Research article

Optimal Control Model for the Spread of *Streptococcus suis* in Human Population

Lapatrada Wanaleesuksan[1], Nichaphat Patanarapeelert[1]* and Klot Patanarapeelert[2]

[1]Department of Mathematics, Faculty of Applied Science, King Mongkut's University of Technology North Bangkok, Bangkok, Thailand
[2]Department of Mathematics, Faculty of Science, Silpakorn University, Nakhon Pathom, Thailand

Curr. Appl. Sci. Technol. 2024, Vol. 24 (No. 6), e0258970; https://doi.org/10.55003/cast.2024.258970

Received: 2 June 2023, Revised: 1 March 2024, Accepted: 11 June 2024, Published: 20 August 2024

Keywords

Streptococcus suis;
zoonotic;
mathematical model;
optimal control

Abstract

Streptococcus suis infection is a zoonotic disease that can spread from pigs to humans. The infection can cause permanent deafness in people. Although it is considered as a neglected zoonotic pathogen, the prevalence of this infection has not measurably decreased in recent years. In this research, we proposed mathematical models of *S. suis* infection in both human and pig populations. Disinfectant sterilization in swine farms and educational campaigns were considered for cooperative control strategies. The aim of this study was to derive an optimal control strategy by using optimal control techniques associated with an existing epidemic model. Equilibrium points and the basic reproduction numbers were analyzed to determine the effect of control parameters in the constant case. For the optimal control problem, we showed numerically that the optimal control functions effectively reduced the number of infectious individuals within a finite time. However, the suggested control functions had more impact on the human group than the swine group. The sensitivity analysis implied that the control of swine population should be focused on the surveillance of weaning piglets.

1. Introduction

Streptococcus suis is a zoonotic bacterial pathogen of swine [1]. *Streptococcus suis* is usually carried in the upper respiratory tract, especially in the tonsils and nasopharynx of pigs, and in the reproductive system [2-4]. The disease can be transmitted from sows to piglets through the womb or vagina, and it is often found when several piglets are brought together during weaning. The

*Corresponding author: Tel.: (+66) 855422599
E-mail: nichaphat.p@sci.kmutnb.ac.th

symptoms in pigs are meningitis, arthritis, blindness, endocarditis, and pneumonia [5]. *Streptococcus suis* can be transmitted from pigs to humans by direct contact with wounds on the skin or around the conjunctiva of infected pigs, and also by the consumption of raw pork contaminated with *S. suis*. In humans, infected patients may develop symptoms ranging from fever, headache, meningitis, and septicemia [6], which can eventually lead to death. Moreover, the complications of *S. suis* infection is myasthenia gravis, and hearing loss to the point of being deaf. [6].

Streptococcus suis infection has been reported in many countries, particularly in countries with significant swine farming. Most of the global cases of infection in patients were reported in Southeast Asia such as China, Japan, Vietnam, and Thailand [7, 8]. In Thailand, there is an infection rate of about 200-350 people per year, with a high mortality rate of about 5-10% [9]. Yet, the risk factors associated with *S. suis* infection in pigs are not well-understood. Several variables such as respiratory syndrome virus co-infection at weaning, inflammation, oxidative stress, and environmental factors have been investigated [10]. It is suggested that control of infections with other pathogens, improvement of environmental conditions and reduction of stress may help reduce the incidence of *S. suis* disease in livestock. Risk factors associated with acquiring *S. suis* infection in human populations included raw pork consumption, pig-related occupation, pigs or pork exposure, and skin injury especially during pork exposure [11]. Due to preventive use of antimicrobials in livestock and lack of effective vaccines, increasing and sharing of knowledge on this pathogen is of utmost importance [12]. Food safety, hygiene, and health education should be encouraged to reduce the threat to humans [13]. Besides the losses in the swine livestock sector because of outbreak of *S. suis*, infections in human can impose a burden on healthcare systems and treatment expenses. Therefore, during the epidemic episode, the control strategy applied in livestock may be questioned regarding the reduction in the transmission potential in the human population.

To address that issue, a theoretical model in which the applied control measures were optimized was our focus. The use of mathematical model can bring a better understanding of the transmission dynamics, can help to predict disease spread patterns, and can be used to evaluate the effectiveness of the control strategy. Mathematical modeling of *S. suis* infection was proposed where the infection took place only in swine livestock [14]. The model described the effectiveness of the disinfection and vaccination measures for swine farms in southern China. Recently, Chaiya *et al.* [15] presented a mathematical model for *S. suis* infection in both swine and human populations that was concerned with the effects of humidity on the infection. However, the control measures were only targeted at livestock. Although such models include the possible relevant factors to bring about a better understanding of the dynamics of transmission and control measures, little is known about how systems evolve with time-dependent control parameters. Thus, the focused problem should aim at determining the optimal values for these control parameters. Since strict control measures on a farm require economic tradeoffs, it is interesting to see whether optimal controls that may balance cost and effectiveness can be formulated.

In this research, we formulated a mathematical model to describe the transmission dynamics of *S. suis* infection in both human and pig populations based on the model of Shen *et al.* [14]. The goal was to determine the optimal control measures applied to swine and human populations. To this end, we define two control variables, sterilization of pig farms and educational campaign strategies to control the transmission of *S. suis* in swine and humans. An epidemic model with constant control parameters was described followed by an analysis of its dynamical properties. The basic reproduction number was derived analytically and used to determine the stability condition of the equilibrium points. Then, the optimal control problem was defined, and a method of solution was described through Pontryagin's maximum principle. Finally, the numerical results for both cases were presented and the sensitivity analysis was performed and discussed.

2. Materials and Methods

2.1 Epidemic model with constant control parameters

We first formulated a mathematical model for the transmission dynamics of *S. suis* in swine and human populations. In the model, $B(t)$ denotes the amount of bacteria in the environment at time t, $S_j\ (t)$ is the number of susceptible piglets at time t, $S_a(t)$ is the number of susceptible adult pigs at time t. $I_p(t)$, $Q(t)$ and $R_p(t)$ represents the numbers of infection, quarantine and recovery of the swine population, respectively. $S_h(t)$, $I_h(t)$ and $R_h(t)$ are the numbers of susceptible, infective and recovered members of human population, respectively. A diagram of the model is presented in Figure 1.

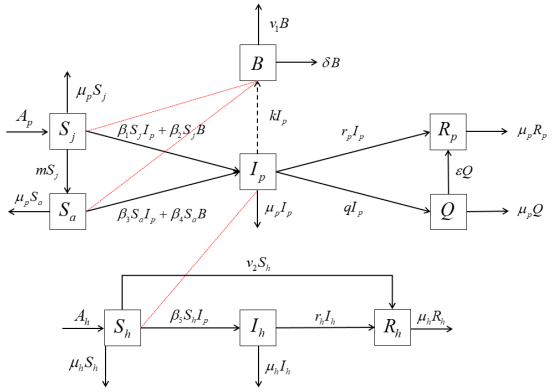


Figure 1. Transmission diagram for transmission of *S. suis*. The red lines represent interactions leading to infections.

The model can be described by a system of differential equations as follows:

$$
\begin{aligned}
\frac{dB}{dt} &= kI_p - \delta B - v_1 B,\\
\frac{dS_j}{dt} &= A_p - mS_j - (\beta_1 I_p + \beta_2 B)S_j - \mu_p S_j,\\
\frac{dS_a}{dt} &= mS_j - (\beta_3 I_p + \beta_4 B)S_a - \mu_p S_a,\\
\frac{dI_p}{dt} &= (\beta_1 I_p + \beta_2 B)S_j + (\beta_3 I_p + \beta_4 B)S_a - (r_p + \mu_p + q)I_p,\\
\frac{dQ}{dt} &= qI_p - (\varepsilon + \mu_p)Q,\\
\frac{dR_p}{dt} &= r_p I_p + \varepsilon Q - \mu_p R_p,\\
\frac{dS_h}{dt} &= A_h - \beta_5 S_h I_p - \mu_h S_h - v_2 S_h,\\
\frac{dI_h}{dt} &= \beta_5 S_h I_p - (r_h + \mu_h)I_h,\\
\frac{dR_h}{dt} &= r_h I_h - \mu_h R_h + v_2 S_h.
\end{aligned}
\tag{1}
$$

In the model, parameter k is the bacteria shedding rate from an infected pig. δ is the decay rate of bacteria in the environment. A_p and A_h represent the recruitment rates of the swine and human population, respectively. m represents the rate which junior pigs grow into adult pigs. β_1, β_2, β_3, β_4 and β_5 describe the transmission rates from infected pigs to the susceptible piglets, bacteria in the environment to the susceptible piglets, infected pigs to the susceptible adult pigs, bacteria in the environment to the susceptible adult pigs, and infected pigs to the susceptible human, respectively. q is the transfer rate from infected pigs to quarantined clinical pigs. r_p, r_h and ε represent the recovery rates of the swine, human, and quarantined population, respectively. μ_p and μ_h are the death rates of swine and human population, respectively. In model (1), we adopt constant parameters v_1 and v_2 to describe the control strategy as follows: v_1 is the rate of sterilization of pig farm to reduce number of bacteria and v_2 is the rate of educational campaign to human population.

2.2 Equilibrium points and reproduction number

By setting the right-hand side of (1) to zero, we obtain two equilibrium points as follows. The disease-free equilibrium (E^0) is in the form

$$E^0 = \left(0, S_j^0, S_a^0, 0, 0, 0, S_h^0, 0, R_h^0\right) \tag{2}$$

where

$$S_j^0 = \frac{A_p}{m+\mu_p}, S_a^0 = \frac{mA_p}{\mu_p(m+\mu_p)}, S_h^0 = \frac{A_h}{\mu_h+v_2}, R_h^0 = \frac{v_2 A_h}{\mu_h(\mu_h+v_2)}.$$

To investigate its stability, we determine the famous epidemic threshold quantity, R_0—the basic reproduction number. In epidemiology, it describes the average number of secondary cases infected by a primary case introduced into a wholly susceptible population. It was shown in general that if $R_0 < 1$, then the disease-free equilibrium is stable, but if $R_0 > 1$, an outbreak occurs [16, 17]. Thus, to gain the stability condition for E^0, it is sufficient to derive only R_0, while the full analysis of stability can be carried out for an ascertaining purpose.

We use a next generation method [18] where the matrix of new infections ($\mathscr{F}$) and the matrix of transfer ($\mathscr{V}$) are given by

$$\mathscr{F} = \begin{pmatrix} 0 \\ (\beta_1 I_p + \beta_2 B)S_j + (\beta_3 I_p + \beta_4 B)S_a \\ 0 \\ \beta_5 S_h I_p \end{pmatrix},$$

and

$$\mathscr{V} = \begin{pmatrix} -kI_p + \delta B + v_1 B \\ r_p I_p + \mu_p I_p + qI_p \\ qI_p + \varepsilon Q + \mu_p Q \\ r_h I_h + \mu_h I_h \end{pmatrix}.$$

The Jacobian matrix of $\mathscr{F}$ and $\mathscr{V}$ at E_0 are

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 \\ \beta_2 S_j^0 + \beta_4 S_a^0 & \beta_1 S_j^0 + \beta_3 S_a^0 & 0 & 0 \\ 0 & \beta_5 S_h^0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

and

$$V = \begin{pmatrix} -\delta - v_1 & k & 0 & 0 \\ 0 & r_p + \mu_p + q & 0 & 0 \\ 0 & -q & \varepsilon + \mu_p & 0 \\ 0 & 0 & 0 & r_h + \mu_h \end{pmatrix},$$

respectively.
Finding the spectral radius [18] of FV^{-1}, we obtain the basic reproduction number as

$$R_0 = \frac{A_p\left[\mu_p(k\beta_2 + (\delta + v_1)\beta_1) + m(k\beta_4 + (\delta + v_1)\beta_3)\right]}{\mu_p(m + \mu_p)(\delta + v_1)(r_p + \mu_p + q)}. \tag{3}$$

If $R_0 < 1$, the disease will die out (E^0 is stable). If $R_0 > 1$, the outbreak will persist.

Next, we consider the endemic equilibrium (E^1), and after some calculations, we obtain

$$E^1 = \left(B^*, S_j^*, S_a^*, I_p^*, Q^*, R_p^*, S_h^*, I_h^*, R_h^*\right) \tag{4}$$

where

$$\begin{aligned} B^* &= \frac{kI_p^*}{\delta + v_1}, S_j^* = \frac{A_p(\delta + v_1)}{(\delta\beta_1 + k\beta_2 + \beta_1 v_1)I_p^* + \delta m + \delta\mu_p + mv_1 + \mu_p v_1}, \\ S_a^* &= \frac{mA_p(\delta + v_1)^2}{\begin{pmatrix}(\delta\beta_1 + k\beta_2 + \beta_1 v_1)I_p^* \\ +\delta m + \delta\mu_p + mv_1 + \mu_p v_1\end{pmatrix}\begin{pmatrix}(\delta\beta_3 + k\beta_4 + \beta_3 v_1)I_p^* \\ +\delta\mu_p + \mu_p v_1\end{pmatrix}}, \\ Q^* &= \frac{qI_p^*}{\varepsilon + \mu_p}, R_p^* = \frac{(\varepsilon q + \varepsilon r_p + \mu_p r_p)I_p^*}{\mu_p(\varepsilon + \mu_p)}, S_h^* = \frac{A_h}{\beta_5 I_p^* + \mu_h + v_2}, \\ I_h^* &= \frac{A_h\beta_5 I_p^*}{(\beta_5 I_p^* + \mu_h + v_2)(\mu_h + r_h)}, R_h^* = \frac{A_h(\beta_5 r_h I_p^* + \mu_h v_2 + r_h v_2)}{\mu_h(\beta_5 I_p^* + \mu_h + v_2)(\mu_h + r_h)}, \end{aligned} \tag{5}$$

and I_p^* can be investigated from the following in equation:

$$I_p^* = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a} \tag{6}$$

Where

$$
\begin{aligned}
a &= \delta^2 q\beta_1\beta_3 + \delta^2\beta_1\beta_3\mu_p + \delta^2\beta_1\beta_3^2 r_p + \delta kq\beta_1\beta_4 + \delta kq\beta_2\beta_3 + \delta k\beta_1\beta_4\mu_p \\
&+\delta k\beta_1\beta_4 r_p + \delta k\beta_2\beta_3\mu_p + \delta k\beta_2\beta_3 r_p + 2\delta q\beta_1\beta_3 v_1 + 2\delta\beta_1\beta_3\mu_p v_1 + 2\delta\beta_1\beta_3 r_p v_1 \\
&+k^2 q\beta_2\beta_4 + k^2\beta_2\beta_4\mu_p + k^2\beta_2\beta_4 r_p + kq\beta_1\beta_4 v_1 + kq\beta_2\beta_3 v_1 + k\beta_1\beta_4\mu_p v_1 \\
&+k\beta_1\beta_4 r_p v_1 + k\beta_2\beta_3\mu_p v_1 + k\beta_2\beta_3 r_p v_1 + q\beta_1\beta_3 v_1^2 + \beta_1\beta_3\mu_p v_1^2 + \beta_1\beta_3 r_p v_1^2, \\
b &= \delta^2 mq\beta_3 + \delta^2 m\beta_3\mu_p + \delta^2 m\beta_3 r_p + \delta^2 q\beta_1\mu_p + \delta^2 q\beta_3\mu_p - \delta^2 A_p\beta_1\beta_3 + \delta^2\beta_1\mu_p^2 \\
&+\delta^2\beta_1\mu_p r_p + \delta^2\beta_3\mu_p^2 + \delta^2\beta_3\mu_p r_p + \delta kmq\beta_4 + \delta km\beta_4\mu_p + \delta km\beta_4 r_p + \delta kq\beta_2\mu_p \\
&+\delta kq\beta_4\mu_p - \delta kA_p\beta_1\beta_4 - \delta kA_p\beta_2\beta_3 + \delta k\beta_2\mu_p^2 + \delta k\beta_2\mu_p r_p + \delta k\beta_4\mu_p^2 + \delta k\beta_4\mu_p r_p \\
&+2\delta mq\beta_3 v_1 + 2\delta m\beta_3\mu_p v_1 + 2\delta m\beta_3 r_p v_1 + 2\delta q\beta_1\mu_p v_1 + 2\delta q\beta_3\mu_p v_1 - 2\delta A_p\beta_1\beta_3 v_1 \\
&+2\delta\beta_1\mu_p^2 v_1 + 2\delta\beta_1\mu_p r_p v_1 + 2\delta\beta_3\mu_p^2 v_1 + 2\delta\beta_3\mu_p r_p v_1 - k^2 A_p\beta_2\beta_4 + kmq\beta_4 v_1 \\
&+km\beta_4\mu_p v_1 + km\beta_4 r_p v_1 + kq\beta_2\mu_p v_1 + kq\beta_4\mu_p v_1 - kA_p\beta_1\beta_4 v_1 - kA_p\beta_2\beta_3 v_1 \\
&+k\beta_2\mu_p^2 v_1 + k\beta_2\mu_p r_p v_1 + k\beta_4\mu_p^2 v_1 + k\beta_4\mu_p r_p v_1 + mq\beta_3 v_1^2 + m\beta_3\mu_p v_2^2 + m\beta_3 r_p v_1^2 \\
&+q\beta_1\mu_p v_1^2 + q\beta_3\mu_p v_1^2 - A_p\beta_1\beta_3 v_1^2 + \beta_1\mu_p^2 v_1^2 + \beta_1\mu_p r_p v_1^2 + \beta_3\mu_p^2 v_1^2 + \beta_3\mu_p r_p v_1^2, \\
c &= \delta^2 mq\mu_p - \delta^2 mA_p\beta_3 + \delta^2 m\mu_p^2 + \delta^2 m\mu_p r_p + \delta^2 q\mu_p^2 - \delta^2 A_p\beta_1\mu_p + \delta^2\mu_p^3 \\
&+\delta^2\mu_p^2 r_p - \delta kmA_p\beta_4 - \delta kA_p\beta_2\mu_p + 2\delta mq\mu_p v_1 - 2\delta mA_p\beta_3 v_1 + 2\delta m\mu_p^2 v_1 \\
&+2\delta m\mu_p r_p v_1 + 2\delta q\mu_p^2 v_1 - 2\delta\ A_p\beta_1\mu_p v_1 + 2\delta\mu_p^3 v_1 + 2\delta\mu_p^2 r_p v_1 - kmA_p\beta_4 v_1 \\
&-kA_p\beta_2\mu_p v_1 + mq\mu_p v_1^2 - mA_p\beta_3 v_1^2 + m\mu_p^2 v_1^2 + m\mu_p r_p v_1^2 + q\mu_p^2 v_1^2 - A_p\beta_1\mu_p v_1^2 \\
&+\mu_p^3 v_1^2 + \mu_p^2 r_p v_1^2.
\end{aligned}
$$

Since $a > 0$, the following conditions are provided for the existence of I_P.

Proposition 1 *Suppose that b and c are the parameters defined above,*

(i) if $c < 0$, then the model (1) has only one endemic equilibrium such that $I_P = \frac{-b+\sqrt{b^2-4ac}}{2a}$,

(ii) if $b < 0$ and $c > 0$, then the model (1) has two endemic equilibrium such that $I_P = \frac{-b\pm\sqrt{b^2-4ac}}{2a}$.

Otherwise, I_P has no positive real root.

To analyze the stability of E^1, we find the Jacobian matrix of (1) at E^1 as given by

$$
J = \begin{bmatrix}
a_{11} & 0 & 0 & a_{14} & 0 & 0 & 0 \\
a_{21} & a_{22} & 0 & a_{24} & 0 & 0 & 0 \\
a_{31} & a_{32} & a_{33} & a_{34} & 0 & 0 & 0 \\
a_{41} & a_{42} & a_{43} & a_{44} & 0 & 0 & 0 \\
0 & 0 & 0 & a_{54} & a_{55} & 0 & 0 \\
0 & 0 & 0 & a_{64} & 0 & a_{66} & 0 \\
0 & 0 & 0 & a_{74} & 0 & a_{76} & a_{77}
\end{bmatrix}
$$

where

$$
\begin{aligned}
&a_{11} = -(\delta + v_1), a_{14} = k, a_{21} = -\beta_2 S_j^*, a_{22} = -\left(\beta_1 I_p^* + \beta_2 B^* + m + \mu_p\right), \\
&a_{24} = -\beta_1 S_j^*, a_{31} = -\beta_4 S_a^*, a_{32} = m, a_{33} = -\left(\beta_3 I_p^* + \beta_4 B^* + \mu_p\right), \\
&a_{34} = -\beta_3 S_a^*, a_{41} = \beta_2 S_j^* + \beta_4 S_a^*, a_{42} = \beta_1 I_p^* + \beta_2 B^*, a_{43} = \beta_3 I_p^* + \beta_4 B^*, \\
&a_{44} = \beta_1 S_j^* + \beta_3 S_a^* - \left(r_p + \mu_p + q\right), a_{54} = q, a_{55} = -\left(\varepsilon + \mu_p\right), a_{64} = -\beta_5 S_h^*, \\
&a_{66} = -\left(\beta_5 I_p^* + \mu_h + v_2\right), a_{74} = \beta_5 S_h^*, a_{76} = \beta_5 I_p^*, a_{77} = -(r_h + \mu_h).
\end{aligned}
$$

Finding roots of the characteristic equation $|J-\lambda I|=0$, we obtain negative eigenvalues $\lambda_1=-(\mu_h+r_h), \lambda_2=-(\varepsilon+\mu_p), \lambda_3=-(I_p^*\beta_5+\mu_h+v_2)$, and the others are determined from the quartic equation

$$\lambda^4+a_1\lambda^3+a_2\lambda^2+a_3\lambda+a_4=0$$

where

$$\begin{aligned}
a_1 =\ & (\beta_2+\beta_4)B^*-\beta_1S_j^*-\beta_3S_a^*+(\beta_1+\beta_3)I_p^*+\delta+m+q+3\mu_p+r_p+v_1,\\
a_2 =\ & \beta_2\beta_4B^{*2}+\beta_1\beta_3I_p^{*2}+(\beta_1\beta_4+\beta_2\beta_3)B^*I_p^*-\beta_1\beta_4B^*S_j^*-\beta_2\beta_3B^*S_a^*-\beta_1\beta_3I_p^*S_j^*-\beta_1\beta_3I_p^*S_a^*\\
& +(\delta\beta_2+\delta\beta_4+m\beta_4+q\beta_2+q\beta_4+2\beta_2\mu_p+\beta_2r_p+\beta_2v_1+2\beta_4\mu_p+\beta_4r_p+\beta_4v_1)B^*\\
& -(\delta\beta_1+k\beta_2+m\beta_1+2\beta_1\mu_p+\beta_1v_1)S_j^*-(\delta\beta_3+k\beta_4+m\beta_3+2\beta_3\mu_p+\beta_3v_1)S_a^*\\
& +(\delta\beta_1+\delta\beta_3+m\beta_3+q\beta_1+q\beta_3+2\beta_1\mu_p+\beta_2r_p+\beta_1v_1+2\beta_3\mu_p+\beta_3r_p+\beta_3v_1)I_p^*\\
& +\delta m+\delta q+3\delta\mu_p+\delta r_p+mq+2m\mu_p+mr_p+mv_1+2q\mu_pqv_1+3\mu_p^2+2\mu_pr_p\\
& +3\mu_pv_1+r_pv_1,\\
a_3 =\ & (\delta\beta_2\beta_4+q\beta_2\beta_4+\beta_2\beta_4\mu_p+\beta_2\beta_4r_p+\beta_2\beta_4v_1)B^{*2}+(\delta\beta_1\beta_3+q\beta_1\beta_3+\beta_1\beta_3\mu_p+\beta_1\beta_3r_p\\
& +\beta_1\beta_3v_1)I_p^{*2}-(\delta\beta_1\beta_4+k\beta_2\beta_4+\beta_1\beta_4\mu_p+\beta_1\beta_4v_1)B^*S_j^*-(\delta\beta_2\beta_3+k\beta_2\beta_4+\beta_2\beta_3\mu_p\\
& +\beta_2\beta_3v_1)B^*S_a^*+(\delta\beta_1\beta_4+\delta\beta_2\beta_3+q\beta_1\beta_4+q\beta_2\beta_3+\beta_1\beta_4\mu_p+\beta_1\beta_4r_p+\beta_1\beta_4v_1+\beta_2\beta_3\mu_p\\
& +\beta_2\beta_3r_p+\beta_2\beta_3v_1)B^*I_p^*-(\delta\beta_1\beta_3+k\beta_2\beta_3+\beta_1\beta_3\mu_p+\beta_1\beta_3v_1)I_p^*S_j^*-(\delta\beta_1\beta_3+k\beta_1\beta_4\\
& +\beta_1\beta_3\mu_p+\beta_1\beta_3v_1)I_p^*S_a^*+(\delta m\beta_4+\delta q\beta_2+\delta q\beta_4+2\delta\beta_2\mu_p+\delta\beta_2r_p+2\delta\beta_4\mu_p+\delta\beta_4r_p\\
& +mq\beta_4+m\beta_4\mu_p+m\beta_4r_p+m\beta_4v_1+q\beta_2\mu_p+q\beta_2v_1+q\beta_4\mu_p+q\beta_4v_1+\beta_2\mu_p^2+\beta_2\mu_pr_p\\
& +2\beta_2\mu_pv_1+\beta_2r_pv_1+\beta_4\mu_p^2+\beta_4\mu_pr_p+2\beta_4\mu_pv_1+\beta_4r_pv_1)B^*-(\delta m\beta_1+2\delta\beta_1\mu_p+km\beta_2\\
& +2k\beta_2\mu_p+m\beta_1\mu_p+m\beta_1v_1+\beta_1\mu_p^2+2\beta_1\mu_pv_1)S_j^*-(\delta m\beta_3+2\delta\beta_3\mu_p+km\beta_4+2k\beta_4\mu_p\\
& +m\beta_3\mu_p+m\beta_3v_1+\beta_3\mu_p^2+2\beta_3\mu_pv_1)S_a^*+(\delta m\beta_3+\delta q\beta_1+\delta q\beta_3+2\delta\beta_1\mu_p+\delta\beta_1r_p\\
& +2\delta\beta_3\mu_p+\delta\beta_3r_p+mq\beta_3+m\beta_3\mu_p+m\beta_3r_p+m\beta_3v_1+q\beta_1\mu_p+q\beta_1v_1+q\beta_3\mu_p\\
& +q\beta_3v_1+\beta_1\mu_p^2+\beta_1\mu_pr_p+2\beta_1\mu_pv_1+\beta_1r_pv_1+\beta_3\mu_p^2+\beta_3\mu_pr_p+2\beta_3\mu_pv_1+\beta_3r_pv_1)I_p^*\\
& +\delta mq+2\delta m\mu_p+\delta mr_p+2\delta q\mu_p+3\delta\mu_p^2+2\delta\mu_pr_p+mq\mu_p+mqv_1+m\mu_p^2+m\mu_pr_p\\
& +2m\mu_pv_1+mr_pv_1+q\mu_p^2+2q\mu_pv_1+\mu_p^3+\mu_p^2r_p+3\mu_p^2v_1+2\mu_pr_pv_1,\\
a_4 =\ & (\delta q\beta_2\beta_4+\delta\beta_2\beta_4\mu_p+\delta\beta_2\beta_4r_p+q\beta_2\beta_4v_1+\beta_2\beta_4\mu_pv_1+\beta_2\beta_4r_pv_1)B^{*2}+(\delta q\beta_1\beta_3\\
& +\delta\beta_1\beta_3\mu_p+\delta\beta_1\beta_3r_p+q\beta_1\beta_3v_1+\beta_1\beta_3\mu_pv_1+\beta_1\beta_3r_pv_1)I_p^{*2}+(\delta q\beta_1\beta_4+\delta q\beta_2\beta_3\\
& +\delta\beta_1\beta_4\mu_p+\delta\beta_1\beta_4r_p+\delta\beta_2\beta_3\mu_p+\delta\beta_2\beta_3r_p+q\beta_1\beta_4v_1+q\beta_2\beta_3v_1+\beta_1\beta_4\mu_pv_1+\beta_1\beta_4r_pv_1\\
& +\beta_2\beta_3\mu_pv_1+\beta_2\beta_3r_pv_1)B^*I_p^*-(\delta\beta_2\beta_2\mu_p+k\beta_2\beta_4\mu_p+\beta_2\beta_3\mu_pv_1)B^*S_a^*-(\delta\beta_1\beta_4\mu_p\\
& +k\beta_2\beta_2\mu_p+\beta_1\beta_4\mu_pv_1)B^*S_j^*-(\delta\beta_1\beta_3\mu_p+k\beta_2\beta_3\mu_p+\beta_1\beta_3\mu_pv_1)I_p^*S_j^*-(\delta\beta_1\beta_3\mu_p\\
& +k\beta_1\beta_4\mu_p+\beta_1\beta_3\mu_pv_1)I_p^*S_a^*+(\delta mq\beta_4+\delta m\beta_4\mu_p+\delta m\beta_4r_p+\delta q\beta_2\mu_p+\delta q\beta_4\mu_p+\delta\beta_2\mu_p^2\\
& +\delta\beta_2\mu_pr_p+\delta\beta_4\mu_p^2+\delta\beta_4\mu_pr_p+mq\beta_4v_1+m\beta_4\mu_pv_1+m\beta_4r_pv_1+q\beta_2\mu_pv_1+q\beta_4\mu_pv_1\\
& +\beta_2\mu_p^2v_1+\beta_2\mu_p\,r_pv_1+\beta_4\mu_p^2v_1+\beta_4\mu_pr_pv_1)B^*+(\delta mq\beta_3+\delta m\beta_3\mu_p+\delta\beta_3r_p+\delta q\beta_1\mu_p\\
& +\delta q\beta_3\mu_p+\delta\beta_1\mu_p^2+\delta\beta_1\mu_pr_p+\delta\beta_3\mu_p^2+\delta\beta_3\mu_pr_p+mq\beta_3v_1+m\beta_3\mu_pv_1+m\beta_3r_pv_1\\
& +q\beta_1\mu_pv_1+q\beta_3\mu_pv_1+\beta_1\mu_p^2v_1+\beta_1\mu_pr_pv_1+\beta_3\mu_p^2v_1+\beta_3\mu_pr_pv_1)I_p^*-(\delta m\beta_1\mu_p+\delta\beta_1\mu_p^2\\
& +km\beta_2\mu_p+k\beta_2\mu_p^2+m\beta_1\mu_pv_1+\beta_1\mu_p^2v_1)S_j^*-(\delta m\beta_3\mu_p+\delta\beta_3\mu_p^2+km\beta_4\mu_p+k\beta_4\mu_p^2\\
& +m\beta_3\mu_pv_1+\beta_3\mu_p^2v_1)S_a^*+\delta mq\mu_p+\delta m\mu_p^2+\delta m\mu_pr_p+\delta q\mu_p^2+\delta\mu_p^3+\delta\mu_p^2r_p+mq\mu_pv_1\\
& +m\mu_p^2v_1+m\mu_pr_pv_1+q\mu_p^2v_1+\mu_p^3v_1+\mu_p^2r_pv_1.
\end{aligned}$$

From the Routh-Hurwitz criteria, the endemic equilibrium is locally stable when $a_1,a_2,a_3,a_4>0$, $a_1a_2>a_3$ and $a_3(a_1a_2-a_3)>a_1^2a_4$.

2.3 Optimal control problem

In this section, we consider the control strategies, i.e., the sterilization rate and educational campaign rate as a function of time by $u_1(t)$ and $u_2(t)$, respectively. Therefore, from (1), the *S. suis* model with two controls variable is in the form

$$\begin{aligned}
\frac{dB}{dt} &= kI_p(t) - \delta B(t) - u_1(t)B(t),\\
\frac{dS_j}{dt} &= A_p - mS_j(t) - \left(\beta_1 I_p(t) + \beta_2 B(t)\right) S_j(t) - \mu_p S_j(t),\\
\frac{dS_a}{dt} &= mS_j(t) - \left(\beta_3 I_p(t) + \beta_4 B(t)\right) S_a(t) - \mu_p S_a(t),\\
\frac{dI_p}{dt} &= \left(\beta_1 I_p(t) + \beta_2 B(t)\right) S_j(t) + \left(\beta_3 I_p(t) + \beta_4 B(t)\right) S_a(t) - (r_p + \mu_p + q) I_p(t),\\
\frac{dQ}{dt} &= qI_p(t) - (\varepsilon + \mu_p) Q(t),\\
\frac{dR_p}{dt} &= r_p I_p(t) + \varepsilon Q(t) - \mu_p R_p(t),\\
\frac{dS_h}{dt} &= A_h - \beta_5 S_h(t) I_p(t) - \mu_h S_h(t) - u_2(t) S_h(t),\\
\frac{dI_h}{dt} &= \beta_5 S_h(t) I_p(t) - (r_h + \mu_h) I_h(t),\\
\frac{dR_h}{dt} &= r_h I_h(t) - \mu_h R_h(t) + u_2(t) S_h(t).
\end{aligned} \tag{7}$$

We call (7) as the optimal control problem.

Next, we construct the objective functional which is an integral that combines the state variables and control variables [19] as given by

$$J(u_1, u_2) = \int_0^{t_f} \left(A_1 B + A_2 I_p + A_3 I_h + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2) \right) dt \tag{8}$$

subjected to the model (7) with a non-negative initial condition where A_i and B_j for $i = 1, 2, 3,\ j = 1, 2$ are positive weight constants. Our goal is to seek (u_1^*, u_2^*) such that function (8) is minimized,

$$J(u_1^*, u_2^*) = \min\{J(u_1, u_2) \mid (u_1, u_2) \in U\} \tag{9}$$

where U is the control set defined by $U = \{(u_1, u_2) \mid 0 \le u_1, u_2 \le 1, t \in [0, t_f]\}$.
To find the necessary condition of the optimal control problem, we define Hamiltonian H [20] as

$$
\begin{aligned}
H = &\left(A_1 B + A_2 I_p + A_3 I_h + \frac{1}{2}(B_1 u_1^2 + B_2 u_2^2)\right) \\
&+\lambda_B\left(kI_p - \delta B - u_1 B\right) + \lambda_{S_j}\left(A_p - mS_j - \left(\beta_1 I_p + \beta_2 B\right)S_j - \mu_p S_j\right) \\
&+\lambda_{S_a}\left(mS_j - \left(\beta_3 I_p + \beta_4 B\right)S_a - \mu_p S_a\right) \\
&+\lambda_{I_p}\left(\left(\beta_1 I_p + \beta_2 B\right)S_j + \left(\beta_3 I_p + \beta_4 B\right)S_a - \left(r_p + \mu_p + q\right)I_p\right) \\
&+\lambda_Q\left(qI_p - \left(\varepsilon + \mu_p\right)Q\right) + \lambda_{R_p}\left(r_p I_p + \varepsilon Q - \mu_p R_p\right) \\
&+\lambda_{S_h}\left(A_h - \beta_5 S_h I_p - \mu_h S_h - u_2 S_h\right) \\
&+\lambda_{I_h}\left(\beta_5 S_h I_p - (r_h + \mu_h)I_h\right) + \lambda_{R_h}(r_h I_h - \mu_h R_h + u_2 S_h)
\end{aligned} \tag{10}
$$

where $\lambda_B, \lambda_{S_j}, \lambda_{S_a}, \lambda_{I_p}, \lambda_Q, \lambda_{R_p}, \lambda_{S_h}, \lambda_{I_h}$ and λ_{R_h} are adjoint variables.

Using Pontryagin's maximum principle [21], we find optimality condition from $\frac{\partial H}{\partial u_i} = 0, i = 1,2$ as given by

$$
\begin{aligned}
\frac{\partial H}{\partial u_1} &= B_1 u_1 - \lambda_B B, \\
\frac{\partial H}{\partial u_2} &= B_2 u_2 - \left(\lambda_{S_h} - \lambda_{R_h}\right)S_h.
\end{aligned} \tag{11}
$$

Hence, we obtain the optimal control characterization

$$
\begin{aligned}
u_1^*(t) &= \min\left\{\max\left\{0, \frac{\lambda_B B}{B_1}\right\}, 1\right\}, \\
u_2^*(t) &= \min\left\{max\left\{0, \frac{\left(\lambda_{S_h} - \lambda_{R_h}\right)}{B_2}\right\}, 1\right\}.
\end{aligned} \tag{12}
$$

Next, we find adjoint equations from $\frac{d\lambda}{dt} = -\frac{\partial H}{\partial x}$ as given by

$$
\begin{aligned}
\lambda_B'(t) &= -A_1 + \lambda_B(\delta + u_1) + \lambda_{S_j}\beta_2 S_j + \lambda_{S_a}\beta_4 S_a - \lambda_{I_p}\left(\beta_2 S_j + \beta_4 S_a\right), \\
\lambda_{S_j}'(t) &= \lambda_{S_j}\left(m + \beta_1 I_p + \beta_2 B + \mu_p\right) - \lambda_{S_a} m - \lambda_{I_p}\left(\beta_1 I_p + \beta_2 B\right), \\
\lambda_{S_a}'(t) &= \lambda_{S_a}\left(\beta_3 I_p + \beta_4 B - \mu_p\right) - \lambda_{I_p}\left(\beta_3 I_p + \beta_4 B\right), \\
\lambda_{I_p}'(t) &= -A_2 - \lambda_B k + \lambda_{S_j}\beta_1 S_j + \lambda_{S_a}\beta_3 S_a + \lambda_{I_p}\left(-\beta_1 S_j - \beta_3 S_a + r_p + \mu_p + q\right) \\
&\quad -\lambda_Q q - \lambda_{R_p} r_p + \lambda_{S_h}\beta_5 S_h - \lambda_{I_h}\beta_5 S_h, \\
\lambda_Q'(t) &= \lambda_Q\left(\varepsilon + \mu_p\right) - \lambda_{R_p}\varepsilon,
\end{aligned} \tag{13}
$$

$$
\begin{aligned}
\lambda_{R_p}'(t) &= \lambda_{R_p}\mu_p, \\
\lambda_{S_h}'(t) &= \lambda_{S_h}\left(\beta_5 I_p + \mu_h + u_2\right) - \lambda_{I_h}\beta_5 I_p - \lambda_{R_h} u_2, \\
\lambda_{I_h}'(t) &= -A_3 + \lambda_{I_h}(r_h + \mu_h) - \lambda_{R_h} r_h, \\
\lambda_{R_h}'(t) &= \lambda_{R_h}\mu_h,
\end{aligned}
$$

with the transversality condition (or boundary conditions) [22]:

$$
\lambda_i\left(t_f\right) = 0, i = B, S_j, S_a, I_p, Q, R_p, S_h, I_h, R_h. \tag{14}
$$

The optimal control problem (7) together with adjoint equation (13) and the optimal control characterization (12) can be solved numerically.

3. Results and Discussion

3.1 Numerical results for the case of constant control parameters

Numerical solutions for the *S. suis* model (1) are presented where the values of parameters are given in Table 1, and the initial populations are given by $B(0) = 0.0303, S_j(0) = 2000, S_a(0) = 2360, I_p(0) = 6, Q(0) = 0, R_p(0) = 0, S_h(0) = 99999, I_h(0) = 1$, and $R_h(0) = 0$. To show that the model dynamic possesses a stable disease-free equilibrium, we choose $v_1 = v_2 = 1$, $\beta_1 = 4.0556 \times 10^{-6}$, and $\beta_4 = 9.7556 \times 10^{-7}$, together with other parameter values in Table 1. This gives $E^0 = (0, 1453, 2913, 0, 0, 0, 4, 0, 99996)$ and $R_0 = 0.6140$. The solution curves for infectious groups and contaminated environments are shown in Figure 2(a). Since the control level is supposed to be extreme, the outbreak does not occur. On the other hand, in the absence of control parameters, i.e., $v_1 = v_2 = 0$, it can be shown that the outbreak occurs in both populations by choosing $\beta_1 = 4.0556 \times 10^{-5}$, and $\beta_4 = 9.7556 \times 10^{-5}$. By substituting these parameter values into (6), we find $c = -4.06 \times 10^{-12}$ and $b = -1.26 \times 10^{-7}$. From Proposition 1, it can be asserted that the model has only one equilibrium in this case. The result is shown in Figure 2(b), where we computed $E^1 = (85, 415, 362, 1538, 233, 1818, 1405, 65, 98530)$ and $R_0 = 4.3686$. By calculating the coefficients of the characteristic equation, we obtain $a_1 = 0.2088$, $a_2 = 0.0136$, $a_3 = 0.0003, a_4 = 2.5750 \times 10^{-6}, a_1a_2 - a_3 = 0.0025, a_3(a_1a_2 - a_3) - a_1^2a_4 = 6.6024 \times 10^{-7}$. Thus, the Routh-Hurwitz condition is satisfied. In this case, the model dynamic possesses a stable endemic equilibrium.

Table 1. Parameter values

Parameter	Value	Reference
k	5.5556×10^{-3}	Estimated
δ	0.1	[14]
A_p	36.3889	[14]
A_h	3.653	Estimated
m	0.0167	[14]
β_2	2.4389×10^{-6}	[14]
β_3	1.6222×10^{-6}	[14]
β_5	1.6667×10^{-6}	Estimated
q	2.7778×10^{-3}	[14]
r_p	8.3333×10^{-3}	[14]
r_h	0.0556	[1]
ε	0.01	Estimated
μ_p	8.3333×10^{-3}	[14]
μ_h	3.653×10^{-5}	Estimated
N_p	4366	[14]
N_h	100000	Estimated

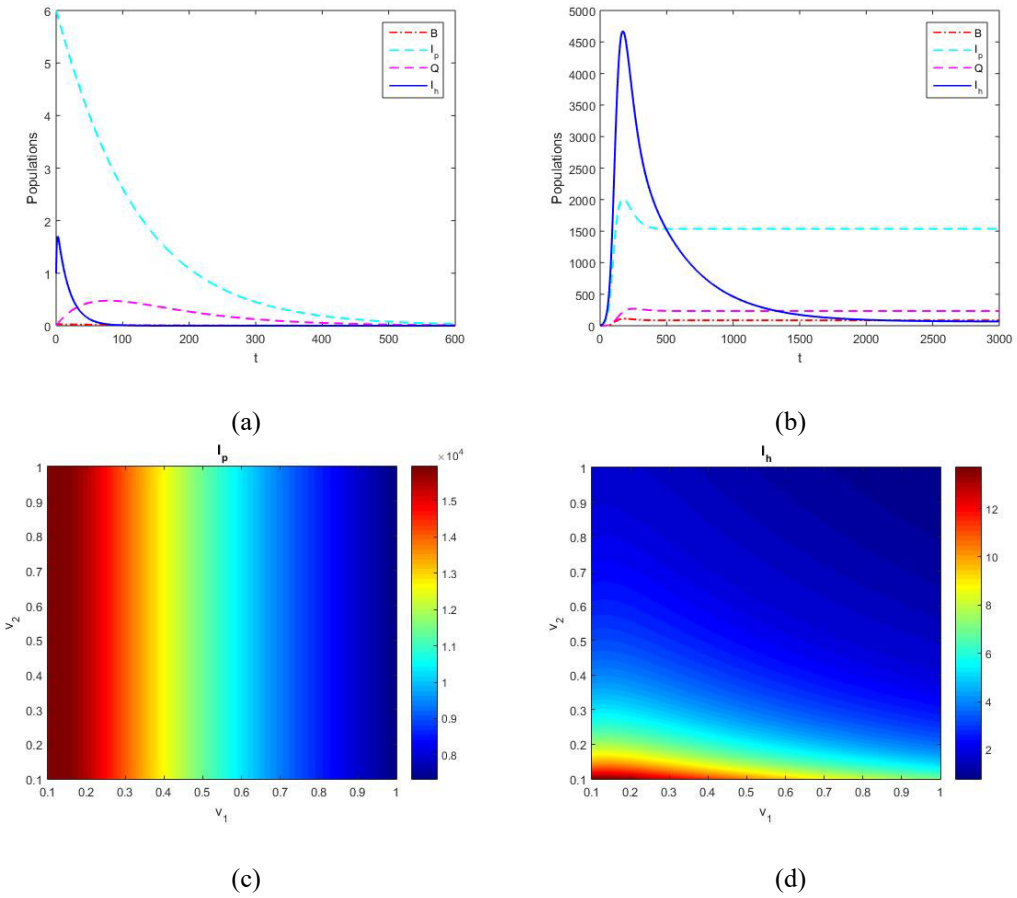
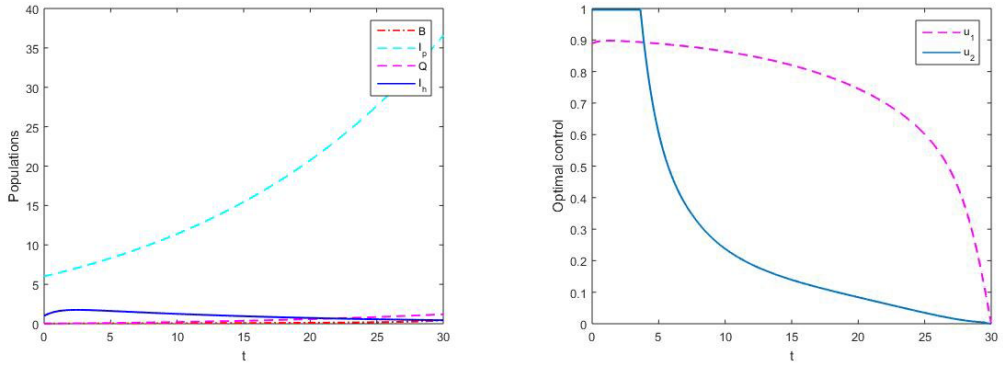


Figure 2. The solution curves ((a)-(b)) and contour plots ((c)-(d)) of the *S. suis* model (1)

Figures 2(c) and (d) illustrate the effects of control parameters on the infectious swine and human populations at the endemic level. It is obvious that the endemic state of the swine population does not depend on v_2, but monotonically decreases as v_1 is increased. Unlike the endemic state of the human population, increasing of v_1 results in the reduction of an endemic level greater than that of v_2.

3.2 Numerical results for the case of optimal control problem

The optimal control problem (7) is numerically solved by the forward-backward Runge-Kutta method [20, 23, 24]. The parameter values analogous to the case of constant control parameters for $R_0 > 1$ is used. To implement the objective function, we choose the weight constants as $A_1 = 5, A_2 = 15, A_3 = 10, B_1 = 10$ and $B_2 = 10$. The dynamic behavior of infectious populations and bacterial environments under dynamic control variables are shown in Figure 3(a).



(a) (b)

Figure 3. The solution of the *S. suis* model with control variables

Importantly, the optimal control strategy is predicted by the model. From Figure 3(b), it is suggested that the sterilization on the farm should be kept at 90% per day at the beginning of the control course and then be gradually relaxed until it turns into a sudden decline approaching zero within a month. Accordingly, it is also suggested that educational campaign should be kept at a maximum level for about four days, and then exponentially decrease to zero within a month. As a consequence, the results from optimal control totally reduce the growth rates and endemic levels of bacteria in the environment, the infected swine population, and the quarantined swine population (see Figure 4(a)-(c)). Although it cannot suppress the outbreak on the farm, it successfully prevents the epidemic in the human population by diminishing the endemic curve below unity (see Figure 3(a) and Figure 4(d)).

3.3 Sensitivity analysis

In order to determine the importance of each parameter on the R_0, we further examine the normalized sensitivity index $\frac{\Omega}{R_0}\left(\frac{\partial R}{\partial \Omega}\right)$ [25] where Ω is the parameter appeared in basic reproduction number. Using the parameter values in Table 1 with $\beta_1 = 4.0556 \times 10^{-5}, \beta_4 = 9.7556 \times 10^{-5}$, and $u_1 = 0.5$, the sensitivity indices of R_0 to the parameters are shown in Table 2.

From Table 2, we see that A_p is the most sensitive parameter for R_0. The second important parameter is β_1. Since the control of A_p is irrelevant, reducing the magnitude of β_1 has the most impact on controlling the epidemic. Therefore, the optimal control strategy should be focused together with reduction of β_1.

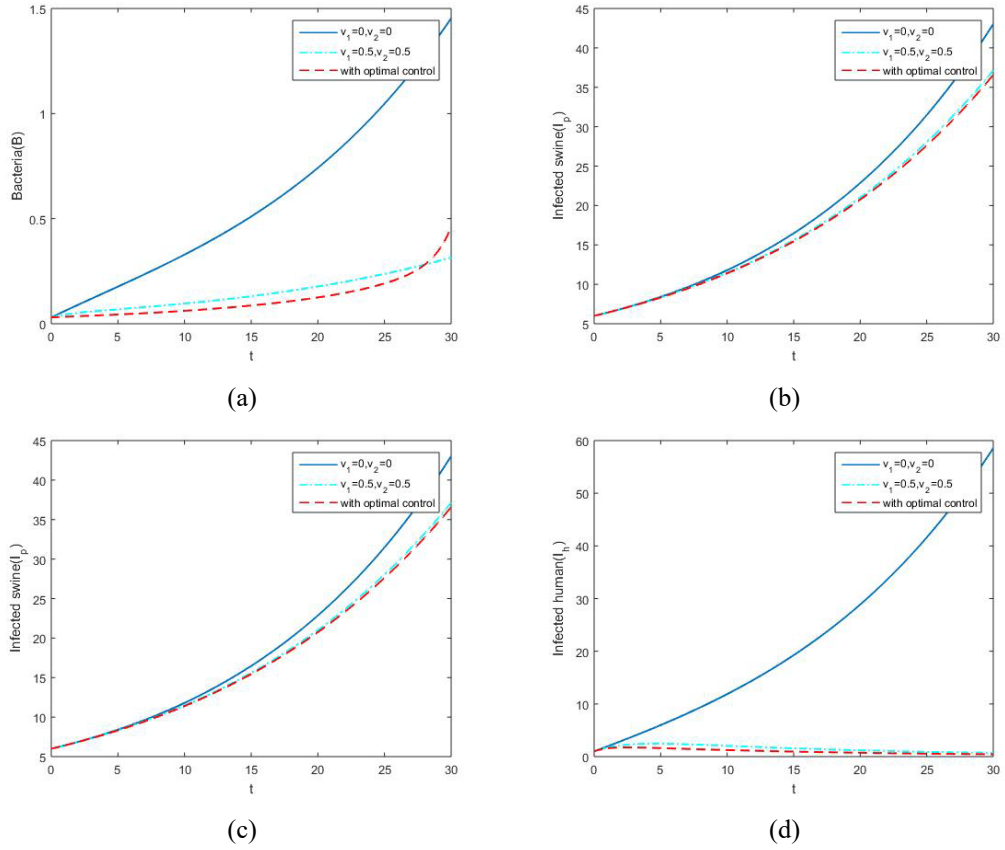


Figure 4. Number of infected population with control and no control

Table 2. Sensitivity indices of the basic reproduction number

Parameters	**Sensitivity indices of R_0**
A_p	1
k	0.0402
δ	−0.0067
m	−0.5562
β_1	0.8886
β_2	0.0005
β_3	0.0712
β_4	0.0397
q	−0.1429
r_p	−0.4286
μ_p	−0.8724
v_1	−0.0335

4. Conclusions

We have formulated a mathematical model of the spread of *S. suis* among two populations where the strategies of sterilize pig farms and educational campaigns are considered. With the constant control parameter, we obtained the disease-free equilibrium which is stable when $R_0 < 1$ and obtain the conditions under which the endemic equilibrium is stable. It was observed that R_0 does not depend on v_2, the rate at which the susceptible individuals were presumably protected after the educational campaign had been operated.

The results from the first model were composed of the basic reproduction number, the disease-free equilibrium and the endemic equilibrium. We also found that the basic reproduction number depended on disinfectant sterilization (the parameter v_1), but it did not depend on the educational campaign (the parameter v_2). However, we observed from the endemic equilibrium (5) that v_2 appeared in I_h and I_p, which showed that the educational campaign would affect the infectious population.

We have shown that the outbreak of *S. suis* occurs if $R_0 > 1$. Under this circumstance, the model might process the stable endemic equilibrium which depends on the constant level of control parameters. The question then became what happens if such control parameters are not constant. In other words, what can we do better to control the outbreak under the same control measures within a particular interval of time? Thus, the second model was formulated to address this question. As we have shown that the analytic formula of the solution of the optimal control problem is impossible, the numerical calculation is thus required.

For the optimal control problem associated with the adjoint equation and the optimal control characterization, we have presented the results numerically. The solution provides an optimal strategy that can be applied to mitigate the spread in both populations. The results show that such strategies can be used to reduce the number of *S. suis* infections. In the present example, the results seem to be more effective in controlling the spread in human populations than the spread in livestock. The reasons for this are two fold: first, the impact of sterilization on the spread in the farm is relatively low. This may be caused by an inappropriate scale of contact rate between the pig and bacterial environment. Since the scale of the bacterial environment is usually low compared with the scale of the pig population, the scale of transmission parameter under the mass action law should be adjusted. Second, the initial number of infected humans is low compared with that of the infected pigs.

From the sensitivity analysis, the most influential transmission parameter is transmission from infectious pigs to susceptible piglets, β_1. As clinical infections are seen mainly in weaned pigs (2–5 weeks after weaning) [26], transmission may occur by the movement and mixing of infected pigs to a naive herd. Hence, reducing the value of β_1 can be achieved by avoiding overcrowding, poor ventilation, and mixing of pigs with an age spread of >2 weeks.

This study highlights several directions for future investigations such as the generalization or restructuring of the pig population by including the asymptomatic carrier group of pig since most clinically healthy pigs are carriers of multiple serotypes of *S. suis*, and the role of carriers in transmission is not completely understood. It is estimated that 100% of pig farms have some *S. suis*, since *S. suis* is a normal inhabitant of the upper respiratory tract [27]. Moreover, incorporating the effects of vaccination into the model may be helpful. As the widely used Bacterin vaccines seem to be ineffective, future research may concentrate on how the burden of control measures can be reduced based on the degree of efficacy of the vaccine.

References

[1] Wertheim, H.F.L., Nghia, H.D.T., Taylor, W. and Schultsz, C., 2009. *Streptococcus suis*: an emerging human pathogen. *Clinical Infectious Diseases*, 48(5), 617-625.

[2] Arends, J.P., Hartwig, N., Rudolphy, M. and Zanen, H.C., 1984. Carrier rate of *Streptococcus suis* capsular type 2 in palatine tonsils of slaughtered pigs. *Journal of Clinical Microbiology*, 20(5), 945-947.

[3] Gottschalk, M. and Segura, M., 2000. The pathogenesis of the meningitis caused by *Streptococcus suis*: the unresolved questions. *Veterinary Microbiology*, 76(3), 259-272.

[4] Padungtod, P., Tharavichitkul, P., Junya, S., Chaisowong, W., Kadohira, M., Makino, S. and Sthitmatee, N., 2010. Incidence and presence of virulence factors of *Streptococcus suis* infection in slaughtered pigs from Chiang Mai, Thailand. *Southeast Asian Journal of Tropical Medicine and Public Health*, 41(6), 1454-1461.

[5] Gottschalk, M., Segura, M. and Xu, J., 2007. *Streptococcus suis* infections in humans: the Chinese experience and the situation in North America. *Animal Health Research Reviews*, 8(1), 29-45.

[6] Segura, M. and Gottschalk, M., 2002. *Streptococcus suis* interactions with the murine macrophage cell line J774: adhesion and cytotoxicity. *Infection and Immunity*, 70(8), 4312-4322.

[7] Fongcom, A., Pruksakorn, S., Netsirisawan, P., Pongprasert, R. and Onsibud, P., 2009. *Streptococcus suis* infection: a prospective study in northern Thailand. *Southeast Asian Journal of Tropical Medicine and Public Health*, 40(3), 511-517.

[8] Ho, D.T.N., Le, T.P.T., Wolbers, M., Cao, Q.T., Nguyen, V.M.H., Tran, V.T.N., Le, T.P.T., Nguyen, H.P., Tran, T.H.C., Dinh, X.S., To, S.D., Hoang, T.T.H., Hoang, T., Campbell, J., Nguyen, V.V.C., Nguyen, T.C., Nguyen, V.D., Ngo, T.H., Spratt, B.G., Tran, T.H., Farrar, J. and Schultsz, C., 2011. Risk factors of *Streptococcus suis* infection in Vietnam. A case-control study. *PLoS ONE*, 6(3), https://doi.org/10.1371/journal.pone.0017604.

[9] NSTDA, 2022. *Streptococcus suis*. [online] Available at: https://www.nstda.or.th/.../sci-update-streptococcus-suis/. (in Thai)

[10] Neila-Ibáñez, C., Napp, S., Pailler-García, L., Franco-Martínez, L., Cerón, J.J., Aragon, V. and Casal, J., 2023. Risk factors associated with *Streptococcus suis* cases on pig farms in Spain. *Veterinary Record*, 193(5), https://doi.org/10.1002/vetr.3056.

[11] Rayanakorn, A., Goh, B.-H., Lee, L.-H., Khan, T.M. and Saokaew, S., 2018. Risk factors for *Streptococcus suis* infection: A systematic review and meta-analysis. *Scientific Reports*, 8(1), https://doi.org/10.1038/s41598-018-31598-w.

[12] Segura, M., Aragon, V., Brockmeier, S.L., Gebhart, C., Greeff, A.D., Kerdsin, A., O'Dea, M.A., Okura, M., Saléry, M., Schultsz, C., Valentin-Weigand, P., Weinert, L.A., Wells, J.M. and Gottschalk, M., 2020. Update on *Streptococcus suis* research and prevention in the era of antimicrobial restriction: 4th International Workshop on *S. suis*. *Pathogens*, 9(5), https://doi.org/10.3390/pathogens9050374.

[13] Kerdsin, A, Takeuchi, D, Nuangmek, A, Akeda, Y, Gottschalk, M and Oishi, K., 2020. Genotypic comparison between *Streptococcus suis* isolated from pigs and humans in Thailand. *Pathogens*, 9(1), https://doi.org/10.3390/pathogens9010050.

[14] Shen, C., Li, M., Zhang, W., Yi, Y., Wang, Y., Hou, Q., Huang, B. and Lu, C., 2014. Modeling transmission dynamics of *Streptococcus suis* with stage structure and sensitivity analysis. *Discrete Dynamics in Nature and Society*, 2014, https://doi.org/10.1155/2014/432602.

[15] Chaiya, I., Trachoo, M., Nonlaopon, K. and Prathumwan, D., 2022. The mathematical model for *Streptococcus suis* infection in pig-human population with humidity effect. *Computers, Materials and Continua*, 71(2), 2981-2998.

[16] Ascher, U.M., Mattheij, R.M. and Russell, R.D., 1995. *Numerical Solution of Boundary Value Problems for Ordinary Differential Equations*. Philadelphia: Society for Industrial and Applied Mathematics.
[17] Dietz, K., 1993. The estimation of the basic reproduction number for infectious diseases. *Statistical Methods in Medical Research*, 2(1), 23-41.
[18] Van den Driessche, P. and Watmough, J., 2002. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Mathematical Biosciences*, 180(1-2), 29-48.
[19] Nyerere, N., Luboobi, L.S., Mpeshe, S.C. and Shirima, G.M., 2020. Optimal control strategies for the infectiology of brucellosis. *International Journal of Mathematics and Mathematical Sciences*, 2020, 1-17.
[20] Lenhart, S. and Workman, J.T., 2007. *Optimal Control Applied to Biological Models*. Boca Raton: CRC Press.
[21] Pontryagin, L.S., 1987. *Mathematical Theory of Optimal Processes*. Boca Raton: CRC Press.
[22] Thamchai, R., 2014. *Stability Analysis of Drinking Epidemic Models and Investigation of Optimal Treatment Strategy*. Ph.D. Curtin University, Australia.
[23] Bakare, E.A., Nwagwo, A., and Danso-Addo, E., 2014. Optimal control analysis of an SIR epidemic model with constant recruitment. *International Journal of Applied Mathematics Research*, 3(3), https://doi.org/10.14419/ijamr.v3i3.2872.
[24] Rodrigues, H.S., Monteiro, M.T.T. and Torres, D.F.M., 2014. Optimal control and numerical software: an overview. *arXiv preprint*, https://doi.org/10.48550/arXiv.1401.7279.
[25] Chitnis, N., Hyman, J.M., and Cushing, J.M., 2008. Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. *Bulletin of Mathematical Biology,* 70, 1272-1296.
[26] Gottschalk, M., 2022. *Streptococcus suis Infection in Pigs*. [online] Available at: https://www.msdvetmanual.com/generalized-conditions/streptococcal-infections-in-pigs/.
[27] Obradovic, M.R., Corsaut, L., Dolbec, D., Gottschalk, M. and Segura, M., 2021. Experimental evaluation of protection and immunogenicity of *Streptococcus suis* bacterin-based vaccines formulated with different commercial adjuvants in weaned piglets. *Veterinary Research*, 52, https://doi.org/10.1186/s13567-021-01004-x.