Controlling Avian Flu and Protecting People's Livelihoods in the Mekong Region

Simulation Modelling of H5N1 Smallholder Poultry Outbreaks in Vietnam

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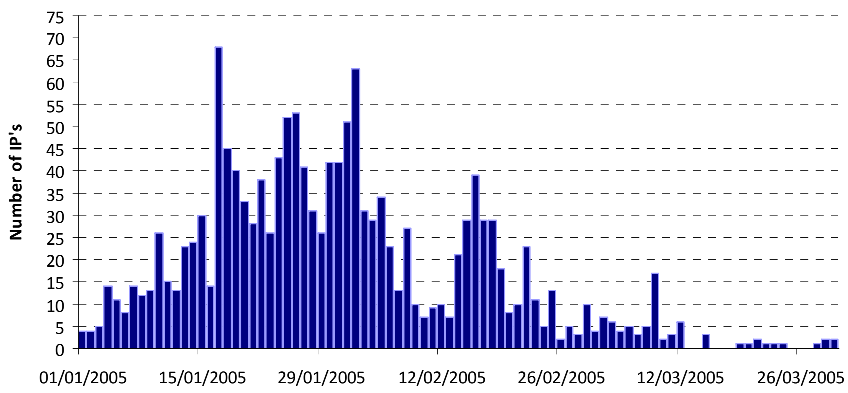
Overview

- Background
- Research questions
- HPAI H5N1 transmission model
- Results of a set of scenario-based simulations
- Discussion

Epidemiology of HPAI H5N1 in Vietnam

(a)



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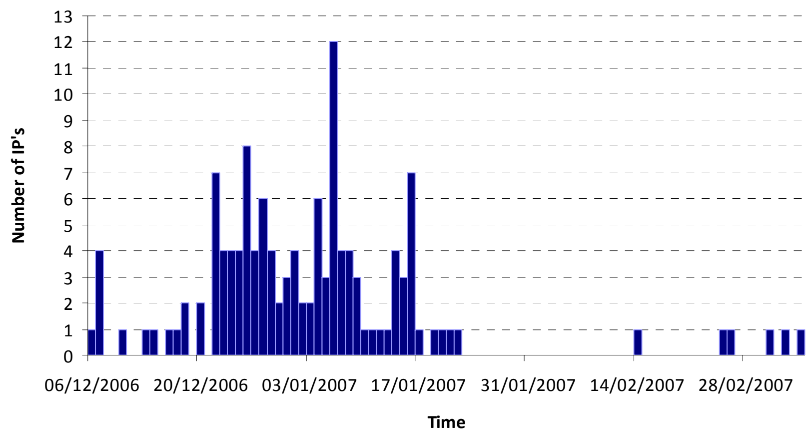
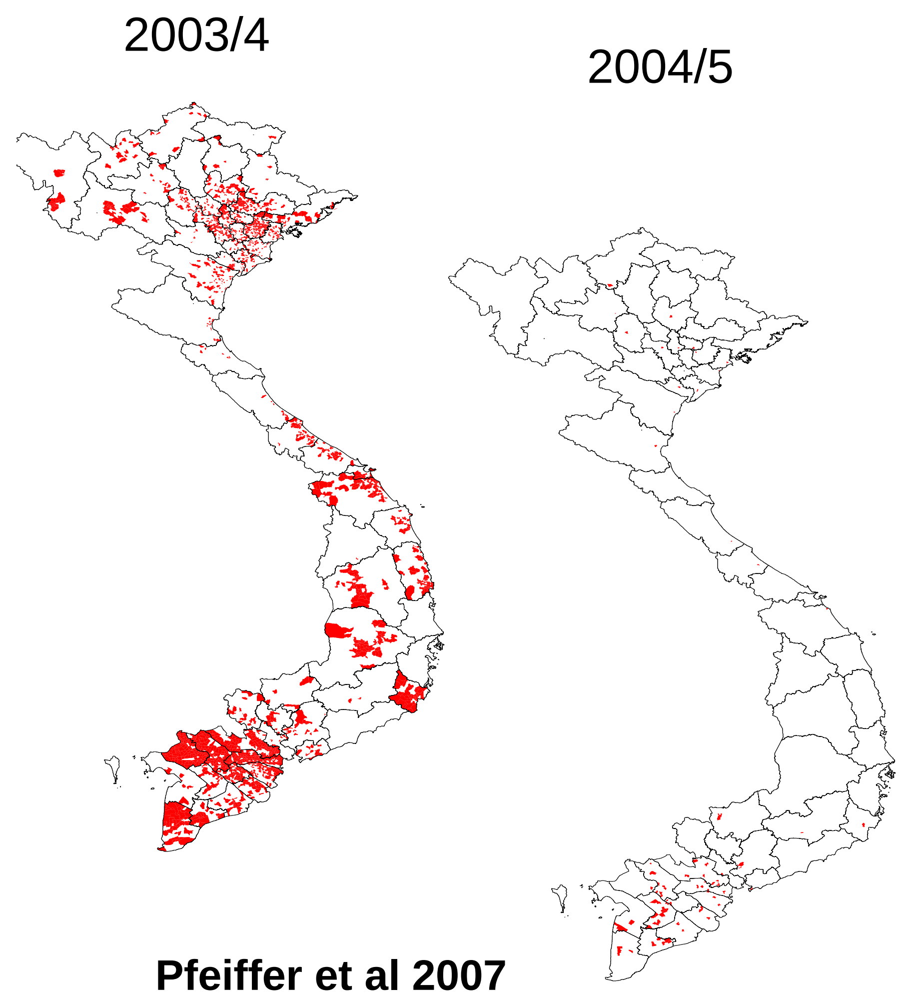
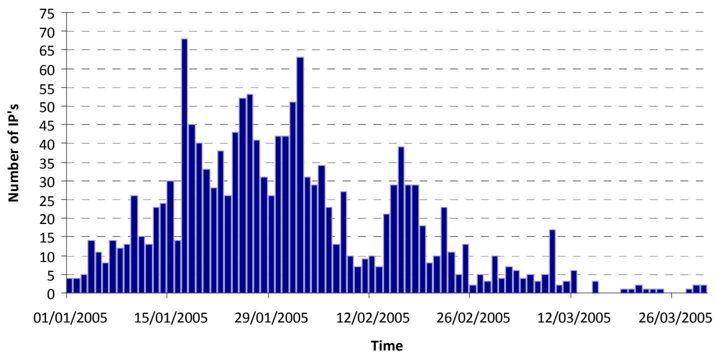




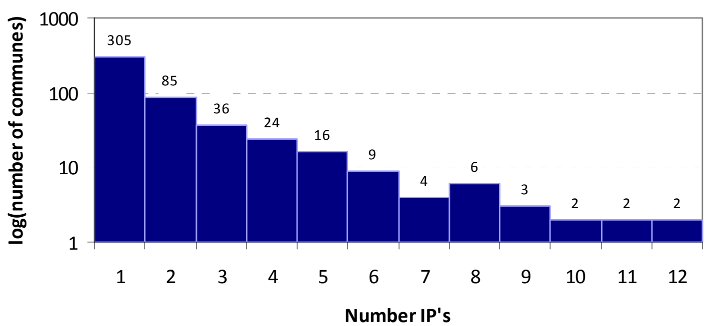
Commune Level Outbreak Expression

2nd Wave

(a)

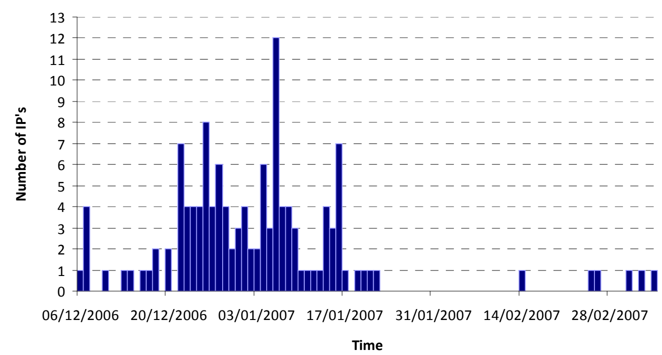


(a)



4th Wave

(b)



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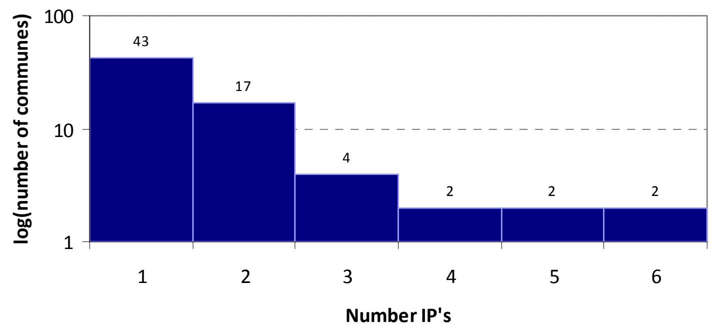
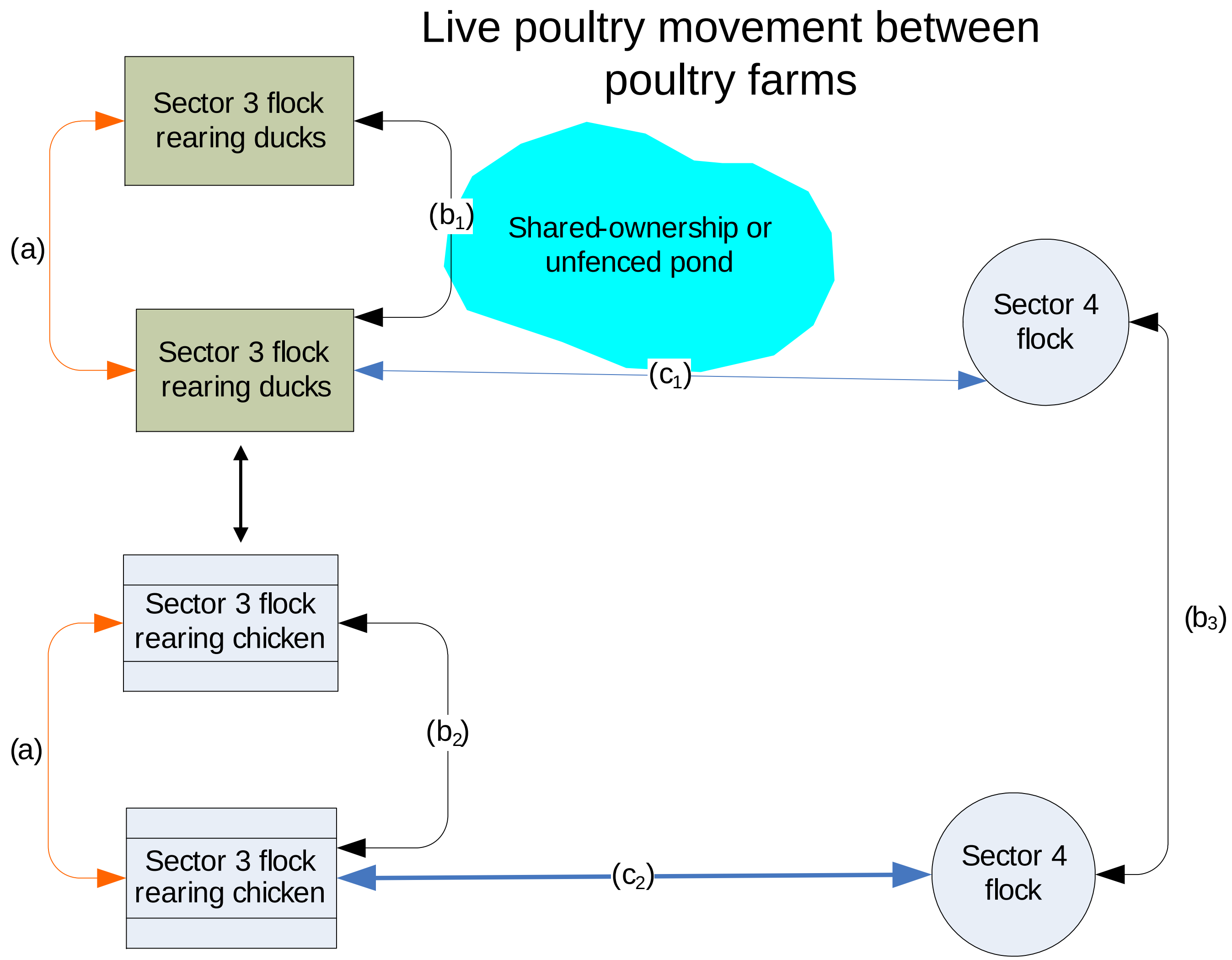


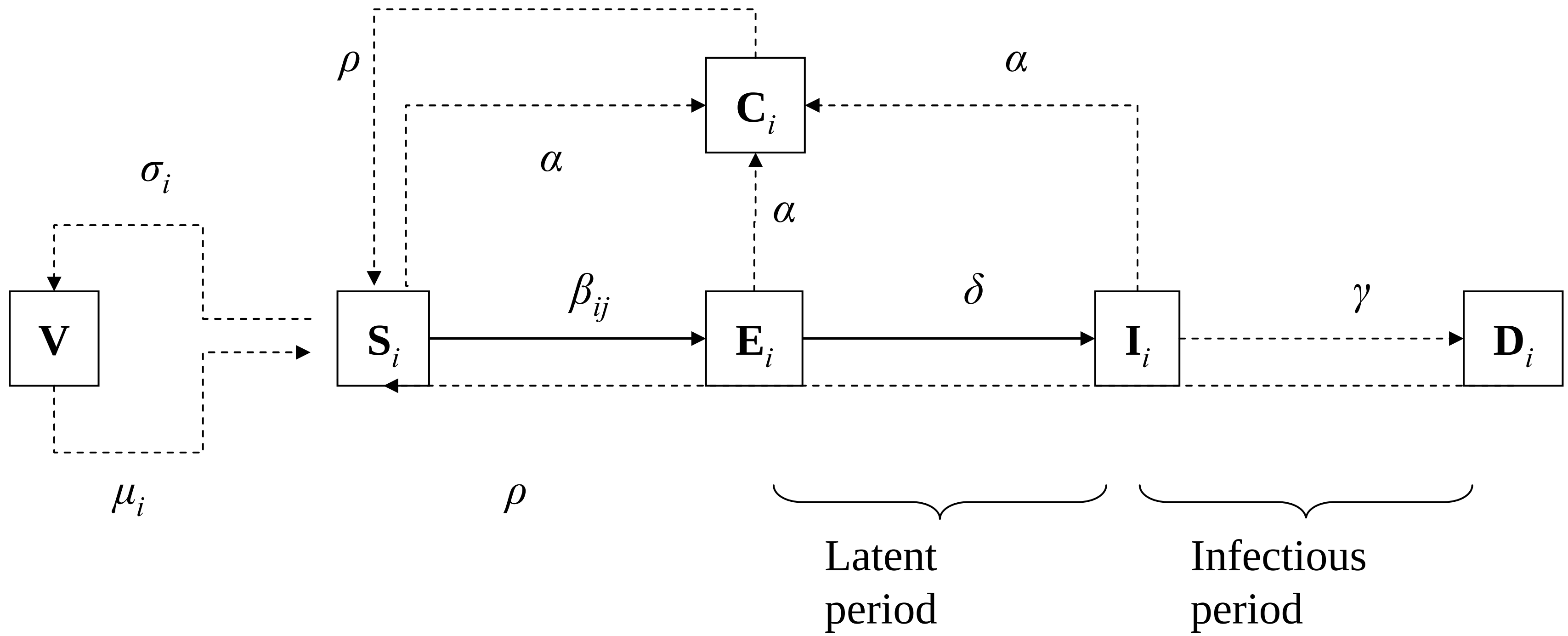
Research Questions

- What is the differential impact of control options in the containment of an outbreak wave at the commune level?
- Conditions for effective long term disease containment at the commune level?
- What is the effect of observed differences in poultry management between North and South Viet Nam on the efficacy of control options?

Poultry Contact Pattern



Transmission Model Framework (SEIDCV)



Mathematical Model

$$\frac{\partial S_i}{\partial t} = -S_i \sum_j \beta_{ij} \frac{I_j}{N_{ij}} - \alpha S_i - \sigma S_i + \rho D_i + \mu V_i$$

$$\frac{\partial E_i}{\partial t} = S_i \sum_j \beta_{ij} \frac{I_j}{N_{ij}} - \delta E_i - \alpha E_i$$

$$\frac{\partial I_i}{\partial t} = \delta E_i - \alpha I_i - \gamma I_i$$

$$\frac{\partial D_i}{\partial t} = \gamma I_i - \rho D_i$$

$$\frac{\partial C_i}{\partial t} = \alpha S_i + \alpha E_i + \alpha I_i$$

$$\frac{\partial V_i}{\partial t} = \sigma S_i - \mu V_i$$

$$E^i_{\Delta t} \sim Poisson\left(S^i_t \sum_j \beta_{ij} \frac{I_j}{N_{ij}} \Delta t \right)$$

$$I^i_{\Delta t} \sim Poisson\left(\delta E^i_t \Delta t \right)$$

Model of Effective Contact Rate

- The annual pattern of movements of birds between and within farms was modeled with reference to the expected seasonality of the contact rate.

$$\beta_{(t)} = \beta_0 \times \left[1 + a_{(t)} \cos\left(2\pi t\right)\right] \times s_{(t)}$$

- Model allows adjustment of values of β when taking seasonality into account

Effective Contact Rate in a Heterogeneous Population of Farms

- Structured, multi-population transmission model
- Model incorporates a poultry population contact matrix for three poultry farm size/type.

$$\beta^{ij} = \begin{bmatrix} \beta_{C3C3} & \beta_{C3D3} & \beta_{C3S4} \\ \beta_{D3C3} & \beta_{D3D3} & \beta_{D3S4} \\ \beta_{S4C3} & \beta_{S4D3} & \beta_{S4S4} \end{bmatrix} \longrightarrow \begin{pmatrix} R_{C3C3} & R_{C3D3} & R_{C3S4} \\ R_{D3C3} & R_{D3D3} & R_{D3S4} \\ R_{S4C3} & R_{S4D3} & R_{S4S4} \end{pmatrix} \begin{pmatrix} i_{C3} \\ i_{D3} \\ i_{S4} \end{pmatrix} = R_n \begin{pmatrix} i_{C3} \\ i_{D3} \\ i_{S4} \end{pmatrix}$$

Reproductive Ratio of Infection (R0)

- **Average number of secondary infected farms produced by a typical infectious farm during its entire infectious period** (Anderson and May, 1991; Diekmann and Heesterbeek 2000)

Uncontrolled scenarios

$$R_{0_{ij}} = \frac{\beta_{ij}}{\gamma_j}$$

Controlled scenarios

$$R_{0_{ij}} = \beta_{ij}\left(\frac{\delta}{\alpha+\delta}\right)\left(\frac{\gamma_j}{\alpha+\gamma_j}\right)$$

Threshold conditions:

R<1 – minor outbreaks may occur
R>1 – minor or major outbreak may occur

Data Sources

- Household census (GSO, 2001; GSO, 1999)
- Poultry census (pre-vaccination campaign)
- Definition of poultry sectors (MARD; FAO; AGI)
- Poultry contact pattern (Soares Magalhaes et al 2007; Tung, 2006; KAP Surveys)
- Outbreak data 2nd (1119) and 4th (114) epidemic waves (DAH)
- Disease control strategies (DAH)

Progression of H5N1 Infection in Chicken and in Ducks

Species	Time to death	Viral shedding	Reference
Chicken			
	2	-	Tian et al., 2005
	3-4	3 days p.i.	Webster et al., 2006
Duck			
	6	3 days p.i.	Tian et al., 2005
		7 days p.i.	Hulse-Post et al., 2005
	0.5 – 4	-	Shortridge et al., 1998
	4 – 6	peaks day 3; day 6	Sturm-Ramirez et al., 2004 and 2005
	No deaths	3 days p.i.	Webster et al., 2006

Natural history in vaccinated birds

Species	Vaccine type	Challenge strain	Clinical disease onset (days p.c.)	Maximum Protection (weeks p.v.)	Shedding onset (days p.c.)	Reference
Chickens						
	Killed	H5N2	9 - 18	4	-	(35)
	Reverse-genetics, inactivated	H5N1	No deaths or clinical signs	43	3	(30)
	Inactivated LPAI	H5N2	-	-	2	(29)
	Inactivated LPAI	H5N2	2	-	2	
	Reverse-genetics, inactivated	H5N3	No deaths or clinical signs	-	3	(28)
Ducks						
	Reverse-genetics, inactivated	H5N1	No deaths or clinical signs	14	3	(30)
	Bivalent, inactivated	H5N9+H7N1	No deaths or clinical signs	-	4	(32)
	Reverse-genetics, inactivated	H5N3	No deaths or clinical signs	-	3	(28)

Vaccine Coverage and Efficacy

Flock type	% of recorded census vaccinated	% of flocks with >=70% of sampled birds with detectable HI antibodies	% of flocks effectively immunized
Chicken	55 (50 - 66)	55	30 (0.28 - 0.36)
Ducks	75 (70 - 80)	55	41 (0.39 – 0.44)

SOURCE: Taylor N, Do Huu D. An analysis of data generated by the post-vaccination sero-monitoring and surveillance activities, following HPAI vaccination in Vietnam (2005-2006): Food and Agriculture Organization of the United Nations; 2007.

Delays in State Transition – Natural History and Field Control

Delay	Without control	Control with/without vaccination	Improved control with/without vaccination
Exposure → Infectious	3-7	3-7	3-7
Infectious →Detection	-	9-18/3-7	**3-7**
Detection → Movement Restriction	-	**0.5**	**0**
Movement Restriction → Depopulation & Disinfection	-	**1.5**	**1**

Model Experimentation and Sensitivity Analysis

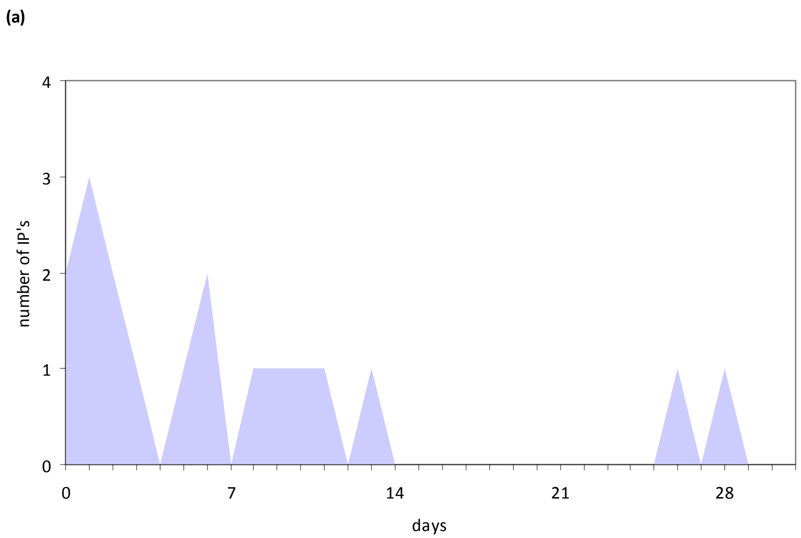
- Impact of uncontrolled scenarios
  - Effect of commune farm structure
  - Effect of infection seeding scenarios (i.e. single introduction; multiple introductions; weekly/monthly introductions)
  - Effect of seasonality (i.e. no seasonality; seasonality in specific farm types; percentage change)

- Impact of disease control interventions
  - Effect of delay times (i.e. latent period; infectious -> detection)
  - Effect of vaccination parameters

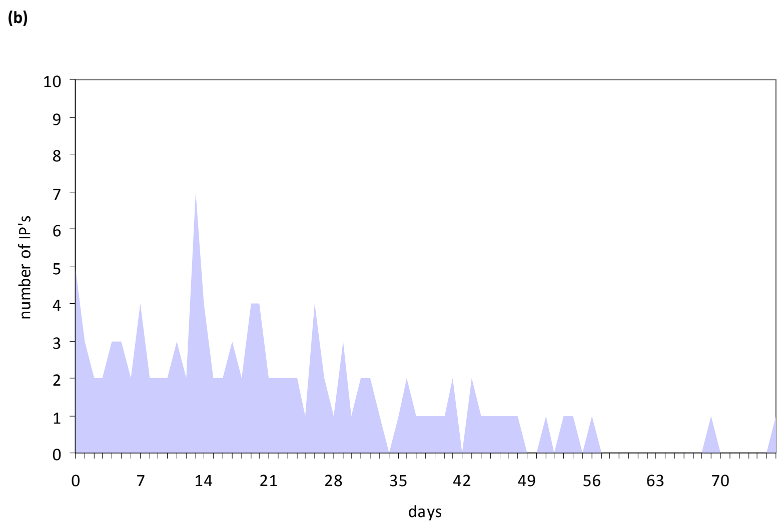
Time to Extinction and Average Number of IP in Second Wave Affected Communes

- Temporal optimization of policies

Northern communes



Southern communes



Sensitivity of the Percentage of Outbreaks Suffering Early Extinction and Conditional Mean Final Outbreak Size to Delays in Detection (I)

(1-year simulations @ 10,000 iterations; IP and 25% commune cull; multiple IP introductions of D3 type; current vaccination efficacy standards (Taylor and Dung 2007)

Policy	% outbreaks extinct within 17 days	Conditional mean final size (IP's)	Commune reproductive number
Uncontrolled	7	597	2.38 (1.98 – 2.84)
Control			
With vaccination			
9d I->D	89	7	1.12(0.71 – 1.44)
18d I->D	74	29	1.67(1.23 -2.17)
Without vaccination			
3d I->D	78	34	1.65(1.21 – 2.20)
7d I->D	66	123	1.89 (1.46 – 2.36)

Sensitivity of the Percentage of Runs Suffering Early Extinction and Conditional Mean Final Outbreak Size to Delays in Detection (II)

Policy	% outbreaks extinct within 17 days	Conditional mean final size (IP's)	Commune reproductive number
Uncontrolled	7	597	2.38 (1.98 – 2.84)
Control			
With vaccination			
9d I->D	89	7	1.12(0.71 – 1.44)
18d I->D	74	29	1.67(1.23 -2.17)
Without vaccination			
3d I->D	78	34	1.65(1.21 – 2.20)
7d I->D	66	123	1.89 (1.46 – 2.36)
Improved control			
With vaccination			
3d I->D	97	2	0.89 (0.54 – 1.07)
7d I->D	85	14	1.23 (0.91 – 1.56)
Without vaccination			
3d I->D	82	11	1.34 (1.11 – 1.58)
7d I->D	70	91	1.79 (1.41 – 2.15)

Research Questions

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- What is the effect of observed differences in poultry management between North and South Viet Nam on the efficacy of control options?

Disease Control Optimization – Vaccination and Detection

(optimization algorithm in Powersim®)

OBJECTIVE	REGION	OPTIMIZED DISEASE CONTROL MEASURES				TRANSMISSION PARAMETERS	
		Vaccine coverage (% farms)			Time to detection (Days)	R_n* (95%CI)	λ** (95%CI)
		C3	D3	S4			
$R_n<1$ $\lambda_{(t)}<1$ $I_{(t)}<1$	**North**	0.95	0.37	1.00	1.5	0.24 (0.11-0.49)	0.011 (0.001-0.08)
	South	0.91	0.76	0.95	2.5	0.47 (0.14-0.72)	0.07 (0.004-0.16)

Conclusion

- Containment and elimination of a wave of HPAI H5N1 outbreaks at the commune level is feasible using a combination of culling and prophylactic vaccination.
- Reduction of delays in disease detection are crucial for the probability of extinction of an outbreak at day 17.
- Prophylactic vaccination of poultry farms is likely to be effective [P(extinct @ day 17)~95%] only when:
  - moderate levels (>40%) of vaccination coverage are achieved in smallholder poultry, and
  - delays in disease detection do not go beyond 3 days.

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Thank you.

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