

Transmissibility of H5N1 avian influenza in Nigeria: The 2006 epidemic

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 - **Case fatality rate:** 59.4 percent

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- A preliminary assessment of the basic reproduction number (\mathcal{R}_0) of the HPAI H5N1 between poultry farms
- Evaluation of the effectiveness of the intervention strategies

Data

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- **Source:** National Veterinary Research Institute of Nigeria

Data

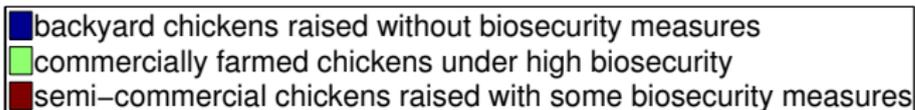
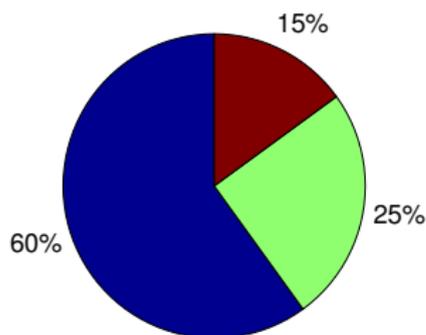
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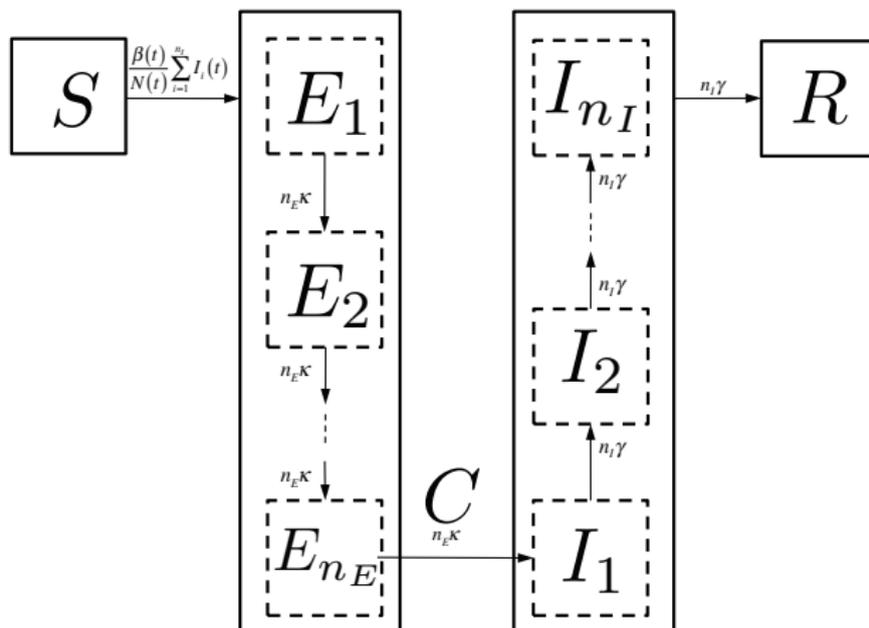
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Deterministic epidemic model

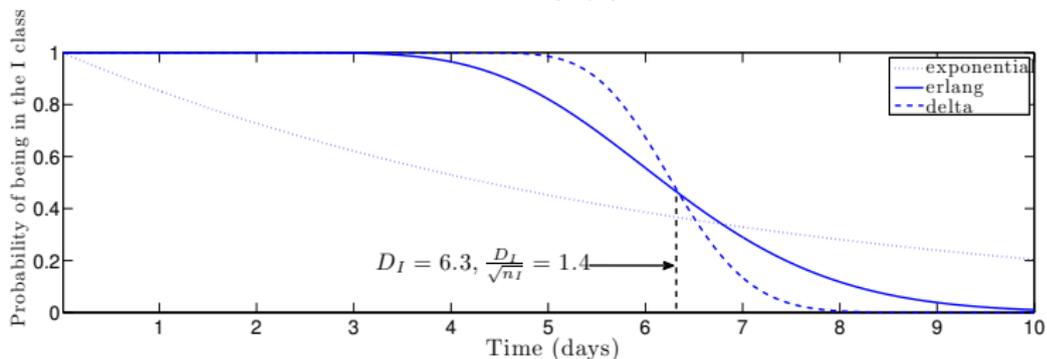
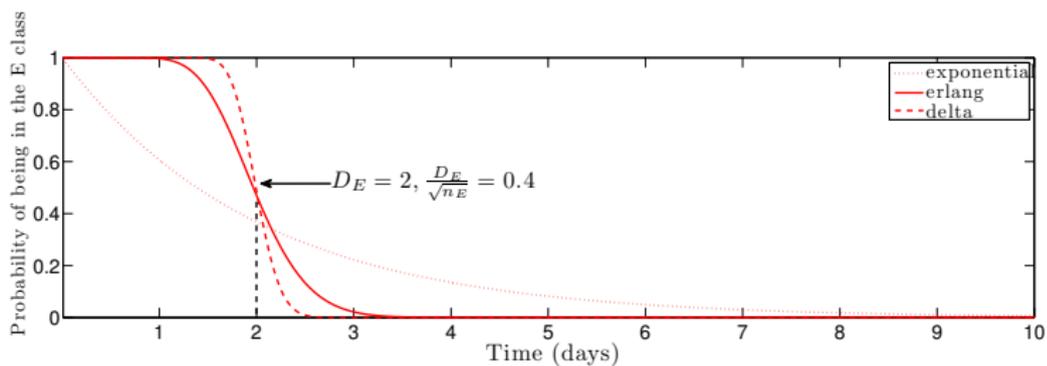
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- Schematic diagram



Survivor functions

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The impact of interventions on the HPAI H5N1 transmission rate

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- The **intervention strategies** to control the spread of HPAI H5N1 include:

Type of intervention	Implementation date
<i>Culling</i> (depopulation of infected premises or decontamination)	Feb. 7 th , 2006
<i>Movement restrictions</i>	Feb. 20 th , 2006
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- Assumption:** the net effect of these interventions have an instantaneous impact on the transmission rate $\beta(t)$

$$\beta(t) = \begin{cases} \beta_0 & \text{for } t < \tau, \\ \beta_1 & \text{for } t \geq \tau, \end{cases}$$

where $\beta_0 > \beta_1$, and τ is the time at which interventions begin

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- **Estimation of $\hat{\theta}$:** (*fminsearch*, *lsqnonlin* and *lsqcurvefit*: MATLAB 7.9.0 (R2009b, The MathWorks))

$$\vec{\theta}^{(k+1)} = \underset{\vec{\theta} \in \mathbb{R}_+^2}{\text{arg min}} J_n(\vec{\theta}^{(k)})$$

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symbol	description
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$$\vec{\theta}^{(k+1)} = \arg \min_{\vec{\theta} \in \mathbb{R}_+^2} J_n(\vec{\theta}^{(k)})$$

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Output: Set the estimator $\hat{\theta}_{LS} = \vec{\theta}^{(k)}$, where $\vec{\theta}^{(k)}$ is a realization of the random variable $\hat{\theta}_{LS}$

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- 1) The **peak epidemic size** is defined as the maximum number of new infected farms throughout the entire course of an epidemic ($\max\{f\}$)
- 2) The **epidemic size** at week ten is defined as the cumulative number of new infected poultry farms at week ten ($C(t = 10)$)

Stochastic epidemic model

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- Markov jump process: $X_t = \{(S_t, E_{1,t}, \dots, E_{n_E,t}, I_{1,t}, \dots, I_{n_I,t}, R_t) : t \in \mathbb{R}_+\}$

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- State space: $\mathbb{Z}_+^{n_E+n_I+2}$

Stochastic epidemic model

- Markov jump process: $X_t = \{(S_t, E_{1,t}, \dots, E_{n_E,t}, I_{1,t}, \dots, I_{n_I,t}, R_t) : t \in \mathbb{R}_+\}$
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Event	From	To	Rate
Exposure of poultry farms	X	$X + (e_2 - e_1)^T$	$\beta SI/N$
Progression from the latent stage E_i to E_{i+1} for $i = 1, \dots, n_E - 1$	X	$X + (e_{i+2} - e_{i+1})^T$	$n_E \kappa E_i$
Infection	X	$X + (e_{n_E+2} - e_{n_E+1})^T$	$n_E \kappa E_{n_E}$
Progression from the infectious stage I_i to I_{i+1} for $i = 1, \dots, n_I - 1$	X	$X + (e_{i+n_E+2} - e_{i+n_E+1})^T$	$n_I \gamma I_i$
Removal	X	$X + (e_{n_E+n_I+2} - e_{n_E+n_I+1})^T$	$n_I \gamma I_{n_I}$

Stochastic epidemic model

Stochastic epidemic model

The corresponding transition probabilities of the events are given by:

$$P(X_{t+\Delta t} - X_t = (e_2 - e_1)^T) = \frac{\beta_t}{N_t} S_t \sum_{j=1}^{n_I} I_{j,t} \Delta t + o(\Delta t)$$

$$P(X_{t+\Delta t} - X_t = (e_{i+2} - e_{i+1})^T) = n_{E^k} E_{i,t} \Delta t + o(\Delta t)$$

for $i = 1, \dots, n_E - 1$

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$$\mu(W_{i-1}) = \left(\frac{\beta(W_{i-1})}{N(W_{i-1})} S(W_{i-1}) \sum_{j=1}^{n_I} I_j(W_{i-1}) + n_{EK} \sum_{j=1}^{n_E} E_j(W_{i-1}) + n_I \gamma \sum_{j=1}^{n_I} I_j(W_{i-1}) \right)^{-1}$$

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Implementation:

- Gillespie's direct algorithm [D. T. Gillespie, 1976]

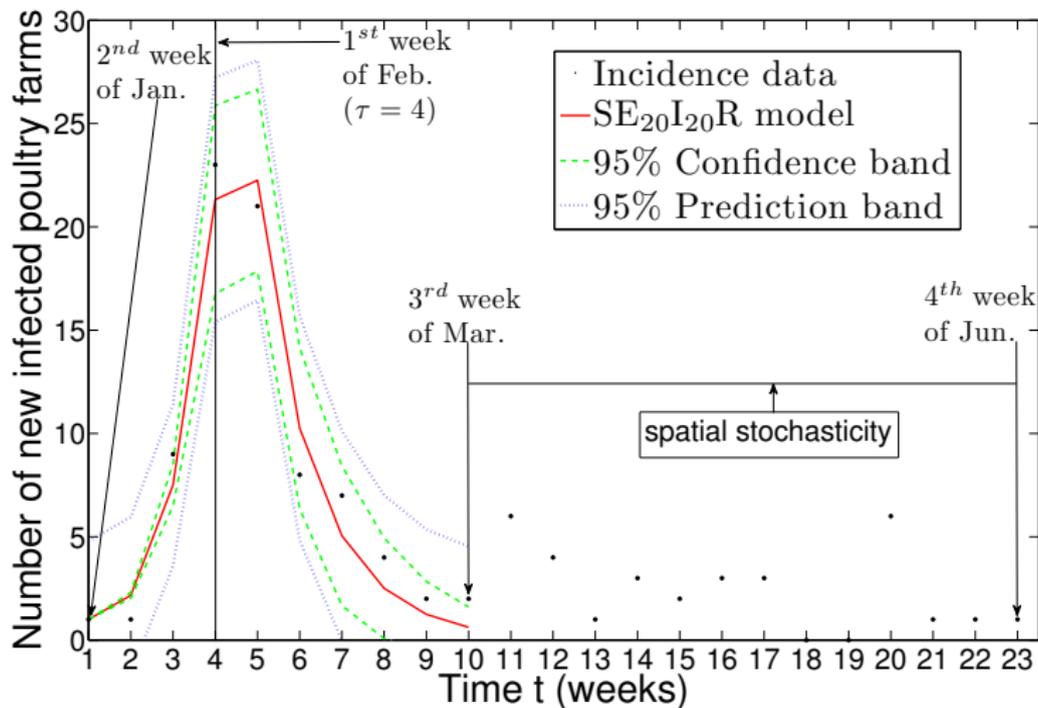
Table 1: Model parameters

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Symbol	Description	Source	Value
β_0	Pre-intervention transmission rate	Estimated	2.33 weeks ⁻¹ (95% CI: 2.26, 2.41)
β_1	Post-intervention transmission rate	Estimated	0.63 weeks ⁻¹ (95% CI: 0.54, 0.73)
$1/\kappa$	Mean incubation period	[J. A. Van der Goot, <i>et. at.</i> , PNAS 2005]	2 days
$1/\gamma$	Mean infectious period	[J. A. Van der Goot, <i>et. at.</i> , PNAS 2005]	6.3 days
$I_1(t_1)$	Initial number of infected poultry farms	From data	1
$N(t_1)$	Initial total number of poultry farms	[Federal Department of Livestock]	7, 000
n_E	Number of sub-compartment for the exposed class	[J. A. Van der Goot, <i>et. at.</i> , PNAS 2005, M. E. Bos, <i>et. at.</i> , Vet. Research 2007]	20
n_I	Number of subcompartment for the infectious class	[J. A. Van der Goot, <i>et. at.</i> , PNAS 2005, M. E. Bos, <i>et. at.</i> , Vet. Research 2007]	20
τ	Time at which interventions begin	[F. O. Fasina, <i>et. at.</i> , Epid. Inf. 2009]	4 th week (Feb. 7 th , 2006)

Data and fit

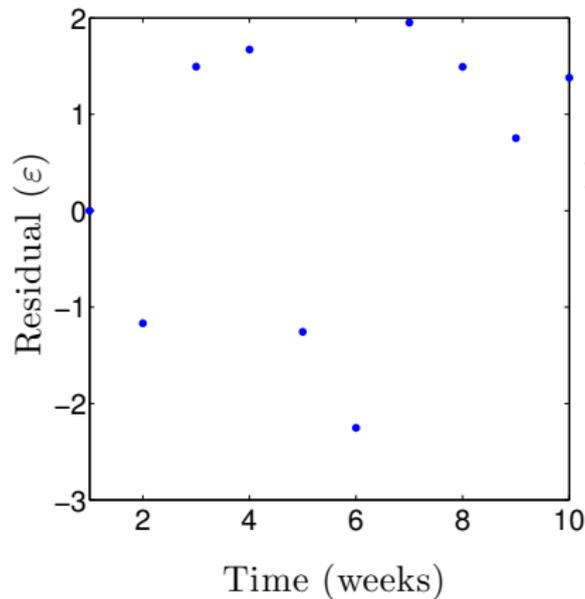
Data and fit



Residual plots

Residual plots

Residual over time assuming constant variance ($\xi = 0$)



Model vs. Residual assuming constant variance ($\xi = 0$)

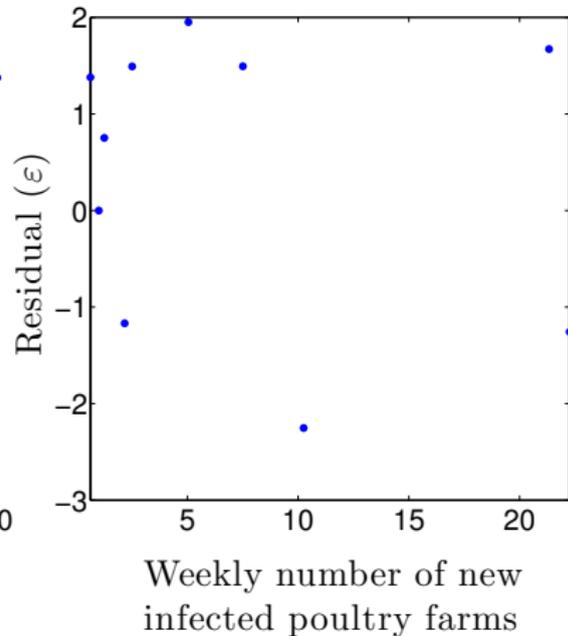


Table 2: Basic reproduction number estimates

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Number of compartments		Basic reproduction number formula	Estimate	$SE(\hat{\mathcal{R}}_0)$	95% CI
n_E	n_I	$(\mathcal{R}_0(\lambda = 1.156, n_E, n_I))$	$(\hat{\mathcal{R}}_0)$		
–	–	$\mathcal{R}_0 = \beta_0 D_I$	2.10	0.03	(2.04, 2.17)
–	–	$\mathcal{R}_p = \beta_1 D_I$	0.57	0.04	(0.48, 0.67)
1	1	$(\lambda D_I + 1)(\lambda D_E + 1)$	2.72	0.04	(2.59, 2.84)
1	$n_I = 20$	$\frac{\lambda D_I(\lambda D_E + 1)}{1 - (\lambda D_I/n_I + 1)^{-n_I}}$	2.17	0.03	(2.08, 2.26)
1	$n_I \rightarrow \infty$	$\frac{\lambda D_I(\lambda D_E + 1)}{1 - e^{-\lambda D_I}}$	2.14	0.03	(2.05, 2.23)
$n_E = 20$	1	$(\lambda D_I + 1)(\lambda D_E/n_E + 1)^{n_E}$	2.83	0.04	(2.69, 2.98)
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[H. J. Wearing *et. al.*, PLoS Medicine 2005]

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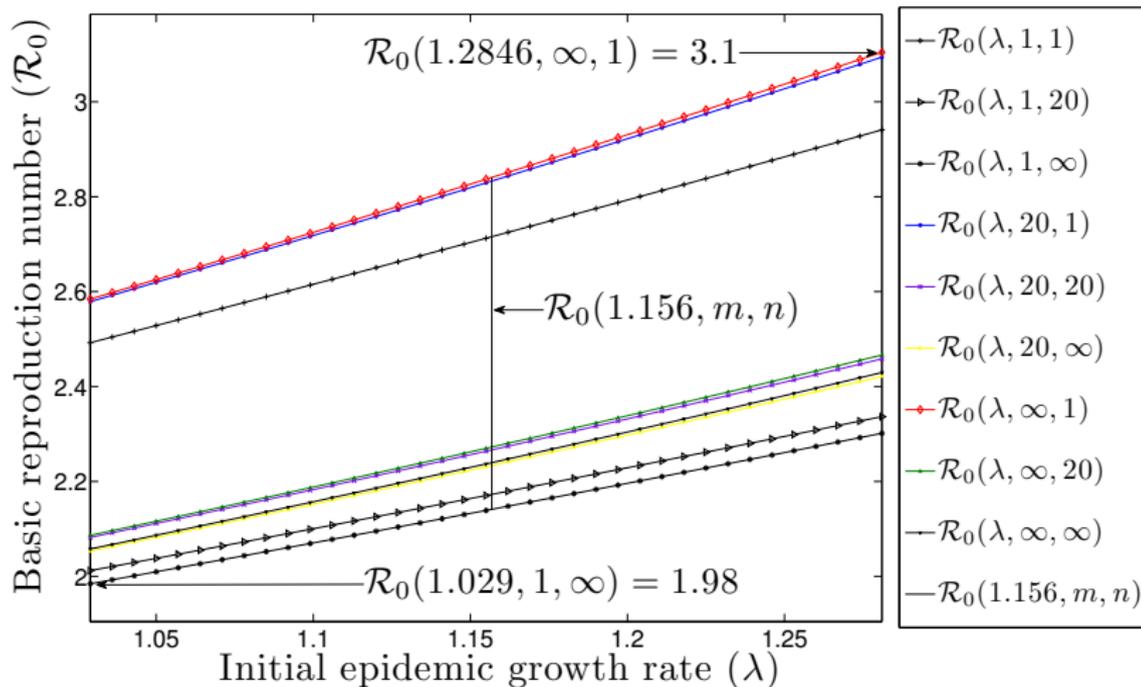
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[H. J. Wearing *et. at.*, PLoS Medicine 2005]

[A.L. Lloyd, 2009]

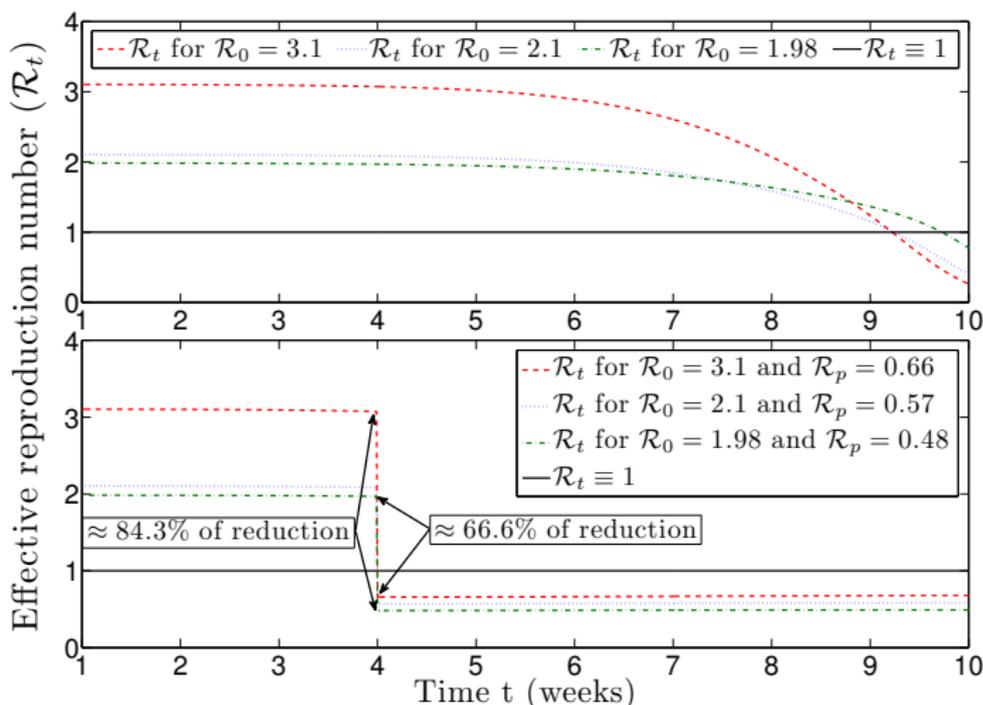
Basic reproduction number

Basic reproduction number



Effective reproduction number

Effective reproduction number



$$66.6\% = \left(1 - \frac{0.66}{1.98}\right) 100\% \leq \left(1 - \frac{\mathcal{R}_p}{\mathcal{R}_0}\right) 100\% \leq \left(1 - \frac{0.48}{3.1}\right) 100\% = 84.3\%$$

Histograms

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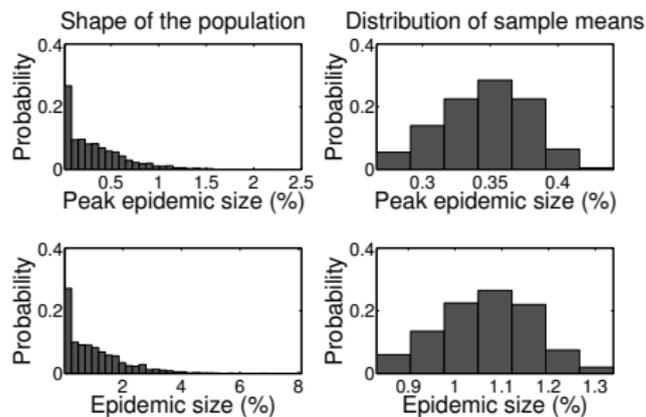


Figure: With interventions

Histograms

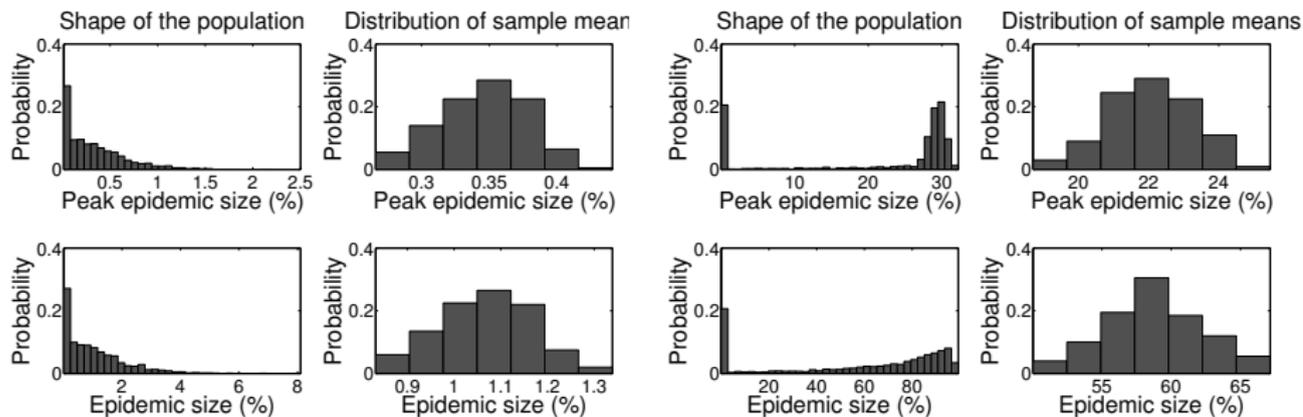


Figure: With interventions

Figure: Without interventions

Table 3: Peak and epidemic size estimates

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		Random variables	
		Peak epidemic size	Epidemic size at the 10 th week
With interventions	No.	29.8 (95% CI: 29.06, 30.7)	92.4 (95% CI: 89.7, 95.1)
	% of the $N(t_1)$	0.42% (95% CI: 0.41%, 0.43%)	1.32% (95% CI: 1.28%, 1.35%)
Without interventions	No.	1906.5 (95% CI: 1891, 1921)	5071.6 (95% CI: 5003, 5140)
	% of the $N(t_1)$	27.2% (95% CI: 27.02%, 27.45%)	72.4% (95% CI: 71.4%, 73.4%)
Reduction	No.	1,876.7	4,979.2
	%	98.4%	98.2%

Table 4: Comparison of basic reproduction number estimates

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Country	Time period	A. I. virus subtype	Serial interval (days)	\mathcal{R}_0	Reference
Nigeria	Jan 2006- Jun 2006	H5N1	12	1.98-3.1	This study
* Thailand	Jul 2004- Nov 2004	H5N1	1-4	2.26-2.64	[T. Tiensin <i>et. al.</i> , J. Infect. Dis. 2004]
Romania	May 2006- Jun 2006	H5N1	7	1.95-2.68	[M. P. Ward, <i>et. al.</i> , Epid. Infect. 2008]
The Netherlands	Feb 2003- May 2003	H7N7	12	3.1-6.5	[A. Stegeman, <i>et. al.</i> , J. Infect. Dis. 2004]
The Netherlands	Feb 2003- May 2003	H7N7	12	4.0-6.9	[A. Le Menach, <i>et. al.</i> , Proc Biol. Sci. 2006]
The Netherlands	Feb 2003- May 2003	H7N7	1.9-3.4	1.1-1.9	[T. Garske, <i>et. al.</i> , PLoS ONE 2007]
Italy	Mar 1999- Apr 2000	H7N7	5	1.9	[T. Garske, <i>et. al.</i> , PLoS ONE 2007]
Canada (British Columbia)	Feb 2004 May 2004	H7N3	8.4	2.4	[T. Garske, <i>et. al.</i> , PLoS ONE 2007]

* With the exception of the Thai study (where \mathcal{R}_0 was estimated at the within-flock level, Tiensin *et al.*, 2007), all of these studies estimated \mathcal{R}_0 between flocks

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- 1) the estimated total number of chickens, where each chicken is treated as an individual epidemiological unit, 2) the spatial coordinates for every poultry farm, 3) the inter-centroid for every county, and 4) the actual number or average number of farms per county, we could potentially analyze the epidemic at both the local and national level

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- Overall, estimates for \mathcal{R}_0 are in line with those estimates for the HPAI H5N1 outbreaks in Romania and an outbreak of H7N3 in British Columbia, Canada
- If spatial data related to the distribution of future outbreaks of HPAI H5N1 in Nigeria were to become available through improved surveillance, it could be incorporated into mathematical models to more accurately estimate key epidemiological parameters at both the local and national level, thus improving our ability to assess intervention strategies, and to predict and prevent future outbreaks

Acknowledgements

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