (Cul10) and emergency vaccination in 3 km (Vac3) around infected flocks; areas: high (HDPA), medium (MDPA) and low (LDPA) density poultry areas.
[b] Defined as the period between first and last detection of an infected flock.
[c] Culled farms comprise detected and pre-emptively culled farms.

Table 4
Sensivity analysis: Effect of between-farm transmission kernel on epidemiological outcomes for different HPAI control strategies of 100 simulated epidemics that started in a high density poultry area (HDPA) in the Netherlands, given as medians and 5th and 95th percentiles.

Transmission kernel	Strategy_Area[a]	Duration (days)[b]			Number of detected farms			Number of culled farms[c]			Number of vaccinated farms		
		Median	5%	95%	Median	5%	95%	Median	5%	95%	Median	5%	95%
Upper Bound	EU_HDPA	184	80	503	872	332	2635	872	332	2635	0	0	0
	Cul1_HDPA	91	0	295	192	1	541	578	12	1023	0	0	0
	Cul3_HDPA	49	0	99	75	1	485	600	12	1423	0	0	0
	Cul10_HDPA	44	0	70	71	1	487	1148	12	2137	0	0	0
	Vac3_HDPA	102	0	156	300	1	723	324	12	765	743	0	1042
Maximum Likelihood Estimate (Default)	EU_HDPA	88	46	203	278	80	491	278	80	491	0	0	0
	Cul1_HDPA	47	0	99	84	1	235	297	12	548	0	0	0
	Cul3_HDPA	30	0	57	44	1	227	412	12	848	0	0	0
	Cul10_HDPA	26	0	48	40	1	225	681	12	1541	0	0	0
	Vac3_HDPA	67	0	113	140	1	331	163	12	374	397	0	678
Lower Bound	EU_HDPA	66	19	116	166	8	289	166	8	289	0	0	0
	Cul1_HDPA	38	0	77	62	1	167	234	12	410	0	0	0
	Cul3_HDPA	24	0	40	32	1	144	341	12	642	0	0	0
	Cul10_HDPA	21	0	38	32	1	146	538	12	1155	0	0	0
	Vac3_HDPA	57	0	91	92	1	215	120	12	264	327	0	482

[a] Strategies: EU measures (EU), pre-emptive culling in 1 km (Cul1), 3 km (Cul3) and 10 km (Cul10) and emergency vaccination in 3 km (Vac3) around infected flocks; areas: high density poultry areas (HDPA).
[b] Defined as the period between first and last detection of an infected flock.
[c] Culled farms comprise detected and pre-emptively culled farms.

emergency vaccination in 3 km radius yields longer epidemics than any of the pre-emptive culling strategies but the lowest number of farms is culled. These differences are more pronounced in the high-transmission setting, but they are also present at the low-transmission setting, indicating that the qualitative results are robust over the range of plausible transmission settings.

Effective control strategies from an epidemiological point of view do not necessarily imply efficient strategies from an economic point of view. The most effective (Cul10) and the least effective (EU) strategies incur the highest total costs. The mean total costs of the strategies Cul1, Cul3 and Vac3 are substantially lower than the EU strategy and the Cul10 strategy. But whereas the culling strategies are more effective than vaccination in terms of duration and size of the epidemics, the total costs of the strategies Cul1, Cul3 and Vac3 differ only marginally.

3.2. Comparison of poultry areas

Epidemics in a HDPA are most severe, from both an epidemic and economic perspective (Table 3). When the epidemic starts in an MDPA, the epidemic durations are similar to the results in the HDPA, but the epidemic sizes (number of detected flocks) are much smaller due to the lower farm densities. The smallest and shortest epidemics are expected in an LDPA, but when considering the upper bounds of the results, the EU strategy yields a much higher epidemic duration and epidemic impact than other strategies. This is caused by the epidemic spreading from a low density area to a higher density area, where the epidemic was subsequently not controlled. Closer analysis of the simulated epidemics reveal that such a jump from LDPA to HDPA during the control phase occurs in 3% of the simulations, irrespective of the control strategy in the LDPA. Similar to the epidemiological results, there is a large variation in costs due to differences in areas in which the first outbreak occurs. The mean total costs are 10–12 times higher when the epidemic starts in a HDPA or MDPA compared to an epidemic that starts in an LDPA. Also there is a large variation in the range of expected losses as indicated by the 5–95% interval per strategy.

3.3. Distribution of costs

Although the total cost of Cul1, Cul3 and Vac3 are more or less equal, the distributions between the direct costs and consequential losses differ substantially between the strategies, but not between the areas (Fig. 2). For example, for the EU minimum strategy in a HDPA the fraction of the direct costs is 37% of the total costs, whereas for the Cul10 strategy in the same area this fraction is 85%. The consequential losses are relatively smaller for Cul3 than for Cul1 or Vac3. For an epidemic in a HDPA the fraction of direct costs as part of the total costs is 51%, 31% and 62% for Cul1, Cul3 and Vac3. The largest part of the direct costs consists of the depopulation of (pre-emptively) culled farms, while most consequential losses originate from the losses in egg delivery.

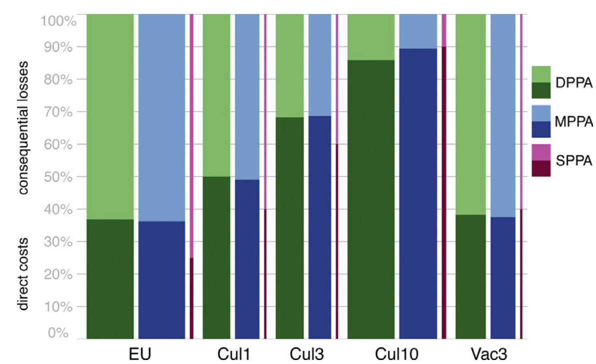

Fig. 2. Mean relative direct costs (darker colours) and consequential losses (lighter colours) of different HPAI control strategies (EU measures (EU), pre-emptive culling in 1 km (Cul1), 3 km (Cul3) and 10 km (Cul10) and emergency vaccination in 3 km (Vac3) around infected flocks) in a high (HDPA), medium (MDPA) and low (LDPA) density poultry area. The areas of the bars correspond to the absolute direct costs and consequential losses.

3.4. Effect of culling capacity and premature slaughter

The course of the epidemic depends on how many and which flocks can be pre-emptively culled. Here we study to what extent culling capacities limit the effective control of an epidemic and whether premature slaughter of broiler flocks in the 10 km surveillance zone adds to the effectiveness of control. Results for 3 km pre-emptive culling in HDPA are shown in Table 5; the epidemiological effects of culling capacities and premature slaughter for the other control strategies and areas are given in Backer et al. (2011).

Table 5
Effect of unlimited culling capacity and premature slaughter of broilers in surveillance zone (10 km around detected farms), in a high density poultry area, with pre-emptive culling in 3 km around detected farms; epidemiological and economic outcomes of 1000 simulated epidemics per strategy given as medians/means and 95th percentiles.

	Duration (days)[b]		Number of detected farms		Number of culled farms		Number of farms in surveillance zone		Total costs (million €)		Direct costs (million €)		Consequential losses (million €)	
Cul3_HDPA[a]	median	95%	median	95%	median	95%	mean	95%	mean	95%	mean	95%	mean	95%
Default (20 farms/day)	30	57	44	227	412	848	761	1428	63	175	43	120	20	53
Unlimited culling capacity	27	50	29	70	357	641	671	1209	50	109	34	77	16	35
Premature slaughter	29	54	43	223	437	939	757	1420	69	170	50	124	19	43

[a] Pre-emptive culling in 3 km (Cul3) in a high density poultry area (HDPA).
[b] Defined as the period between first and last detection of an infected flock; restrictions are lifted 40 days after the last detection in an infected area.

With a culling capacity of 20 farms/day, the model results show that infected flocks are culled with little delay of 0.1 (0.05–0.6) days, having the highest priority for culling. The delay for a pre-emptively culled farm in a 3 km radius however is 4.2 (0.2–18.2) days. To study this limiting effect of the culling capacity, the simulations were repeated with unlimited resources. Unlimited culling capacity lowers the size and duration of the epidemic, resulting in substantial lower costs of an epidemic, both direct and consequential (Table 5).

Like pre-emptive culling, premature slaughter is aimed at reducing the density of susceptible flocks in surveillance zones, by depopulating the broiler farms with broilers younger than 21 days of age. As these young birds cannot be slaughtered in the regular way (because of size limitations in the slaughterhouses), they will be slaughtered on site by the same teams that are used for (pre-emptive) culling, but with a lower priority. Simulation results show that premature slaughter does not add much to the effectiveness of the Cul3 control strategy (Table 5), presumably because of a limited number of broiler farms in the HDPA and because of the lowest culling priority. Due to the higher number of depopulated farms, the direct and total costs increase. For an individual farmer however there might be an incentive for premature slaughter when the expected revenues of the broilers at slaughter age (here assumed to be 70% of normal revenues) do not outweigh the additional expenditures to fully raise the birds in the remaining rearing period.

4. Discussion

By means of a stochastic modeling approach several control strategies for HPAI epidemics were compared, in an epidemiological and economic analysis. Effective control strategies from an epidemiological point of view do not necessarily imply efficient strategies from an economic point of view, as was illustrated by the different control strategies and the areas of different poultry farm densities. Although the ranking of the different control strategies seems to be robust over a range of plausible transmission settings, it should be kept in mind that the transmission kernel is estimated from a specific outbreak (H7N7 in the Netherlands in 2003) and is therefore only valid for poultry populations of similar composition and farming structure.

In general, emergency vaccination yielded longer and larger epidemics than pre-emptive culling, even when the vaccination radius is larger than the culling radius. Although the ranking of the studied strategies is in agreement with the comparable control strategies of the EU, 1 km pre-emptive culling and 3 km emergency vaccination in the study of Longworth et al. (2014b), some notable differences are observed. The difference between the epidemiological results for 1 km pre-emptive culling and 3 km emergency vaccination is smaller than in our results. This might be attributed to the explicit within-flock transmission in our model; vaccination does reduce the probability of infection, but once infected, vaccination only slows the spread within and consequently also between farms. In the Longworth study, epidemics in the HDPA are larger and longer than indicated by our results, presumably due to the chosen transmission parameters based on expert opinion (Longworth et al., 2014a), while our kernel model was parameterized by observed outbreak data. Conversely, the majority of epidemics in the MDPA seem to be effectively controlled by either pre-emptive culling or emergency vaccination, whereas our results show only slightly smaller and shorter epidemics in the MDPA compared to the HDPA. This seems to indicate a more localized spread mechanism compared to our model, which could be attributed to the assumption that transports are severely reduced during the control phase and that local spread is limited to 3 km (Longworth et al., 2014a). Despite the different underlying epidemiological models, the total costs of 1 km pre-emptive culling and 3 km emergency vaccination in the study of Longworth et al. (2014b) are comparable, in agreement with our results. It should be noted though that the absolute costs cannot be compared directly as our results are based on a partial budget model whereas Longworth et al. (2014b) use a 'total' budget model.

For HPAI the time scale of the vaccine induced immune response within the animal (one to two weeks) is long compared to the time scale of transmission within and between farms. For livestock diseases with less discrepancy between immune response and transmission time scales, emergency vaccination can be a viable control strategy, as shown in previous model analyses for classical swine fever (Backer et al., 2009) and foot-and-mouth disease (Backer et al., 2012).

From the simulation results for unlimited culling capacity it was concluded that an increased culling capacity would substantially decrease the epidemic and economic impact. These results indicate that it is worthwhile to invest in preparedness and in resources that enable an adequate response, for example in training and maintaining a basic infrastructure for quick response. Increasing vaccination capacity would not be as effective, as the immune response time in a vaccinated bird is most likely just as limiting for effective control as the vaccination capacity. It should also be kept in mind that the assumed vaccination capacity of 20 farms/day is optimistic for the current method of administration by injecting individual birds. In practice, vaccination capacities will be much lower, which would disqualify vaccination as an emergency measure. An alternative is to apply vaccination in a more preventive manner, e.g., vaccination of flocks in HDPAs when another area in the country is infected. This would however still pose considerable logistical challenges (e.g., most teams are needed in the outbreak area), incur high vaccination costs, and disrupt exports for a prolonged period.

Vaccination also introduces the potential problem of reduced market access for products of vaccinated birds. Irrespective of the applied control strategy, export is prohibited to the EU and third country markets. Some of these restrictions specifically apply for the infected areas, but poultry farmers outside the infected zones might also be confronted with consequences since trade bans can occur. Especially for the Dutch poultry sector, an epidemic of HPAI has large consequences, because of the export of large numbers of breeding eggs and one-day-old chicks. After the last detected outbreak it takes time until all restrictions in trade are lifted and the export situation returns to normal. Because of the longer duration of epidemics, compared to Cul1 and Cul3, the Vac3 strategy will disturb export more profoundly.

Shifts in costing components have implications for stakeholders involved. EU community measures related to HPAI epidemics include 50% co-financing of veterinary emergency measures. Eligible costs components are costs of compulsory and pre-emptive slaughter and related operational expenditures (Bergevoet et al., 2011). In addition, the remaining costs for these specific components are shared between the government and the Dutch poultry farmers by means of a compulsory statutory levy and compensation scheme (Van Asseldonk et al., 2006). Business interruption and adverse price effects are not reimbursed by EU or the national compensation scheme. For this reason farmers may prefer pre-emptive culling to emergency vaccination because a larger share of the costs is reimbursed.

Since the objective of this study was to compare different HPAI control strategies the partial budget model only includes those costing components that differ between the evaluated alternatives. Therefore, the types of costs that do not or only marginally differ between strategies, and thus do not alter the ranking of the strategies, were excluded from the calculations. Excluded costs were for example domestic price effects due to export restrictions within the EU and to third countries, and the effect of the epidemic on prices in infected regions versus non-infected regions. Also impacts from HPAI epidemics felt upstream and downstream along the poultry value chain are excluded: breeding, feed production, input supply, slaughter, processing, final sale and consumption (i.e., ripple effects). The same holds for non-AI sensitive livestock branches and non-agricultural industries as tourism (i.e., spill-over effects) because losses are incurred mainly due to the fact of an occurring epidemic and to a lesser extent to the applied control strategy. Since other than typical agricultural production is becoming more important for the rural economy these spill-over effects are likely to become a large part of the total epidemic costs.

HPAI virus transmission from birds to humans occasionally occurs (Katz et al., 1999; Koopmans et al., 2004). It is therefore essential to control an HPAI epidemic in poultry to minimize risk for humans. For the same reason, hobby flocks should be critically considered. Using randomly generated locations of an estimated number of 110 000 hobby flocks in the Netherlands (Treep et al., 2004) and assuming a relative susceptibility of 0.014 compared to commercial poultry farms (Bavinck et al., 2009), 57 (2–243) hobby flocks are expected to be infected by commercial poultry farms under the Cul3_HDPA strategy (Backer et al., 2011). Infected hobby flocks are often dead ends in HPAI transmission because of limited contacts with other farms and thus play a minor role in the epidemic. They can however still pose a considerable threat to their owners, and should be taken into account in HPAI eradication.

A specific feature of the applied simulation method is that at the start of the epidemic the decision is made which control measure will be used, and the decision makers do not deviate from this decision during the epidemic. This is often not what happens in practice during an epidemic. In reality, it is a process of monitoring and adapting the control strategy based on a series of decisions rather than on one decision. Or, as Ge (2008) puts it: "the epidemic can only be understood backwards, but it must be controlled forwards".

Decision making in controlling contagious animal diseases is a complex process, characterized by a mixture of epidemiological, economic and social ethical value judgments. Different stakeholders will have different ideas about which strategy should prevail (Cohen et al., 2007). Their views may, for instance, represent the interests of the farming community, the processing industry, the animals, the consumer or the general public. This may create a situation of conflicting interests, as economic motives may prevail in the views of some, while animal or human welfare motives may be prominent in the view of others (Mourits et al., 2010). This study emphasizes the strength of combining epidemiological and economic model analysis to gain insight in a range of consequences and thus to serve as a decision support tool in the control of HPAI epidemics.

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