



Commune-level Simulation Model of HPAI H5N1 Poultry Infection and Control in Viet Nam

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1. Summary

With the aim of contributing to evidence-based and equitable disease control strategies FAO's Pro-Poor Livestock Policy Initiative is promoting a systematic approach, referred to as *Strategic Pathogen Assessment for Domesticated Animals (SPADA)*, which combines rigorous epidemiological and economic analysis with risk management. In the case of HPAI, the epidemiological component focuses on development of stochastic simulation models of disease transmission to identify control policies that might be beneficial in the reduction of the transmission of HPAI virus at the local, sub-national and national level.

This report describes a farm-based disease transmission model that approximates the dynamics of HPAI H5N1 outbreaks in Vietnam poultry farms. During model experimentation the impact of varying different sets of epidemiological parameters on the number of infected farms, the force of infection and on the net reproductive number within a commune were simulated. The average net reproductive number (secondary cases arising from one infected farm in a vaccinated population), R_n , in the most lenient control scenario was 2.26. Current disease control measures are predicted to significantly reduce disease transmission but do not completely eliminate the possibility for circulation of residual infection ($R_n = 1.05$). A disease control optimization process which takes into account the differences in farm structure between geographical regions shows that optimal disease control policies differ, depending on local conditions. However, they also suggest that complete elimination of HPAI H5N1 from domestic poultry in Vietnam requires high levels of vaccination coverage of S4 backyard farms, levels that are unlikely to be achievable. Therefore, more attention must be paid to early detection of infection and reduced response time.

Future research foresees validation of the model with more complete data, economic assessment of the financial and economic implications of the different disease control scenarios, and field studies to assess incentive mechanisms for early disease reporting.

2. Background

Outbreaks of highly pathogenic avian influenza H5N1 (HPAI) viruses in poultry and their threatening zoonotic consequences emphasize the need for effective control measures (Ferguson et al. 2005). This becomes most significant in countries where poultry and human cases have reached relatively high incidences.

All four countries in the Mekong region have reported viral circulation in their poultry populations since late 2001 (Webster et al 2002). Incidence in poultry was specially high in Vietnam where outbreaks were reported seasonally from early 2003 to late 2005 with the highest incidence around the Tet-holiday festivities (Pfeiffer 2005). In addition to cases in poultry Viet Nam is the country with most HPAI H5N1-related human fatalities of all countries reported infected (OIE, 2006; WHO, 2006).

In Viet Nam most outbreaks of HPAI H5N1 in poultry were observed in small commercial farms which rear chicken or ducks and in backyard flocks (Morris et al. 2005). These backyard flocks, subsistence (Sector 4) and market oriented (Sector 3), account for about two-thirds of poultry production and half of direct marketing in Viet Nam. In rural areas, typically seven out of ten households, that is around eight million households, many of them living below the international poverty line, own chickens. If serious adverse impacts on these poor are to be avoided, it is essential to develop and implement control strategies that are adapted to initial conditions and local institutions.

Containment policies applied in Viet Nam were irregular and different throughout the country for the three outbreak waves (Dung, pers. comm). These included movement control and a set of culling policies. Their differential efficacy and socio-economic impacts have not yet been quantified. Currently the country is not reporting outbreaks and is implementing a systematic vaccination campaign of their poultry flocks, which is regarded as a transitory policy (Dung, pers. comm).

Effective strategies for eradication of highly pathogenic avian influenza H5N1 infection in smallholder poultry flocks require an understanding of the dynamics of the infection process between flocks, as well as the factors influencing them. We model HPAI H5N1 transmission within a heterogeneous population of poultry farms at the commune level and quantify the differential effectiveness of different disease containment scenarios.

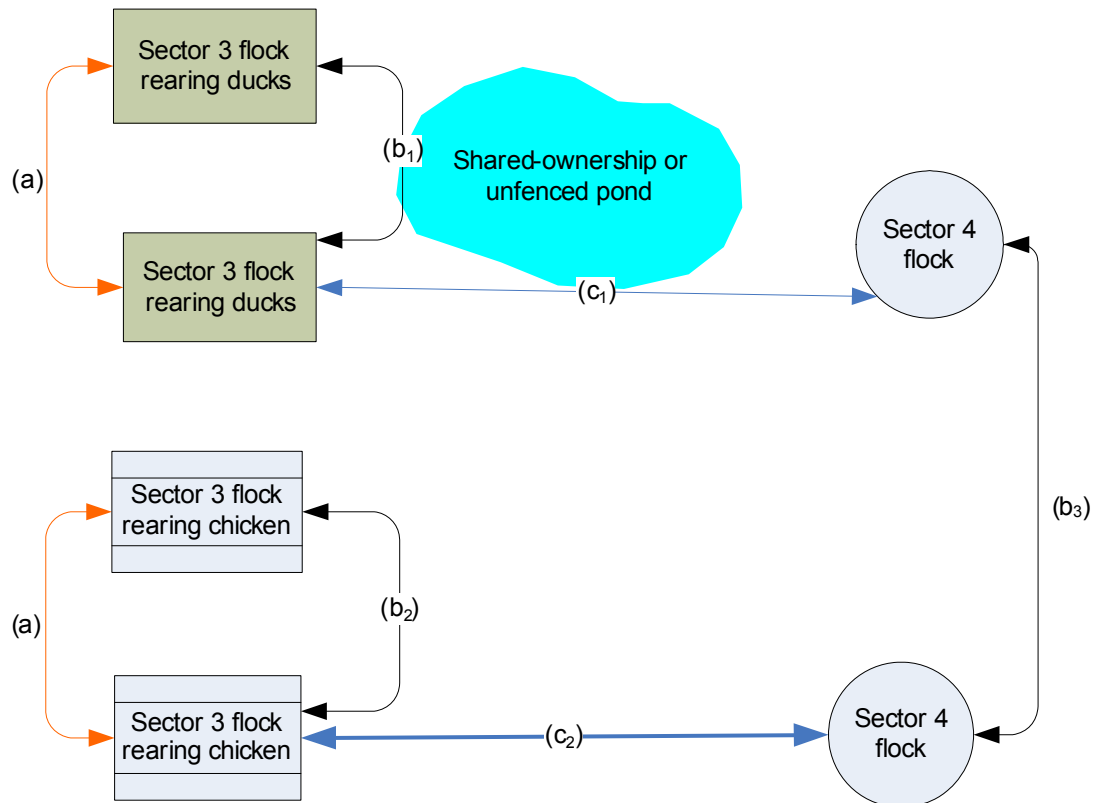
This report summarizes the current status of the epidemiological research component initiated by FAO's Pro-Poor Livestock Policy Initiative within the SPADA framework and sets the direction for future research.

3. Conceptual Setting

The risk of infection by a HPAI H5N1 strain has been found to differ in chicken and ducks (Gilbert et al. 2004). In order for the transmission model to take this biological feature into account, the small commercial farms of a commune were categorized according to their predominant poultry populations. This was achieved by disaggregating the Sector 3 farm population into two strata: Sector 3 farms rearing ducks only (D3) and Sector 3 farms rearing chicken only (C3). In our approximations we have considered Sector 4 farms (S4) as meta-populations of multiple species of poultry.

In our model we assume that virus is introduced and transmitted within and between Sector 3 and Sector 4 poultry farms by the movement of live poultry. Other risk pathways for virus introduction are not considered in our approximations. The conceptual structure describing live poultry movements between farms which can lead to the circulation of HPAI H5N1 infection in a commune is shown in Figure 1.

Figure 1: Schematic of the structure of contact between Sector 3 and Sector 4 poultry holdings. The arrows in orange represent the observed movement of poultry between Sector 3 holdings due to the seasonally-driven trade of unfinished birds. The arrows in blue represent the opportunity of direct contact between farms of different sectors due to the free ranging activity of individual birds. The arrows in black represent the opportunity of contact between farms of the same sector due to the free ranging activity of individual birds. (a) Trade of unfinished birds between sector 3 farms; (b1) Direct contact between Sector 3 duck farms; (b2) Direct contact between sector 3 chicken farms; (b3) Direct contact between Sector 4 farms; (c1) Direct contact between Sector 3 duck farms and Sector 4 farms; (c2) Direct contact between sector 3 chicken farms and sector 4 farms.



Contact between poultry farms is facilitated either by trade of birds or by the free ranging activity of individual birds. We assume that the likelihood of Sector 3 farms to get into contact with other Sector 3 farms is maximized through the trade of unfinished birds (a). The birds involved in this movement are expected to resume their growth cycle on the farm that bought them. This movement of poultry is dependent on local dynamics which are driven by the seasonal variation in demand. The movement of unfinished birds between Sector 3 farms can be defined as seasonally-driven, age-dependent with a species-specific intensity.

It has been observed that Sector 3 duck farms can rear their flocks in a pond of shared-ownership. Despite the frequent separation by fences we assume that flocks under such a

rearing system can come into direct contact with each other since they are managed in a common aquatic environment (b_1).

It is common for Sector 3 chicken farms to have a separate backyard flock, mainly comprising finished birds, for own consumption. This sub-population of birds within Sector 3 farms may be kept under free range conditions and its movement pattern may lead to contact with another Sector 3 farm (b_2).

Sector 4 farms which rear their birds under a free-range system will have the opportunity to contact Sector 3 duck farms if these are reared in unfenced ponds (c_1) and also with other Sector 4 farms with the same characteristics in the vicinity (b_3). Similarly, individual movements of birds belonging to Sector 4 may also lead to contact with Sector 3 chicken farms that have an uncontained backyard flock (c_2).

These theoretical contact links form the basis of the epidemiological framework underlying the transmission model.

4. Data Sources

Outbreak Data

Data regarding HPAI H5N1 infection at the commune level was obtained from the Department of Animal Health - Ministry of Agriculture and Rural Affairs for Viet Nam (DAH) for the three epidemic waves occurring between January 2003 and November 2005. These included time of reporting and estimated number of farms infected per commune.

Disease Control Data

Country level disease control data was obtained from the DAH to inform the parameters of the control model. This included information relating to the level of culling and the coverage of vaccination campaigns.

Commune Farm Structure Data

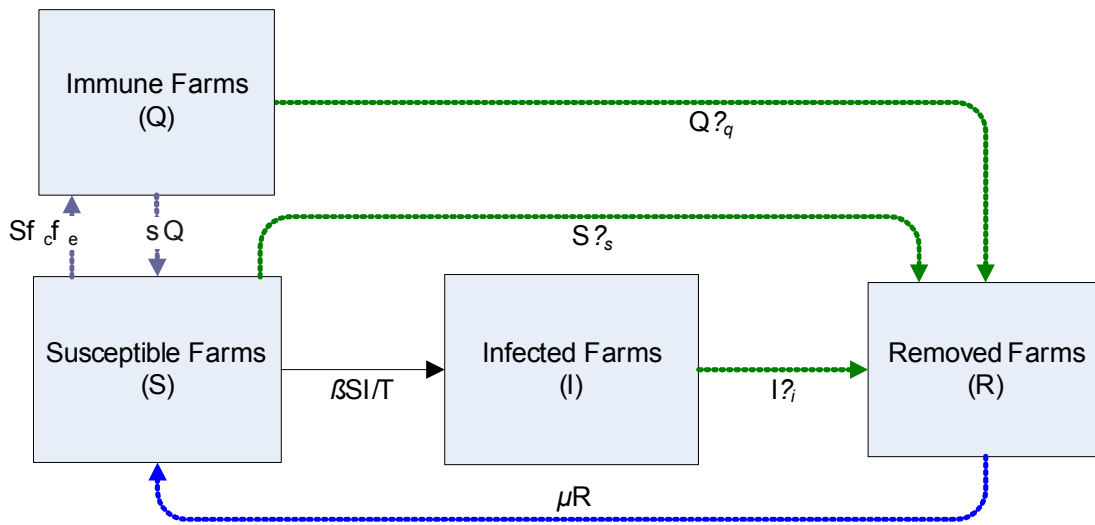
The model used household census data from 2001 obtained from the General Statistics Office of Viet Nam (GSO) and animal census data from 4 provinces (two within the Red River Delta and two in the Mekong River Delta) obtained during the pre-vaccination census in Viet Nam. Datasets were combined to obtain the number of farms per category of subpopulation for each study area.

5. Transmission Model

Structure and Dynamic Assumptions of the Core Model

We have developed a stochastic, farm-based compartmental transmission model where different poultry farms in a commune can be in one of the following four states: susceptible, immune, infected, removed and again susceptible upon restocking (SQIRS). The basic structure of the model is shown in Figure 2.

Figure 2: Schematic of the HPAI H5N1 SQIRS model structure illustrating the dynamic assumptions between the four states and the parameters involved in the state transitions



In the core model we have used the following set of non-linear differential equations to express the changes in state:

$$\frac{\partial S_{(t)}}{\partial t} = \mu R_{(t)} + \sigma Q_{(t)} - \left(\beta S_{(t)} \frac{I_{(t)}}{T_{(t)}} \right) - \gamma_s S_{(t)} - \varphi_c \varphi_e S_{(t)} \quad (1)$$

$$\frac{\partial Q_{(t)}}{\partial t} = \varphi_c \varphi_e S_{(t)} - \sigma Q_{(t)} - \gamma_q Q_{(t)} \quad (2)$$

$$\frac{\partial I_{(t)}}{\partial t} = \left(\beta S_{(t)} \frac{I_{(t)}}{T_{(t)}} \right) - \gamma_i I_{(t)} \quad (3)$$

$$\frac{\partial R_{(t)}}{\partial t} = \gamma_s S_{(t)} + \gamma_i I_{(t)} + \gamma_q Q_{(t)} - \mu R_{(t)} \quad (4)$$

We have assumed that in a commune farms mix randomly and that all are equally susceptible to infection. These expressions are based on a frequency-dependent transmission function where S , I , R and Q are the numbers of susceptible, infected, removed and immune farms in a commune per unit time step.

The structure of the core model assumes a dynamic expression $\beta SI / T$ which characterizes the rate of change from the susceptible state to the infected state which (I/T) (1). This rate is dependent on the frequency of infective farms and is controlled by the effective contact rate parameter, β , which is derived considering a constant per farm contact rate and the probability that contact results in infection. We consider that this effective contact rate is independent of farm density.

Based on the theoretical contact structure presented in Figure 1, the heterogeneous population (multi-population; C3, D3 and S4 farms) model incorporated a farm contact matrix (β_{ij}) which included the effective contact rates for each modeled interaction.

The reproductive number of a typical infectious farm (R_0) is an important theoretical epidemiological measure of the potential of disease spread. It is defined as the average expected number of secondary infectious cases resulting from a typical infectious case in totally susceptible population (Diekmann and Heesterbeek 2000). The average number of secondary cases per infectious individual in a vaccinated population is termed the net reproduction number (R_n). This measure is a function of the contact rate and the duration of infectiousness and in a heterogeneous population it can be explained by the following relationship:

$$R_{n[ij]} = \frac{\beta_{ij}}{\alpha_j} \quad \text{where } 1/\alpha_j \text{ is the mean duration of the infectious period of the infected case.}$$

However, for heterogeneously mixing subpopulations a typical infectious commune farm is best described as partially belonging to one of the three sub-populations. The calculation of the net reproductive number of a commune under heterogeneity can be approximated by considering the next generation matrix (R_{ij}) at each time-step and a matrix constituted by subpopulation fractions of the typical infectious farm.

Control Model

We assume that, once detected, infected farms are culled at a rate γ_i (4) moving to the state R where they will remain for a defined period of time (time-to-restocking). Farms in state R are characteristically empty farms. In reality, once an infected farm was identified, removal (culling) policies were also targeting susceptible farms in a variety of strategies for the different outbreak

waves (Dung, pers.comm). Therefore, removal of susceptible farms was entirely dependent on prior detection of an infected farm. We developed an approximation of this (1) where susceptible farms were allowed to be culled at a rate γ_s and computed at the next time step together with the removed infected farms (4).

The core model utilized an semi-open population design where removed (culled) farms re-enter at each time step the susceptible state S conditioned by a time dependent restocking rate, μ (1)

The incorporation of the immune state (Q) allowed us to model prophylactic vaccination of each subpopulation. This was modeled as a transition between the (S) state to the (Q) state at a rate φ_c (2). Overall, the fraction of susceptible farms being properly immunized and thus entering state (Q) is dependent on the level of coverage of the vaccination, φ_c (proportion vaccinated farms), and on the efficacy of the vaccination, φ_e .

Immunity provided by vaccination is assumed to be lost at a rate σ . This determines the transition of immune farms back to the (S) state (Eq. 1 and 3).

6. Model Experimentation

The transmission model was developed in Powersim studio software. Simulation outputs were recorded after 1,000 iterations. Each iteration corresponds to a model run over a 10 year period.

During model experimentation we have simulated the impact of varying different sets of epidemiological parameters on the number of infected farms, the force of infection and on the net reproductive number within a commune. Epidemiological parameters used in the model include farm and housing parameters, virus parameters and disease control parameters. These were either entered as fixed values or as distributions. When entered as distributions values were set to be sampled in each iteration using Latin Hypercube sampling method.

Initially we considered a commune constituted by a homogeneous group of farms by averaging out the farm structure across all study communes. This approach allowed us to assess the robustness of the simulation outputs under homogeneity.

During simulations with the heterogeneous population model some parameter values were set as common across all poultry sectors while others were allowed to assume values specific to a given poultry sector.

Model experimentation also included the assessment of varying the initial conditions of an outbreak. This procedure allowed evaluation of the impact of geographical differences of

commune poultry farm structure on the size and duration of an outbreak wave. Using geographically disaggregated data we have separately simulated HPAI H5N1 outbreaks using a commune farm structure of the North and a commune farm structure of the South of Viet Nam. In addition to this we have used an evolutionary search algorithm included in Powersim Studio software for the optimization of disease control policies for the different geographical regions considered in the study. This analysis was performed by defining a set of disease control objectives and control decisions. The search algorithm allowed the generation of robust values for disease control decisions that best meet the disease control objectives.

7. Simulation Results

Homogeneous Commune Structure

We have assessed the impact of four disease containment policies on the development of an HPAI H5N1 outbreak wave assuming an average commune structure in Viet Nam. The scenarios considered in these simulations are outlined in Table 1.

Table 1: Disease control interventions considered in different simulated scenarios

Scenario	Intervention(s)
I	Cull reported cases.
II	I + Pre-emptive cull (3 km radius) around reported cases.
III	II + Vaccination of all Sector 3 farms
IV	III + Vaccination of 25% of S4 farms

Scenarios I and II reflect disease containment measures used in the first and second waves (2003-2004; 2004-2005), respectively. Scenarios III and IV have taken into consideration the antiviral prophylaxis of poultry flocks which was initiated after the second outbreak wave. In Scenario IV a proportion (25%) of backyard flocks (S4) are also included in the vaccination campaign. The epidemiological impact of each control scenario is presented in Table 2.

When considering culling of infected farms only (Scenario I) the maximum R_n estimate obtained was 4.03. This means that a typical infected farm can infect up to 4 susceptible farms during its entire life expectancy (up to the moment it is culled). The variation of this maximum estimate was largely dependent on the time between infection and reporting (data not shown).

Table 2: Mean impact of disease control scenarios on HPAI H5N1 epidemiological parameters for all study communes. Simulations were run for a period of 10 years and each simulation was run over 1000 iterations.

Scenario	Disease Outcome		
	R_n^* (95%CI)	Cases (95%CI)	Force of infection** (95%CI)
I	2.26 (0.97-4.06)	6.88 (2.86-25.11)	3.43 (0.94-9.47)
II	2.24 (0.97-4.03)	6.19 (2.69-21.98)	3.09 (0.89-8.24)
III	1.05 (0.32-2.62)	3.6 (1.5-18.7)	1.24 (0.13-5.05)
IV	0.23 (0.07-0.58)	1.6 (1.4-1.9)	0.01 (0.003-0.04)

* farm; ** farm/day

However inclusion of a 3km pre-emptive culling ring (culling of all susceptible farms) around an index case (Scenario II) did not significantly reduce the commune reproductive number despite the force of infection being significantly reduced ($P=0.038$). This reduction however is not sufficient to contain disease spread as an average of 6 farms can still become infected per time step.

Inclusion of antiviral prophylaxis seems to produce the best disease containment results with all epidemiological parameters approaching threshold values. For $R_n < 1$ transmission is expected to give rise to minor outbreaks while for $R_n > 1$ the outcome of transmission may be either minor or major outbreaks (Diekmann and Heesterbeek 2000). The results from simulations of Scenario III show that this policy may either lead to major or minor outbreaks. This finding is also supported by the estimates for the force of infection. This suggests that under the homogeneous population assumption vaccination of Sector 3 farms may not be sufficient to contain progression to major outbreak waves.

The inclusion of 25% vaccination coverage of backyard flocks seems to reduce disease transmission below threshold values. However from the resulting number of cases residual infection circulating amongst the poultry populations appears possible. The impact on commune outbreak status and progression of each scenario can be further understood by analyzing Figure 3.

Figure 3: Cumulative probability distributions of the values of R_n for different disease control scenarios at commune level. The R_n values plotted are the mean value per time-step (per day).

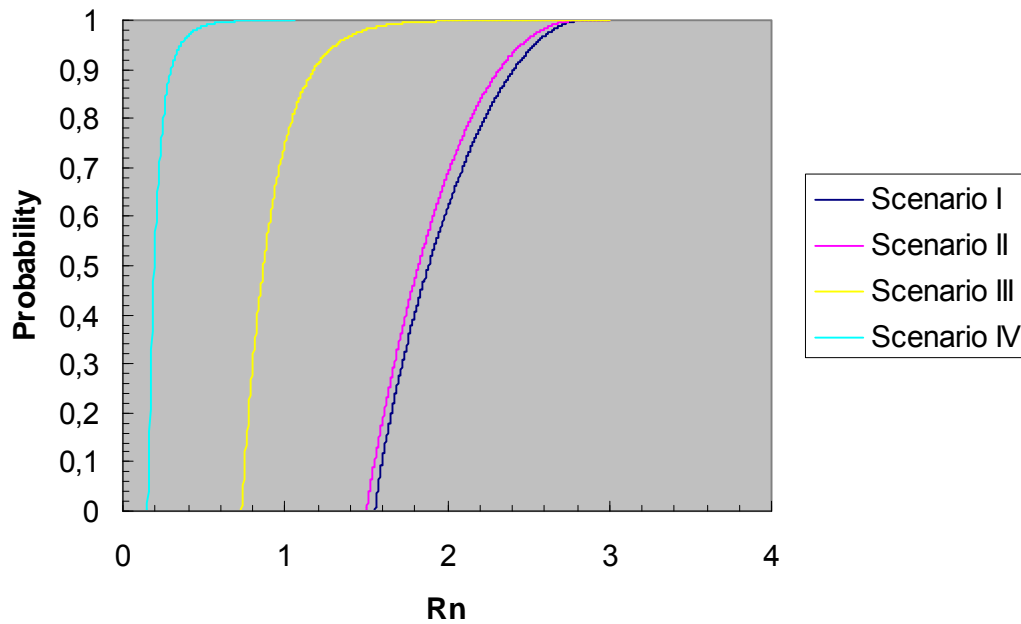
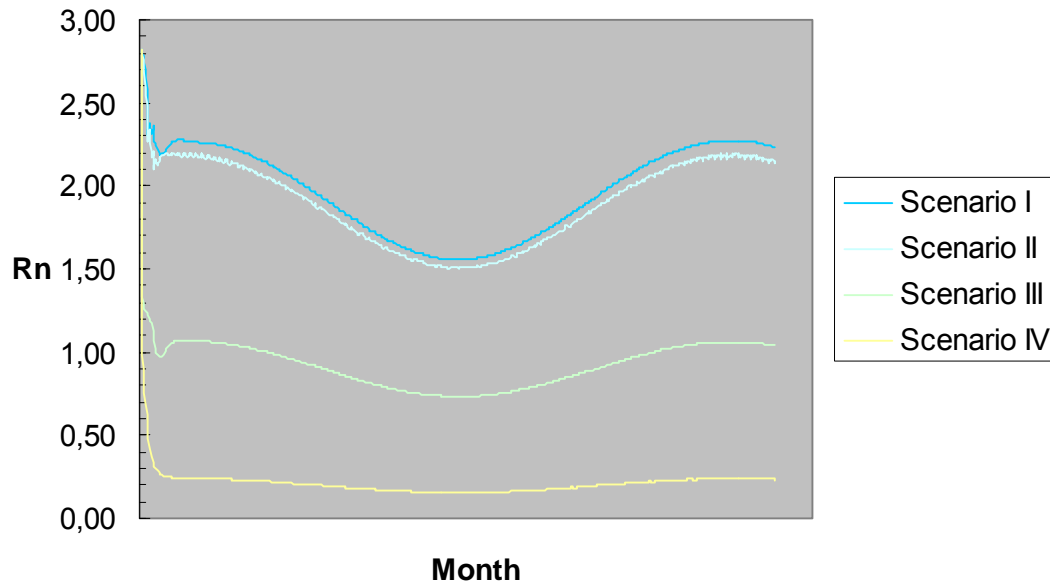


Figure 3 suggests that containment Scenarios I and II result in the highest probability of major outbreaks. Clearly Scenario IV is the one predicted to best control an active outbreak wave although there seems to be a probability for circulation of residual infection in the commune (95%CI: $0.07 < R_n < 0.58$).

The simulations show that commune R_n estimates vary considerably over the year reaching their peak values around January-February and their lowest values around July-August. Figure 4 shows the annual variation of the commune reproductive number for the four containment scenarios.

Figure 4: Mean monthly distribution of R_n for different disease control scenarios at commune level (total of 1000 iterations, each run for 10 year period, time-step for integration: 1 day).



This apparent seasonality is most likely driven by the observed movement of birds between farms around and shortly after the first weeks of February (Tet-holiday festivities) which we approximate in our model using a trigonometric function. The disease containment measures in Scenario IV seem to be most effective to level the expected seasonality of the outbreak waves and hence to control spread of the disease.

Geographical Heterogeneity of Poultry Farm Structure

We have simulated disease containment scenarios considering the observed differences in flock and husbandry structure of the northern and southern communes in Viet Nam (data not shown). The observed differences in farm structure between these geographical regions have previously been shown to require different disease control approaches.

For our purposes we consider disease transmission to be controlled when the commune reproductive number, the number of infected farms and the force of infection are all below the threshold value of one. We have performed a disease control optimization process which achieves the above criteria and takes into account the farm structure differences between geographical regions. The results are summarized in Table 3.

Table 3: Optimized disease control interventions of a typical epidemic wave and their impact on the net reproductive number and on the force of infection for northern and southern communes.

Objective	Region	Optimized Disease Control Measures			Transmission Parameters		
		Vaccine coverage (% farms)			Radius of pre-emptive cull (km)	R_n^* (95%CI)	λ^{**} (95%CI)
		C3	D3	S4			
$R_n < 1$ $\lambda_{(t)} < 1$ $I_{(t)} < 1$	North	0.97	0.30	1.00	10.5	0.23 (0.08-0.56)	0.009 (0.001-0.03)
	South	0.89	0.23	0.95	4.5	0.25 (0.08-0.61)	0.01 (0.002-0.03)

* farm; ** farm/day

The optimized mix of disease control measures suggests that both sectors C3 and S4 farms play an important role for disease transmission in both geographical regions given the high requirement for vaccination coverage of small commercial farms of chickens and backyard flocks to achieve disease control objectives. It is expected that in Northern communes reaching the control objectives requires vaccination coverage of both sectors of close to 100%. In addition model optimization suggests that pre-emptive culling should be applied in Northern communes at double the radius compared to Southern communes. Optimized disease containment options have a positive impact on the epidemiological parameters of disease spread resulting in effective long-term control of infection at the commune level.

8. Conclusions and Future Research Directions

Our model predicts that containment and elimination of a wave of HPAI H5N1 outbreaks at the commune level is feasible using a combination of vaccination and culling. An important conclusion, however, is the need for disease control policies that are adapted to local conditions, i.e. mixture of flock types, in order to achieve high levels of containment, with pre-emptive culling being particularly important in Northern communes.

Our simulations also suggest that disease control policies based on vaccination of poultry farms are likely to be effective only when high levels of vaccination coverage are achieved in backyard flocks (S4). Virus circulation, which may be sufficient to trigger another outbreak wave, is predicted to occur in poultry populations when this sector is left with a low level of coverage. Thus, the major caveat against the vaccination policy is that vaccination coverage of S4 is currently not reaching the required level for elimination of infection and that it is not realistic to expect to be able to systematically reach most of the backyard flock population for a number of years to come. Therefore, it would be important to improve on the rate of detection of infection and shorten response time to culling (within the smallest possible radius).

We are in the process of validating model predictions with more complete data on the containment operations currently in progress such as the vaccination campaign and sero-surveillance results of the vaccinated flocks.

The financial and socio-economic burdens associated with the four disease control scenarios and the distribution of these burdens among different sectors will be subject to analysis by the economic component of the SPADA framework. Furthermore, we are designing field studies to test incentive schemes for disease reporting and for the assessment of traceability schemes that decrease surveillance costs.

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10. Disclaimer & Contacts

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