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MODELING AND EVALUATING TARGETED INTERVENTIONS TO CURB AVIAN INFLUENZA SPREAD AMONG HUMANS AND DOMESTIC BIRDS

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Abstract. Avian influenza, caused by influenza A viruses, has drawn substantial attention globally due to increased deaths from time to time. This study examines control interventions for avian influenza transmission in humans and domestic birds using a deterministic mathematical model. The model incorporates three time-dependent interventions: vaccinating susceptible birds, maintaining proper hygiene practice, and culling infected birds. The next-generation matrix method is used to determine the effective reproduction number. Optimal control theory is applied by incorporating: vaccination, proper human hygiene practices, and culling of infected birds. To determine the necessary conditions for the existence of optimal controls, the Pontryagin's Maximum Principle is employed. The optimal control problem is then solved using the forward-backward sweep method based on the fourth-order Runge-Kutta algorithm, implemented in MATLAB. Results from the optimal control analysis show that the strategy combining all interventions is the most effective approach for controlling the disease. Furthermore, the Incremental Cost-Effectiveness Ratio (ICER) is used to identify the most cost-effective strategy for disease control. The findings show that Strategy VII has a negative ICER, indicating that it is less costly and averts

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more infections. Therefore, to eliminate the disease, we recommend the implementation of all the aforementioned control measures.

Keywords: avian influenza; effective reproduction number; optimal control; numerical simulation.

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1. INTRODUCTION

Avian influenza is a serious respiratory infectious disease caused by the influenza A virus, which belongs to the influenza genus and the Orthomyxoviridae family [1]. Avian influenza virus is categorized into low-pathogenic avian influenza (LPAI) virus and highly pathogenic avian influenza (HPAI) virus [1]. The viruses naturally exist among wild aquatic birds globally, and they have the capacity to infect domestic birds, other bird species, and various animal populations [2]. Wild aquatic birds release avian influenza viruses into the environment through their mucus, feces, and saliva during migration. Humans and domestic birds can become infected by coming into contact with these contaminated fluids [3]. Some symptoms that can be observed in domestic birds during a disease outbreak include decreased egg production, soft-shelled eggs, swelling, loss of appetite, diarrhea, respiratory issues, and sudden death [4]. In humans, it may cause fever, cough, sore throat, muscle pain, shortness of breath, headache, and eye infections [5, 6]. This infectious disease not only threatens public health but also results in significant economic losses for farmers relying on income from domestic birds [7]. In 2020, Europe reported 302 cases of highly pathogenic avian influenza (HPAI), with wild birds accounting for the majority of these cases [8]. Moreover, between 2003 and 2022, 868 human cases of avian influenza, which resulted in 457 deaths, were reported worldwide [9]. Additionally, in 2023, 37 domestic bird outbreaks and 120 wild bird outbreaks were reported across various countries globally. These outbreaks led to the culling of approximately 2.5 million domestic birds worldwide, with the H5N1 sub-type being predominant [9]. These economic hardships can deepen poverty and force migration as families seek new livelihoods. Public fear and healthcare burdens may increase, especially in areas with human cases [10]. Frequent outbreaks of avian influenza worldwide highlight the need for a thorough understanding of its transmission dynamics and the identification of the most sensitive parameters influencing its spread. Such knowledge is essential for implementing appropriate interventions to control the disease.

Most existing studies have focused on developing mathematical models for the transmission dynamics of avian influenza, incorporating control interventions targeting humans and domestic poultry, while other domestic bird species, such as pigeons, peacock have been largely overlooked. For example, [11] formulated a deterministic model to assess various intervention measures against avian influenza A (H7N9) infection. The results revealed that minimizing the interaction rate and culling infected poultry are highly effective in eliminating infections in both populations. [12] studied the nonlinear adaptive control of an avian influenza model, incorporating slaughter, educational campaigns, and treatment found that poultry slaughtering is essential in eliminating the source of avian influenza virus in the population. The study of [13] established that awareness programs through education and information dissemination, treatment, and psychological support are key in managing the disease. Additionally, [14] established that more saturation and psychological levels significantly decrease the number of infected humans, and in turn, reduces infection in the community. Furthermore [15] formulated an optimal control model and found that vaccination and medical treatment can significantly reduce the numbers of exposed and infectious individuals. Despite numerous studies, the contribution of non-domestic poultry which follows in a large category of domestic birds such as pigeons, peacocks remain poorly understood. This study intends to use a mathematical deterministic model incorporating humans and domestic birds to assess the impacts of different control interventions. The rest of the paper is organized as follows; model formulation is presented in Section 2. Section 3 discusses an Objective functional for an avian influenza, while Section 4 presents numerical results. Conclusion and recommendation are done in Section 5.

2. MODEL FORMULATION

2.1. Description of state variables and parameters. The flow diagram by [16] has been extended to include a vaccination class for domestic birds. Thus, the mathematical model for the transmission dynamics of avian influenza and its control measures such as vaccination of domestic birds (η_1), proper hygiene practice (η_2), and culling of infected birds (η_3) is formulated by considering the interactions among the human population, domestic birds, and the contaminated environment containing the avian influenza virus. The total human population $N_H(t)$ is

divided into three compartments: susceptible humans $S_H(t)$, infected humans $I_H(t)$, and recovered humans $R_H(t)$. The susceptible humans are those who currently not infected with avian influenza but have the potential to become infected. These individuals are not in danger of avian influenza infections whenever they maintain proper hygiene practices at a rate of η_2 , where $0 < \eta_2 \leq 1$. On the other hand, a proportion $(1 - \eta_2)$ of the total susceptible populations that do not maintain proper hygiene practices become infected through contact with infected domestic birds and a contaminated environment at the force of infection, as defined by

$$(1) \quad \lambda_1 = \gamma_1 B + \gamma_2 I_D.$$

Where γ_1 signifies the transmission rate from contaminated environments while γ_2 denotes the rate at which susceptible humans contract infections through direct contact with infected domestic birds. Infected humans shed the virus into the environment through respiratory secretions, such as coughs and sneezes, as well as other bodily fluids, including saliva, mucus, and occasionally feces. The recovered population from avian influenza infection consists of individuals who develop temporary protective immunity but gradually lose this immunity over time, eventually rejoining the susceptible population.

The domestic bird population is categorized into three compartments: susceptible domestic birds $S_D(t)$, who are healthy but at risk of infection; vaccinated domestic birds $V_D(t)$, who have been immunized and do not carry avian influenza; and infected domestic birds $I_D(t)$, who are infected with the virus, shed it into the environment and can transmit the disease to others. The susceptible class is recruited by $(1 - \eta_1)\Lambda_2$ and ρV_D , while it decreases due to natural deaths at rate μ_2 and the force of infections at rate λ_2 that is defined by

$$(2) \quad \lambda_2 = \beta_1 B + \beta_2 I_D.$$

Parameter β_1 indicates the transmission rate of infection from contaminated environments whereas β_2 represents the rate at which susceptible domestic birds contract an infection through direct contact with infected domestic birds. The susceptible domestic birds are vaccinated at a rate of $\eta_1(t)$, where $0 \leq \eta_1 \leq 1$. When $\eta_1 = 0$, it signifies that vaccination is not implemented. Conversely, when $\eta_1 = 1$, it indicates that vaccination is maximally implemented. We assess the effectiveness of the vaccine not only by its reported efficacy (ω) but also by considering the

rate at which its protection wanes (ρ) over time. The vaccinated class declines due to waning of the vaccine at a rate ρ , where $0 < \rho \leq 1$. When ρ is closer to zero, the waning rate is very slow, meaning that immunity lasts for a long time. In contrast, when ρ is closer to one, the waning rate is much faster, indicating that immunity is quickly lost. The vaccinated population decreases due to imperfect vaccine efficacy, occurring at a rate of $(1 - \omega)$, where ω represents the efficacy of the vaccine. The value of ω lies within the range $(0, 1]$. The population of infected domestic birds decreases due to natural death (μ_2), disease-induced mortality (τ), and the culling of infected birds (η_3). Migratory waterfowl and shorebirds are natural carriers of avian influenza viruses that contaminate the environment (B) at rate θ . Furthermore, infected humans and domestic birds also contribute to this contamination by shedding avian influenza viruses at rates of δ_1 and δ_2 , respectively. Avian influenza viruses naturally decrease in the environment at a rate of σ . The model is constructed based on the following assumptions: The exposed classes are not included in the analysis because of their short incubation period [17]; The model does not account for direct interactions between susceptible domestic birds and infected wild birds or other animals, as it focuses on assessing the role of a contaminated environment in avian influenza transmission; direct human-to-human transmission of avian influenza is excluded due to its rarity [18]. Vaccine efficacy is imperfect and denoted by $\omega < 1$, where ω represents the level of protection conferred [19].

2.2. System of equations. The avian influenza transmission dynamics model is presented by a non-linear system of ordinary differential equations as shown in Eq. (3).

$$(3) \quad \left. \begin{aligned} \dot{S}_H &= \Lambda_1 + \psi R_H - (\mu_1 + (1 - \eta_2)\lambda_1)S_H, \\ \dot{I}_H &= (1 - \eta_2)\lambda_1 S_H - (\mu_1 + \varepsilon + \alpha)I_H, \\ \dot{R}_H &= \alpha I_H - (\psi + \mu_1)R_H, \\ \dot{S}_D &= (1 - \eta_1)\Lambda_2 + \rho V_D - (\mu_2 + \eta_1 + \lambda_2)S_D, \\ \dot{I}_D &= \lambda_2 S_D + (1 - \omega)\lambda_2 V_D - (\mu_2 + \tau + \eta_3)I_D, \\ \dot{V}_D &= \eta_1 \Lambda_2 + \eta_1 S_D - (\mu_2 + (1 - \omega)\lambda_2 + \rho)V_D, \\ \dot{B} &= \theta + \delta_1 I_H + \delta_2 I_D - \sigma B. \end{aligned} \right\}$$

The initial conditions are:

$$S_H(0) > 0; I_H(0) \geq 0; R_H(0) \geq 0; S_D(0) > 0; I_D(0) \geq 0; V_D(0) \geq 0; \text{ and } B(0) > 0.$$

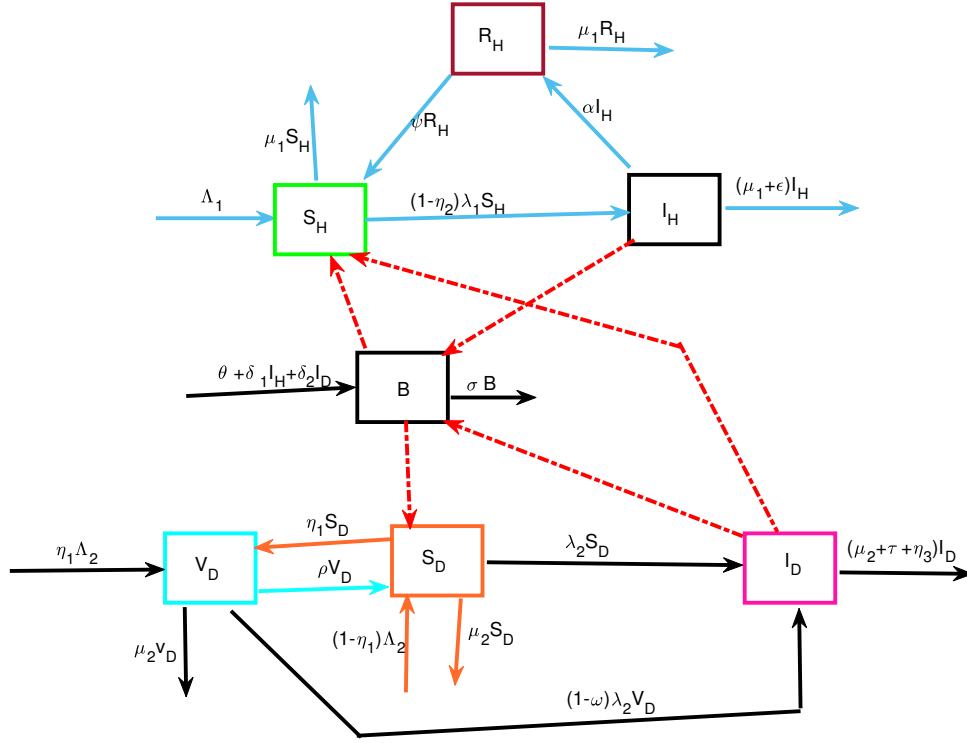


FIGURE 1. The flow diagram for the avian influenza transmission dynamics with control measures for humans and domestic birds.

2.3. Theoretical analysis.

2.3.1. Positivity of the model solution. In this section, we show the solution of model system (3) is non negative for $t \geq 0$

Theorem 2.1. *If the initial conditions are non negative, then the solution*

$\Gamma = \{(S_H, I_H, R_H, S_D, I_D, V_D, B) \in \mathbb{R}_+^7\}$ *of model (3) maintains positive value for $t \geq 0$.*

Proof. Consider 1st equation of model (3). $\frac{dS_H}{dt} = \Lambda_1 + \psi R_H - (\mu_1 + (1 - \eta_2)\lambda_1)S_H$, which reduces to

$$(4) \quad \frac{dS_H}{dt} \geq -(\mu_1 + (1 - \eta_2)\lambda_1)S_H$$

By separation of variables and integrating inequality (4), we get

$$S_H(t) \geq S_H(0)e^{-\int_0^t (\mu_1 + (1 - \eta_2)\lambda_1)ds} > 0,$$

With the same procedures, the rest equations will be

$$I_H(t) \geq I_H(0)e^{-(\mu_1 + \epsilon + \alpha)t} > 0, R_H(t) \geq R_H(0)e^{-(\psi + \mu_1)t} > 0, S_D \geq S_D(0)e^{-\int_0^t (\mu_2 + \eta_1 + \lambda_2)ds} > 0,$$

$$I_D(t) \geq I_D(0)e^{-(\mu_2+\tau+\eta_3)t} > 0, V_D \geq V_D(0)e^{-\int_0^t(\mu_2+(1-\omega)\lambda_2+\rho)ds} > 0, B(t) \geq B(0)e^{-\sigma t} > 0.$$

Thus the solution of model (3) is non negative for all $t \geq 0$ \square

2.3.2. Disease free equilibrium (E^0) and effective reproduction number (R_e). Disease free equilibrium, denoted as (E^0), is a state where the avian influenza disease does not persist in both human and domestic bird populations. To obtain $E^0 = (S_H^0, I_H^0, R_H^0, S_D^0, I_D^0, V_D^0, B^0)$ set the left-hand side of Eq. (3) to zero. Upon solving the resulting system, we obtain:

$$E^0 = \left(\frac{\Lambda_1}{\mu_1}, \quad 0, \quad 0, \quad \frac{\Lambda_2(\mu_2(1-\eta_1)+\rho)}{\mu_2(\eta_1+\mu_2+\rho)}, \quad 0, \quad \frac{\Lambda_2\eta_1(\mu_2+1)}{\mu_2(\eta_1+\mu_2+\rho)}, \quad \frac{\theta}{\sigma} \right).$$

The effective reproduction number (R_e) is the average number of secondary infections produced by a single infected human or domestic bird in a population where some humans and domestic birds are already immune due to vaccination or other factors. The next-generation method which is given by $FV^{-1} = \left(\frac{\partial \mathcal{F}_i(E^0)}{\partial x_j} \right) \left(\frac{\partial \mathcal{V}_i(E^0)}{\partial x_j} \right)$ is applied to compute the effective reproduction number. $\mathcal{F}(x_i)$ represents the newly infected individuals enter in the compartment and $\mathcal{V}(x_i)$ denotes the individual leaving or exiting the infected compartment.

From the model system (3), we followed the same procedure used by [16], and the effective reproduction number (R_e) was found to be:

$$R_e = \frac{R_{HB} + R_{DB} + \sqrt{(R_{HB} - R_{DB})^2 + 4R_{HDB}}}{2},$$

where,

$$\begin{aligned} R_{HB} &= \frac{(1-\eta_2)\gamma_1\delta_1\Lambda_1}{b_3\mu_1\sigma}, \quad R_{DB} = \frac{b_2(\beta_1\delta_2+\beta_2\sigma)\Lambda_2}{b_1b_4\sigma}, \\ R_{HDB} &= \frac{(1-\eta_2)b_2\beta_1\delta_1(\gamma_1\delta_2+\gamma_2\sigma)\Lambda_1\Lambda_2}{b_1b_3b_4\mu_1\sigma^2}, \quad b_1 = \mu_2(\mu_2+\rho+\eta_1), \\ b_2 &= \mu_2(1-\eta_1)+\rho+(1-\omega)(\eta_1\mu_2+\eta_1), \quad b_3 = \mu_1+\varepsilon+\alpha, \quad b_4 = \mu_2+\tau+\eta_3. \end{aligned}$$

R_{HB} represents the expected number of humans who become infected with avian influenza in environments where control measures are implemented, while R_{DB} represents the expected number of domestic birds infected in the same environments under those control measures.

In the absence of control measures ($\eta_i = 0, \forall i \in \{1, 2, 3\}$), the effective reproduction number (R_e) reduces to the basic reproduction number (R_0).

2.4. The impact of control strategies on the persistence of avian influenza. . Based on the sensitivity analysis results by [16], it was observed that the bird-to-bird transmission rate (β_2), contaminated environment-to-human transmission rate (γ_2), infected bird-to-human transmission rate (γ_1), contaminated environment-to-domestic bird transmission rate (β_1), and infected human-to-environment transmission rate (δ_1) are the most influential parameters in the spread of the disease. To reduce these parameters, the study proposes the following intervention programs: a bird vaccination program, denoted by η_1 , which is introduced to enhance immunity during disease outbreaks. This program aims to lower the transmission rate from the contaminated environment (β_1). Encouraging proper hygiene practices for humans (η_2), especially when exposed to contaminated environments, It helps reduce the transmission rate from these areas (γ_2). It also prevents the spread of avian influenza virus to the environment (δ_1) through coughing or sneezing. Moreover, the culling of infected domestic birds (η_3), aims to prevent the spread of the virus to other species.

TABLE 1. Model parameters and their values

Symbol	Values (day^{-1})	Source	Symbol	Values (day^{-1})	Source
Λ_1	300	[20]	γ_1	0.00008	[14]
α	0.9	[21]	β_1	0.00004	assumed
μ_1	0.0000391	[22]	β_2	0.00002	[23]
ε	0.000001	[20]	δ_2	0.008	assumed
ψ	0.5	assumed	δ_1	0.0006	assumed
σ	0.875	[24]	τ	0.05	[23]
Λ_2	1000	[22]	γ_2	0.0008	assumed
μ_2	0.01	[23]	θ	100	assumed

Using the parameter values provided in Table 1, we substitute the control rates (η_1, η_2, η_3) $\in [0, 1]$ and vaccination efficacy $\omega \in (0, 1]$ into the model. These parameter values represent the effectiveness of the three control interventions: vaccination of domestic birds (η_1), proper hygiene practices (η_2) and culling of infected flocks (η_3). Then, we use Matlab codes to draw

line graphs and contour plots to study the effect of each control intervention individually as well as the combined impact of two control interventions.

From Fig. 2 (a), we observe that the disease is eliminated from the population when proper hygiene of at least 95% is practiced. Based on the information provided in Fig. 2 (b), it shows that the culling of infected domestic birds alone, without implementing any other control strategies, is not sufficient to eradicate the disease.

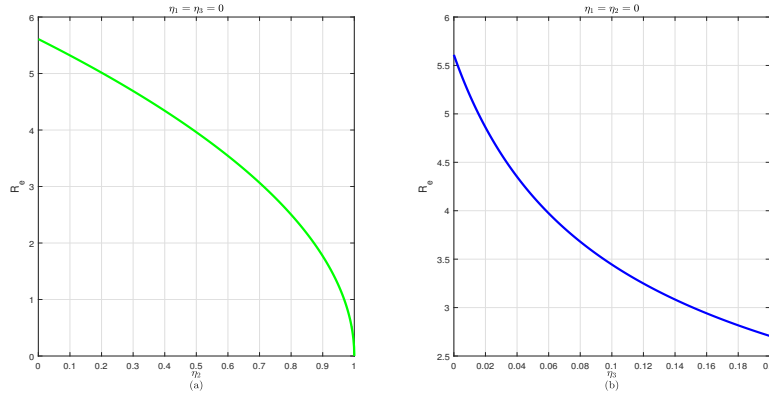


FIGURE 2. The effects of η_2 and η_3 on R_e independently.

According to the information presented in Fig. 3, highly effective vaccines play a crucial role in the eradication of avian influenza. The results indicate that a vaccine with 100% efficacy can lead to the elimination of avian influenza, provided that the susceptible domestic bird population is vaccinated at a minimum rate of 0.1 per day.

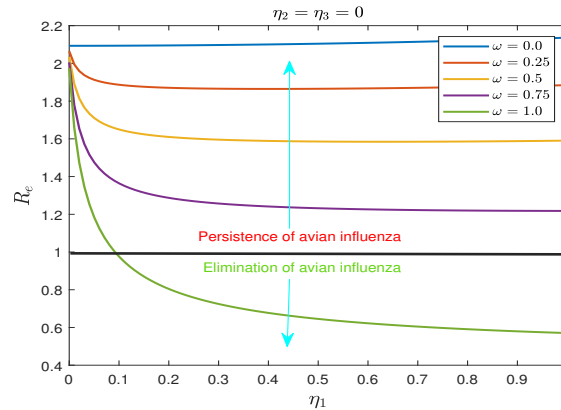


FIGURE 3. The effect of vaccination η_1 on R_e with different vaccine efficacy (ω).

Fig. 4 demonstrates that by employing a combination of improved hygiene practices (η_2) and vaccination (η_1) with varying levels of vaccine efficacy, the disease can be effectively eradicated without the need for culling infected birds. The findings in Fig. 4 (a-d) show that to eradicate avian influenza using vaccination η_1 with at least vaccine efficacy of 50% is recommended, combined with maintaining hygiene practices at a minimum rate of 60% consistently, will result in the elimination of avian influenza

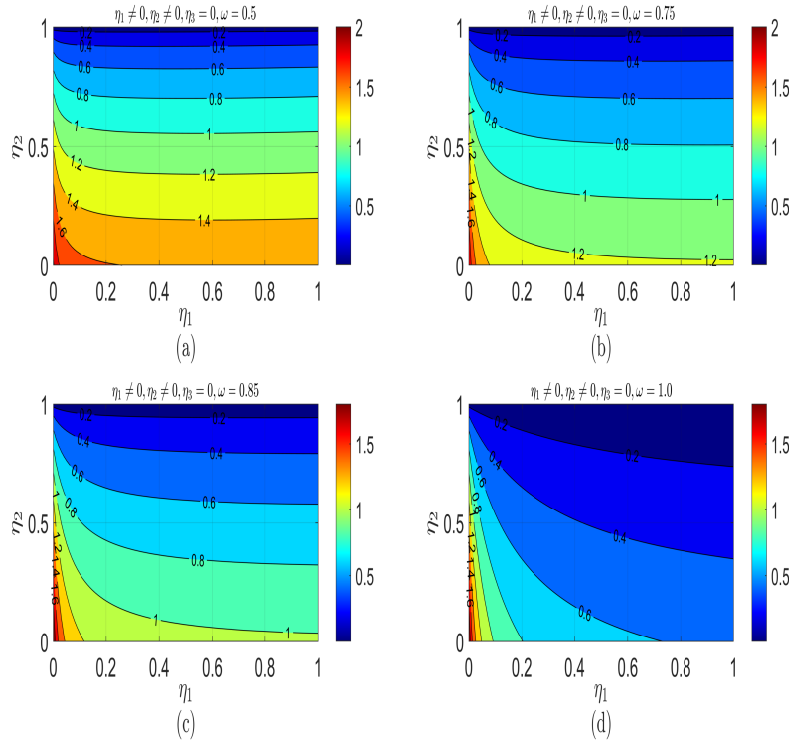


FIGURE 4. The effect of proper hygiene practices (η_2) and vaccination (η_1) on the R_e with different vaccine efficacy rate (ω).

Fig. 5 illustrates that increasing vaccine efficacy from 0.5 to 1.0, along with culling infected domestic birds, leads to a reduction in the effective reproduction number (R_e). This emphasizes the important role of vaccination in controlling disease transmission, especially when combined with interventions like culling infected birds.

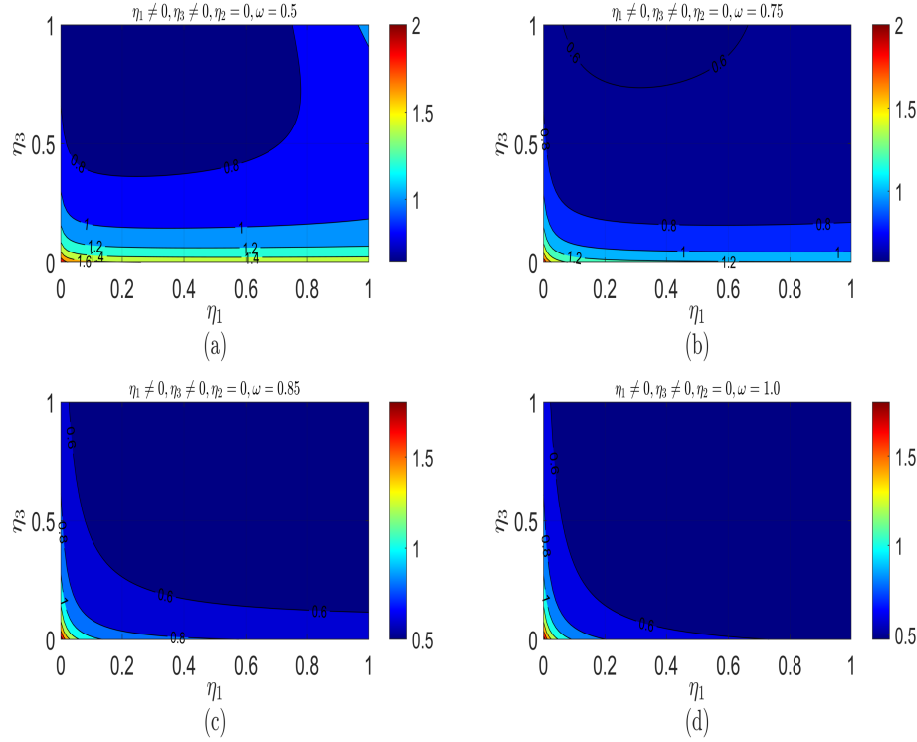


FIGURE 5. The effect of culling the infected domestic birds (η_3) and vaccination (η_1) on the R_e with varying vaccine efficacy rate (ω).

Fig. 6 highlights how different levels of proper hygiene practices (η_2) and culling (η_3) influence the effective reproduction number (R_e). It shows that both measures are important for controlling the epidemic and that their combined application can achieve more effective results.

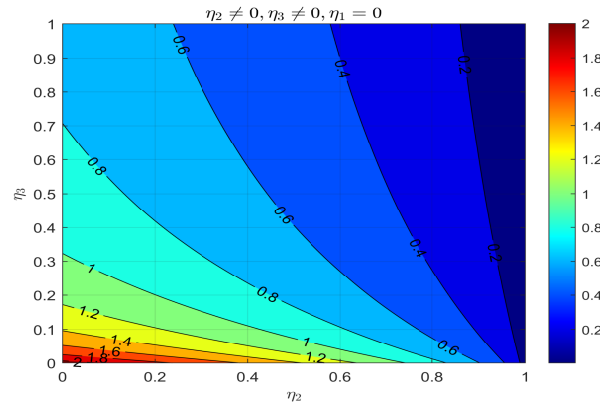


FIGURE 6. The effect of proper hygiene practices (η_2) and culling the infected flock (η_3) on R_e

3. OBJECTIVE FUNCTIONAL

The application of optimal control theory aims to identify the most cost-effective strategies for managing the spread of avian influenza. This approach involves determining the best combination of interventions that can effectively reduce the outbreak while simultaneously minimizing economic costs and resource utilization. Therefore, the objective functional that is subject to the non-linear system (3) is defined by

$$(5) \quad J(I_H, I_D, \eta_1, \eta_2, \eta_3) = \int_0^{tf} \left(Q_1 I_H + Q_2 I_D + \frac{1}{2} g_1 \eta_1^2 + \frac{1}{2} g_2 \eta_2^2 + \frac{1}{2} g_3 \eta_3^2 \right) dt.$$

The values Q_i and g_j refer to the weighting coefficients for the infected state variables and the control variables, respectively, where $i \in \{1, 2\}$ and $j \in \{1, 2, 3\}$. The linear terms $Q_1 I_H$ and $Q_2 I_D$ of the Lagrangian represent the overall social cost associated with infected humans and domestic birds, respectively. Social costs refers to expenses incurred from hospital admissions and outpatient care, as well as costs associated with responding to infected domestic birds. The $\frac{1}{2} g_1 \eta_1^2$, $\frac{1}{2} g_2 \eta_2^2$ and $\frac{1}{2} g_3 \eta_3^2$ terms are quadratic expressions that indicate the costs associated with declining saturation effects from the implementation of vaccination programs, proper hygiene and culling interventions, respectively. The value tf denotes the duration over which control interventions are implemented.

The aim is to determine the controls η_1 , η_2 , and η_3 that simultaneously lower the number of infected humans and infected domestic birds at the minimum costs implemented, such that:

$$(6) \quad J(\eta_1^*, \eta_2^*, \eta_3^*) = \min_{\Omega} J(\eta_1, \eta_2, \eta_3)$$

where $\Omega = \{(\eta_1^*, \eta_2^*, \eta_3^*) \in L^1(0, T) | 0 \leq \eta_1 \leq 1, 0 \leq \eta_2 \leq 1, 0 \leq \eta_3 \leq 1\}$.

For the minimization problem, the Pontryagin's Maximum Principle, which is a powerful tool in optimal control theory [25] is applied to provides the necessary conditions for optimality of a control problem. When dealing with non-linear differential equations with complex dependencies, directly calculating derivatives is computationally expensive and numerically unstable. However, by incorporating adjoint variables, which are derived from the Hamiltonian function H , it is possible to simplify and facilitate the computation of the optimal solution. Thus,

$$(7) \quad H(y_j, \eta_q, A_j, t) = L(I_H, I_D, \eta_q, t) + \sum_{j=1}^7 A_j f(y_j, \eta_q, t)$$

for $j \in \{1, 2, 3, 4, 5, 6, 7\}$ and $q \in \{1, 2, 3\}$,

where y_j represents model state variables, η_q represent control strategies, A_j represent adjoint or Co-state variable, $L(I_H, I_D, \eta_q, t)$ represent Lagrangian function, $f(y_j, \eta_q, t)$ represent model dynamical system includes control strategies.

$H(y_j, \eta_q, A_j, t)$ is expanded as;

$$(8) \quad \left. \begin{aligned} H = & Q_1 I_H + Q_2 I_D + \frac{1}{2} (g_1 \eta_1^2 + g_2 \eta_2^2 + g_3 \eta_3^2) \\ & + A_1 (\Lambda_1 + \psi R_H - ((1 - \eta_2)(\gamma_1 B + \gamma_2 I_D) + \mu_1) S_H) \\ & + A_2 ((1 - \eta_2)(\gamma_1 B + \gamma_2 I_D) S_H - (\mu_1 + \varepsilon + \alpha) I_H) \\ & + A_3 (\alpha I_H - (\mu_1 + \psi) R_H) \\ & + A_4 ((1 - \eta_1) \Lambda_2 + \rho V_D - (\mu_2 + \eta_1 + \beta_1 B + \beta_2 I_D) S_D) \\ & + A_5 ((\beta_1 B + \beta_2 I_D) S_D + (1 - \omega)(\beta_1 B + \beta_2 I_D) V_D - (\mu_2 + \tau + \eta_3) I_D) \\ & + A_6 (\eta_1 \Lambda_2 + \eta_1 S_D - (\mu_2 + (1 - \omega)(\beta_1 B + \beta_2 I_D) + \rho) V_D) \\ & + A_7 (\theta + \delta_1 I_H + \delta_2 I_D - \sigma B). \end{aligned} \right\}$$

To obtain optimal control, the adjoint functions must obey the following:

$$A'_j = -\frac{\partial H}{\partial y_j}, \forall y_j \in \{S_H, I_H, R_H, S_D, I_D, V_D, B\} \text{ and } j \in \{1, 2, 3, 4, 5, 6, 7\}.$$

Thus, by applying Pontryagin's maximum principle and the existence result for optimal control, as detailed by [26] we obtain: There exist three optimal controls: η_1^* , η_2^* and η_3^* , along with the solution $S_H^*, I_H^*, R_H^*, S_D^*, I_D^*, V_D^*, B^*$ of the corresponding model system (3), that minimize the objective function $J(\eta_1, \eta_2, \eta_3)$ over Ω . Then there exist adjoint function A_i for $i = 1, 2, 3, 4, 5, 6, 7$ such as

$$(9) \quad \left. \begin{aligned} \frac{dA_1}{dt} &= (1 - \eta_2)(\gamma_1 B + \gamma_2 I_D)(A_1 - A_2) + A_1 \mu_1, \\ \frac{dA_2}{dt} &= A_2(\mu_1 + \varepsilon + \alpha) - (\delta_1 A_7 + \alpha A_3 + Q_1), \\ \frac{dA_3}{dt} &= A_3(\mu_1 + \psi) - A_1 \psi, \\ \frac{dA_4}{dt} &= (\beta_1 B + \beta_2 I_D)(A_4 - A_5) + \eta_1(A_4 - A_6) + \mu_2 A_4, \\ \frac{dA_5}{dt} &= -Q_2 + (1 - \eta_2)\gamma_2 S_H(A_1 - A_2) + \beta_2 S_D(A_4 - A_5) + (1 - \omega)\beta_2 V_D(A_6 - A_5) - \delta_2 A_7, \\ \frac{dA_6}{dt} &= (1 - \omega)(\beta_1 B + \beta_2 I_D)(A_6 - A_5) + (\mu_2 + \rho)A_6 - \rho A_4 \\ \frac{dA_7}{dt} &= (1 - \eta_2)\gamma_1 S_H(A_1 - A_2) + \beta_1 S_D(A_4 - A_5) + (1 - \omega)\beta_1 V_D(A_6 - A_5) + A_7 \sigma. \end{aligned} \right\}$$

with transversality condition

$$(10) \quad A_i(t_f) = 0, i = 1, 2, 3, 4, 5, 6, 7.$$

Then, the following characterizations hold

$$(11) \quad \left. \begin{aligned} \eta_1^* &= \min \left(\max \left(0, \frac{(A_4 - A_6)S_D}{g_1} \right), 1 \right), \\ \eta_2^* &= \min \left(\max \left(0, \frac{(A_2 - A_1)\lambda_1 S_H}{g_2} \right), 1 \right), \\ \eta_3^* &= \min \left(\max \left(0, \frac{A_5 I_D}{g_3} \right), 1 \right). \end{aligned} \right\}$$

where A_1, A_2, A_4, A_5, A_6 are solutions of the system (9)

Proof. The adjoint (or costate) system and transversality conditions, as described in Eqs. (9) and (10), respectively, are standard results derived from Pontryagin's Maximum Principle for determining optimal control strategies. Thus, the costate system (9) is obtained by computing the partial derivatives of the Hamiltonian (H) Eq. (8) with respect to each state variable as follows:

$$\begin{aligned} \frac{dA_1}{dt} &= -\frac{\partial H}{\partial S_H}, \quad A_1(t_f) = 0, \\ &\vdots \\ \frac{dA_7}{dt} &= -\frac{\partial H}{\partial B}, \quad A_7(t_f) = 0. \end{aligned}$$

We derive the optimality Eq. (11) by taking the partial derivatives of the Hamiltonian Eq. (8) with respect to each control parameter and solving for the optimal values of η_i^* .

Thus

$$(12) \quad \left. \begin{aligned} \frac{\partial H}{\partial \eta_1} &= g_1 \eta_1 - A_4 S_D + A_5 S_D = 0, \\ \frac{\partial H}{\partial \eta_2} &= g_2 \eta_2 + \lambda_1 S_H (A_1 - A_2) = 0, \\ \frac{\partial H}{\partial \eta_3} &= g_3 \eta_3 - A_5 I_D = 0. \end{aligned} \right\}$$

Upon solving the Eq. (12), we obtain the control values as follows:

$$\eta_1^* = \frac{(A_4 - A_6)S_D}{g_1}, \eta_2^* = \frac{(A_2 - A_1)\lambda_1 S_H}{g_2}, \text{ and } \eta_3^* = \frac{A_5 I_D}{g_3}.$$

□

4. NUMERICAL SIMULATION FOR AN OPTIMAL CONTROL PROBLEM

This section provides a detailed numerical analysis of the optimal control model system (8) for avian influenza. It focuses on vaccination (η_1), proper hygiene practices (η_2), and culling of the infected domestic birds (η_3). The optimal control problem is solved numerically using the forward-backward sweep method to implement both the model system (3) and the adjoint system (9) in MATLAB, applying the parameter values listed in Table 1. The process starts by solving the model system (3) forward in time using the fourth-order Runge-Kutta method, based on the provided initial values of the state variables. Thereafter, the backward fourth-order Runge-Kutta method utilizes the calculated values of the state variables along with the initial control values to solve the adjoint Eq. (9) with given transversality conditions Eq. (10). The adjoint and state variables are then utilized to update the control variables using MATLAB code, based on the initial cost estimates for vaccination, proper hygiene, and culling of infected birds. The costs for η_1 , η_2 , and η_3 are assumed to be 1.30 dollars, 3.50 dollars, and 0.75 dollars, respectively [9]. The control strategies we consider involve both single and multiple interventions, as detailed below.

4.1. Strategy I: The use of vaccination alone (η_1). The implementation of this strategy aimed to minimize the objective function (J) by using a single control option, η_1 , while setting all other control options to zero.

Fig. 7 focuses on implementing domestic bird vaccination solely to control disease transmission in humans and birds. The results show a reduction in the number of cases among domestic birds and a decrease in avian influenza viruses in the environment. However, this strategy alone is not sufficient to control the disease. The control profile in Fig. 7(d) suggests that vaccination should be sustained at maximum levels consistently throughout the entire avian influenza outbreak.

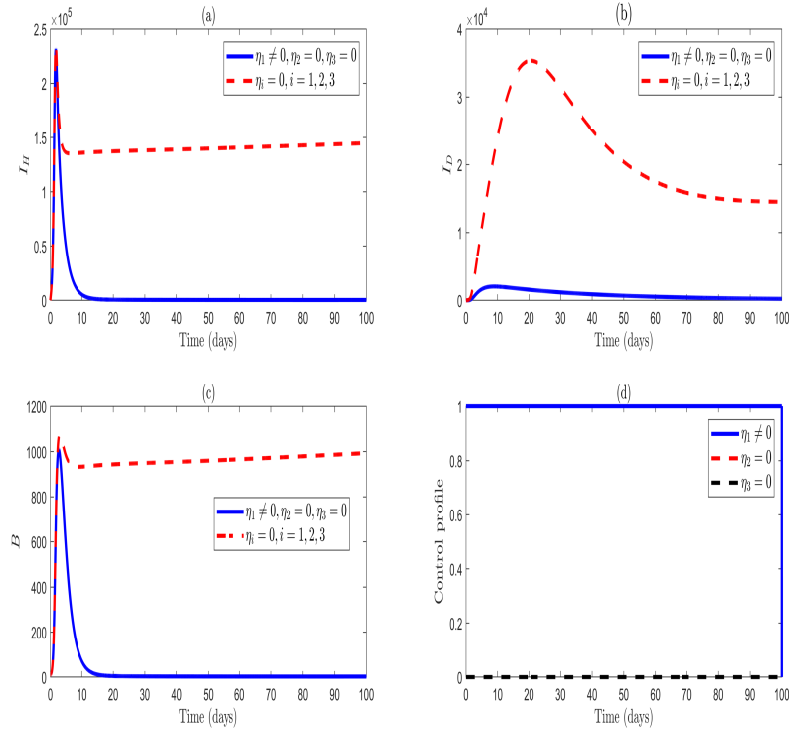


FIGURE 7. The impact of vaccination on domestic birds.

4.2. Strategy II: The use of proper hygiene alone (η_2). This strategy is implemented to minimize the objective function (J) by using only one control option, η_2 , with all other controls set to zero. Fig. 8 shows that implementing hygiene practices alone can significantly reduce the number of infected humans. However, relying solely on human hygiene practices is not sufficient to prevent avian influenza infections in domestic birds, although it can help reduce the concentration of the virus in the environment. The control profile in Fig. 8 (d) suggests that consistently maintaining maximum hygiene throughout the intervention period can effectively reduce the number of infected individuals.

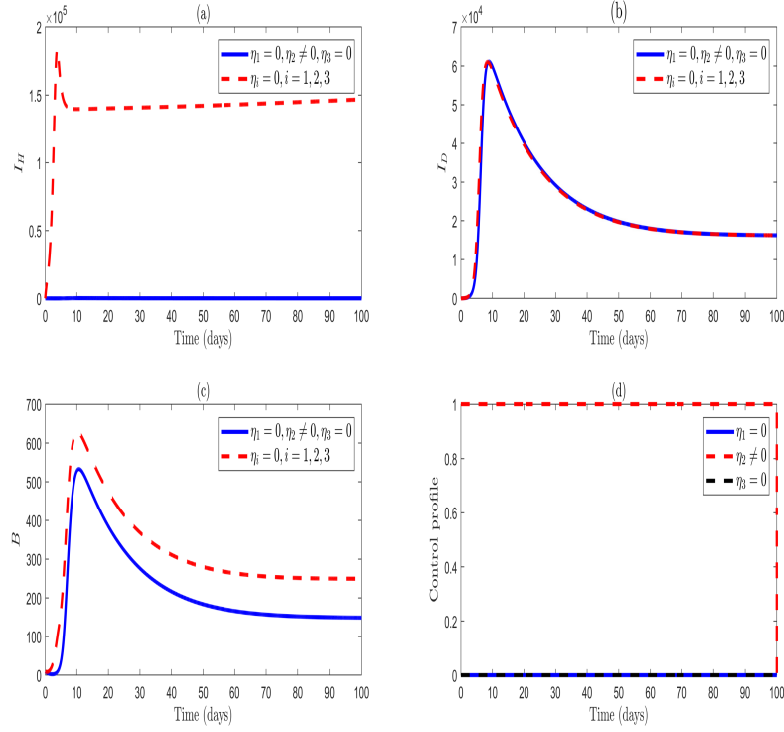


FIGURE 8. The impact of proper hygiene practices among humans.

4.3. Strategy III: The use of culling alone (η_3). This strategy aims to minimize the objective function (J) by using only control option η_3 and setting all other controls to zero. Fig. 9 demonstrates that culling infected birds alone results in a slight reduction in the number of infected humans and the concentration of avian influenza in the environment. Fig. 9(d) indicates that culling should be implemented at maximum intensity and sustained consistently throughout the duration of the outbreak.

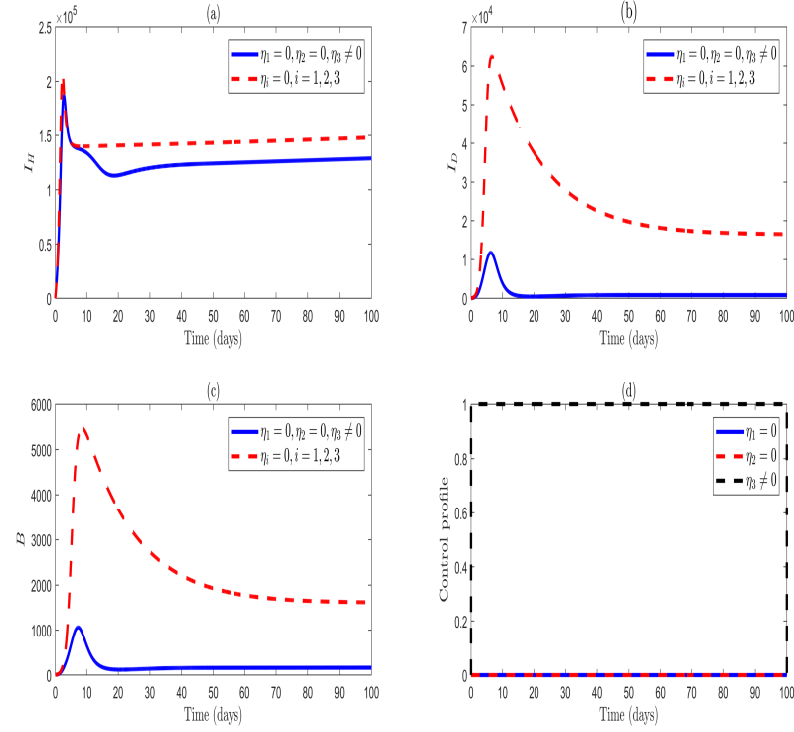


FIGURE 9. The impact of culling the infected domestic birds.

4.4. Strategy IV: The use of proper hygiene and vaccination (η_1 and η_2). This strategy focuses on minimizing the objective function (J) by utilizing control options η_1 and η_2 while keeping all other controls to zero. Fig. 10 demonstrates a notable decrease in the populations of infected humans and domestic birds, as well as in the environmental concentrations of the avian influenza virus, due to the implementation of hygiene and vaccination measures. The control profiles in Fig. 10(d) suggest that both proper hygiene practice and vaccination need to be maintained at the highest level from the beginning to the end of the disease outbreak.

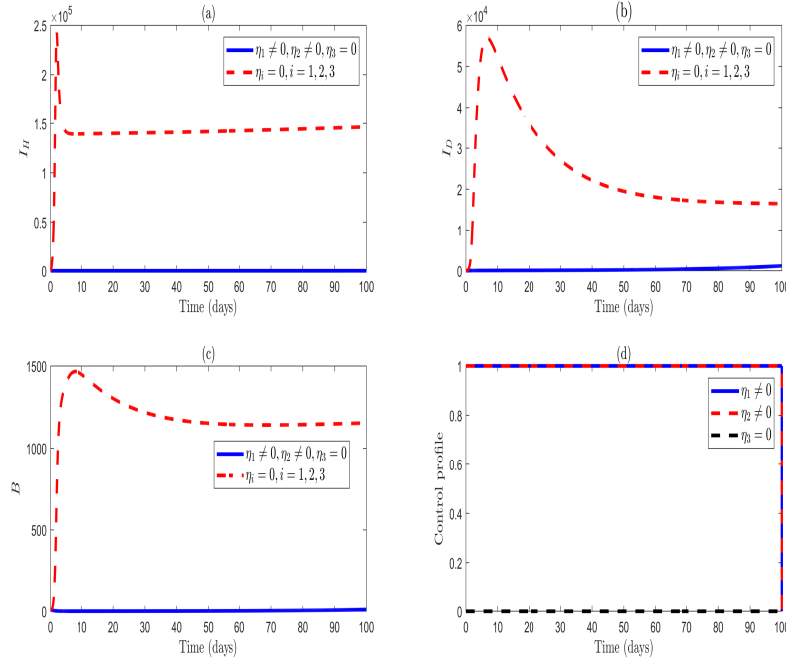


FIGURE 10. The impact of proper hygiene practices on humans and vaccination on domestic birds.

4.5. Strategy V: The use of vaccination and culling (η_1 and η_3). This strategy seeks to minimize the objective function (J) by employing control options η_1 and η_3 while setting all other controls to zero. Fig. 11 illustrates the use of domestic bird vaccination combined with culling of infected birds to control disease transmission in both humans and birds. As depicted in Fig. 11(a), the number of infected humans drops to zero within the first 20 days, while Fig. 11(c) demonstrates that avian influenza viruses are eliminated within the first 17 days. Fig. 11(b) further indicates that the number of infected domestic birds falls to zero on the first day. The control profile in Fig. 11(d) suggests that vaccination and culling should be maintained at maximum levels within the first 95 and 97 days, respectively, after which they gradually decline to zero.

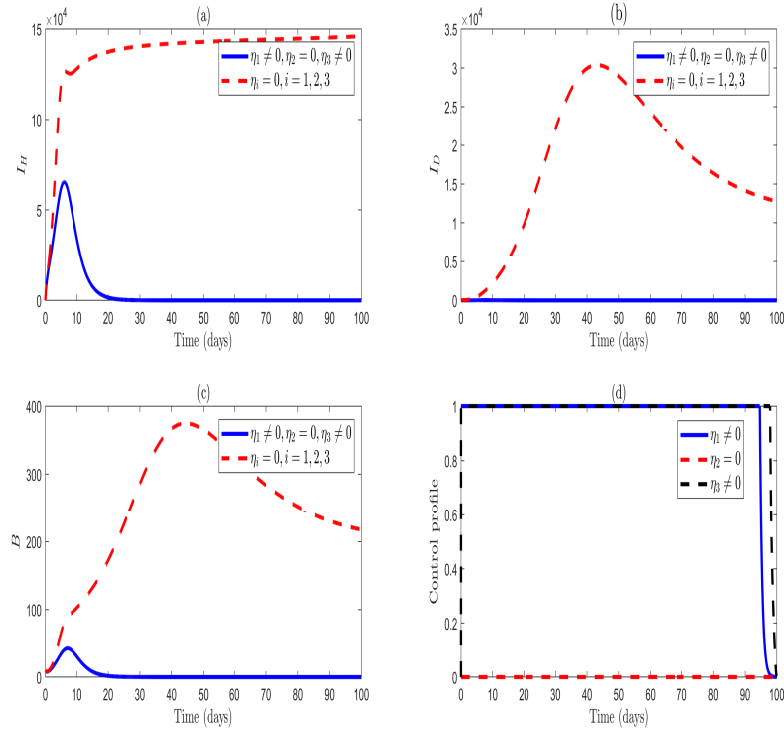


FIGURE 11. The impact of vaccination and culling the infected domestic birds.

4.6. Strategy VI: The use of proper hygiene and culling (η_2 and η_3). This strategy aims to minimize the objective function (J) by using control options η_2 and η_3 while setting all other controls to zero. Fig. 12 illustrates a significant reduction in the populations of infected humans and domestic birds, as well as a decrease in environmental concentrations of the avian influenza virus, resulting from the implementation of hygiene practices and the culling of infected birds. The control profile in Fig. 12(d) indicates that hygiene and culling should be sustained at maximum levels within the first 80 and 85 days, respectively, before abruptly declining to zero.

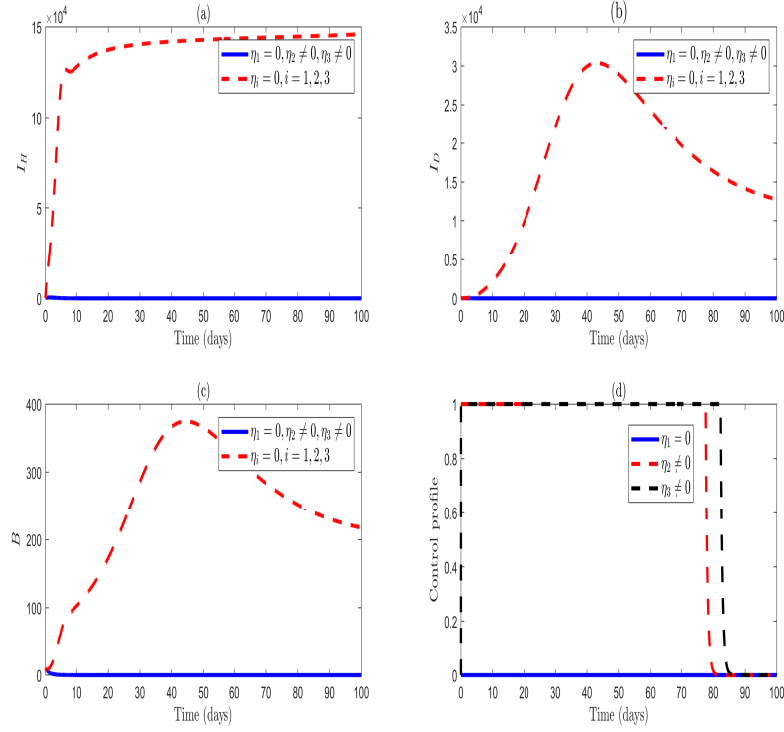


FIGURE 12. The impact of human proper hygiene practices and culling the infected domestic birds.

4.7. Strategy VII: The use of vaccination, proper hygiene and culling (η_1 , η_2 and η_3).

This strategy aims to minimize the objective function (J) by employing all the suggested control options. Fig. 13 shows a substantial decrease in the populations of infected humans and domestic birds, along with a reduction in environmental concentrations of the avian influenza virus, due to the implementation of all suggested control measures. The control profile in Fig. 13(d) suggests maintaining both controls at maximum levels for the first 68, 70 and 73 days before they sharply decline to zero. Among all strategies, strategy VII is the most effective approach, as it significantly reduces avian influenza infections in humans, domestic birds, and the viral concentration in the environment for a short period of time compared to other strategies.

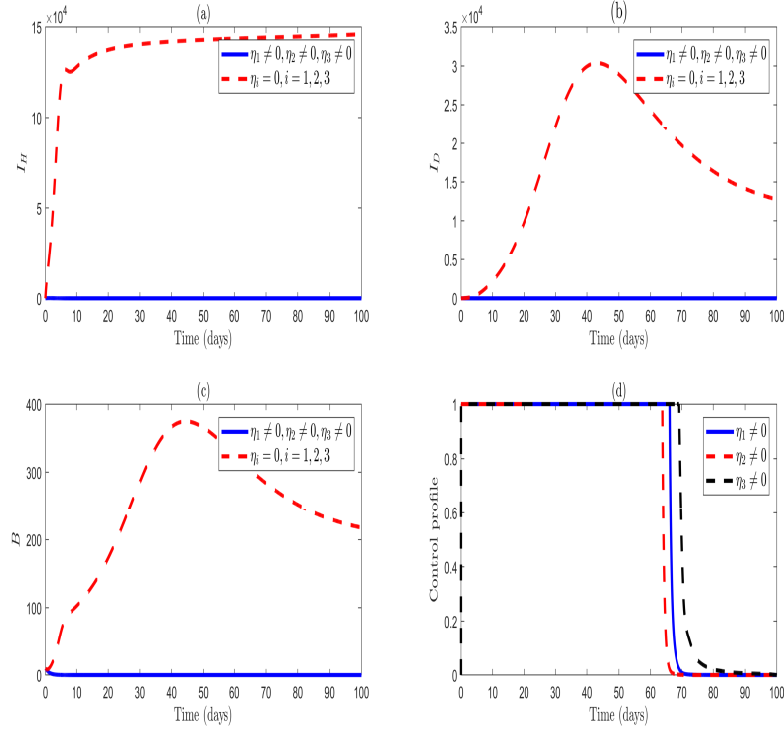


FIGURE 13. The impact of both control measures.

COST-EFFECTIVENESS ANALYSIS

By following [27, 28, 29] procedure, we perform a cost-effectiveness analysis using the Incremental Cost-Effectiveness Ratio (ICER) to justify the expenses associated with various control strategies, including domestic bird vaccination, proper hygiene practices, and the culling of infected domestic birds. ICER is calculated by dividing the difference in costs between two strategies by the difference in their effectiveness. We selected this method because it allows for the comparison of the cost-effectiveness of interventions that combine at least two control strategies. Mathematically is defined by:

$$\text{ICER} = \frac{\text{Cost of the new strategy} - \text{Cost of the baseline strategy}}{\text{Effectiveness of the new strategy} - \text{Effectiveness of the baseline strategy}}$$

TABLE 2. Incremental cost-effective ratio in ascending order of total infection averted

Strategy	Total cost (\$)	Total infection averted	ICER
IV	2.6551×10^9	3.9859×10^9	0.6662
V	6.2433×10^8	3.9966×10^9	-189.7916
VII	1.5213×10^7	4.0093×10^9	-47.9620
II	1.0336×10^{10}	4.0103×10^9	10,320.787

Table 2 shows that strategy II has a higher ICER than strategy IV, making it more costly to implement. To conserve limited resources, strategy II is excluded, and the more cost-effective strategy IV is compared with the remaining strategies.

TABLE 3. Incremental Cost-Effective Ratio in ascending order of total infection averted

Strategy	Total cost (\$)	Total infection averted	ICER
IV	2.6551×10^9	3.9859×10^9	0.6662
V	6.2433×10^8	3.9966×10^9	-189.7916
VII	1.5213×10^7	4.0093×10^9	-47.9620

Similarly, comparing Strategies IV and V in Table 3 shows a \$189.79 cost saving for Strategy V. Its lower ICER indicates that Strategy IV is more costly and less effective, so it is excluded to save resources.

TABLE 4. Incremental Cost-Effective Ratio in ascending order of total infection averted

Strategy	Total cost (\$)	Total infection averted	ICER
V	6.2433×10^8	3.9966×10^9	0.1562
VII	1.5213×10^7	4.0093×10^9	-47.9620

Table 4 shows that Strategy VII is less costly and more effective than Strategy V. This suggests that combining domestic bird vaccination, proper hygiene practices, and culling of infected birds results in greater cost savings and better outcomes. Therefore, it is the most cost-effective strategy for controlling transmission in both humans and domestic birds.

5. CONCLUSIONS AND RECOMMENDATIONS

This study presents a mathematical model, formulated using ordinary differential equations, to analyze the transmission dynamics and control of avian influenza in human and domestic bird populations. It focuses on interventions such as vaccinating susceptible domestic birds, promoting proper hygiene practices, and culling infected birds. The effective reproduction number was determined using the next-generation matrix method to evaluate the likelihood of avian influenza persisting or being eliminated in regions where the proposed control interventions are applied. Additionally the Pontryagin's Maximum Principle approach is used to analyze the optimal control problem and evaluate the cost-effectiveness of the control strategies. The findings show that implementing all three control measures is timely and cost-effective in reducing infections and environmental virus levels. By comparing all seven strategies, it is evident that strategy VII is the most effective in eliminating the avian influenza outbreak, as it requires fewer days to achieve eradication compared to the other strategies. We also use the Incremental Cost-Effectiveness Ratio (ICER) to identify the strategy that is less costly and averts more infections compared to the other strategies. The results show that Strategy VII, which combines vaccination, proper hygiene practices, and culling of infected domestic birds, has a negative ICER, indicating it is less costly and averts more infections. Therefore, it is the most cost-effective strategy among all options.

Based on the observations of avian influenza transmission, we recommend a comprehensive set of measures to be implemented. Fundamentally, vaccination programs should be put in place for domestic bird populations. This is crucial in reducing the risk of co-infection with avian influenza viruses. Furthermore, to maintain vaccine effectiveness, regular updates are needed to match the rapidly mutating influenza strains. The government should enforce hygiene measures like handwashing, equipment disinfection, and restricted access to prevent virus spread, focusing on sanitation and limiting disease entry points. Lastly, the culling or isolation of infected

domestic birds should be carried out in a timely manner to minimize the further propagation of the disease. Prompt action in identifying the containing infected populations will help prevent the virus from spreading further and potentially spilling over into human communities. A coordinated implementation of these measures is crucial to controlling the avian influenza outbreak and protecting human and domestic bird health.

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AUTHORS' CONTRIBUTIONS

- S.P. Soka conceptualization, model analysis, writing the original manuscript, editing and submitting the final draft of the manuscript.
- M. M. Mayengo has contributed by providing insightful suggestions on the methodology, reviewing, and editing the manuscript, supervision.
- M. Kgosimore has contributed by providing insightful suggestions on the methodology, reviewing, and editing the manuscript, supervision.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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