OPTIMAL CONTROL OF AN AVIAN INFLUENZA MODEL WITH MULTIPLE TIME DELAYS IN STATE AND CONTROL VARIABLES

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ABSTRACT. In this paper, we consider an optimal control model governed by a class of delay differential equation, which describe the spread of avian influenza virus from the poultry to human. We take three control variables into the optimal control model, namely: slaughtering to the susceptible and infected poultry \(u_1(t)\), educational campaign to the susceptible human population \(u_2(t)\) and treatment to infected population \(u_3(t)\). The model involves two time delays that stand for the incubation periods of avian influenza virus in the infective poultry and human populations. We derive first order necessary conditions for existence of the optimal control and perform several numerical simulations. Numerical results show that different control strategies have different effects on controlling the outbreak of avian influenza. At the same time, we discuss the influence of time delays on objective function and conclude that the spread of avian influenza will slow down as the time delays increase.

1. Introduction. Avian influenza is an infectious viral disease especially of birds. These viruses occur generally among wild birds worldwide and can infect domestic poultry and other bird species. Avian influenza virus (Influenza type A virus) do not normally infect human. In addition to that, there have been reported and revealed that some of the virus cross the species barrier and lead to serious infections in human and other mammals, such as A (H5N1) and A (H7N9) [12, 23, 13]. If the Avian influenza virus is transmitted to humans, it will lead to serious problems. For

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example, Hong Kong reported 18 cases (including 6 death cases) of human infection with avian influenza A (H5N1) for the first time in 1997, which caused widespread concern worldwide [8]. Further, H7N9, H9N2 and other avian influenza viruses have great potential threat to human. Especially, the virus subtype H7N9 is mainly transmitted through the respiratory tract, infected poultry and their secretions, excreta, and water contaminated by the virus. There are 3 cases firstly infected H7N9 virus in February 2013, and by May 31, 132 cases were found, including 37 deaths, and the mortality rate reached 30%. These cases were distributed in Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, etc [34]. Recently, infected humans of H7N9 are still sporadic, and it has not yet found the ability that the virus can spread among humans. Sporadic infections almost contact with poultry mainly in poultry farms, live-poultry markets and other regions [35, 2]. All the above facts indicate that avian influenza still remains a significant threat to public health in China, thus, it is necessary to deepen our understanding of transmission dynamics of avian influenza, and further control the spread of the avian influenza.

Mathematical models have become extremely useful and important tools in understanding and analyzing the transmission mechanisms of infectious diseases [21]. Considering the high morbidity and mortality in poultry and humans, there are some scholars have addressed transmission dynamics of avian influenza recently [31, 6]. For example, Iwami et al. have developed the mathematical models to investigate the spread of the mutant avian influenza and assessed the effectiveness of the elimination and quarantine policies [16, 15, 17, 18]. Liu and Ruan [26] constructed two bird-to-human avian influenza models with different growth laws of the avian population, and proved the globally asymptotic stability. Liu et al. [24] incorporated the psychological effect of the human population into avian influenza model and studied the dynamical behavior of the model, they found that the psychological effect cannot change the stability of equilibria but may affect the number of infected cases. Gourley et al. [4] established a patch model with delay to investigate the role of migratory birds in the spread of H5N1 avian influenza, they proved globally asymptotic stability of the disease-free equilibrium, and the persistence of infection, they also fitted the data of H5N1 infected ducks in the Poyang Lake region of China. More works can be found in related references [7, 27, 28, 29, 25].

On the other hand, as is known to all that avian influenza has posed huge economic burden which primarily includes opportunity loss, health care related expenditures, loss of employment and so on. It is also costly to implement control interventions, such as therapy, vaccination, isolation and educational campaigns. Therefore, how to formulate optimal control strategies of avian influenza balanced the costs and benefits is an important and meaningful question from the epidemiological and social economic viewpoint. To address these issues, optimal control strategies of avian influenza should be established. In last two decades, many optimal control problems in epidemiology have been studied for various control interventions (both pharmaceutical and non-pharmaceutical). Recently, many optimal control problems with respect to avian influenza have appeared in literatures. In [20], the authors chose the slaughter intensity and the effect of education campaign as control variables, formulated an optimal control problem to minimize the cost of controlling disease outbreaks. Eunok et al. [19] found that the quarantine policy is important rather than the elimination policy during the disease spread, even if the unit execution cost of the quarantine policy is more expensive than that of the elimination policy. Sharma et al. [30] took the incubation periods of avian influenza
A (H7N9) virus into the model, set up an optimal control problem and used a quadratic control to reduce the spread of the disease and the cost of treatment. For avian influenza, poultry is the main animal population responsible for transmitting the disease to humans, but it is difficult to track and diagnose the infected poultry, so the control strategies should be posed on both poultry and human populations. Generally, slaughtering, vaccination and treatment are the common control strategies. More precisely, slaughtering aims to eliminate exposed poultry in the early stages of an outbreak, and it is a reactive control measure which is employed differently from region to region due to high socioeconomic loses [36]. Meanwhile, at the beginning of the outbreak of avian influenza, relevant government departments will broadcast the information of avian influenza through the mass media, internet, etc., which may prompt the humans’ public health awareness, and further avoid contacting with the source of infection [33]. In addition, during the outbreak of avian influenza, the treatment capacity is related to the limited medical resources, which plays an important role in reducing the mortality and preventing the transmission of avian influenza [38]. Based on the above discussion, mixed control strategies are useful to control and prevent the transmission of avian influenza at different stages, so it is necessary to investigate the optimal control strategies of combination of slaughtering to poultry, educational campaign to the susceptible human population and treatment to infected humans.

As far as we know, there are rare results about the optimal mixed control strategies of delayed avian influenza model. In this paper, we propose an optimal control problem of delayed avian influenza model (time delays stand for the incubation periods of avian influenza virus in the infective poultry and human populations) by considering slaughtering to poultry, educational campaign to the susceptible human population and treatment to infected humans as control variables. The main purpose is to find the optimal control pair of slaughter, response intensity via educational campaign and treatment, which seeks to minimize the number of infected poultry, the number of infected humans, and the cost during the implementing these three control strategies.

The organization of the rest of this article is as follows: in section 2, the avian influenza model with multiple time delays is formulated and the stability of equilibria is presented. In section 3, the optimal control problem of this delayed avian influenza model is described. The section 4 is mainly devoted to proving the existence of the optimal control and solving the optimal control problem. A numerical example is provided to illustrate the effectiveness of theoretic results, and the influence of time delays are also indicated in section 5. Finally, a brief discussion about the biological interpretation and conclusion is given in Section 6.

2. Model formulation and equilibria analysis. In this section, we formulate a compartmental model that can be used to describe the transmission of the avian influenza and discuss some simple properties of our model.

2.1. Model formulation. Although the avian influenza virus spreads between wild birds and poultry, and between poultry and humans. We will only consider the transmission dynamics of avian influenza between poultry and humans because of poultry is an important factor in the spread of the virus. The poultry population is divided into two sub-populations depending on the state of the disease: susceptible poultry \( S_a(t) \) and infected poultry \( I_a(t) \). The total poultry population at time \( t \) is denoted by \( N_a(t) = S_a(t) + I_a(t) \). The human population is divided into
three sub-populations, which are susceptible human $S_h(t)$, infected human with avian influenza $I_h(t)$ and recovered human from avian influenza $R_h(t)$. The total population of human at time $t$ is given by $N_h(t) = S_h(t) + I_h(t) + R_h(t)$. The number of susceptible poultry (human) is increased by new recruitment, but decreases by natural death and infection (moving to class $I_s$ $(I_s)$). The number of infected poultry (human) is increased by the infection of susceptible poultry (human) and reduced through natural and disease-related death. In addition, the number of infected humans is also reduced by recovery from the disease (moving to class $R_h$).

Motivated by the discussion above, we obtain the schematic diagram of our model (see Figure 1). The model with Bendington-DeAngelis incidence is presented by the following delayed differential equations:

$$
\begin{align*}
\frac{dS_s(t)}{dt} &= \Lambda_a - \frac{\beta_a S_s(t) I_a(t)}{1 + \alpha_1 S_s(t) + \alpha_2 I_s(t)} - \mu_a S_s(t), \\
\frac{dI_s(t)}{dt} &= \frac{\beta_a e^{-\mu \tau} S_s(t - \tau_1) I_s(t - \tau_1)}{1 + \alpha_1 S_s(t - \tau_1) + \alpha_2 I_s(t - \tau_1)} - (\mu_a + \delta_a) I_s(t), \\
\frac{dS_h(t)}{dt} &= \Lambda_h - \frac{\beta_h S_h(t) I_a(t)}{1 + \beta_1 S_h(t) + \beta_2 I_a(t)} - \mu_h S_h(t), \\
\frac{dI_h(t)}{dt} &= \frac{\beta_h e^{-\mu \tau} S_h(t - \tau_2) I_a(t - \tau_2)}{1 + \beta_1 S_h(t - \tau_2) + \beta_2 I_a(t - \tau_2)} - (\mu_h + \delta_h + \gamma) I_h(t), \\
\frac{dR_h(t)}{dt} &= \gamma I_h(t) - \mu_h R_h(t).
\end{align*}
$$

For the sake of simplicity, we denote $S_s(t), I_s(t), S_h(t), I_h(t)$ and $R_h(t)$ as $S_a, I_a, S_h, I_h$ and $R_h$, respectively. All parameters in model (1) are assumed non-negative and described as follows: $\Lambda_a$ represents new recruitment of the poultry population; $\beta_a$ is the transmission rate from infective poultry to susceptible poultry; $\mu_a$ and $\delta_a$ are the natural and disease-related death rate of the poultry population, respectively; $\Lambda_h$ is the new recruitment of the human population; $\beta_h$ is the transmission rate from infective poultry to susceptible human; $\mu_h$ and $\delta_h$ are the natural and disease-related death rate of the human population; $\gamma$ is the recovery rate of the infective human. $\alpha_i (i = 1, 2)$ and $\beta_i (i = 1, 2)$ are parameters that measure the inhibitory effect.

Because the removed population has no effect on the dynamics of $S_h$ and $I_h$, system (1) can be decoupled to the following system:

$$
\begin{align*}
\frac{dS_s(t)}{dt} &= \Lambda_a - \frac{\beta_a S_s(t) I_a(t)}{1 + \alpha_1 S_s(t) + \alpha_2 I_s(t)} - \mu_a S_s(t), \\
\frac{dI_s(t)}{dt} &= \frac{\beta_a e^{-\mu \tau} S_s(t - \tau_1) I_s(t - \tau_1)}{1 + \alpha_1 S_s(t - \tau_1) + \alpha_2 I_s(t - \tau_1)} - (\mu_a + \delta_a) I_s(t), \\
\frac{dS_h(t)}{dt} &= \Lambda_h - \frac{\beta_h S_h(t) I_a(t)}{1 + \beta_1 S_h(t) + \beta_2 I_a(t)} - \mu_h S_h(t), \\
\frac{dI_h(t)}{dt} &= \frac{\beta_h e^{-\mu \tau} S_h(t - \tau_2) I_a(t - \tau_2)}{1 + \beta_1 S_h(t - \tau_2) + \beta_2 I_a(t - \tau_2)} - (\mu_h + \delta_h + \gamma) I_h(t).
\end{align*}
$$

The initial conditions of model (2) take the following form:

$$
\begin{align*}
S_a(\theta) &= \phi_1(\theta), & I_a(\theta) &= \phi_2(\theta), & S_s(\theta) &= \phi_3(\theta), & I_h(\theta) &= \phi_4(\theta), \\
\phi_i(\theta) &\in C([-\tau, 0], \mathbb{R}_+), & \theta &\in [-\tau, 0], & i &= 1, 2, 3, 4,
\end{align*}
$$
There are two equilibria for model (2): a disease-free equilibrium $E^0$ given by $E^0 = (\frac{\Lambda_h}{\mu_h}, 0, \frac{\Lambda_a}{\mu_a}, 0)$, which always exists; and an endemic equilibrium $E^\ast = (S_a^\ast, I_a^\ast, S_h^\ast, I_h^\ast)$, which exists whenever $R_0 > 1$, where $S_a^\ast = \frac{\Lambda_a}{\beta_a(\mu_a + \alpha_1\Lambda_a)(\alpha_2\mu_a + \beta_a\mu_a - \alpha_1\beta_a\Lambda_a)}$, $I_a^\ast = R_0(\mu_a + \alpha_1\Lambda_a)(\Lambda_a - \mu_a S_a^\ast)/\beta_a\Lambda_a$, $I_h^\ast = \frac{\beta_a e^{-\nu_2 S_a^\ast}}{(\mu_h + \beta_a + \gamma)(1 + \beta_1 S_a^\ast + \beta_2 I_a^\ast)}$ and

$$S_h^\ast = \frac{1}{2\mu_h\beta_1} \left( \sqrt{[\mu_h(1 + \beta_2 I_a^\ast) + \beta_h I_h^\ast - \beta_1\Lambda_h]^2 + 4\beta_1\mu_h\Lambda_h(1 + \beta_2 I_a^\ast)} - \mu_h(1 + \beta_2 I_a^\ast) - \beta_h I_h^\ast + \beta_1 \Lambda_h \right).$$

We further observe that all populations will remain positive and bounded when we start with a positive initial condition. The positively invariant bounded set for

![Schematic diagram of the model with delay.](image-url)

**Figure 1.** Schematic diagram of the model with delay.
system (2) is
\[ \Gamma = \left\{ (S_a, I_a, S_h, I_h) \in \mathbb{R}^+_4 : S_a(t - \tau_1) + I_a(t) \leq \frac{\Lambda_a}{\mu_a} S_a, S_h(t - \tau_2) + I_h(t) \leq \frac{\Lambda_h}{\mu_h} \right\}. \]
All the solution initiating anywhere in the non-negative cone of \( \mathbb{R}^+_4 \) will enter into \( \Gamma \) and then remain there for all time.

**Proposition 1.** The two equilibria of system (1) have the following properties:

(i) The disease-free equilibrium \( E_0 \) is locally asymptotically stable if \( R_0 < 1 \) and unstable if \( R_0 > 1 \);

(ii) The endemic equilibrium \( E^e \) whenever exists (i.e. \( R_0 > 1 \)), is locally asymptotically stable when \( \alpha_2 > \alpha_1 \) and
\[ S^e_a > \frac{\mu_a [\alpha_1 (\mu_a + \delta_a) - (\alpha_2 \mu_a + \beta_a)]}{(\mu_a + \delta_a)(\alpha_1 \Lambda_a + \alpha_2 e^{\mu_a \tau_1} (\mu_a + \delta_a)) - \Lambda_a (\alpha_2 \mu_a + \beta_a)}. \]

**Proof.** The proof idea is similar to the literature [30]. For the sake of completeness, a brief proof is given in the A.

**Theorem 2.1.** For system (1):

(i) The disease-free equilibrium \( E_0 \) of (2) is globally asymptotically stable when \( R_0 < 1 \);

(ii) The endemic equilibrium \( E^e \) is globally asymptotically stable if \( R_0 > 1 \).

**Proof.** The proof is similar to the literature [30], and a brief proof can be found in the B.

3. Description of optimal control problem. In this section, we describe the optimal control problem for delayed avian influenza system (1) and introduce three control variables \( u_1(t) \), \( u_2(t) \) and \( u_3(t) \):

(i) The control \( u_1(t) \) represents the slaughtering to the susceptible and infected poultry. In the early stage of avian influenza outbreak, slaughtering the poultry is an essential measure to control the spread of disease. Hence, we consider poultry slaughtering \( u_1(t) \) as control variable such that \( 0 \leq u_1(t) \leq 1 \). Here 0 represents no slaughter and 1 full slaughter.

(ii) The control \( u_2(t) \) represents educational campaign to the susceptible human population. In reality, there has a negative correlation between the intensity of educational campaign to susceptible human population and infected number, so, we adopt \( 1 - u_2(t) \) instead of \( u_2(t) \) to describe the negative relationship between control variable \( u_2(t) \) and state variables. On the other hand, the disease information can be considered as a possible tool to trigger the responsiveness of the susceptible humans, and people do not react timely to disease information, so it is more reasonable to introduce a time delay \( \tau_2 \) into \( 1 - u_2(t) \). Therefore, we consider this response intensity \( 1 - u_2(t) \) with time delay as a control variable such that \( 0 \leq u_2(t) \leq 1 \). Here 0 represents no response and 1 full response of informed humans.

(iii) The control \( u_3(t) \) represents treatment to infected population. In general, providing treatment to infected individuals can not only reduces the number of infections but also inhibit the development of disease. Because the medical resources (medical diagnosis, medical beds, medicines, treatment, health care, etc.) are usually limited, therefore, we take saturated treatment rate function \( \frac{c u_3(t) I_h}{1 + \alpha I_h} \) into consideration with treatment rate \( c \) and saturation constant \( \alpha \),
where $\alpha$ is the maximal medical resource supplied per unit time. So, the treatment intensity $u_3(t)$ is a control variable such that $0 \leq u_3(t) \leq 1$.

By introducing these three control variables $u_1(t)$ (poultry slaughtering), $u_2(t)$ (educational campaign of susceptible humans) and $u_3(t)$ (treatment of infected humans), (1) becomes

\[
\begin{aligned}
\frac{dS_a}{dt} &= \Lambda_a - \frac{\beta_a S_a I_a}{1 + \alpha_1 S_a + \alpha_2 I_a} - (\mu_a + u_1(t))S_a, \\
\frac{dI_a}{dt} &= \frac{\beta_a e^{-\mu_1 t_1} S_a(t - t_1)I_a(t - t_1)I_a(t - t_1)}{1 + \alpha_1 S_a(t - t_1) + \alpha_2 I_a(t - t_1)} - (\mu_a + \delta_a + u_1(t))I_a, \\
\frac{dS_h}{dt} &= \Lambda_h - (1 - u_2(t))\frac{\beta h S_h I_a}{1 + \beta_1 S_h + \beta_2 I_a} - \mu h S_h, \\
\frac{dI_h}{dt} &= (1 - u_2(t - \tau_2))\frac{\beta h e^{-\mu_1 t_2} S_h(t - t_2)I_a(t - t_2)}{1 + \beta_1 S_h(t - t_2) + \beta_2 I_a(t - t_2)} - (\mu_h + \delta_h + \gamma)I_h - \frac{c u_3(t) I_h}{1 + \alpha I_h}, \\
\frac{dR_h}{dt} &= \gamma I_h - \mu_h R_h + \frac{c u_3(t) I_h}{1 + \alpha I_h}.
\end{aligned}
\]

The main purpose of optimal control problem is to find optimal pair of slaughter, response intensity via educational campaign and treatment $(u_1(t), u_2(t), u_3(t))$, which seeks to minimize the number of infected poultry, the number of infected humans, and the cost during the implementing these three control strategies. To do this, we construct the following objective functional

\[
J(u_1(t), u_2(t), u_3(t)) = \int_0^T L(S_a(t), I_a(t), S_h(t), I_h(t), R_h(t), u_1(t), u_2(t), u_3(t))dt,
\]

with

\[
L = A_1 S_a(t) + A_2 I_a(t) + A_3 I_h(t) + B_1 u_1(t) (S_a(t) + I_a(t)) + B_2 u_2(t) S_h(t) + B_3 u_3(t) I_h(t) + \frac{1}{2} (C_1 u_1(t)^2 + C_2 u_2(t)^2 + C_3 u_3(t)^2),
\]

where $[0, T]$ is the entire time interval over which the three control strategies (slaughter, educational campaign and treatment) are applied, and the constants $A_i, B_i, C_i (i = 1, 2, 3)$ are positive weighted constants to make the terms of integrand keep balance in objective functional $J$. The meaning of the objective functional $J$ is described as follows

(i) The term $\int_0^T [A_1 S_a(t) + A_2 I_a(t) + A_3 I_h(t)]dt$ gives the total number of susceptible and infected poultry infected with avian influenza virus and the total number of infected human over the time period $T$.

(ii) The term $u_1(t)(S_a(t) + I_a(t))$ depicts the total number of poultry being slaughtered, so, the term $\int_0^T [B_1 u_1(t)(S_a(t) + I_a(t)) + C_1 u_1(t)^2]dt$ gives the total cost of slaughtering for susceptible and infected avian.

(iii) The term $u_2(t)S_h(t)$ depicts the total number of susceptible humans being given educational campaign, so the term $\int_0^T [B_2 u_2(t)S_h(t) + C_2 u_2(t)^2]dt$ gives the total cost of educational campaign for susceptible humans.
(iv) The term \( u_3(t)I_h(t) \) depicts the total number of infected humans being receiving the treatment, so, the term \( \int_0^T [B_3u_3(t)I_h(t) + C_3u_3(t)^2]dt \) gives the total cost of treatment for infected humans.

Our goal is to find an optimal control pair \((u_1(t), u_2(t), u_3(t))\) such that

\[
J(u_1^*, u_2^*, u_3^*) = \min \{ J(u_1(t), u_2(t), u_3(t)) | (u_1(t), u_2(t), u_3(t)) \in U \},
\]

where the admissible control set \( U \) is given as

\[
U = \{(u_1(t), u_2(t), u_3(t)) | u_i(t) (i = 1, 2, 3) \text{ is Lebesgue measurable, } u_i(t) \in [0, 1], t \in [0, T] \}.
\]

For the sake of simplicity, we also denote \( u_i(t) = u_i(i = 1, 2, 3) \) in the subsequent sections when confusion not occurs.

4. Existence and characterization of the optimal control. In this section, we discuss the existence of the optimal control pair in finite time for the system (6) with the initial conditions (3), and then construct the Hamiltonian of the optimal control problem to derive the first order necessary conditions for the optimal control.

4.1. Existence of the Optimal Control. For the existence of optimal control problem (6) and (7), we have the following result.

**Theorem 4.1.** There exists an optimal control pair \( u^* = (u_1^*, u_2^*, u_3^*) \) \( \in U \) and a corresponding optimal state \((S_a^*, I_a^*, S_h^*, I_h^*, R_h^*)\) such that

\[
J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in U} J(u_1, u_2, u_3),
\]

subject to the control system (6) with the initial conditions (3).

**Proof.** In order to prove the existence of optimal control, we take three steps based on the results in [10, 11]. Firstly, we can easily get \( S_a(t-\tau_i) + I_a(t) \leq \frac{A_a}{\mu_a}, S_h(t-\tau_2) + I_h(t) + R_h(t) \leq \frac{A_h}{\mu_h} \) from the system (6), which means the solutions of system (6) are bounded for each bounded control variable \( u_i \in U (i = 1, 2, 3) \). Obviously, the right side functions of system (6) satisfy the Lipschitz condition about state variables. Therefore, we can obtain that the set of solutions to the system (6) is nonempty without control variables in \( U \). Secondly, it follows from (9) that the admissible control set \( U \) is closed and convex, and the system (6) can be written as linear function of control variables, the coefficients of which depend on state variables. Thirdly, from the definition of \( L \) in (8), we can obtain \( L \) is convex because the Hessian matrix \( H(L) = \text{diag}\{C_1, C_2, C_3\} \) is positive definite with \( C_i > 0 \) \((i = 1, 2, 3)\). Also \( L(S_a, I_a, S_h, I_h, R_h, u_1, u_2, u_3) \geq \frac{1}{2}(C_1u_1(t)^2 + C_2u_2(t)^2 + C_3u_3(t)^2) = g(u_1, u_2, u_3) \), clearly \( g(u_1, u_2, u_3) \) is continuous and satisfies \( g(u_1, u_2, u_3) [u_1, u_2, u_3] \rightarrow \infty \) as \( |(u_1, u_2, u_3)| \rightarrow \infty \), here \( \cdot \) denotes the \( L^2(0, T) \) norm of vector. Therefore, we conclude that there exists an optimal control pair \( u^* = (u_1^*, u_2^*, u_3^*) \in U \) such that \( J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in U} J(u_1, u_2, u_3) \). 

4.2. Characterization of the Optimal Control. In this subsection, we solve the optimal control problem presented in (6) and (7) by constructing the Hamiltonian \( H \) and using the Pontryagin’s maximum principle. For the sake of simplicity, we first define a characteristic function \( \chi_{[a,b]}(t) \) as

\[
\chi_{[a,b]}(t) = \begin{cases} 
1, & \text{if } t \in [a, b] \\
0, & \text{otherwise}. 
\end{cases}
\]
In the following, the first order necessary conditions for the optimal control problem is given.

**Theorem 4.2.** Let \( u_1^*, u_2^* \) and \( u_3^* \) be optimal control variables, \( S_a^*, I_a^*, I_h^* \) and \( R_h^* \) are corresponding optimal state variables of the control system (6) and (3). Then there exists adjoint variable \( \lambda(t) = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t)) \in \mathbb{R}^5 \) that satisfies the following adjoint equations:

\[
\frac{d\lambda_1(t)}{dt} = - (A_1 + B_1 u_1) + \lambda_1(t)[(\mu_a + u_1) + \frac{\beta_a I_a^*(1 + \alpha_2 I_a^*)}{(1 + \alpha_1 S_a^* + \alpha_2 I_a^*)^2}] + \chi_{[0,T - \tau_1]}(t) \lambda_2(t + \tau_1) \frac{\beta_a e^{-\mu_\tau_1 I_a^*}}{(1 + \alpha_1 S_a^* + \alpha_2 I_a^*)^2},
\]

\[
\frac{d\lambda_2(t)}{dt} = - (A_2 + B_1 u_1) + \lambda_2(t) \frac{\beta_a S_a^*(1 + \alpha_1 S_a^*)}{(1 + \alpha_1 S_a^* + \alpha_2 I_a^*)^2} + \lambda_2(t)(\mu_a + \delta_a + u_1) + \lambda_3(t)(1 - u_2) \frac{\beta_h S_h^*(1 + \beta_1 S_h^*)}{(1 + \beta_1 S_h^* + \beta_2 I_a^*)^2}
\]

\[
+ \chi_{[0,T - \tau_1]}(t) \lambda_2(t + \tau_1) \frac{\beta_a e^{-\mu_\tau_1 S_a^*}}{(1 + \alpha_1 S_a^* + \alpha_2 I_a^*)^2} - \chi_{[0,T - \tau_2]}(t) \lambda_4(t + \tau_2) \frac{(1 - u_2) \beta_h e^{-\mu_\tau_2 S_h^*}}{(1 + \beta_1 S_h^* + \beta_2 I_a^*)^2},
\]

\[
\frac{d\lambda_3(t)}{dt} = - B_2 u_2 + \lambda_3(t)(1 - u_2) \frac{\beta_a I_a^*(1 + \beta_2 I_a^*)}{(1 + \beta_1 S_h^* + \beta_2 I_a^*)^2} + \mu_h
\]

\[
+ \chi_{[0,T - \tau_2]}(t) \lambda_4(t + \tau_2) \frac{(1 - u_2) \beta_h e^{-\mu_\tau_2 I_a^*}}{(1 + \beta_1 S_h^* + \beta_2 I_a^*)^2},
\]

\[
\frac{d\lambda_4(t)}{dt} = - (A_3 + B_3 u_3) + \lambda_4(t)(\mu_h + \delta_h) + (\lambda_4(t) - \lambda_5(t))(\gamma + \frac{c}{1 + \alpha I_h^*}),
\]

\[
\frac{d\lambda_5(t)}{dt} = \lambda_5(t) \mu_h,
\]

with transversality conditions \( \lambda_i(T) = 0 (i = 1, 2, 3, 4, 5) \). Furthermore, the corresponding optimal controls are give as follows:

\[
u_i^*(t) = \min \{ \max \{ D_i, 0 \}, 1 \}, \quad i = 1, 2, 3, 4, 5
\]

where

\[
D_1 = \frac{1}{C_1} [ (\lambda_1(t) - B_1) S_a^* + (\lambda_2(t) - B_1) I_a^* ],
\]

\[
D_2 = \frac{1}{C_2} \chi_{[0,T - \tau_2]}(t) \lambda_4(t + \tau_2) \frac{\beta_h e^{-\mu_\tau_2 S_h^* I_a^*}}{(1 + \beta_1 S_h^* + \beta_2 I_a^*)^2} - \lambda_3(t) \frac{\beta_h S_h^* I_a^*}{1 + \beta_1 S_h^* + \beta_2 I_a^*} - B_2 S_h^*,
\]

\[
D_3 = \frac{1}{C_3} (\lambda_4(t) - \lambda_5(t)) \frac{c I_a^*}{1 + \alpha I_h^*} - B_3 I_a^*.
\]

**Proof.** To simplify the notations, we let \( x(t) = (S_a(t), I_a(t), S_h(t), I_h(t), R_h(t))^T \), \( u(t) = (u_1(t), u_2(t), u_3(t))^T \) and \( \lambda(t) = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t))^T \). We also
define \( x_{\tau_1}(t) := x(t - \tau_1), x_{\tau_2}(t) := x(t - \tau_2), u_{\tau_1}(t) := u(t - \tau_1) \). The Hamiltonian is given by

\[
H = H(x, x_{\tau_1}, x_{\tau_2}, u, u_{\tau_1}, \lambda)(t) = A_1 S_a + A_2 I_a + A_3 h + [B_1 u_1(t)(S_a + I_a) + B_2 u_2(t)S_h + B_3 u_3(t)I_h]
\]

\[
+ \frac{1}{2} (C_1 u_1^2(t) + C_2 u_2^2(t) + C_3 u_3^2(t))
\]

\[
+ \lambda_1(t)[A_a - \frac{\beta_a S_a I_a}{1 + \alpha_1 S_a + \alpha_2 I_a} - (\mu_a + u_1(t))S_a]
\]

\[
+ \lambda_2(t)[\beta_a e^{\mu_a \tau_1} S_{a, \tau_1} I_{a, \tau_1} + \frac{\beta_a e^{\mu_a \tau_1} S_{a, \tau_1} I_{a, \tau_1}}{1 + \alpha_1 S_{a, \tau_1} + \alpha_2 I_{a, \tau_1}} - (\mu_a + \delta_a + u_1(t))I_a]
\]

\[
+ \lambda_3(t)[A_h - (1 - u_2(t)) \frac{\beta_h S_h I_a}{1 + \beta_1 S_h + \beta_2 I_a} - \mu_h S_h]
\]

\[
+ \lambda_4(t)[(1 - u_{2, \tau_1}) \frac{\beta_h e^{\mu_h \tau_2} S_{h, \tau_2} I_{a, \tau_2}}{1 + \beta_1 S_{h, \tau_2} + \beta_2 I_{a, \tau_2}} - (\mu_h + \delta_h + \gamma)I_h - \frac{c u_3(t) I_h}{1 + \alpha I_h}]
\]

\[
+ \lambda_5(t)[\gamma I_h - \mu_h R_h + \frac{c u_3(t) I_h}{1 + \alpha I_h}].
\]

Let \( u^*(t) = (u_1^*(t), u_2^*(t), u_3^*(t))^T \) be the optimal control and \( x^*(t) = (S_a^*(t), I_a^*(t), S_h^*(t), I_h^*(t), R_h^*(t))^T \) be the corresponding optimal trajectory. By the Pontryagin’s maximum principle with delay in state [14, 3], there exists \( \lambda(t) \in \mathbb{R}^5 \) such that the first order necessary conditions for the existence of optimal control are given by the following three equations, that is, the state equations

\[
\frac{dx}{dt} = \frac{\partial H}{\partial \lambda},
\]

the optimal condition

\[
0 = [\frac{\partial H}{\partial u_1}(t) + \chi_{[0, T-\tau_1]}(t)(\frac{\partial H}{\partial u_{\tau_1}}(t))_{t=\tau_1}]_{u=u^*},
\]

and the adjoint equation

\[
\frac{d\lambda}{dt} = -[\frac{\partial H}{\partial x}(t) + \chi_{[0, T-\tau_1]}(t)(\frac{\partial H}{\partial x_{\tau_1}}(t))_{t=\tau_1} + \chi_{[0, T-\tau_2]}(t)(\frac{\partial H}{\partial x_{\tau_2}}(t))_{t=\tau_2}]_{x=x^*}.
\]

In the componentwise form, the above conditions are expressed as

(i) The state equations: given by the system (6).

(ii) The optimality conditions:

\[
\frac{\partial H}{\partial u_1(t)} = 0,
\]

\[
\frac{\partial H}{\partial u_2(t)} + \chi_{[0, T-\tau_1]}(t) \frac{\partial H}{\partial u_{\tau_1}}(t) |_{t=\tau_1} = 0,
\]

\[
\frac{\partial H}{\partial u_3(t)} = 0.
\]

Substituting (13) into (14), we have

\[
B_1(S_a^* + I_a^*) + C_1 u_1^*(t) - \lambda_1(t) S_a^* - \lambda_2(t) I_a^* = 0,
\]

\[
B_2 S_h^* + C_2 u_2^*(t) + \lambda_3(t) \frac{\beta_h S_h^* I_a^*}{1 + \beta_1 S_h^* + \beta_2 I_a^*} = 0.
\]
(iii) The adjoint equations:

\[- \chi_{[0,T-\tau_2]}(t) \lambda_4(t + \tau_2) \frac{\beta_h e^{-\mu_s \tau_2} S_{h_{\tau_2}}^* h_{\tau_2}^*}{1 + \beta_1 S_{h_{\tau_2}}^* + \beta_2 I_{h_{\tau_2}}^*} = 0, \]

\[B_3 h_{\tau_2}^* + C_3 \nu_3(t) - \lambda_4(t) \frac{c h_{\tau_2}^*}{1 + \alpha h_{\tau_2}^*} + \lambda_5(t) \frac{c h_{\tau_2}^*}{1 + \alpha h_{\tau_2}^*} = 0. \]  

(15)

Further simplification of (15) yields

\[ u_i^*(t) = D_i, \quad i = 1, 2, 3. \]

It follows from the bounds for the control \( u_i(t)(i = 1, 2, 3) \) that (12) holds.

(iii) The adjoint equations:

\[ \frac{d\lambda_1(t)}{dt} = - \left[ \frac{\partial H}{\partial S_a} + \chi_{[0,T-\tau_1]}(t) \frac{\partial H}{\partial S_{a_{\tau_1}}} \right]_{(x,u)=(x^*,u^*)} \]

\[= - (A_1 + B_1 u_1(t)) + \alpha_1(t) \frac{\beta_a S_{a_1}^*(1 + \alpha_1 S_{a_1}^* + \alpha_2 I_{a_1}^*)}{1 + \beta_1 S_{a_1}^* + \beta_2 I_{a_1}^*} \]

\[+ \chi_{[0,T-\tau_1]}(t) \lambda_2(t + \tau_1) \frac{\beta_a e^{-\mu_s \tau_1} S_{a_{\tau_1}}^*}{1 + \alpha_1 S_{a_{\tau_1}}^* + \alpha_2 I_{a_{\tau_1}}^*} \]

\[\frac{d\lambda_2(t)}{dt} = - \left[ \frac{\partial H}{\partial I_a} + \chi_{[0,T-\tau_1]}(t) \frac{\partial H}{\partial I_{a_{\tau_1}}} \right]_{(x,u)=(x^*,u^*)} \]

\[+ \chi_{[0,T-\tau_2]}(t) \frac{\partial H}{\partial I_{a_{\tau_2}}} \right]_{(x,u)=(x^*,u^*)} \]

\[= - (A_2 + B_1 u_1(t)) + \alpha_1(t) \frac{\beta_a S_{a_2}^*(1 + \alpha_1 S_{a_2}^* + \alpha_2 I_{a_2}^*)}{1 + \beta_1 S_{a_2}^* + \beta_2 I_{a_2}^*} + \lambda_2(t)(\mu_a + \delta_a + u_1(t)) \]

\[+ \lambda_3(t)(1 - u_2(t)) \frac{\beta_h S_{h_{\tau_2}}^*(1 + \beta_1 S_{h_{\tau_2}}^*)}{1 + \beta_1 S_{h_{\tau_2}}^* + \beta_2 I_{h_{\tau_2}}^*} \]

\[\frac{d\lambda_3(t)}{dt} = - \left[ \frac{\partial H}{\partial S_h} + \chi_{[0,T-\tau_2]}(t) \frac{\partial H}{\partial S_{h_{\tau_2}}} \right]_{(x,u)=(x^*,u^*)} \]

\[= - B_2 u_2(t) + \lambda_3(t) \left[ (1 - u_2(t)) \frac{\beta_h I_{h_{\tau_2}}^*(1 + \beta_1 S_{h_{\tau_2}}^* + \beta_2 I_{h_{\tau_2}}^*)}{1 + \beta_1 S_{h_{\tau_2}}^* + \beta_2 I_{h_{\tau_2}}^*} \right] \]

\[- \chi_{[0,T-\tau_2]}(t) \lambda_4(t + \tau_2) \frac{1 - u_{2_{\tau_2}}(t)) \beta_h e^{-\mu_s \tau_2} S_{h_{\tau_2}}^* (1 + \beta_1 S_{h_{\tau_2}}^*)}{1 + \beta_1 S_{h_{\tau_2}}^* + \beta_2 I_{h_{\tau_2}}^*} \]

\[\frac{d\lambda_4(t)}{dt} = - \left[ \frac{\partial H}{\partial I_h} \right]_{(x,u)=(x^*,u^*)} \]

\[= - (A_3 + B_3 u_3(t)) + \lambda_4(t) (\mu_h + \delta_h + \gamma + \frac{c u_3(t)}{1 + \alpha I_h^*}) \]

\[- \lambda_5(t) \left[ \gamma + \frac{c u_3(t)}{1 + \alpha I_h^*} \right] \]

\[= - (A_3 + B_3 u_3(t)) + \lambda_4(t) (\mu_h + \delta_h) + (\lambda(t) - \lambda_5(t)) (\gamma + \frac{c u_3(t)}{1 + \alpha I_h^*}), \]
positive integers. Then, time interval \( t \geq t_m \), we assume the step size is \( \Delta \).

5. **Numerical simulations.** This section aims to illustrate the effectiveness of our theoretical results that obtained in previous sections and the influence of time delays on objective function also performed.

5.1. **Numerical examples.** In order to obtain the discrete optimal control problem, we assume the step size is \( \Delta > 0 \), and \( \tau = m \Delta \) and \( T = n \Delta \), where \( m, n \) are positive integers. Then, time interval \( [-\tau, T + \tau] \) can be divided as

\[
t_{-m} < \cdots < t_0 = 0 < t_1 < \cdots < t_n = T < t_{n+1} < \cdots < t_{n+m}.
\]

Table 1. Algorithm

| Step 1: for \( k = -m, -(m-1), \ldots, 0 \) do: |
| --- |
| \( S_a^k = S_a(0); I_a^k = I_a(0); S_h^k = S_h(0); I_h^k = I_h(0); R_h^k = R_h(0) \) |
| end for |
| for \( k = n, n+1, \ldots, n+m \) do: |
| \( \lambda_1^k = 0; \lambda_2^k = 0; \lambda_3^k = 0; \lambda_4^k = 0; \lambda_5^k = 0 \) |
| end for |
| \( m_1 = \lfloor \tau_1/\Delta \rfloor; m_2 = \lfloor \tau_2/\Delta \rfloor \) |

| Step 2: for \( k = 0, 1, \ldots, n-1 \) do: |
| --- |
| \( S_a^{k+1} = S_a^k + \Delta \left[ \Lambda_a - \frac{\beta_a S_a^k I_a^k}{1 + \alpha_1 S_a^k + \alpha_2 I_a^k} - (\mu_a + u_1(t)) S_a^k \right] \) |
| \( I_a^{k+1} = I_a^k + \Delta \left[ \frac{\beta_a e^{-\mu_a \tau_1} S_a^k S_h^k}{1 + \alpha_1 S_a^k + \alpha_2 I_a^k} - (\mu_a + \delta_a + u_1^a(t)) I_a^k \right] \) |
| \( S_h^{k+1} = S_h^k + \Delta \left[ \Lambda_h - (1 - u_2^k) \frac{\beta_a e^{-\mu_a \tau_2} S_h^k}{1 + \alpha_1 S_a^k + \alpha_2 I_a^k} - \mu_h S_h^k \right] \) |
| \( I_h^{k+1} = I_h^k + \Delta \left[ (1 - u_2^{k-1}) \frac{\beta_a e^{-\mu_a \tau_2} S_h^k I_a^k}{1 + \alpha_1 S_a^k + \alpha_2 I_a^k} - (\mu_h + \delta_h + \gamma) I_h^k - \frac{c u_1^a I_h^k}{1 + \alpha_1 I_h^k} \right] \) |
| \( R_h^{k+1} = R_h^k + \Delta \left[ \gamma I_h^k - \mu_h R_h^k + \frac{c u_1^a I_h^k}{1 + \alpha_1 I_h^k} \right] \) |
| for \( j = 1, 2, 3, 4, 5 \) do: |
| \( \lambda_j^{n-k-1} = \lambda_j^{n-k} - \Delta \times \text{Temp}_j \) |
| end for |
| \( D_1^{k+1} = (\lambda_1^{n-k} - \beta_1) S_a^k + (\lambda_2^{n-k} - \beta_1) I_a^k )/C_1; D_2^{k+1} = \text{Temp}_a/C_2 \) |
| \( D_3^{k+1} = (\lambda_4^{n-k} - \lambda_5^{n-k}) I_a^k / C_3 \) |
| \( u_1^{k+1} = \min \{ \max(0, D_1^{k+1}), 1 \}; u_2^{k+1} = \min \{ \max(0, D_2^{k+1}), 1 \} \) |
| end for |

| Step 3: for \( k = 1, 2, \ldots, n \) do: |
| --- |
| \( S_a^k(t_k) = S_a^k; I_a^k(t_k) = I_a^k; S_h^k(t_k) = S_h^k; I_h^k(t_k) = I_h^k; R_h^k(t_k) = R_h^k \) |
| \( u_1^k(t_k) = u_1^k; u_2^k(t_k) = u_2^k; u_3^k(t_k) = u_3^k \) |
| end for |

\[ \dfrac{d\lambda_5(t)}{dt} = - \left[ \dfrac{\partial H}{\partial R_h(t)} \right]_{(x,u) = (x^*, u^*)} = \lambda_5(t) \mu_h, \]

with transversality conditions \( \lambda_i(T) = 0 (i = 1, 2, 3, 4, 5) \).

This is completed the proof. \( \square \)
So we can define the values of $S_a(t), I_a(t), S_h(t), I_h(t), R_h(t), \lambda_k(t)$ and $u_i(t)$ at nodal points by $S_a^j, I_a^j, S_h^j, I_h^j, R_h^j, \lambda_k^j$ and $u_i^j$, respectively, where $-m \leq i \leq n + m, j = 1, 2, 3, k = 1, \ldots, 5$. In order to obtain the discrete form of equation (6) and adjoint equation (13), we use the first order forward difference to approximate the time derivative and first order backward difference approximation [22] to those two equations, respectively. Then applying the algorithm presented in Table 1, we can solve our optimal control problem numerically, with the parameters value shown in Table 2 and initial conditions $S_a(0) = 10000, I_a(0) = 500, S_h(0) = 1000, I_h(0) = 10$ and $R_h(0) = 1$.

Table 2. Parameter values of numerical experiments for model (2)

| Parameter | Value                     | Source of data |
|-----------|---------------------------|----------------|
| $\Lambda_a$ | 1000/245 per day         | [5, 9]         |
| $\beta_a$   | $5.1 \times 10^{-4}$ per day | [5],          |
| $\mu_a$     | 1/245 per day             | [5, 9]         |
| $\delta_a$  | 1/400 per day             | [5]            |
| $\Lambda_h$ | 2000/36500 per day        | [5]            |
| $\beta_h$   | $2 \times 10^{-6}$ per day | [5]            |
| $\mu_h$     | $5.48 \times 10^{-5}$ per day | [26, 37]   |
| $\delta_h$  | 0.001 per day             | [26, 37]       |
| $\gamma$    | 0.1 per day               | [26, 37]       |
| $c$         | 0.5                       | Assumed        |
| $\alpha$    | 0.1                       | Assumed        |
| $\alpha_1$  | 0.01                      | Assumed        |
| $\alpha_2$  | 0.03                      | Assumed        |
| $\beta_1$   | 0.01                      | Assumed        |
| $\beta_2$   | 0.01                      | Assumed        |

Figure 2(a) and (b) present the population of infected poultry and infected human with and without control, and Figure 2(c) shows the values of control variables $u_1(t), u_2(t)$ and $u_3(t)$ in each time, which illustrate that the infected population of poultry and human decrease remarkably under control. For poultry population, when $t \approx 20$, the number of infected poultry has dramatically reduce; when $t \approx 90$, the number of infected poultry goes to zero. And the number of infected human gradually decreases when $t \approx 25$ under control. Subsequently, the disease gradually goes to extinction in human population. Thus, the control strategies in our model have significant influence on the spread of avian influenza.

However, the cost of control strategies must be considered by disease control department and the cost of each measure is different, so we spontaneously want to know: under only one or two control strategies, how will the influenza change compared with three control strategies? In order to do this, we make simulations under only $u_1(t), u_2(t)$ or $u_3(t)$ (see Figure 3); and only $(u_1(t), u_2(t)), (u_2(t), u_3(t))$ or $(u_1(t), u_3(t))$ (see Figure 4). Figure 3(a) shows the effect of $u_1(t)$ (poultry slaughtering) is evident, namely, the infected poultry population has rapidly decrease, while the control $(u_2(t)$ (educational campaign) and $u_3(t))$ (treatment to infected
human population) seem not have any influence on infected avian, which is reasonable because $u_2(t)$ and $u_3(t)$ act on human population. From Figure 3(b), we see $u_1(t)$ also is an effective measure to suppress the outbreak of influenza, because poultry slaughtering is an immediate and rapid control measure in the source of disease. Also, the effect of educational campaign ($u_2(t)$) is obvious, so educational campaign, as a convenient and low cost measure, should be adopted firstly. Figure 4 shows the effect of two control strategies (the other one sets as zero). From Figure 4(a), control ($u_1(t), u_2(t)$) and ($u_1(t), u_3(t)$) have same effect on the influenza, which are also equivalent to the three control in Figure 2(a) and control $u_1(t)$ in Figure 3(a), approximately. Control ($u_2(t), u_3(t)$) are also verified that there is no effect on poultry population (as $u_2(t)$ and $u_3(t)$ in Figure 3(a)). It follows from Figure 4(b) that ($u_1(t), u_3(t)$) or ($u_2(t), u_3(t)$) are more effective measures than ($u_1(t), u_2(t)$). Motivated by the discussion above, we may conclude that the poultry slaughtering is the most effective control measure for poultry population and treatment to infected human population is the most effective one for human population, while educational campaign is also a measure that can not be ignored.

In addition, we calculate the values of objective function (7) with all/part of control and without control. Using Simpson’s quadrature formula, the objective function (7) takes the following discrete form:
\[ \hat{J}(\mathbf{u}) = \Delta \frac{\Delta}{3} \left( f(x_0, u_0) + f(x_n, u_n) + \frac{[n/2]}{2} \sum_{i=1}^{[n/2]} f(x_{2i-1}, u_{2i-1}) + \frac{[n/2]}{2} \sum_{i=1}^{[n/2]} f(x_{2i}, u_{2i}) \right), \]

where \( f(x, u) = L(S_a(t), I_a(t), S_h(t), I_h(t), R_h(t), u_1(t), u_2(t), u_3(t)) \) is the integrand part of objective function \( (7) \) and \([\cdot]\) denotes integer-valued function.

The calculating results for the discrete form \( (17) \) are shown in Table 3. We can see from Table 3 that, compared with the case of without control, the value of \( \hat{J}(\mathbf{u}) \) under part/all of control strategies not significantly increase, which indicate that we can adopt some control strategies to reduce the number of the infected poultry and human population while the total cost related this disease is relatively low. Meanwhile, it is clear that the value of \( \hat{J}(\mathbf{u}) \) will decrease as long as \( u_1(t) \neq 0 \), and the possible reason is that poultry slaughtering is a measure that can curb the disease from source. Therefore, we can mainly adopt control strategies \( u_1(t), (u_1(t), u_2(t)), (u_1(t), u_3(t)) \) or \( (u_1(t), u_2(t), u_3(t)) \), and others in the second when influenza outbreak.
Table 3. Values of objective function under different control variables for model (2)

| Value of control \(u(t)\) | Value of objective function \((\times 10^4)\) |
|--------------------------|-------------------------------|
| \(u_1(t), u_2(t), u_3(t) \equiv 0\) (Without control) | 1.4681 |
| \(u_1(t) \neq 0, u_2(t), u_3(t) \equiv 0\) | 1.2038 |
| \(u_2(t) \neq 0, u_1(t), u_3(t) \equiv 0\) | 1.4692 |
| \(u_3(t) \neq 0, u_1(t), u_2(t) \equiv 0\) | 1.4684 |
| \(u_1(t), u_2(t) \neq 0, u_3(t) \equiv 0\) | 1.2039 |
| \(u_1(t), u_3(t) \neq 0, u_2(t) \equiv 0\) | 1.2041 |
| \(u_2(t), u_3(t) \neq 0, u_1(t) \equiv 0\) | 1.4692 |
| \(u_1(t), u_2(t), u_3(t) \neq 0\) (With all of controls) | 1.2043 |

5.2. Influence of time delays to objective function. This numerical example is devoted to indicating the effect of time delays on avian influenza in model (6). We will compute the value of objective function \(J(u)\) by (17) under different time delays and the results are presented in Figure 5. Since delays \(\tau_1\) and \(\tau_2\) denote the delay of transmission rate for avian and human, respectively, the speed of transmission of disease decreases as the increasing of \(\tau_1\) or \(\tau_2\), which are clearly illustrated by Figure 5(a) and (b). Thus, in order to curb the transmission of disease, related department should provide some protect advices (such as educational campaign) to humans as fast as possible to increase the time delay of disease transmission, which will cut the cost of disease control.

![Figure 5](image1.png)

\(\text{Figure 5. Values of objective function under different time delays for model (6).}\)

5.3. Effect of the basic reproduction number \(R_0\). The basic reproduction number \(R_0\) is an important index to describe the spread of disease. Generally, the higher value of \(R_0\) means the high epidemic peaks. Thus, we will investigate the effects of \(R_0\) on the peak value of \(I_a (I_h)\) under different control combinations.

Based on the discussion in subsection 5.1, the control strategy \(u_1\) is only considered for avian population, while the controls \(u_1, u_2\) or \(u_3\) are considered for human population. The simulation results are shown in Figure 6, which are the plots of
epidemic peaks of the infected poultry and human population under different basic reproduction number and different control strategies. We can see from Figure 6(a) that, for the poultry population, the epidemic peaks rapidly increase with the raise of $R_0$, while under the control measure $u_1$ (slaughtering to the susceptible and infected poultry), the effect of $R_0$ on epidemic peak largely decrease, i.e., the epidemic peak of infected poultry has not significant increase with the raise of $R_0$. Meanwhile, Figure 6(b) indicate that the slaughtering to the susceptible and infected poultry (i.e., control strategy $u_1$) also has significate influence to suppress the outbreak of influenza among human population whenever the basic reproduction number is small or large, but for the other two control strategies $u_2$ and $u_3$, the effect of $R_0$ on epidemic peaks is distinct only when $R_0$ is relatively large, which may because slaughtering is a control measure in the source of disease.

![Figure 6. Effect of $R_0$.](image)

5.4. Effect of treatment saturation constant $\alpha$ on the optimal control. This numerical example is devoted to exploring the influence of treatment saturation constant $\alpha$ on the spreading of influenza under different basic reproduction number. Because the treatment is only acted on the human population, we just consider the infected human population here. The simulation results are presented by Figure 7, which indicate that the strategy $u_1$ (slaughtering) is the most effective control measure in both $\alpha = 0.1$ and $1.0$, compared with the other two control combinations. For different values of $\alpha$, the control strategies $u_2$ and $u_3$ almost have no impact on $I_h$ when $R_0$ is small, while their suppressing effect to disease gradually enlarge for a relatively large basic reproduction number. In particular, one can easily observe that, small $\alpha$ can lead to low epidemic peaks under same $R_0$, which means that small treatment saturation constant is more effective to suppress the influenza.

5.5. Effect of parameter $\alpha_1$ in model (6). As we can see from the form of $R_0$ (see (4)), the different choice of $\alpha_1$ can lead to different values of $R_0$. By choosing $\alpha_1 = 0.1, 0.06, 0.04$ and $0.03$, we can obtain $R_0 = 0.7365, 1.2195, 1.8144$ and $2.3997$, respectively, and plot the epidemic peaks of $I_a(t)$ and $I_h(t)$ under different control strategies, which are shown in Figure 8. Figure 8(a) shows that the peak value of $I_h$ abruptly increase as the decrease of $\alpha_1$ (i.e., as the increase of $R_0$). We also know that $u_1$ can dramatically curb the outbreak of influenza whenever $\alpha_1$ is small or large. Figure 8(a) illustrates that all the three control strategies have
good performance to curb the outbreak of avian influenza among humans when \( \alpha \) is small. Especially, \( u_3 \) is more effective than \( u_2 \) for large \( \alpha_1 \), but the result is opposite for small \( \alpha_1 \). According to the analysis above, we may conclude that for small value of \( \alpha_1 \), the effects of control strategies are more significant.

5.6. Effect of parameter \( \alpha_2 \) in model (6). Because the value of \( \alpha_2 \) can not change \( R_0 \), we explore the effects of \( \alpha_2 \) on peak values of \( I_a \) and \( I_h \) under different \( R_0 \). The simulation results are presented in Figure 9. Figure 9(a) and (b) indicate that the epidemic peaks of avian population rapidly rise with the increasing of \( R_0 \) when the control measure is in the absence, and the small \( \alpha_2 \) means the large peaks of \( I_a \). On the contrary, under the control strategy \( u_1 \), the peaks of \( I_a \) sharply reduce, and the influence of \( \alpha_2 \) is also not obvious. For humans, it follows from Figure 9(c) and (d) that the large \( \alpha_2 \) also can suppress the outbreak of avian influenza, and the effect of \( \alpha_2 \) is more evident when the peak of infected humans is large.

5.7. Effect of parameters \( \beta_1 \) and \( \beta_2 \) in model (6). In order to study the effects of \( \beta_1 \) and \( \beta_2 \), we consider the peak of infected humans under three different control strategies, and the results are shown in Figure 10 and 11. It follows from Figure
that large $\beta_1$ will lead to a small peak value of $I_h$ when the control is $u_1$. For the other two strategies $u_2$ and $u_3$, their effects are similar to that of $u_1$. Form Figure 11, we can see that the increase of $\beta_2$ will result in the decreasing of peak of $I_h$ whichever control strategies are adopted. It is also worth pointing out that the control measure $u_1$ is the most effective strategy to suppress the outbreak of influenza among humans under different parameters $\beta_1$ and $\beta_2$.

6. Concluding remarks. Poultry and birds always suffer from the threat of avian influenza, such as H5N1, H7N9, which can further influence the health of humans and the development of economy. Therefore, it is necessary to investigate the transmission dynamics of avian influenza, which also provide the theoretical reference for relevant departments to set out effective control strategies. In order to study the effects of different control strategies, we consider an optimal control problem described by a delay differential equation with multiple time delays in state and control variables, and derive the first order necessary conditions for existence of the optimal control. Through numerical examples, we find that the number of infected poultry and humans decrease remarkably under control strategies, and the speed of disease spread will decrease as the increasing of time delays $\tau_1$ or $\tau_2$. Recently, the age-structure and multi-patch models have been widely studied because of its extensive application in epidemic. Our future work is to investigate the stochastic avian influenza models with age-structure or multi-patch.
Appendix A. Proof of Proposition 1.

Proof of Proposition 1. (i) The characteristic equation takes the following form

\[(\lambda + \mu_a)(\lambda + \mu_h)(\lambda + \mu_h + \delta_h + \gamma)(\lambda + \mu_a + \delta_a - \frac{\beta_a \Lambda_a e^{-(\mu_a + \lambda)\tau_1}}{\mu_a + \alpha_1 \Lambda_a}) = 0.\]  \hspace{1cm} (18)

It is obvious that the first three eigenvalues of (18) are \(\lambda_1 = -\mu_a < 0, \lambda_2 = -\mu_h < 0\) and \(\lambda_3 = -(\mu_h + \delta_h + \gamma) < 0\), respectively, and the last one is given by

\[f(\lambda) = \lambda + \mu_a + \delta_a - \frac{\beta_a \Lambda_a e^{-(\mu_a + \lambda)\tau_1}}{\mu_a + \alpha_1 \Lambda_a} = 0.\]  \hspace{1cm} (19)

If \(\tau_1 = 0\), \(\mathcal{R}_0\) can be simplified as \(\mathcal{R}_0^* = \frac{\beta_a \Lambda_a}{(\mu_a + \alpha_1 \Lambda_a)(\mu_a + \tau_1)}\). The unique root of (19) therefore is \(\lambda = (\mu_a + \delta_a)(\mathcal{R}_0^* - 1) < 0\), which indicate the asymptotic stability of \(E_0^*\) whenever \(\tau_1 = 0\).

If \(\tau_1 \neq 0\), let us consider the following two cases.
Case I: $\tau_1 > \tau_1^*$ (i.e., $\mathcal{R}_0 < 1$). Suppose $\lambda = iv(v > 0, i^2 = -1)$ is a root of equation (19), which implies that

$$iv + \mu_a + \delta_a = \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{\mu_a + \alpha_1 \Lambda_a} \cdot e^{-iv \tau_1} = 0.$$  

Applying the Euler formula $e^{a+bi} = e^a (\cos b + i \sin b)$, separating real and imaginary parts, we derive that

$$\left\{ \begin{array}{l}
\frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{\mu_a + \alpha_1 \Lambda_a} \cdot \cos(v \tau_1) = \mu_a + \delta_a, \\
\frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{\mu_a + \alpha_1 \Lambda_a} \cdot i \sin(v \tau_1) = iv.
\end{array} \right. \quad (20)$$

Squaring and adding the two equations of (20) yields

$$v^2 = \left( \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{\mu_a + \alpha_1 \Lambda_a} \right)^2 - (\mu_a + \delta_a)^2. \quad (21)$$

Noting $\mathcal{R}_0 < 1$, we observe that $\left( \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{\mu_a + \alpha_1 \Lambda_a} \right)^2 < (\mu_a + \delta_a)^2$. This means $v^2 < 0$, which contradict the fact that $v > 0$ is a real number. All the eigenvalues of (18) therefore have negative real part, that is, $E^0$ is locally asymptotically stable.

Case II: $0 \leq \tau_1 \leq \tau_1^*$ (i.e., $\mathcal{R}_0 > 1$). We from (19) know that $f(0) = \mu_a + \delta_a - \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{\mu_a + \alpha_1 \Lambda_a} = (\mu_a + \delta_a)(1 - \mathcal{R}_0) < 1$, and $f(\lambda) \to +\infty$ as $\lambda \to +\infty$, which means that there must exists a $\lambda_0 > 0$ such that $f(\lambda_0) = 0$. Hence, the characteristic equation (19) has at least one root with positive real part. In other words, $E^0$ is unstable.

(ii) The characteristic equation corresponding to $E^e$ is of the form

$$(\lambda + \mu_h + \delta_h + \gamma)(\lambda + \mu_h + \beta_h L_3)(\lambda^2 + M_1 \lambda + M_2 e^{-\lambda \tau_1} + M_3 + M_4 e^{-\lambda \tau_1}) = 0, \quad (22)$$

here $M_1 = 2\mu_a + \delta_a + \beta_a L_1$, $M_2 = -\beta_a L_2 e^{-\mu_a \tau_1}$, $M_3 = \mu_a^2 + \mu_a \delta_a + \beta_a (\mu_a + \delta_a) L_1$, $M_4 = -\mu_a \beta_a L_2 e^{-\mu_a \tau_1}$, $L_1 = \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{(1 + \alpha_1 \Lambda_a)}$, $L_2 = \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{(1 + \alpha_1 \Lambda_a) L_1}$, $L_3 = \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{(1 + \alpha_1 \Lambda_a) L_2}$. It is easily to know that two eigenvalues $\lambda_1 = -(\mu_h + \delta_h + \gamma)$ and $\lambda_2 = -(\mu_h + \beta_h L_3)$ of (22) are negative. So we only need to examine the last two eigenvalues of (22), which are determined by

$$\lambda^2 + M_1 \lambda + M_2 e^{-\lambda \tau_1} + M_3 + M_4 e^{-\lambda \tau_1} = 0. \quad (23)$$

If $\tau_1 = 0$, then (23) becomes $\lambda^2 + (M_1 + M_2) \lambda + (M_3 + M_4) = 0$. All the eigenvalues obviously have negative real parts if $\alpha_2 > \alpha_1$ and (5) hold. If $0 \leq \tau_1 < \tau_1^*$ (i.e., $\mathcal{R}_0 > 1$), let $\lambda = iv(v > 0)$ be a root of (23), then by using the same manner as in (21), one has

$$v^4 + (M_1^2 + 2M_3 - M_2^2) v^2 + M_3^2 - M_4^2. \quad (24)$$

Let $N_1 = M_1^2 - 2M_3 - M_2^2$, $N_2 = M_3^2 - M_4^2$. Owing to $\mathcal{R}_0 < 1$, we can get

$$\left( \frac{\beta_a \Lambda_s e^{-\mu_a \tau_1}}{(\mu_a + \alpha_1 \Lambda_a)} \right)^2 < 1.$$  

Noting that $\alpha_2 > \alpha_1$ and (5) hold, we easily observe that $N_1 > 0$ and $N_2 > 0$. Therefore, (24) has no positive root, which means that all eigenvalues of (23) have negative real parts. In a word, the endemic equilibrium $E^e$ is locally asymptotically stable for all $0 \leq \tau_1 < \tau_1^*$. \qed
Appendix B. Proof of Theorem 2.1.

Proof. In order to prove the global stability of the equilibria, we firstly study the following avian-only subsystem:

\[
\begin{align*}
\frac{dS_a(t)}{dt} &= \Lambda_a - \frac{\beta_a S_a(t) I_a(t)}{1 + \alpha_1 S_a(t) + \alpha_2 I_a(t)} - \mu_a S_a(t), \\
\frac{dI_a(t)}{dt} &= \frac{\beta_a e^{-\mu_a \tau_1} S_a(t - \tau_1) I_a(t - \tau_1)}{1 + \alpha_1 S_a(t - \tau_1) + \alpha_2 I_a(t - \tau_1)} - (\mu_a + \delta_a) I_a(t).
\end{align*}
\]

(25)

In fact, the avian-only subsystem (25) are independent of the full system (2). System (25) always has a unique disease-free equilibrium \(A^0(\frac{\Lambda_a}{\mu_a}, 0)\) and a unique endemic equilibrium \(A^e(S^e_a, I^e_a)\) if \(0 \leq \tau_1 < \tau^*_1\). Similarly, we can easily get that the disease-free equilibrium \(A^0\) is locally asymptotically stable if \(\tau_1 \geq \tau^*_1\) and endemic equilibrium \(A^e\) is locally asymptotically stable if \(0 \leq \tau_1 < \tau^*_1\). Let now consider the global stability of \(A^0\) and \(A^e\).

In order to show that \(A^0\) is globally asymptotically stable, we define a Lyapunov function as follows

\[
V_1 = (S_a - S^0_a - S^0_a \ln \frac{S_a}{S^0_a}) e^{-\mu_a \tau_1} + I_a + \int_{t-\tau_1}^{t} \frac{\beta_a e^{-\mu_a \tau_1} S_a I_a}{1 + \alpha_1 S_a + \alpha_2 I_a} ds,
\]

the derivative of \(V_1\) is

\[
\frac{dV_1}{dt} = - \frac{e^{-\mu_a \tau_1} \mu_a (S_a - S^0_a)^2}{S_a} - (\mu_a + \delta_a)(1 - R_0) I_a.
\]

(26)

Since \(\{(S_a, I_a) \in \mathbb{R}^2_+ : \frac{dV_1}{dt} = 0\} = \{(S_a, I_a) \in \mathbb{R}^2_+ : S_a = S^0_a = \frac{\Lambda_a}{\mu_a}, I_a = I^0_a = 0\}\), and by LaSalle’s Invariance Principle, we easily obtain that the disease-free equilibrium \(A^0(\frac{\Lambda_a}{\mu_a}, 0)\) of subsystem (25) is globally asymptotically stable when \(R_0 < 1\).

To prove the global stability of \(E^0\), we therefore only need to discuss model (2) at the disease-free steady state, i.e., the following system

\[
\begin{align*}
\frac{dS_h}{dt} &= \Lambda_h - \mu_h S_h, \\
\frac{dI_h}{dt} &= -(\mu_h + \delta_h + \gamma) I_h.
\end{align*}
\]

(27)

The solution of (27) is as follows

\[
\begin{align*}
S_h &= \frac{\Lambda_h}{\mu_h} + C e^{-\mu_h t}, \\
I_h &= C e^{-(\mu_h + \delta_h + \gamma) t},
\end{align*}
\]

(28)

where \(C\) is a constant. Obviously, we can see that \(S_h \rightarrow \frac{\Lambda_h}{\mu_h}\) and \(I_h \rightarrow 0\) when \(t \rightarrow \infty\). Hence, the disease-free equilibrium \(E^0\) of system (2) is globally asymptotically stable.

The global stability of the avian-only subsystem (25) at endemic equilibrium \(A^e = (S^e_a, I^e_a)\) can be easily prove according to the method in [1]. Therefore, in order to prove the global stability of the endemic equilibrium \(E^e\) of system (2), we only consider system (25) again with avian components already at the endemic
steady state as follows
\[
\begin{align*}
\frac{dS_h}{dt} &= \Lambda_h - \frac{\beta_h S_h I_a^e}{1 + \beta_1 S_h + \beta_2 I_a^e} - \mu_h S_h, \\
\frac{dI_h}{dt} &= \frac{\beta_h e^{-\mu_h \tau} S_h (t - \tau_2) I_a^e}{1 + \beta_1 S_h (t - \tau_2) + \beta_2 I_a^e} - (\mu_h + \delta_h + \gamma) I_h.
\end{align*}
\tag{29}
\]
Let \( \xi = 1 + \beta_1 S_h + \beta_2 I_a^e \) in the first equation of (29), we have
\[
\frac{d}{dt} \left( \frac{\beta_h \Lambda_h \xi - \beta_h I_a^e \xi + \beta_h I_a^e + \frac{\beta_2 \beta_h (I_a^e)^2}{\beta_1} - \mu_h \xi^2 + \mu_h \xi + \mu_h I_a^e \xi}{\beta_1 \xi} \right) = \frac{2 \mu_h \xi - h_1}{\mu_h \xi^2 - h_1 \xi - h_2} + \frac{h_1}{\mu_h \xi^2 - h_1 \xi - h_2} \frac{dt}{h_1} = -\frac{1}{\beta_1} \frac{dx}{dt}.
\]
Integrating the both sides of (31), we have
\[
\frac{\beta_1}{2 \mu_h} \left[ \frac{\xi - h_1}{\beta_1} - \frac{\sqrt{h_1^2 + \frac{h_2}{\mu_h}}}{\beta_1} \right] = C e^{-2 \mu_h t},
\tag{32}
\]
where \( C \) is a constant. It is easily obtained from (32) that \( S_h \to S_h^e \) when \( t \to \infty \), which also implies that \( S_h (t - \tau_2) \to S_h^e (t \to \infty) \). We therefore only need to discuss the second equation of (29) in the steady state \( S_h^e \). Similarly, from the second equation of (29), we have
\[
I_h = \frac{\beta_h e^{-\mu_h \tau} S_h^e I_a^e}{(\mu_h + \delta_h + \gamma) (1 + \beta_1 S_h^e + \beta_2 I_a^e)} + C e^{-(\mu_h + \delta_h + \gamma) t} \tag{C is a constant}. \tag{33}
\]
So, \( I_h \to I_a^e \) when \( t \to \infty \) based on (33). Therefore, the endemic equilibrium \( E^e \) of system (2) is globally asymptotically stable.

**Appendix C. Some variables in table 1.**

\[
\begin{align*}
\text{Temp}_1 &= -(A_1 + B_1 u_1^k) + \lambda_{1}^{k-n} \left( (\mu_a + u_1^k) + \frac{\beta_a I_a^k (1 + \alpha_2 I_a^k)}{(1 + \alpha_1 S_a^k + \alpha_2 I_a^k)^2} \right) \\
&\quad + \chi(\alpha_b + \tau_1) (t_n - k) \lambda_{2}^{n-k+1} \frac{\beta_b S_h^k (1 + \beta_1 S_h^k)^k}{(1 + \alpha_1 S_a^k + \alpha_2 I_a^k)^2}, \\
\text{Temp}_2 &= -(A_2 + B_1 u_1(t)) + \lambda_{1}^{n-k} \frac{\beta_a S_h^k (1 + \alpha_1 S_a^k + \alpha_2 I_a^k)^2}{(1 + \alpha_1 S_a^k + \alpha_2 I_a^k)^2} \\
&\quad + \lambda_{2}^{k-n} (\mu_a + \delta_a + u_1^k) + \lambda_{3}^{k-n} (1 - u_2^k) \frac{\beta_b S_h^k (1 + \beta_1 S_h^k)^k}{(1 + \alpha_1 S_a^k + \alpha_2 I_a^k)^2} \\
&\quad + \chi(\alpha_b + \tau_1) (t_n) \lambda_{2}^{n-k+1} \frac{\beta_b S_h^k (1 + \beta_1 S_h^k)^k}{(1 + \alpha_1 S_a^k + \alpha_2 I_a^k)^2} \\
&\quad - \chi(\alpha_b + \tau_2) (t_n - k) \lambda_{4}^{k-n+2} \frac{1 - u_2^{k-m_2}}{(1 + \beta_2 I_a^{k-m_2})^2} \frac{\beta_b e^{-\mu_h \tau} S_h^{k-m_2} (1 + \beta_1 S_h^{k-m_2})}{(1 + \beta_1 S_h^{k-m_2} + \beta_2 I_a^{k-m_2})^2}, \\
\text{Temp}_3 &= -B_2 u_2(t) + \lambda_3(t) [(1 - u_2(t)) \frac{\beta_h I_a^e (1 + \beta_2 I_a^e)}{(1 + \beta_1 S_h^e + \beta_2 I_a^e)^2} + \mu_h]
\end{align*}
\]
\[ -\chi_{[0,T-t_{2}]}(t_{n-k})\lambda_{4}^{n-k+m_{2}}(1-u_{2}^{k-m_{2}})\beta_{h}e^{-\mu_{h}t_{2}}I_{a}^{k-m_{2}}(1 + \beta_{2}I_{a}^{k-m_{2}}) \\
\left(1 + \beta_{1}S_{h}^{k-m_{2}} + \beta_{2}I_{a}^{k-m_{2}}\right)^{2}, \]

Temp4 = \( - (A_{3} + B_{3}u_{3}(t)) + \lambda_{4}^{n-k}(\mu_{h} + \delta_{h}) + (\lambda_{4}^{n-k} - \lambda_{5}^{n-k})(\gamma + \frac{c_{u_{3}}^{k}}{(1 + \alpha I_{h}^{k})^{2}}) \),

Temp5 = \( \lambda_{5}^{n-k} \mu_{h} \),

Temp6 = \( \chi_{[0,T-t_{2}]}(t_{n-k})\lambda_{4}^{n-k+m_{2}}\beta_{h}e^{-\mu_{h}t_{2}}S_{h}^{k-m_{2}}I_{a}^{k-m_{2}} \\
1 + \beta_{1}S_{h}^{k-m_{2}} + \beta_{2}I_{a}^{k-m_{2}} \)

\[ - \lambda_{5}^{n-k} \frac{\beta_{h}S_{h}^{k}I_{a}^{k}}{1 + \beta_{1}S_{h}^{k} + \beta_{2}I_{a}^{k}} - B_{2}S_{h}. \]

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REFERENCES

[1] A. Abta, A. Kaddar and H. T. Alaoui, Global stability for delay SIR and SEIR epidemic models with saturated incidence rates, Electronic Journal of Differential Equations, 2012 (2012), 1–13.

[2] C. Bao, L. Cui, M. Zhou et al., Live-animal markets and influenza a (H7N9) virus infection, New England Journal of Medicine, 368 (2013), 2337–2339.

[3] E. B. M. Bashier and K. C. Patidar, Optimal control of an epidemiological model with multiple delay poultry and its role in sustaining avian influenza, SIAM Journal on Applied Mathematics, 71 (2011), 487–516.

[4] L. Bourouiba, S. A. Gourley, R. Liu and J. Wu, The interaction of migratory birds and domestic poultry and its role in sustaining avian influenza, SIAM Journal on Applied Mathematics, 71 (2011), 487–516.

[5] F. Chen and J. Cui, Cross-species epidemic dynamic model of influenza, in 2016 9th International Congress on Image and Signal Processing, BioMedical Engineering and Informatics (CISP-BMEI), IEEE, 2016.

[6] Z. Chen and Z. Xu, A delayed diffusive influenza model with two-strain and two vaccinations, Applied Mathematics and Computation, 349 (2019), 439–453.

[7] N. S. Chong, J. M. Tchuenche and B. J. Smith, A mathematical model of avian influenza with half-saturated incidence, Theory in Biosciences, 133 (2014), 23–38.

[8] E. Claas, A. Osterhaus, R. Van-Beek et al., Human influenza a H5N1 virus related to a highly pathogenic avian influenza virus, The Lancet, 351 (1998), 472–477.

[9] C. A. Y. E. Committee, China agriculture yearbook, 2012.

[10] W. H. Fleming and R. W. Rishel, Deterministic and stochastic optimal control, Springer Verlag, New York, 1975.

[11] H. Gaff and E. Schaefer, Optimal control applied to vaccination and treatment strategies for various epidemiological models, Mathematical Biosciences and Engineering, 6 (2009), 469–492.

[12] N. Gao, Z. Lu, B. Cao et al., Clinical findings in 111 cases of influenza A (H7N9) virus infection, New England Journal of Medicine, 369 (2013), 1869–1869.

[13] R. Gao, B. Cao, Y. Hu et al., Human infection with a novel avian-origin influenza A (H7N9) virus, New England Journal of Medicine, 368 (2013), 1888–1897.

[14] L. G"ollmann, D. Kern and H. Maurer, Optimal control problems with delays in state and control variables subject to mixed control-state constraints, Optimal Control Applications and Methods, 30 (2009), 341–365.

[15] S. Iwami, Y. Takeuchi, A. Kurobeinikov and X. Liu, Prevention of avian influenza epidemic: what policy should we choose?, Journal of Theoretical Biology, 252 (2008), 732–741.

[16] S. Iwami, Y. Takeuchi and X. Liu, Avian-human influenza epidemic model, Mathematical Biosciences, 207 (2007), 1–25.

[17] S. Iwami, Y. Takeuchi and X. Liu, Avian flu pandemic: Can we prevent it?, Journal of Theoretical Biology, 257 (2009), 181–190.

[18] S. Iwami, Y. Takeuchi, X. Liu and S. Nakaoka, A geographical spread of vaccine-resistance in avian influenza epidemics, Journal of Theoretical Biology, 259 (2009), 219–228.
[19] E. Jung, S. Iwami, Y. Takeuchi et al., Optimal control strategy for prevention of avian influenza pandemic, Journal of Theoretical Biology, 260 (2009), 220–229.

[20] T. Kang, Q. Zhang and L. Rong, A delayed avian influenza model with avian slaughter: Stability analysis and optimal control, Physica A: Statistical Mechanics and its Applications, 529 (2019), 1215–44.

[21] M. J. Keeling and P. Rohani, Modeling infectious diseases in humans and animals, Princeton University Press, 2008.

[22] A. Lahrouz, H. El Mahjour, A. Settati et al., Dynamics and optimal control of a non-linear epidemic model with relapse and cure, Physica A: Statistical Mechanics and its Applications, 496 (2018), 299–317.

[23] D. Liu, W. Shi, Y. Shi et al., Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: Phylogenetic, structural, and coalescent analyses, The Lancet, 381 (2013), 1926–1932.

[24] S. Liu, L. Pang, S. Ruan and X. Zhang, Global dynamics of avian influenza epidemic models with psychological effect, Computational and Mathematical Methods in Medicine, 2015, Article ID 913726.

[25] S. Liu, S. Ruan and X. Zhang, On avian influenza epidemic models with time delay, Theory in Biosciences, 134 (2015), 75–82.

[26] S. Liu, S. Ruan and X. Zhang, Nonlinear dynamics of avian influenza epidemic models, Mathematical Biosciences, 283 (2017), 118–135.

[27] F. K. Mbabazi, J. Y. T. Mugisha and M. Kimathi, Modeling the within-host co-infection of influenza A virus and pneumococcus, Applied Mathematics and Computation, 339 (2018), 488–506.

[28] O. P. Misra and D. K. Mishra, Spread and control of influenza in two groups: A model, Applied Mathematics and Computation, 219 (2013), 7982–7996.

[29] G. P. Samanta, Permanence and extinction for a nonautonomous avian-human influenza epidemic model with distributed time delay, Mathematical and Computer Modelling, 52 (2010), 1794–1811.

[30] S. Sharma, A. Mondal, A. K. Pal et al., Stability analysis and optimal control of avian influenza virus A with time delays, International Journal of Dynamics and Control, 6 (2018), 1351–1366.

[31] Z. Shi, X. Zhang and D. Jiang, Dynamics of an avian influenza model with half-saturated incidence, Applied Mathematics and Computation, 355 (2019), 399–416.

[32] P. Van den Driessche and J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Mathematical Biosciences, 180 (2002), 29–48.

[33] A. Wang and Y. Xiao, A filippov system describing media effects on the spread of infectious diseases, Nonlinear Analysis: Hybrid Systems, 11 (2014), 84–97.

[34] World Health Organization, WHO risk assessments of human infection with avian influenza A(H7N9) virus, 2017, https://www.who.int/influenza/human_animal_interface/influenza_h7n9/Risk_Assessment/en/.

[35] Y. Xiao, X. Sun, S. Tang et al., Transmission potential of the novel avian influenza A(H7N9) infection in mainland China, Journal of Theoretical Biology, 352 (2014), 1–5.

[36] H. Yoko, K. Yoshinari, Y. Takehisa et al., Potential risk associated with animal culling and disposal during the foot-and-mouth disease epidemic in Japan in 2010, Research in Veterinary Science, 102 (2015), 228–230.

[37] X. Zhang, Global dynamics of a stochastic avian-human influenza epidemic model with logistic growth for avian population, Nonlinear Dynamics, 90 (2017), 2331–2343.

[38] X. Zhang and X. Liu, Backward bifurcation of an epidemic model with saturated treatment function, Journal of Mathematical Analysis and Applications, 348 (2008), 433–443.

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