MODELING THE RAPID SPREAD OF AVIAN INFLUENZA (H5N1) IN INDIA

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ABSTRACT. Controlling the spread of avian bird flu has become a challenging tasks for Indian agriculture and health administrators. After the first evidence and control of the virus in 2006, the virus attacked five states by January 2008. Based on the evidence of rapid spread of the avian bird flu type H5N1 among the Indian states of Maharashtra, Manipur, and West Bengal, and in the partially affected states of Gujarat and Madhya Pradesh, a model is developed to understand the spread of the virus among birds and the effect of control measures on the dynamics of its spread. We predict that, in the absence of control measures, the total number of infected birds in West Bengal within ten and twenty days after initial discovery of infection were 780,000 and 2.1 million, respectively. When interventions are introduced, these values would have ranged from 65,000 to 225,000 after ten days and from 16,000 to 190,000 after twenty days. We show that the farm and market birds constitute the major proportion of total infected birds, followed by domestic birds and wild birds in West Bengal, where a severe epidemic hit recently. Culling 600,000 birds in ten days might have reduced the current epidemic before it spread extensively. Further studies on appropriate transmission parameters, contact rates of birds, population sizes of poultry and farms are helpful for planning.

1. Introduction. Avian bird flu (H5N1) epidemics among Indian birds were reported for the first time on a large scale during 2006 in the states of Maharashtra, Gujarat, and Madhya Pradesh; subsequent epidemics appeared in July 2007 in Manipur and in January 2008 in West Bengal[9]. In Maharashtra the number of birds infected was more than one million and in Manipur this number was 150,000. In West Bengal, five days after confirmation of H5N1 (among bird samples), the number of birds to be culled was half a million; twenty days later this target was raised to two million. It is not given that all the birds culled are infected, nor that all infected birds are carriers of the virus. So far, no suspected human cases of this deadly bird virus have appeared in India, where the mechanisms for spreading the disease and its potentially serious public health dangers in India are understood [9, 45, 19, 17]. Information on containing the spread of the virus through vaccines and other preventive measures is widely available [46, 7, 8]. There is a possibility that H5N1 came to India through migratory birds[18, 29, 43]. Usually, in the initial stage, domestic birds are infected by migratory wild birds and then the virus is spread to farm birds and market birds through contaminated clothes, equipment, and through poultry staff or direct contact with infected birds, cages, etc. There were studies

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that explain how bird flu is transferred and rates of reproduction in South Asian countries[12, 24, 36], Europe[2, 32, 44, 15], and globally[6]. General discussions on the methods used in understanding the spread and public health implications can be seen elsewhere[25].

In the January 2008 outbreak in the state of West Bengal, the World Health Organization (WHO) identified more serious risk factors than those of the July 2007 outbreak in the state of Manipur. The Ministry of Health and Family Welfare (Mo-HFW) and the Department of Animal Husbandry, Dairying, and Fisheries (DAHD) in New Delhi have launched large-scale culling operations and interventions to control the virus's spread[9]. In West Bengal's Birbhum and South Dinajpur districts, epicenters of the epidemic, the estimated number of infected birds to be culled within ten days after the reported first case is 378,000[13]. By January 10, about 9,500 deaths had occurred; by January 18, this number had risen to 35,000[14], indicating the virus was prevalent at least a week before the first reported case. Another news report suggests that the number of diseased birds that died within ten days after January 8 was 55,000[14]. Within five days of confirmation of the H5N1 in the samples from West Bengal, reports of the virus appeared in four more districts of the state; within two weeks the virus spread to eleven districts [40]. In China, it was observed that rapid spread of H5N1 in a short period makes it difficult to control the disease[35]. Assuming a growth of 9,500 infected birds to 378,000 infected birds in ten days in West Bengal gives us an alarming rate of 0.36 new cases per day, with a doubling period of 1.18 days. Although, the spread of the virus among birds might be controlled by effective culling operations, we need to understand the dynamics of the spread mechanisms so that other regions of the country can be well prepared for future epidemics. There are several unknown quantitative questions: What is the rate at which wild birds (such as wild ducks and other waterfowl) get infected? How many infections (on average) does an infected bird initiate before dying? Does this rate depend on the type and location of the bird? In India or any part of the world, data collection and estimation procedures involved in answering such questions may be not straight forward. These require a properly designed studies, detection of an infected bird at an early stage, and avian follow-ups. A number of interesting modeling questions present themselves: At what rate is the disease spreading among birds in the state and in neighboring states? What is the infection's time-lag from its epicenter to its nearest next center? And what is the basic reproductive rate R_0 ; i.e., the average number of secondary infections generated by one infected bird in a predominantly susceptible population[1]? If $R_0 > 1$, then the epidemic explodes, but if $R_0 < 1$ then the epidemic will fade away in a short period. The survival time of an infected bird is not very long (at most, about ten days), migratory and domestic birds spread more virus than poultry birds unless proper care is taken for their containment. Some studies report survival of birds after infection as twelve days and spread is more in densely populated farm houses[50].

As a first step in understanding these dynamics, we have formulated a model for the spread of H5N1 among birds in India. In this system, domestic birds acquire infection from migratory wild birds, and spread occurs within all types of birds in a region; meanwhile, migratory birds in this region carry virus to other locations. Some studies supported the idea that migratory birds carry H5N1 virus, travel long distances, and may die with or without infecting other wild birds[49, 26, 11].

We focus here in developing a mathematical model that explains the dynamics of the recent avian influenza (H5N1) epidemic in the bird population in West Bengal. We study the effects of different levels of intervention strategies in controlling the virus's spread. Although the spread was explained retrospectively, we hope the present analysis will help to control the spread in future outbreaks in the other parts of India.

2. Mathematical model. We model the spread of the H5N1 in birds by taking transmission from wild birds to domestic birds, domestic birds to market birds, farm birds, and infecting poultry worker's equipment and cloths. Infected farm birds carry the virus to their counterparts in other farms when they are carried by vehicles and eventually spread to wild birds in another region. We assume that all the infected birds are equally infectious, spread the virus, and eventually die from the disease[46, 41, 47, 42]. There is a time-lag of T units before farm birds infect their counter parts of other regions. See Figure 1 for the description of these flows. See model equations, description of the variables, and parameters given this section. Our results are based on the model developed for the transmissions described in Figure 1. We have indirectly estimated the mean and median number of days of birds' life after being infected with H5N1. See Section 2.1 for the estimation procedures implemented for this purpose.

Suppose W_B, D_B, M_B, F_B and P_w are variables corresponding to populations of wild birds, domestic birds, market birds, farm birds, and poultry workers (poultry workers need not be carrying infection, but their cloths or equipment has virus particles which comes into contact with birds). Let $W_{B_0}, D_{B_0}, M_{B_0}, F_{B_0}$ and P_{w_0} be the variables corresponding to the infected population at epicenter (this epicenter can be treated as a location where domestic birds acquired infection from migratory birds). Suppose after a time-gap of T time units (say) birds at neighboring block/village are detected with the virus (call cycle 0) and let $W_{B_1}, D_{B_1}, M_{B_1}, F_{B_1}$ and P_{w_1} be the corresponding variables. This process continues and let W_{B_i} , D_{B_i} , M_{B_i} , F_{B_i} and P_{w_i} are variables for the i^{th} cycle, where i=0,1,2,...,n. Once the infection is triggered among domestic birds, virus spreads to other subpopulations and there will be time-lag T to bring infection to the birds in cycle 1 (from cycle 0). $S_{i1}, S_{i2}, S_{i3}, S_{i4}$ and S_{i5} are five coefficients that determine the spread of infection among the subpopulations of wild birds, domestic birds, market birds, farm birds, and poultry workers at i^{th} cycle. $a_{i1}, \alpha_{i2}, \gamma_{i3}, \beta_{i4}$ and λ_{i5} and $c_{i1}, c_{i2}, c_{i3}, c_{i4}$, and c_{i5} are corresponding rates of transmission and contact. Each category, birds die at a rate u. The model equations below use these variables, coefficients, and parameters explain the corresponding dynamics. A schematic diagram of this model can be seen in Figure 1.

$$\begin{array}{lll} \frac{dW_{B_0}}{dt} & = & S_{01}W_{B_0} - uW_{B_0} & \frac{dW_{B_1}}{dt} = S_{11}W_{B_1} - uW_{B_1} \\ \frac{dD_{B_0}}{dt} & = & S_{02}D_{B_0} - uD_{B_0} & \frac{dD_{B_1}}{dt} = S_{12}D_{B_1} - uD_{B_1} \\ \frac{dM_{B_0}}{dt} & = & S_{03}M_{B_0} - uM_{B_0}, & \frac{dM_{B_1}}{dt} = S_{13}M_{B_1} - uM_{B_1}, \dots \\ \frac{dF_{B_0}}{dt} & = & S_{04}F_{B_0} - uF_{B_0} & \frac{dF_{B_1}}{dt} = S_{14}F_{B_1} - uF_{B_1} \\ \frac{dP_{w_0}}{dt} & = & S_{05}P_{w_0} - uP_{w_0} & \frac{dP_{w_1}}{dt} = S_{15}P_{w_1} - uP_{w_1} \end{array}$$

$$\frac{dW_{B_{n-1}}}{dt} = S_{(n-1)1}W_{B_{n-1}} - uW_{B_{n-1}}$$

$$\frac{dW_{B_n}}{dt} = S_{n1}W_{B_n} - uW_{B_n}$$

$$\frac{dD_{B_{n-1}}}{dt} = S_{(n-1)2}D_{B_{n-1}} - uD_{B_{n-1}}$$

$$\frac{dD_{B_n}}{dt} = S_{n2}D_{B_n} - uD_{B_n}$$

$$\frac{dM_{B_{n-1}}}{dt} = S_{(n-1)3}M_{B_{n-1}} - uM_{B_{n-1}},$$

$$\frac{dM_{B_n}}{dt} = S_{n3}M_{B_n} - uM_{B_n},$$

$$\frac{dF_{B_{n-1}}}{dt} = S_{(n-1)4}F_{B_{n-1}} - uF_{B_{n-1}}$$

$$\frac{dF_{B_n}}{dt} = S_{n4}F_{B_n} - uF_{B_n}$$

$$\frac{dP_{w_{n-1}}}{dt} = S_{(n-1)5}P_{w_{n-1}} - uP_{w_{n-1}}$$

$$\frac{dP_{w_n}}{dt} = S_{n5}P_{w_n} - uP_{w_n}$$

where the coefficients of the spread are given by

$$S_{i1} = a_{i1}c_{i1} \left[\frac{D_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}}{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}} \right]$$

$$S_{i2} = \alpha_{i2}c_{i2} \left[\frac{W_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}}{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}} \right]$$

$$S_{i3} = \gamma_{i3}c_{i3} \left[\frac{W_{B_i} + D_{B_i} + F_{B_i} + P_{w_1}}{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}} \right]$$

$$S_{i4} = \beta_{i4}c_{i4} \left[\frac{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}}{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_i} + P_{w_1}} \right]$$

$$S_{i5} = \lambda_{i5}c_{i5} \left[\frac{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_1}}{W_{B_i} + D_{B_i} + M_{B_i} + F_{B_1}} \right].$$

We have simulated the epidemic in West Bengal with following parameterizations. Note that very few published studies give quantitative information on H5N1 transmission rates between birds[2, 32, 44, 15, 42, 23]. Such studies need careful design, and the sample size may not be very large. For the Thailand poultry data R_0 was estimated between 2.26 and 2.64[42]. Suppose D is the infectious period and A is transmission parameter between birds then the product of these two was taken as an approximation of basic reproductive rate, (i.e., $R_0 = AD$)[1, 42]. Additionally, the Thai study found that the transmission parameter will be lesser for backyard chickens than for poultry chickens. The study estimates value of A for D=3 days and D=4 days as 0.87 per day and 0.66 per day for all birds and 0.75 per day and 0.60 per day for backyard chickens. Based on the Thailand poultry data, we first predicted the number of infected birds with parameter values $a_{i1} = 0.4, \alpha_{i2} = 0.60, \gamma_{i3} = 0.79, \beta_{i4} = 0.79, \text{ and } \lambda_{i5} = 0.5.$ These values are given in Table 1. We have estimated the mean duration of death as three days (see section 2.1) and for this duration the Thailand parameters may overestimate the Indian epidemic intensity. Hence, we perturbed our parameters values a bit and choose them as $a_{i1} = 0.4$, $\alpha_{i2} = 0.60$, $\gamma_{i3} = 0.79$, $\beta_{i4} = 0.79$, and $\lambda_{i5} = 0.5$. We have no evidence that the rates of infection depend on the season, nor do we know whether these rates change from one spread cycle to another in neighboring blocks or villages. Death rates are found not to be same for the all birds; after H5N1 infection, some birds

survive longer than others[46, 37, 38]. Laboratory experiments in Korea indicate that virus-inoculated birds died within a day[21, 22]. Contact rates between birds are naturally higher than those between birds and poultry workers [7, 6]. These contact rates may also depend upon the distances traveled by birds. Based on the poultry data from the Netherlands, infectious contact rates were calculated for short-range, medium-range, and long-range distances travelled [23]. These values range between 0.016 and 0.336. We believe these contact rates not apply in the recent spread of the virus. Within five days after detection of the virus, the number of infected birds was expected to reach half a million. Hence, we assume somewhat higher contact rates and predict for a range of values. Numerical values for the contact rates are $c_{ij} = (0.5, 0.9)$ for j = 1, 2, 3, 4 and $c_{i5} = 0.5$. Initial sizes of the infected subpopulations are $W_{B_0} = 10,000, D_{B_0} = 50,000, M_{B_0} = 100,000,$ $F_{B_0} = 100,000$, and $P_{w_0} = 10,000$. We have studied the dynamics of the spread with varying contact rates of birds ranging between 0.5 and 0.9 (see Table 3). We have studied the dynamics of the spread with control measures. These measures include culling operations and containment operations. $S_{ij} = S_{ij}(1-\epsilon)$, where ϵ is efficacy of the intervention. We assumed efficacy of these interventions between 40 per cent and 80 per cent and demonstrated the effect in terms of reduction in infected birds.

2.1. Mean survival time after infection. We have estimated mean survival time of birds after infection with avian flu. Let $d_0, d_1, d_2, ..., d_n$ be the reported number of bird deaths in the bird flu affected region. We use the general idea of back calculation applied to AIDS epidemiology [3, 4, 5]. Methodology explained in this section is same as the one used to estimate incubation period in epidemiology [27] and instead of estimating the mean duration from infection to the development of disease, we estimate mean survival time from infection. Suppose G(t) is the cumulative number of reported death cases up to time t_n and h(x) to be the infection density. If H(t) is the survival distribution at time t, then the cumulative number of reported number of deaths can be expressed as the following convolution of infection density and survival distribution:

$$G(t) = \int_{t_0}^{t_n} h(x)H(t-x)dx. \tag{1}$$

From the above equation we have estimated the survival distribution for the infected birds. Using equation 1, the cumulative number of deaths during (t_{i-1}, t_i) can be written as

$$G(t) = \int_{t_{i-1}}^{t_i} h(x)H(t-x)dx.$$
 (2)

Suppose q_i is the conditional probability of death before time t_n , which can be treated as actually occurring in one of the intervals $(t_0, t_1), (t_1, t_2), ..., (t_{n-1}, t_n)$. Hence, q_i can be expressed as

$$q_i = [G(0 \le x \le t_t) - G(0 \le x \le t_{i-1})] [G(0 \le x \le t_n)]^{-1}.$$
(3)

By substituting the convolution of infection density with survival function in equation (3), we get

$$q_{i} = \left[\int_{t_{0}}^{t_{i}} h(x)H(t-x)dx - \int_{t_{0}}^{t_{i-1}} h(x)H(t-x)dx \right] \left[\int_{t_{0}}^{t_{n}} h(x)H(t-x)dx \right]^{-1}.$$

We assume the d'_i s follow a multinomial distribution with probabilities of dying in each of the intervals (t_{i-1}, t_i) being q_i . Then the likelihood function for q_i is

$$L(q_i) = \prod_{i=1}^{t_n} q_i^{d_i}. \tag{4}$$

We estimate the parameters of G(t) by the method of maximum likelihood. The complete likelihood equation for maximization is

$$L(q_{i}) = \prod_{i=1}^{t_{n}} \left[\int_{t_{0}}^{t_{i}} h(x)H(t-x)dx - \int_{t_{0}}^{t_{i-1}} h(x)H(t-x)dx \right]^{d_{i}} \times \left[\int_{t_{0}}^{t_{n}} h(x)H(t-x)dx \right]^{-d_{i}} \times \left[\int_{t_{0}}^{t_{n}} h(x;\theta)H(t-x;b_{1},b_{2})dx - \int_{t_{0}}^{t_{i-1}} h(x;\theta)H(t-x;b_{1},b_{2})dx \right]^{d_{i}} \times \left[\int_{t_{0}}^{t_{n}} h(x;\theta)H(t-x;b_{1},b_{2})dx \right]^{-d_{i}}.$$

$$(5)$$

We assume h(x) follows exponential with $\theta=0.5$ per cent growth. We assume the survival distribution follows a Weibull distribution (which is known to mimic several functional shapes), $1-b_1exp(-t/b_2)$, where b_1 is scale parameter and b_2 is shape parameter. We estimate $b_1=3.30$ and $b_2=1.35$. We have calculated a 95 percent bootstrap[10] based confidence intervals. This gives us mean and median durations from infection to death of infected bird as 3.02 days (95 percent CI, 1.82 - 4.12) and 2.51 days. This kind of back-calculation with much more mathematical analysis is under consideration to study the impact of anti-retroviral therapies for AIDS[28].

3. Results. We predict almost 0.78 million birds were infected during first ten days of the epidemic in the West Bengal. Farm birds and market birds constitute the largest proportion of total infected birds. These two subpopulations together comprise 620,000; the next largest consists of domestic birds, at around 120,000. We also predicted that the infected would reach 2.1 million in twenty days (with 0.79 million market birds and 0.95 million farm birds). Although migratory birds are assumed to bring the infection to the domestic level, spread rates among migratory wild birds are comparatively low at 20,000 (See Figure 2). MoHFW and DAHD, New Delhi, supplied expert teams to the state of West Bengal, and intervention operations began on January 14, 2008. The government also supplied protective equipment, medicines, and other essentials for culling[9]. Using the above model, we have studied the effect of the interventions and simulated five scenarios based on five efficacy levels for controlling operations. See Figures 3 through 11 for the effectiveness of interventions in reducing the viral spread. If the efficacy level is at 40 percent, then the total infected birds by the end of ten days after first detection

could be restricted to 230,000, and if the efficacy level reaches 60 percent, then the estimated number of total infected birds in the first ten days could be restricted at 121,000. It is to be noted that the culling operations were not very successful even after a week of operations; by January 20 the virus spread to six districts [30], by January 21 to seven districts [39] and by January 25 to eleven districts [40]. If this level of intervention continues then in twenty days the infection will come down to 103,500. There was evidence that lack of proper protection to the uninfected flock could lead to spread of the virus[31]. Increasing the controlling operations to 80 percent would have reduced the infected birds number from 820,000 to 66,000 and 16,500 after tens and twenty days of infection, respectively. However such a reduction depends on various factors, such as earlier detection of virus in the bird population, understanding of the appropriate dynamics of spread in the region of infection, knowledge of the initial bird population, and an estimate of the size of the initial infected group. We estimate the mean number of days to death of an infected bird is 3.02 days and the median is 2.51 days. We believe that the spread of the infected birds was overestimated when we fitted transmission parameters obtained from the Thailand-based poultry study [42] into our model (see Table 2). However, this study provided very interesting results on transmission parameters and reproduction rates with respect to the duration of infectious period among birds. The time-lag of spread between two cycles could have occurred at a constant rate or at a rate which is a function of variables such as distance from the epicenter to other locations or prevalence.

We have no evidence from Indian data on the time lag. In our analysis, we have assumed a one-day lag between infection cycles. A small number of surviving infected birds could spread the virus to many uninfected birds in a short period. Some have predicted that H5N1 might become a threat to global poultry market[31]. Culling plays one of the important intervention strategies in India. Table 2 (last column) shows the total number of birds infected in ten days is 760,000, which 610,000 consists farm and market birds. These two bird populations are estimated to be from 160,000 to 1.4 million (in ten days), depending upon range of values for contact rates (see Table 3). We believe if a similar epidemic occurs in another large state like West Bengal, the spread would be similar. If such a situation arises, then to control the disease's spread, the number of birds needing to be culled would be between 600,000 and 1.4 million (in ten days). If such operation is conducted, then infected bird populations would drop to 10,000 in twenty days.

4. Conclusions. Given the insufficient information on poultry sizes and the lack of programs to train owners and managers of bird farms and markets in early detection of bird flu, it is unlikely that bird flu in India could be brought into control in ten days to two weeks after initial screening (unless the epidemic is mild). This situation holds true for any region of the country. We suggest educating the people involved in farming and marketing birds about the precautions to be taken and training them to identify infected birds. These interventions will help to prepare the country for future epidemics. The density of birds in various regions and the proportion of infected birds change the transmission rates between birds. In India large-scale avian diseases are uncommon, and governments have tackled outbreaks in a timely way.

Mathematical models can help to provide a range of values for planning and organization for the future epidemics[48]. Instead of assuming the spread of flu as

shown in Figure 1, one can think of developing a model that spreads when migratory birds infect domestic birds at an epicenter (i.e., at cycle 0) and same flock of birds infect at cycle 1, cycle 2, and so on. Nonetheless, there is a need for specially designed studies to investigate some of the transmission aspects of this deadly virus, and government needs to initiate a research team on vaccines. Vaccine researchers have had some success in identifying potential candidate vaccines for subtypes of H5N1[23, 33, 16, 20, 34]. There is a great scope for developing mathematical models in understanding the efficacy of vaccination in controlling the spread of bird flu [34] and in developing cost-effective studies to handle different vaccination strategies in India. We hope that the modeling predictions presented in this work help in timely planning and early control of future bird flu epidemics in India.

Table 1. Parameter description and numerical values

Parameter	Description	Value	Relevant References
$\frac{1}{u}$	Average time to death after infection	3.02 days (95% CI, 1.82-4.12	Section 2.1
$a_{i1}, \alpha_{i2}, \gamma_{i3},$ β_{i4}, λ_{i4}	Transmission rates of infection among the sub-populations of wild birds, domestic birds, market birds, farm birds and poultry workers at <i>i</i> th cycle	0.4, 0.5, 0.68, 0.78, 0.5	14-17, 31, 32, Section 2.1
$c_{i1}, c_{i2}, c_{i3}, c_{i4}, c_{i5}$	Contact rates of infection among the sub-populations of wild birds, domestic birds, market birds, farm birds and poultry workers at <i>i</i> th cycle	0.5 - 0.8, 0.5 - 0.8,	6, 18, 32, Section 2.1
ϵ	Intervention Efficacy	40%-80%	Section 2.1
b_1,b_2	Scale and shape parameters in the Weibull distribution	3.30, 1.35	1, 20-22, 39-40, Section 2.1

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Table 2. Number of birds infected with H5N1 during the first ten days

	Based on Thailand transmission data						
Bird type	Infectious period $= 3 \text{ days}$			Infectious period $= 4 \text{ days}$			
	Low	Mean	High		Low	Mean	High
Wild birds	20,749	20,856	21,488		19,534	20,641	21,302
Domestic birds	243,281	395,720	1,365,660		74,562	205,441	817,092
Market birds	441,432	532,524	3,056,430		111,821	421,358	1,543,320
Farm birds	551,173	594,622	4,165,680		124,413	417,621	1,986,180
Total	1,256,635	1,543,722	8,609,258		330,330	1,065,061	4,367,894
	Based on 1	parameters	de-				
	scribed in the Section 2		2				
Wild birds	20,404						
Domestic birds	123,899						
Market birds	281,694						

Note: We have used Thailand poultry based data for transmission parameters for domestic, farm birds and used intermediate value for market birds. See Section 2 for parametrization

338,793

764,790

Farm birds

Total

TABLE 3. Number of birds infected with H5N1 during the first ten days by varying contact rates between birds

Bird type	Contact rates					
Did type	c = 0.5	c = 0.6	c = 0.8	c = 0.9		
Wild birds	11,311	13,832	30,114	44,462		
Domestic birds	53,929	81,647	188,166	285,982		
Market birds	120,072	183,638	431,959	662,229		
Farm birds	142,049	219,333	521,932	802,604		
Total	327,361	498,450	1,172,171	1,795,277		

Note: Predictions for c = 0.7 are given in the last column of the Table 2

REFERENCES

- [1] R. M. Anderson, and R. M. May, *Infectious diseases of Humans: Dynamics and Control*, Oxford University Press, Oxford, 1991.
- [2] G. J. Boender, T. J. Hagenaars, A. Bouma, G. Nodelijk, A. R. Elbers, M. C. de Jong, and M. van Boven, Risk maps for the spread of highly pathogenic avian influenza in poultry, PLoS Comput. Biol., 3(2007):e71.
- [3] R. Brookmeyer, and M. H. Gail, Minimum size of the acquired immunodeficiency syndrome (AIDS) epidemic in the United States, Lancet, 2(1986):1320–2.
- [4] R. Brookmeyer, and M. H. Gail, A method for obtaining short-term projections and lower bounds on the size of the AIDS epidemic, J. Am. Stat. Assoc., 83(1988):301–308.
- [5] R. Brookmeyer, and M. H. Gail, AIDS Epidemiology A Quantitative Approach, Oxford University Press, New York, 1994.
- [6] V. Colizza, A. Barrat, M. Barthelemy, A. J. Valleron, and A. Vespignani Modeling the world-wide spread of pandemic influenza: baseline case and containment interventions, PLoS Med., 4(2007):e13.
- [7] Communicable Disease Alert, Monthly Newsletter, 9:9, 2005, National Institute of Communicable Diseases, Directorate General of Health Services, Government of India.
- [8] M. D. de Jong, and T. T. Hien, Avian influenza A (H5N1), J. Clin. Virol., $\mathbf{35}(2006):2-13$.

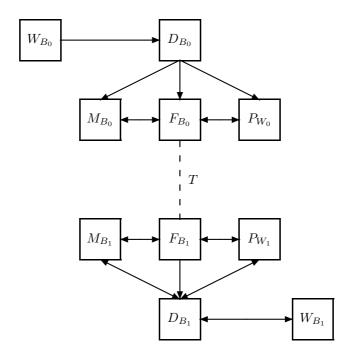


FIGURE 1. Spread of bird flu from one cycle (block/cycle) to neighboring cycles. Migratory wild birds infect domestic birds and spread of virus is due to traveling of farm birds to neighboring places and mixing with other farm birds. In this case virus transfer from farm birds to domestic birds and domestic birds to wild birds and hence virus is spread to another block/village.

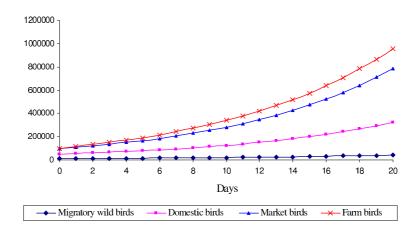


Figure 2. Spread of H5N1 among bird populations

^[9] Department of Animal Husbandry, Dairying and Fisheries, Ministry of Health and Family Welfare, New Delhi, http://dahd.nic.in and http://mohfw.nic.in.

^[10] B. Efron, and R. J. Tibshirani, An Introduction to the Bootstrap, Chapman & Hall, London, 1993.

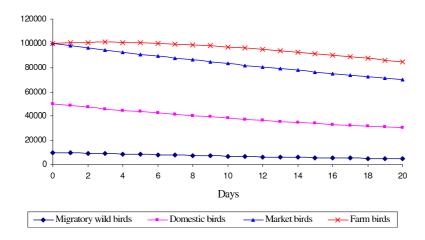


FIGURE 3. Controlled Spread of H5N1 (Interventions level = 40%)

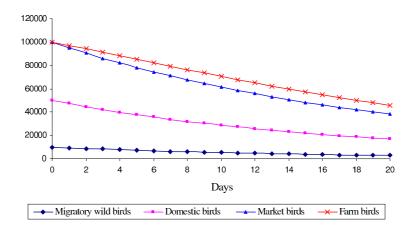


FIGURE 4. Controlled Spread of H5N1 (Interventions level = 50%)

- [11] C. J. Feare, The role of wild birds in the spread of HPAI H5N1, Avian. Dis., 51(2007):440-7.
- [12] N. M. Ferguson, D. A. Cummings, S. Cauchemez, C. Fraser, S. Riley, A. Meeyai, S. Iamsirithaworn, and D. S. Burke, Strategies for containing an emerging influenza pandemic in Southeast Asia, Nature, 437(2005):209–214.
- [13] FluRadar.com West Bengal Begins Culling to Combat Bird Flu, (browsed on 19 January, 2008).
- [14] Freshnews.in Brid Flu: culling on in West Bengal, states on alert, (browsed on 19th January, 2008).
- [15] T. Garske, P. Clarke, and A. C. Ghani, The transmissibility of highly pathogenic avian influenza in commercial poultry in industrialised countries, PLoS ONE., 2(2007):e349.
- [16] J. Ge, G. Deng, Z. Wen, et al. Newcastle disease virus-based live attenuated vaccine completely protects chickens and mice from lethal challenge of homologous and heterologous H5N1 avian influenza viruses, J. Virol., 81(2007):150-8.
- [17] T. J. John, Bird Flu: Public Health Implications for India, Econ. Polit. Weekly, (2005):4792–4795.

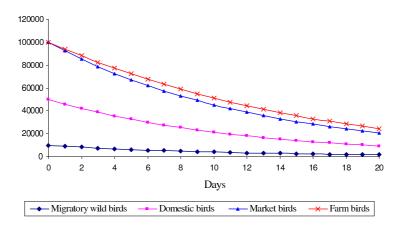


FIGURE 5. Controlled Spread of H5N1 (Interventions level = 60%)

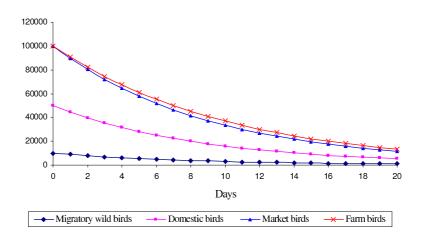


FIGURE 6. Controlled Spread of H5N1 (Interventions level = 70%)

- [18] R. P. Kamal, C. Tosh, B. Pattnaik, et al., Analysis of the PB2 gene reveals that Indian H5N1 influenza virus belongs to a mixed-migratory bird sub-lineage possessing the amino acid lysine at position 627 of the PB2 protein, Arch. Virol., 152(2007):1637-44.
- [19] S. Khare, R. Agarwal, R. Singh, and S. Lal, Overview of avian influenza, J. Indian. Med. Assoc., 104(2006):379–380.
- [20] J. H. Kreijtz, Y. Suezer, and G. van Amerongen, Recombinant modified vaccinia virus Ankarabased vaccine induces protective immunity in mice against infection with influenza virus H5N1, J. Infect. Dis., 195(2007):1598–606.
- [21] Y. K. Kwon, H. W. Sung, S. J. Joh., et al., An outbreak of highly pathogenic avian influenza subtype H5N1 in broiler breeders, Korea, J. Vet. Med. Sci., 67(2005):1193-6.
- [22] Y. K. Kwon, S. J. Joh, M. C. Kim, et al., Highly pathogenic avian influenza (H5N1) in the commercial domestic ducks of South Korea, Avian. Pathol., 34(2005):367-70.
- [23] A. Le Menach, E. Vergu, R. F. Grais, D. L. Smith, and A. Flahault, Key strategies for reducing spread of avian influenza among commercial poultry holdings: 'lessons for transmission to humans, Proc. Biol. Sci., 273(2006):2467-75.

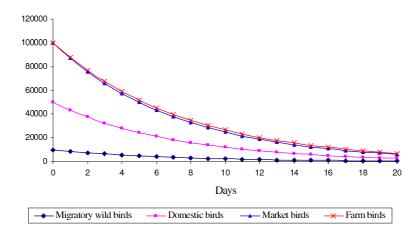


FIGURE 7. Controlled Spread of H5N1 (Interventions level = 80%)

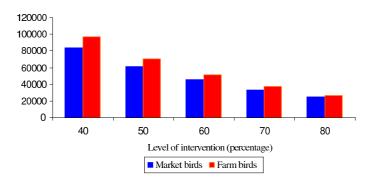


FIGURE 8. Decline in Sub-population sizes in ten days due to control measures

- [24] I. M. Longini Jr., A. Nizam, S. Xu, K. Ungchusak, W. Hanshaoworakul, D. A. Cummings, and M. E. Halloran, Containing pandemic influenza at the source, Science, 309(2005):1083-7.
- [25] R. M. May, Infectious Disease: Can we Avert a Lethal Flu Pandemic?, Curr. Biol., 15(2006):R922-R924.
- [26] A. T. Peterson, B. W. Benz, and M. Pape, Highly pathogenic H5N1 avian influenza: entry pathways into North America via bird migration, PLoS ONE, 2(2007):e261.
- [27] Arni S. R. Srinivasa Rao, and M. Kakehashi, A combination of differential equations and convolution in understanding the spread of an epidemic, Sadhana. Academy Proc. Engg. Sci., 29(2004):305–313.
- [28] Arni S. R. Srinivasa Rao, Incubation periods under various anti-retroviral therapies in homogeneous mixing and age-structured dynamical models: A theoretical approach, arXiv:qbio/060828v2.
- [29] K. Ray, V. A. Potdar, S. S. Cherian, S. D. Pawar, S. M. Jadhav, S. R. Waregaonkar, A. A. Joshi, and A. C. Mishra, Characterization of the complete genome of influenza A (H5N1) virus isolated during the 2006 outbreak in poultry in India, Virus Gen., 36(2008):345– 53.
- [30] Reuters, http://in.reuters.com/article/topNews/idINIndia-31499720080121, (Browsed on 21 Jan, 2008).

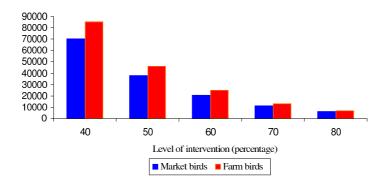


FIGURE 9. Decline in Sub-population sizes in twenty days due to control measures

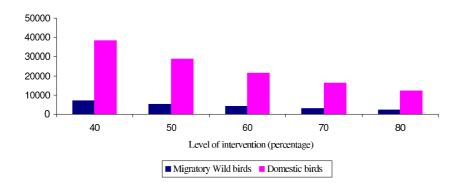


FIGURE 10. Decline in Sub-population sizes in ten days due to control measures

- [31] N. J. Savill, S. G. St. Rose, M. J. Keeling, and M. E. Woolhouse, Silent spread of H5N1 in vaccinated poultry, Nature, 442(2007):757.
- [32] K. J. Sharkey, R. G. Bowers, K. L. Morgan, S. E. Robinson, and R. M. Christley, Epidemiological consequences of an incursion of highly pathogenic H5N1 avian influenza into the British poultry flock, Proc Biol Sci., 275(2008):19–28.
- [33] H. Shi, X. F. Liu, X. Zhang, S. Chen, L. Sun, and J. Lu, Generation of an attenuated H5N1 avian influenza virus vaccine with all eight genes from avian viruses, Vaccine, 25(2007):7379– 84.
- [34] D. J. Smith, Predictability and Preparedness in Influenza Control, Science, 312(2006):392–394.
- [35] G. J. Smith, X. H. Fan, J. Wang, et al., Emergence and predominance of an H5N1 influenza variant in China, Proc. Natl. Acad. Sci. U S A, 103(2006):16936-41.
- [36] G. J. Smith, T. S. Naipospos, T. D. Nguyen, et al., Evolution and adaptation of H5N1 influenza virus in avian and human hosts in Indonesia and Vietnam, Virology, 350(2006):258– 68
- [37] T. Songserm, R. Jam-On, N. Sae-Heng, N. Meemak, D. J. Hulse-Post, K. M. Sturm-Ramirez, and R. G. Webster, *Domestic ducks and H5N1 influenza epidemic, Thailand.*, Emerg. Infect. Dis., 12(2006):575–81.
- [38] K. M. Sturm-Ramirez, D. J. Hulse-Post, E. A. Govorkova, et al., Are ducks contributing to the endemicity of highly pathogenic H5N1 influenza virus in Asia?, J. Virol., 79(2005):11269-79.

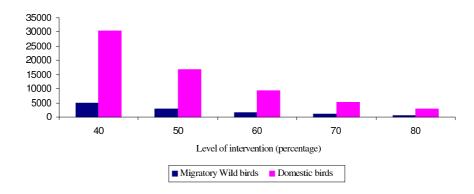


FIGURE 11. Decline in Sub-population sizes in twenty days due to control measures

- [39] The Hindu, http://www.hindu.com/2008/01/22/stories/2008012259780800.htm, (Browsed on 22 Jan, 2008).
- [40] The Indian Express More than half of West Bengal slips in Bird flu grip, http://www.expressindia.com, (browsed on 25th January, 2008).
- [41] G. Tian, S. Zhang, Y. Li, Z. Bu, P. Liu, J. Zhou, C. Li, J. Shi, K. Yu, and H. Chen, Protective efficacy in chickens, geese and ducks of an H5N1-inactivated vaccine developed by reverse genetics, Virology, 341(2005):153–62.
- [42] T. Tiensin, M. Nielen, H. Vernooij, et al., Transmission of the highly pathogenic avian influenza virus H5N1 within flocks during the 2004 epidemic in Thailand, J. Infect. Dis., 196(2007):1679–84.
- [43] C. Tosh, H. V. Murugkar, S. Nagarajan, et al., Outbreak of avian influenza virus H5N1 in India, Vet. Rec., 161(2007):279.
- [44] J. Truscott, T. Garske, I. Chis-Ster, J. Guitian, D. Pfeiffer, L. Snow, J. Wilesmith, N. M. Ferguson, and A. C. Ghani, Control of a highly pathogenic H5N1 avian influenza outbreak in the GB poultry flock, Proc Biol Sci., 274(2007):2287–95.
- [45] R. Uma Shaanker, Guest Editorial, Challenges fly in the wake of bird flu, Curr. Sci., 90(1997):1585–1586.
- [46] R. G. Webster, and D. J. Hulse-Post, Controlling avian flu at the source, Nature, 435(2005):415-417.
- [47] R. G. Webster, R. J. Webby, E. Hoffmann, et al., The immunogenicity and efficacy against H5N1 challenge of reverse genetics-derived H5N3 influenza vaccine in ducks and chickens, Virology, 35(2006):303-11.
- [48] R. G. Webster, D. J. Hulse-Post, K. M. Sturm-Ramirez, Y. Guan, M. Peiris, G. Smith, and H. Chen, Changing epidemiology and ecology of highly pathogenic avian H5N1 influenza viruses, Avian Dis., 51(2007):269-72.
- [49] K. Winker, K. G. McCracken, D. D.Gibson, et al., Movements of birds and avian influenza from Asia into Alaska, Emerg. Infect. Dis., 13(2007):547–52.
- [50] H. Yoon, C. K. Park, H. M. Nam, and S. H. Wee, Virus spread pattern within infected chicken farms using regression model: the 2003-2004 HPAI epidemic in the Republic of Korea, J. Vet. Med. B Infect. Dis. Vet. Public Health, 52(2005):428-31.

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