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Optimal isolation control strategies and cost-effectiveness analysis of a two-strain avian influenza model

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ABSTRACT

The most important and effective measures against disease outbreaks in the absence of valid medicines or vaccine are quarantine and isolation strategies. In this paper optimal control theory is applied to a system of ordinary differential equation describing a two-strain avian influenza transmission via the Pontryagin's Maximum Principle. To this end, a pair of control variables representing the isolation strategies for individuals with avian and mutant strains were incorporated into the transmission model. The infection averted ratio (IAR) and the incremental cost-effectiveness ratio (ICER) were calculated to investigate the cost-effectiveness of all possible combinations of the control strategies. The simulation results show that the implementation of the combination strategy during the epidemic is the most cost-effective strategy for avian influenza transmission. This is followed by the control strategy involving isolation of individuals with the mutant strain. Also observed was the fact that low mutating and more virulent virus results in an increased control effort of isolating individuals with the avian strain; and high mutating with more virulent virus results in increased efforts in isolating individuals with the mutant strain.

1. Introduction

Influenza pandemics have periodically affected humanity since ancient times, they are rare but recurring events. Three pandemics occurred in the last century: in 1918 (Spanish flu), 1957 (Asian flu) and 1968 (Hong Kong flu). The 1918 pandemic is the most lethal, it killed 40–50 million people within a year, its heaviest toll were among young adults in the prime of life (WHO, 2005). Subsequent pandemics were much milder, with an estimated two million deaths in 1957 and one million deaths in 1968 (WHO, 2005). The world may yet face another pandemic. Health experts at World Health Organization (WHO) and elsewhere have been monitoring the extremely severe influenza virus, the highly pathogenic H5N1 strain.

The human cases of the highly pathogenic H5N1 influenza A viruses is on the increase due to the fact that the virus is now endemic within avian populations in Southeast Asia (Ferguson et al., 2005). However, H5N1 represents a serious pandemic threat owing to the risk of mutation or reassortment generating a virus with increased transmissibility, although it is currently incapable of sustained human-to-human transmission (Gumel, 2009; WHO, 2005). To help combat and curtail the burden of a possible potential influenza pandemic, there is a need for a coordinated global effort. In line with this need, a number of countries have formulated their public health preparedness plans which are primarily based on the use of non-pharmaceutical interventions (such as increased hygiene, use of protective devices (e.g. face masks), isolation in hospital wards, and quarantine of suspected cases) and pharmaceutical interventions (such as the use of antivirals and vaccine) (Butler, 2006; Gumel, 2009; WHO, 2005).

A number of mathematical modeling studies have been carried out on influenza pandemic in humans to quantify the potential burden of the pandemic and the various control strategies (see, for instance, Ferguson et al., 2005; Gani et al., 2005; Germann et al., 2006; Gumel et al., 2008; Longini et al., 2004; Longini and Halloran, 2005; Nuño et al., 2007, 2008; van Genugten et al., 2003). Many of these studies emphasize the use of pharmaceutical interventions, it is generally believed that such interventions (antivirals and vaccine) would not be readily and widely available at the onset of the pandemic. Thus, it is highly imperative to carry out modeling studies that focuses on non-pharmaceutical interventions (such as isolation of those with symptoms) in-line with WHO recommendation for alternative measures to reduce transmission and prevent or at least delay further spread of avian influenza should the pandemic occur (WHO, 2005). A number of mathematical modeling studies have been carried out along this direction (see Chowell et al., 2004,

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Table 1
Description of parameters of the two-strain avian model (1).

Parameter	Description	Baseline value	Reference
Π_H	Recruitment rate for humans	30 per day	Gumel (2009)
Π_W	Birth rate of wild birds	1000 per day	Agusto and Gumel (2010)
Π_D	Birth rate of domestic birds	1000 per day	Agusto and Gumel (2010)
μ_H	Natural mortality rate for humans	$1/(70\times 365)$ per day	Bowman et al. (2005)
μ_A	Natural mortality rate of avian	1/100 per day	Agusto and Gumel (2013), Gumel (2009)
δ_W, δ_D	Avian mortality rate	0.05 per day	Agusto and Gumel (2010)
δ_H	Human mortality rate	0.06 per day	Iwami et al. (2007)
β_W, β_D	Effective contact rate for avian strain	0.4/200,000 per day	Agusto and Gumel (2013), Gumel (2009), Menach et al. (2006)
β_M	Effective contact rate for mutant strain	$0.3\times(0.4/20{,}000)$ per day	Gumel (2009)
η_M	Modification parameters	1	Gumel (2009)
τ	Infection-reduction parameter in humans	0.1	Gumel (2009)
θ_J	Reduction of transmission of mutant strain due to isolation	0.6	Gumel (2009)
θ_M	Relative variability of mortality of mutant strain	1.5	Gumel (2009)
θ_D	Relative reduction in mortality due to isolation	0.6	Gumel (2009)
ξ_A	Mutation rate	0.01	Iwami et al. (2007)
γ_A	Recovery rate of humans with avian strain	0.05 per day	Gumel (2009)
γ_M	Recovery rate of humans with mutant strain	0.01 per day	Gumel (2009)

2003; Gumel et al., 2004). For instance, Chowell et al. (2004) uses the uncertainty and sensitivity analysis of the basic reproductive number ($\mathcal{R}_0$) to assess the role model parameters play in outbreak control and their result shows that transmission and isolation rates have the largest effect on $\mathcal{R}_0$. Furthermore, Chowell et al. (2003) and Gumel et al. (2004) obtained the threshold for the basic reproductive number $\mathcal{R}_0$ for assessing the strategies of quarantine and isolation; they both discuss the control of SARS by looking at the role of disease transmission parameters in the reduction of $\mathcal{R}_0$ and the prevalence of the disease.

In this paper, a time dependent optimal control strategies associated with isolating symptomatic individuals is considered using the two-strain avian influenza transmission model by Gumel (2009). In Gumel (2009), however, optimal control strategies were not considered; the discussions are based on prevalence of the disease at equilibrium. Time dependent control strategies have been applied for the studies of HIV models (Kirschner et al., 1997), tuberculosis models (Agusto, 2009; Jung et al., 2002), SARS (Yan et al., 2007), avian influenza (Agusto and Ogunye, 2010; Jung et al., 2009) and malaria (Agusto and Lenhart, in press; Agusto et al., 2012; Okosun et al., 2013). Introduced into the model are two control mechanisms representing the rate of isolating the symptomatic individuals infected with avian and mutant strains, respectively. And the following questions are addressed: given high disease transmission rate, which control strategy is the most beneficial to apply in reducing disease transmission? Which control strategy is the most cost effective? And lastly, what is the impact of mutation on the control efforts? The paper is organized as follows: Section 2 describes the two-strain avian influenza model. The objective functional is introduced in Section 3, followed by the analysis of the optimal controls. Section 4 includes some numerical studies of the optimal controls and discussion of the results. And Section 5, focuses on the control strategies cost-effectiveness.

2. A two-strain avian model

The state equation is the system of ordinary differential equations from Gumel (2009). The model sub-divides the total avian population at time t, denoted by $N_A(t)$, into susceptible wild birds ($S_W(t)$), susceptible domestic birds ($S_D(t)$), infected wild birds ($I_W(t)$) and infected domestic birds ($I_D(t)$), so that $N_A(t)=S_W(t)+S_D(t)+I_W(t)+I_D(t)$. Similarly, the total human population at time t, denoted by $N_H(t)$, is sub-divided into susceptible humans ($S_H(t)$), humans infected with the avian strain ($H_A(t)$), humans infected with the mutant strain ($H_M(t)$), isolated humans with avian ($J_A(t)$) and mutant ($J_M(t)$) strains and recovered humans ($R_H(t)$). Thus, $N_H(t)=S_H(t)+H_A(t)+H_M(t)+J_A(t)+J_M(t)+R_H(t)$.

Thus, the two-strain avian influenza transmission model from Gumel (2009) is given by the following nonlinear system of differential equations:

$$\begin{aligned}
\frac{dS_W}{dt} &= \Pi_W - \lambda_W S_W - \mu_A S_W,\\
\frac{dS_D}{dt} &= \Pi_D - \lambda_D S_D - \mu_A S_D,\\
\frac{dI_W}{dt} &= \lambda_W S_W - \mu_A I_W - \delta_W I_W,\\
\frac{dI_D}{dt} &= \lambda_D S_D - \mu_A I_D - \delta_D I_D,\\
\frac{dS_H}{dt} &= \Pi_H - \tau(\lambda_W+\lambda_D+\lambda_M)S_H - \mu_H S_H,\\
\frac{dH_A}{dt} &= \tau(\lambda_W+\lambda_D)S_H - \xi_A H_A - \psi_A H_A - \mu_H H_A - \delta_H H_A,\\
\frac{dH_M}{dt} &= \tau\lambda_M S_H + \xi_A H_A - \psi_M H_M - \mu_H H_M - \theta_M\delta_H H_M,\\
\frac{dJ_A}{dt} &= \psi_A H_A - \gamma_A J_A - \mu_H J_A - \theta_D\delta_H J_A,\\
\frac{dJ_M}{dt} &= \psi_M H_M - \gamma_M J_M - \mu_H J_M - \theta_D\theta_M\delta_H J_M,\\
\frac{dR_H}{dt} &= \gamma_A J_A + \gamma_M J_M - \mu_H R_H.
\end{aligned} \tag{1}$$

where $\lambda_W=\beta_W(I_D+I_W)$, $\lambda_D=\beta_D(I_D+I_W)$ and $\lambda_M=\beta_M\eta_M(H_M+\theta_J J_M)$. And the initial condition $S_W(0)$, $S_D(0)$, $I_W(0)$, $I_D(0)$, $S_H(0)$, $H_A(0)$, $H_M(0)$, $J_A(0)$, $J_M(0)$, $R_H(0)$ are given and the definitions of above model parameters are listed in Table 1.

The model synthesizes some demographic effects by assuming a proportional natural death rate $\mu_A>0$ in the domestic and wild birds and constant recruitment rates Π_D, Π_W. It is assumed that domestic and wild birds have the same natural death rate