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MODELING AND ANALYZING THE TRANSMISSION DYNAMICS OF VISCERAL LEISHMANIASIS

Lan Zou*

Department of Mathematics
Sichuan University
Chengdu, Sichuan 610064, China

Jing Chen and Shigui Ruan

Department of Mathematics
University of Miami
Coral Gables, FL 33146, USA

Abstract. In this paper, we develop a mathematical model to study the transmission dynamics of visceral leishmaniasis. Three populations: dogs, sandflies and humans, are considered in the model. Based on recent studies, we include vertical transmission of dogs in the spread of the disease. We also investigate the impact of asymptomatic humans and dogs as secondary reservoirs of the parasites. The basic reproduction number and sensitivity analysis show that the control of dog-sandfly transmission is more important for the elimination of the disease. Vaccination of susceptible dogs, treatment of infective dogs, as well as control of vertical transmission in dogs are effective prevention and control measures for visceral leishmaniasis.

1. **Introduction.** Leishmaniasis is a vector-borne disease that is transmitted by sandflies and caused by obligate intracellular protozoans of the genus *Leishmania*.There are three main forms of the disease:Visceral leishmaniasis (VL), Cutaneous leishmaniasis (CL) and Mucocutaneous leishmaniasis (ML). Among these forms, VL is fatal if left untreated in over 95% of cases. It is a chronic and systemic disease caused by *Leishmania infantum* whose characteristics include irregular long term fever, weight loss, asthenia, adynamia, anemia with visible cutaneous and mucosal pallor, splenomegaly, hepatomegaly, leucopenia, thrombocytopenia, and complications of bacterial infections. VL is maintained in a cycle between sandflies and animal hosts, in which domestic dogs and humans are predominant reservoir hosts. *L. infantum* infection often does not equate with clinical disease since some people may have a silent infection without any symptoms or signs. Typical clinical signs of VL include fever, weight loss, anemia, lymphadenopathy, and hepato- and splenomegaly ([3]).

A total of 98 countries and three territories reported endemic VL transmissions. The map in Figure 1 given by WHO shows the status of endemicity of VL worldwide in 2013. From the available data, WHO estimated that 90% of global VL cases occurred in six countries: Bangladesh, Brazil, Ethiopia, India, South Sudan, and

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* Corresponding author: Lan Zou (E-mail: lanzou@163.com).

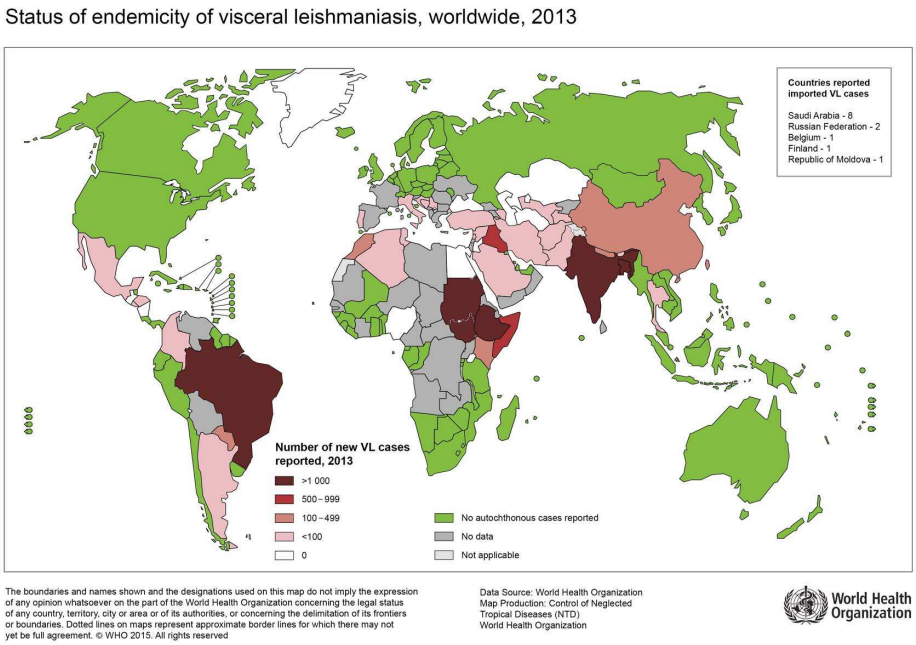


FIGURE 1. Status of endemicity of VL worldwide in 2013 ([31]).

Sudan. Brazil is the only country with a high burden of both VL and CL among the 25 countries with burden of leishmaniasis ([32]). In the last 20 years, Brazil registered a marked increase in the incidence of VL (Figure 2).

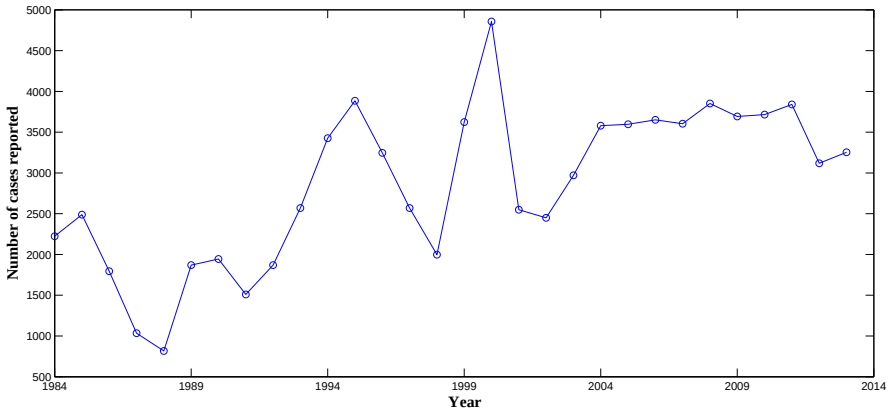


FIGURE 2. The reported cases of VL in Brazil from 1984 to 2013 ([30, 31]).

Prior to the initiation of a national control program in 1951, VL was one of the major parasitic diseases in China, endemic in 17 provinces, cities and autonomous

regions. About 530,000 VL cases were estimated in China in 1951 ([28]). Though it was virtually under control through active detection of human infections for treatment and vector control since the 1960s, VL currently occurs in more than 50 counties in six provinces and autonomous regions in western China, including Xinjiang, Gansu, Sichuan, Shaanxi, Shanxi, and Inner Mongolia ([27]). More than 90% of the new infections are found in Xinjiang, Gansu and Sichuan. The data reported by Chinese Center for Disease Control and Prevention (China CDC) revealed that human VL cases did not decrease in these endemic areas during the past years (Figure 3).

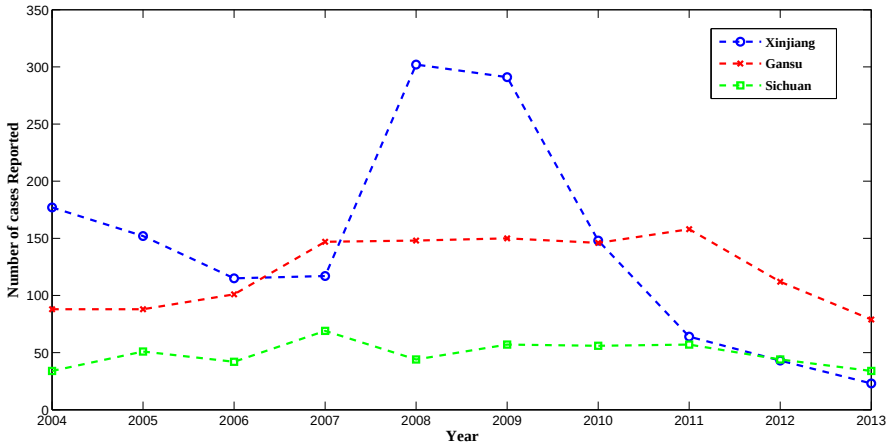


FIGURE 3. The reported cases of VL in the most serious provinces (Xinjiang, Gansu, Sichuan) in China ([5]).

Domestic dogs are considered as the predominant reservoir of *Leishmania infantum chagasi* (*L. infantum*) in hyperendemic foci, with canine seroprevalence between 8% and 40% ([24]). Both subclinically infected and diseased dogs can be infectious to phlebotomine vectors, but infectiousness is higher in dogs with overt clinical signs ([6, 10]). Recent research indicates that mother-to-child transmission, also called vertical (transplacental or transmammary) transmission, may be an additional important mechanism maintaing the canine reservoir ([2, 11, 21]). It has been reported that both symptomatic and asymptomatic *Leishmania*-infected dogs act as a source of parasites for VL transmission ([17, 18]).

Mathematical models have been proposed to describe the transmission dynamics of visceral leishmaniasis. Hasibeder et al. ([13]) and Dye ([7]) proposed models of canine and zoonotic VL, respectively. Burrattini et al. [4] developed a transmission dynamics model of leishmaniasis including vector, human and canine populations. Reithinger [23] developed a mathematical model to investigate whether widespread provision of deltamethrin-impregnated colars in Brazil is likely to lead to greater zoonotic VL control than the current dog culling program. ELmojitaba et al. [8] used a mathematical model to study the transmission of VL in Sudan. Zhao et al. [33] proposed a model and calculated optimal control strategies. However, there has been very little research on modeling the vertical transmission of VL.

In this paper, we propose a model for the transmission of visceral leishmaniasis which describes the transmission between canine reservoirs and sandflies as well

as the transmission from sandflies to humans. To investigate the role of vertical transmission in the spread and control of VL, we take into consideration the canine vertical transmission in this model. The structure of this paper is as follows: a mathematical model for VL is constructed in Section 2. The basic reproduction number of the model is calculated in Section 3. The sub-system of blocking dog-sandfly transmission is discussed in Section 4 and the sub-system of blocking human-sandfly transmission is discussed in Section 5. Sensitivity analysis and simulations are performed in Section 6. Some conclusions and discussions are presented in Section 7.

2. **Mathematical modeling.** We assume that humans and dogs are the hosts, with the biological vector sandflies transmitting the infection within and between the two host populations. We take the asymptomatic dog and human reservoirs as crucial roles in the transmission and persistence of VL. Moreover, we take these into account: (i) vertical transmission in dog reservoir; (ii) vaccination of susceptible dogs, culling of exposed and infective dogs, and treatment of infective dogs.

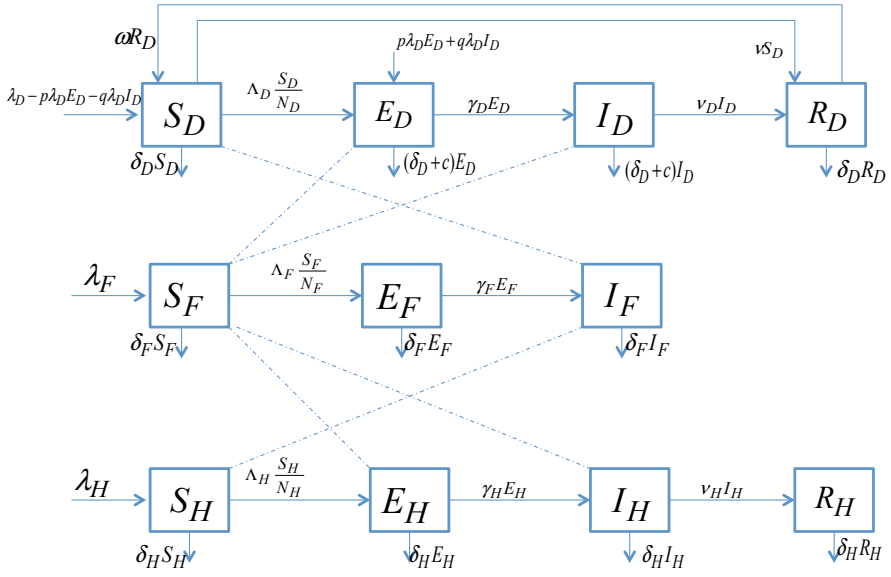


FIGURE 4. Flowchart of Leishmaniasis transmission, where $\Lambda_D = \beta_{FD} I_F a_D$, $\Lambda_F = (\beta'_{DF} E_D + \beta_{DF} I_D) a_D + (\beta'_{HF} E_H + \beta_{HF} I_H) a_H$ and $\Lambda_H = \beta_{FH} I_F a_H$.

The total populations of dogs N_D and humans N_H are divided into the following epidemiological compartments: susceptible (S_D and S_H), exposed (E_D and E_H), infectious (I_D and I_H), recovered or vaccinated (R_D and R_H), respectively. The total population of sandflies N_F is also divided into three compartments: susceptible S_F, exposed E_F and infectious I_F. Newborn exposed dogs are described as $p\lambda_D E_D + q\lambda_D I_D$, which reflects the vertical transmission of VL in dogs. Following the transmission diagram shown in Figure 4, we adapt a SEIRS structure for dogs, a SEI structure for sandflies and a SEIR structure for humans, and the VL model

takes the following form:

$$\begin{cases} \frac{dS_D}{dt} = \lambda_D - p\lambda_D E_D - q\lambda_D I_D - \beta_{FD} a_D I_F \frac{S_D}{N_D} - (\delta_D + \nu) S_D + \omega R_D, \\ \frac{dE_D}{dt} = \beta_{FD} a_D I_F \frac{S_D}{N_D} + p\lambda_D E_D + q\lambda_D I_D - (\delta_D + \gamma_D + c) E_D, \\ \frac{dI_D}{dt} = \gamma_D E_D - (\delta_D + \nu_D + c) I_D, \\ \frac{dR_D}{dt} = \nu S_D + \nu_D I_D - (\delta_D + \omega) R_D, \\ \frac{dS_F}{dt} = \lambda_F - (\beta'_{DF} E_D + \beta_{DF} I_D) a_D \frac{S_F}{N_F} - (\beta'_{HF} E_H + \beta_{HF} I_H) a_H \frac{S_F}{N_F} - \delta_F S_F, \\ \frac{dE_F}{dt} = (\beta'_{DF} E_D + \beta_{DF} I_D) a_D \frac{S_F}{N_F} + (\beta'_{HF} E_H + \beta_{HF} I_H) a_H \frac{S_F}{N_F} - (\delta_F + \gamma_F) E_F, \\ \frac{dI_F}{dt} = \gamma_F E_F - \delta_F I_F, \\ \frac{dS_H}{dt} = \lambda_H - \beta_{FH} a_H I_F \frac{S_H}{N_H} - \delta_H S_H, \\ \frac{dE_H}{dt} = \beta_{FH} a_H I_F \frac{S_H}{N_H} - (\delta_H + \gamma_H) E_H, \\ \frac{dI_H}{dt} = \gamma_H E_H - (\delta_H + \nu_H) I_H, \\ \frac{dR_H}{dt} = \nu_H I_H - \delta_H R_H \end{cases} \tag{1}$$

with nonnegative initial conditions. Parameters used in system (1) are nonnegative and listed in Table 1.

TABLE 1. Model parameters and their descriptions

Parameters	Interpretations
λ_D	Recruitment rate of susceptible dogs
λ_F	Recruitment rate of susceptible sandflies
λ_H	Recruitment rate of susceptible humans
$1/\delta_D$	Average lifespan of dogs
$1/\delta_F$	Average lifespan of sandflies
$1/\delta_H$	Average lifespan of humans
β_{FD}	Prob. of transmission from infectious sandflies to dogs
β'_{DF}	Prob. of transmission from exposed dogs to sandflies
β_{DF}	Prob. of transmission from infectious dogs to sandflies
β_{FH}	Prob. of transmission from infectious sandflies to humans
β'_{HF}	Prob. of transmission from exposed humans to sandflies
β_{HF}	Prob. of transmission from infectious humans to sandflies
p	Fraction of offspring of exposed dogs born to be exposed
q	Fraction of offspring of infectious dogs born to be exposed
a_D	Rate of biting on dogs by sandflies
a_H	Rate of biting on humans by sandflies
$1/\gamma_D$	Incubation period in dogs
$1/\gamma_F$	Incubation period in sandflies
$1/\gamma_H$	Incubation period in humans
c	Culling rate of exposed and infective dogs
ν	Vaccination rate of dogs
ω	Loss rate of vaccination in dogs
ν_D	Recovery rate of dogs
ν_H	Recovery rate of humans

3. **Basic reproduction number.** The equilibria of system (1) satisfy

$$\begin{cases} \lambda_D - p\lambda_D E_D - q\lambda_D I_D - \beta_{FD} a_D I_F \frac{S_D}{N_D} - (\delta_D + \nu) S_D + \omega R_D = 0, \\ \beta_{FD} a_D I_F \frac{S_D}{N_D} + p\lambda_D E_D + q\lambda_D I_D - (\delta_D + \gamma_D + c) E_D = 0, \\ \gamma_D E_D - (\delta_D + \nu_D + c) I_D = 0, \\ \nu S_D + \nu_D I_D - (\delta_D + \omega) R_D = 0, \\ \lambda_F - (\beta'_{DF} E_D + \beta_{DF} I_D) a_D \frac{S_F}{N_F} - (\beta'_{HF} E_H + \beta_{HF} I_H) a_H \frac{S_F}{N_F} - \delta_F S_F = 0, \\ (\beta'_{DF} E_D + \beta_{DF} I_D) a_D \frac{S_F}{N_F} + (\beta'_{HF} E_H + \beta_{HF} I_H) a_H \frac{S_F}{N_F} - (\delta_F + \gamma_F) E_F = 0, \\ \gamma_F E_F - \delta_F I_F = 0, \\ \lambda_H - \beta_{FH} a_H I_F \frac{S_H}{N_H} - \delta_H S_H = 0, \\ \beta_{FH} a_H I_F \frac{S_H}{N_H} - (\delta_H + \gamma_H) E_H = 0, \\ \gamma_H E_H - (\delta_H + \nu_H) I_H = 0, \\ \nu_H I_H - \delta_H R_H = 0. \end{cases} \tag{2}$$

We obtain a unique disease-free equilibrium $E_0 = (S_D^0, 0, 0, R_D^0, S_F^0, 0, 0, S_H^0, 0, 0, 0)$, where

$$S_D^0 = \frac{(\delta_D + \omega)\lambda_D}{\delta_D(\delta_D + \omega + \nu)},\ R_D^0 = \frac{\nu\lambda_D}{\delta_D(\delta_D + \omega + \nu)},\ S_F^0 = \frac{\lambda_F}{\delta_F},\ S_H^0 = \frac{\lambda_H}{\delta_H}.$$

Rewrite system (1) as the form

$$\dot{x} = \mathcal{F}(x) - \mathcal{V}(x), \tag{3}$$

where $x = (E_D, I_D, E_F, I_F, E_H, I_H, S_D, R_D, S_F, S_H, R_H)$,

$$\mathcal{F} = \begin{pmatrix} \beta_{FD} a_D I_F \frac{S_D}{N_D} + p\lambda_D E_D + q\lambda_D I_D \\ 0 \\ (\beta'_{DF} E_D + \beta_{DF} I_D) a_D \frac{S_F}{N_F} + (\beta'_{HF} E_H + \beta_{HF} I_H) a_H \frac{S_F}{N_F} \\ 0 \\ \beta_{FH} a_H I_F \frac{S_H}{N_H} \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix},$$

and

$$\mathcal{V} = \begin{pmatrix} (\delta_D + \gamma_D + c) E_D \\ -\gamma_D E_D + (\delta_D + \nu_D + c) I_D \\ (\delta_F + \gamma_F) E_F \\ -\gamma_F E_F + \delta_F I_F \\ (\delta_H + \gamma_H) E_H \\ -\gamma_H E_H + (\delta_H + \nu_H) I_H \\ -\lambda_D + p\lambda_D E_D + q\lambda_D I_D + \beta_{FD} a_D I_F \frac{S_D}{N_D} + (\delta_D + \nu) S_D - \omega R_D \\ -\nu S_D - \nu_D I_D + (\delta_D + \omega) R_D \\ -\lambda_F + (\beta'_{DF} E_D + \beta_{DF} I_D) a_D \frac{S_F}{N_F} + (\beta'_{HF} E_H + \beta_{HF} I_H) a_H \frac{S_F}{N_F} + \delta_F S_F \\ -\lambda_H + \beta_{FH} a_H I_F \frac{S_H}{N_H} + \delta_H S_H \\ -\nu_H I_H + \delta_H R_H \end{pmatrix}.$$

Then, the derivatives of $\mathcal{F}$ and $\mathcal{V}$ at the disease-free equilibrium E_0 are given by

$$D\mathcal{F}(E_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix},\ D\mathcal{V}(E_0) = \begin{pmatrix} V & 0 \\ J_3 & J_4 \end{pmatrix}, \tag{4}$$

where

$$F=\begin{pmatrix} p\lambda_D & q\lambda_D & 0 & \frac{(\delta_D+\omega)\beta_{FD}a_D}{\delta_D+\omega+\nu} & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0\\ \beta'_{DF}a_D & \beta_{DF}a_D & 0 & 0 & \beta'_{FH}a_H & \beta_{FH}a_H\\ 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & \beta_{FH}a_H & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V=\begin{pmatrix} \delta_D+\gamma_D+c & 0 & 0 & 0 & 0 & 0\\ \gamma_D & \delta_D+\nu_D+c & 0 & 0 & 0 & 0\\ 0 & 0 & \delta_F+\gamma_F & 0 & 0 & 0\\ 0 & 0 & -\gamma_F & \delta_F & 0 & 0\\ 0 & 0 & 0 & 0 & \delta_H+\gamma_H & 0\\ 0 & 0 & 0 & 0 & -\gamma_H & \delta_H+\nu_H \end{pmatrix},$$

and all eigenvalues of J_4 have positive real parts.

Since F is non-negative and V is a non-singular M-matrix, it follows from [26] that the maximum real part of all eigenvalues of the matrix $F-V$ is negative if and only if the spectral radius of the next generation matrix $\rho(FV^{-1})<1$. Moreover,

$$V^{-1}=\begin{pmatrix} \frac{1}{\delta_D+\gamma_D+c} & 0 & 0 & 0 & 0 & 0\\ \frac{\gamma_D}{(\delta_D+\gamma_D+c)(\delta_D+\nu_D+c)} & \frac{1}{\delta_D+\nu_D+c} & 0 & 0 & 0 & 0\\ 0 & 0 & \frac{1}{\delta_F+\gamma_F} & 0 & 0 & 0\\ 0 & 0 & \frac{\gamma_F}{(\delta_F+\gamma_F)\delta_F} & \frac{1}{\delta_F} & 0 & 0\\ 0 & 0 & 0 & 0 & \frac{1}{\delta_H+\gamma_H} & 0\\ 0 & 0 & 0 & 0 & \frac{\gamma_H}{(\delta_H+\gamma_H)(\delta_H+\nu_H)} & \frac{1}{\delta_H+\nu_H} \end{pmatrix}.$$

The eigenvalues of the matrix FV^{-1} for system (1) satisfy the following equation:

$$H(\lambda):=\lambda^3(\lambda^3-a_1\lambda^2-(c_3b_5+b_1a_3)\lambda+a_1b_5c_3)=0, \tag{5}$$

where

$$a_1=\frac{\lambda_D(p(c+\delta_D+\nu_D)+q\gamma_D)}{(\delta_D+\gamma_D+c)(\delta_D+\nu_D+c)},\ a_3=\frac{\beta_{FD}a_D\gamma_F(\delta_D+\omega)}{\delta_F(\delta_D+\omega+\nu)(\delta_F+\gamma_F)},$$
$$b_1=\frac{a_D(\beta'_{DF}(c+\delta_D+\nu_D)+\beta_{DF}\gamma_D)}{(\delta_D+\gamma_D+c)(\delta_D+\nu_D+c)},\ b_5=\frac{a_H(\beta'_{HF}(\delta_H+\nu_H)+\beta_{HF}\gamma_H)}{(\delta_H+\gamma_H)(\delta_H+\nu_H)},$$
$$c_3=\frac{\beta_{FH}a_H\gamma_F}{\delta_F(\delta_F+\gamma_F)}.$$

The basic reproduction number R_0, defined as the average number of secondary cases arising from an average primary case in an entirely susceptible population, is the spectral radius of FV^{-1} ([26]). Let $A_2=a_1$, $A_2=c_3b_5+a_3b_1$, $A_0=a_1b_5c_3$, $B=81A_0^2-12A_1^3-3A_1^2A_2^2-54A_0A_1A_2-12A_0A_2^3$, and $D=36A_1A_2-108A_0+8A_2^3+12\sqrt{B}$. The basic reproduction number is

$$R_0=\frac{2A_1}{D}+\frac{2A_2^2}{3D}+\frac{D}{6}+\frac{A_1}{3}.$$

Then we obtain that

$$R_0>R_-:=\frac{1}{3}(a_1+\sqrt{a_1^2+3(c_3b_5+a_3b_1)}).$$

In fact, R_- is the positive real root of equation $H'(\lambda)=3\lambda^2-2a_1\lambda-(c_3b_5+b_1a_3)=0$. Furthermore, the disease-free equilibrium is unstable if $R_0>1$. It leads to the following result:

Theorem 3.1. *If $R_- \geq 1$, the disease-free equilibrium E_0 is unstable.*

To further analyze the basic reproduction number, we make the following assumption:

Assumption 1. $p = q = 0$, *that is, no offsprings are born to be exposed.*

We obtain the basic reproduction number under Assumption 1 as follows

$$\tilde{R}_0 = \sqrt{R_H + R_D},$$

where

$$R_H := \frac{\gamma_F \beta_{FH} a_H^2 (\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H)}{(\delta_F + \gamma_F)\delta_F(\delta_H + \gamma_H)(\delta_H + \nu_H)},$$
$$R_D := \frac{\gamma_F \beta_{FD} a_D^2 (\beta'_{DF}c + \beta'_{DF}\delta_D + \beta'_{DF}\nu_D + \beta_{DF}\gamma_D)(\delta_D + \omega)}{(\delta_D + \gamma_D + c)(\delta_D + \nu_D + c)(\delta_D + \omega + \nu)}.$$

Remark 1. Since $\tilde{R}_0 = R_0|_{p=q=0}$, it follows that $R_0 \geq \tilde{R}_0$. That is, the basic reproduction number with vertical transmission in dogs is greater than that without vertical transmission in dogs.

Moreover, we obtain the following result.

Theorem 3.2. *Under Assumption 1, the disease-free equilibrium is locally stable if $\tilde{R}_0 < 1$ and unstable if $\tilde{R}_0 > 1$.*

When Assumption 1 does not hold, we further discuss the basic reproduction number and equilibria in two cases: (i) blocking the transmission between dogs and sandflies and (ii) blocking the transmission between human and sandflies. In the next two sections, we will study not only the transmission between one host and sandfly, but also the transmission in the host without sandflies.

4. **Blocking dog-sandfly transmission.** For the case of blocking the transmission between dogs and sandflies, we make the following assumption.

Assumption 2. $a_D = 0$.

Under this assumption, the eigenvalues of the matrix FV^{-1} satisfy the equation

$$x^3[\delta_F(\gamma_H + \delta_H)(\gamma_F + \delta_F)(\delta_H + \nu_H))x^2 - a_H^2\beta_{FH}\gamma_F(\beta'_{HF}\nu_H + \beta'_{HF}\delta_H + \beta_{HF}\gamma_H)]$$
$$[(\gamma_D + \delta_D + c)(\delta_D + \nu_D + c)x - \lambda_D(q\gamma_D + p\delta_D + p\nu_D + pc)] = 0.$$

Thus, the basic reproduction number is

$$R_0^H := \max\{R_0^{HD}, R_0^{HH}\},$$

where

$$R_0^{HD} := \frac{\lambda_D(q\gamma_D + p(\delta_D + \nu_D + c))}{(\gamma_D + \delta_D + c)(\delta_D + \nu_D + c)},$$
$$R_0^{HH} := a_H\sqrt{\frac{\beta_{FH}\gamma_F(\beta'_{HF}\nu_H + \beta'_{HF}\delta_H + \beta_{HF}\gamma_H)}{\delta_F(\gamma_H + \delta_H)(\gamma_F + \delta_F)(\delta_H + \nu_H)}}.$$

To discuss the existence of the endemic equilibria of system (1), we first consider the dog-only system

$$\begin{cases} \frac{dS_D}{dt} = \lambda_D - p\lambda_D E_D - q\lambda_D I_D - (\delta_D + \nu)S_D + \omega R_D, \\ \frac{dE_D}{dt} = p\lambda_D E_D + q\lambda_D I_D - (\delta_D + \gamma_D + c)E_D, \\ \frac{dI_D}{dt} = \gamma_D E_D - (\delta_D + \nu_D + c)I_D, \\ \frac{dR_D}{dt} = \nu S_D + \nu_D I_D - (\delta_D + \omega)R_D \end{cases} \tag{6}$$

and then the sandfly-human system

$$\begin{cases} \frac{dS_F}{dt} = \lambda_F - (\beta'_{HF}E_H + \beta_{HF}I_H)a_H\frac{S_F}{N_F} - \delta_F S_F, \\ \frac{dE_F}{dt} = (\beta'_{HF}E_H + \beta_{HF}I_H)a_H\frac{S_F}{N_F} - (\delta_F+\gamma_F)E_F, \\ \frac{dI_F}{dt} = \gamma_F E_F - \delta_F I_F, \\ \frac{dS_H}{dt} = \lambda_H - \beta_{FH}a_H I_F\frac{S_H}{N_H} - \delta_H S_H, \\ \frac{dE_H}{dt} = \beta_{FH}a_H I_F\frac{S_H}{N_H} - (\delta_H+\gamma_H)E_H, \\ \frac{dI_H}{dt} = \gamma_H E_H - (\delta_H+\nu_H)I_H, \\ \frac{dR_H}{dt} = \nu_H I_H - \delta_H R_H. \end{cases} \tag{7}$$

If $R_0^{HD} \neq 1$, the disease-free equilibrium $(S_D^0, 0, 0, R_D^0)$ is the unique equilibrium of the sandfly-human system (6). It is stable if $R_0^{HD} < 1$ and unstable if $R_0^{HD} > 1$. If $R_0^{HD} = 1$, the equilibrium $(S_D^*, E_D^*, I_D^*, R_D^*)$ lies on a singular line, where $I_D^* > 0$ and

$$\begin{aligned} S_D^* &= \frac{1}{\gamma_D\delta_D(\delta_D+\omega+\nu)}[-\delta_D I_D^*\lambda_D(p\nu_D + pc + p\delta_D + q\gamma_D) - \omega\lambda_D I_D^*(p\delta_D \\ &\quad + p\nu_D + pc + q\gamma_D) + \lambda_D\gamma_D(\delta_D+\omega) + \omega I_D^*(c^2 + \nu_D\gamma_D + c\delta_D + c\nu_D + c\gamma_D)], \\ E_D^* &= \frac{(\delta_D+\nu_D+c)}{\gamma_D}I_D^*, \\ R_D^* &= \frac{1}{\gamma_D\delta_D(\delta_D+\omega+\nu)}[\nu\lambda_D\gamma_D - \nu\lambda_D I_D^*(p\delta_D + p\nu_D + pc + q\gamma_D) \\ &\quad + \delta_D I_D^*(c\gamma_D + c\delta_D + \nu_D\gamma_D + c^2) + \nu_D I_D^*(\nu\gamma_D + c^2 + c\delta_D) \\ &\quad + \nu c I_D^*(\delta_D + \nu_D + \gamma_D)]. \end{aligned}$$

Particularly, when $p = q = 0$, $R_0^{HD} \equiv 0$, the disease will be eliminated within dogs in this case.

For the sandfly-human system, we obtain the following result for the endemic equilibrium.

Theorem 4.1. *The disease-free equilibrium $(S_F^0, 0, 0, S_H^0, 0, 0, 0)$ of system (7) is stable if $R_0^{HH} < 1$ and unstable if $R_0^{HH} > 1$. Moreover, if $R_0^{HH} > 1$, a unique disease endemic equilibrium $E_{FH}^* = (S_F^*, E_F^*, I_F^*, S_H^*, I_H^*, E_H^*, R_H^*)$ exists, where*

$$\begin{aligned} S_F^* &= \lambda_F(\gamma_H+\delta_H)(\delta_H+\nu_H)(\lambda_H\delta_F\gamma_F + \beta_{FH}a_H\gamma_F\lambda_F + \lambda_H\delta_F^2) \\ &\quad /\delta_F\beta_{FH}a_H\gamma_F[\delta_H\lambda_F(\delta_H+\gamma_H+\nu_H) + a_H\lambda_H(\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H) \\ &\quad + \nu_H\lambda_F\gamma_H], \\ E_F^* &= \frac{\lambda - \delta_F S_F^*}{\delta_F+\gamma_F}, \quad I_F^* = \frac{\gamma_F(\lambda - \delta_F S_F^*)}{\delta_F(\delta_F+\gamma_F)}, \\ S_H^* &= \frac{\delta_F\lambda_H^2(\delta_F+\gamma_F)}{\delta_H[\beta_{FH}a_H\gamma_F(\lambda_F - \delta_F S_F^*) + \lambda_H\delta_F(\delta_F+\gamma_F)]}, \\ E_H^* &= \frac{\lambda_F\gamma_H(\lambda_F - \delta_F S_F^*)(\delta_H+\nu_H)}{a_H\gamma_H S_F^*\delta_F(\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H)}, \\ I_H^* &= \frac{\lambda_F\gamma_H(\lambda_F - \delta_F S_F^*)}{a_H S_F^*\delta_F(\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H)}, \\ R_H^* &= \frac{\nu_H\lambda_F\gamma_H(\lambda_F - \delta_F S_F^*)}{a_H S_F^*\delta_F\delta_H(\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H)}. \end{aligned}$$

Proof. For the sandfly-human system (7), when $R_0^{HH} < 1$ the disease-free equilibrium $(S_F^0, 0, 0, S_H^0, 0, 0, 0)$ is the unique equilibrium. It is stable if $R_0^{HH} < 1$ and unstable if $R_0^{HH} > 1$.

For the endemic equilibrium of sandfly-human system (7), from $\frac{dS_F}{dt} = \frac{dE_F}{dt} = \frac{dI_F}{dt} = \frac{dI_H}{dt} = 0$, the equilibrium $(S_F^*, E_F^*, I_F^*, S_H^*, E_H^*, I_H^*, R_H^*)$ satisfies

$$I_F^* = \frac{\gamma_F}{\delta_F} E_F^*,\ E_F^* = \frac{\lambda_F - \delta_F S_F^*}{\delta_F + \gamma_F},\ E_H^* = \frac{\delta_H + \nu_H}{\gamma_H} I_H^*,$$
$$I_H^* = \frac{\lambda_F \gamma_H (\lambda_F - \delta_F S_F^*)}{a_H S_F^* \delta_F (\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H)}. \tag{8}$$

On the other hand, from $\frac{dS_H}{dt} = \frac{dE_H}{dt} = \frac{dI_H}{dt} = \frac{dR_H}{dt} = 0$, we have

$$E_H^* = \frac{\delta_H + \nu_H}{\gamma_H} I_H^*,\ R_H^* = \frac{\nu_H}{\delta_H} I_H^*,\ E_F^* = \frac{\lambda_H \delta_F (\lambda_H - \delta_H S_H^*)}{\beta_{FH} a_H \gamma_F \delta_H S_H^*},$$
$$I_H^* = \frac{\gamma_H (\lambda_H - \delta_H S_H^*)}{\delta_H (\delta_H + \gamma_H + \nu_H) + \nu_H \gamma_H}. \tag{9}$$

Because E_F^* and I_H^* in (8) are equivalent to those in (9), the following equations for S_H^* and S_F^* hold:

$$\frac{\lambda_F - \delta_F S_F^*}{\delta_F + \gamma_F} = \frac{\lambda_H \delta_F (\lambda_H - \delta_H S_H^*)}{\beta_{FH} a_H \gamma_F \delta_H S_H^*},$$
$$\frac{\lambda_F \gamma_H (\lambda_F - \delta_F S_F^*)}{a_H S_F^* \delta_F (\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H)} = \frac{\gamma_H (\lambda_H - \delta_H S_H^*)}{\delta_H (\delta_H + \gamma_H + \nu_H) + \nu_H \gamma_H}, \tag{10}$$

which have solutions

$$S_{F1}^* = \frac{\lambda_F}{\delta_F},\ S_{H1}^* = \frac{\lambda_H}{\delta_H},$$

and

$$\begin{aligned} S_{F2}^* &= \lambda_F(\gamma_H + \delta_H)(\delta_H + \nu_H)(\lambda_H \delta_F \gamma_F + \beta_{FH} a_H \gamma_F \lambda_F + \lambda_H \delta_F^2)/\delta_F \beta_{FH} a_H \gamma_F \\ &\quad [\delta_H \lambda_F (\delta_H + \gamma_H + \nu_H) + a_H \lambda_H (\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H) + \nu_H \lambda_F \gamma_H], \\ S_{H2}^* &= \frac{\delta_F \lambda_H^2 (\delta_F + \gamma_F)}{\delta_H [\beta_{FH} a_H \gamma_F (\lambda_F - \delta_F S_F^*) + \lambda_H \delta_F (\delta_F + \gamma_F)]}. \end{aligned}$$

Note that for the endemic equilibrium, $E_F^*, I_F^*, E_H^*, I_H^* > 0$. Therefore, the solution (S_{F1}^*, S_{F2}^*) is ignored. Moreover, if $R_0^{HH} > 1$, we have

$$\begin{aligned} &\lambda - \delta_F S_F^* \\ &= \frac{\lambda_F \lambda_H [a_H^2 \beta_{FH} \gamma_F (\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H) - \delta_F (\gamma_H + \delta_H)(\delta_F + \gamma_F)(\delta_H + \nu_H)]}{\beta_{FH} a_H \gamma_F [\delta_H \lambda_F (\delta_H + \gamma_H + \nu_H) + a_H \lambda_H (\beta'_{HF}\delta_H + \beta'_{HF}\nu_H + \beta_{HF}\gamma_H) + \nu_H \lambda_F \gamma_H]} \\ &> 0. \end{aligned}$$

Then, the sandfly-human system (7) always has a unique endemic equilibrium $(S_F^*, E_F^*, I_F^*, S_H^*, E_H^*, I_H^*, R_H^*)$. □

Therefore, we can conclude the following results under Assumption 2 for the full system (1).

Theorem 4.2. *Assume that Assumption 2 holds.*

(i) If $R_0^H < 1$, the disease-free equilibrium $E^0 = (S_D^0, 0, 0, R_D^0, S_F^0, 0, 0, S_H^0, 0, 0, 0)$ is the unique equilibrium of system (1), and it is locally stable; if $R_0^H > 1$, E^0 is unstable.

(ii) If $R_0^{HH} > 1$, the disease-endemic equilibrium of system (1) exists. Moreover, if $R_0^{HH} > 1$ and $R_0^{HD} \neq 1$, there is only one diseaseendemic equilibrium $E^* = (S_D^0, 0, 0, R_D^0, S_F^*, E_F^*, I_F^*, S_H^*, I_H^*, E_H^*, R_H^*)$ (only sandfly-human disease endemic); if $R_0^{HH} > 1$ and $R_0^{HD} = 1$, there is a disease-endemic singular line $(S_D^*, E_D^*, I_D^*, R_D^*, S_F^*, E_F^*, I_F^*, S_H^*, I_H^*, E_H^*, R_H^*)$. Here S_D^0, R_D^0, S_F^0, S_H^0, S_D^*,

E_D^*, I_D^*, R_D^*, S_F^*, E_F^*, I_F^*, S_H^*, I_H^*, E_H^* and R_H^* are the same as the above statement.

Remark 2. When vertical transmission of dogs exists, VL is still able to be endemic in dogs even if the transmission between sandflies and dogs is blocked.

5. **Blocking human-sandfly transmission.** To discuss the case that the human-sandfly transmission is blocked, we make the following assumption.

Assumption 3. $a_H = 0$.

Under this assumption, the eigenvalues of the matrix FV^{-1} satisfy the equation

$$\begin{aligned}&\lambda^4[\delta_F(\gamma_F+\delta_F)(\gamma_D+\delta_D+c)(\delta_D+\nu_D+c)(\nu+\omega+\delta_D)\lambda^2\\&-\delta_F\lambda_D(\gamma_F+\delta_F)(\nu+\omega+\delta_D)(q\gamma_D+p(\delta_D+\nu_D+c))\lambda\\&-a_D^2\beta_{FD}\gamma_F(\delta_D+\omega)(\beta'_{DF}\delta_D+\beta'_{DF}c+\beta'_{DF}\nu_D+\beta_{DF}\gamma_D]=0.\end{aligned}$$

Thus, the basic reproduction number is

$$R_0^D := \frac{\lambda_D(q\gamma_D+p(\delta_D+\nu_D+c))}{2(\gamma_D+\delta_D+c)(\delta_D+\nu_D+c)}+\sqrt{\Delta},$$

where

$$\begin{aligned}\Delta \;=\;& \frac{\lambda_D^2(q\gamma_D+p(\delta_D+\nu_D+c))^2}{4(\gamma_D+\delta_D+c)^2(\delta_D+\nu_D+c)^2}\\&+\frac{a_D^2\beta_{FD}\gamma_F(\delta_D+\omega)(\beta'_{DF}(\delta_D+c+\nu_D)+\beta_{DF}\gamma_D)}{\delta_F^2(\gamma_F+\delta_F)^2(\gamma_D+\delta_D+c)^2(\delta_D+\nu_D+c)^2(\nu+\omega+\delta_D)^2}.\end{aligned}$$

Similar to Theorem 4.2(i), we have the following result:

Theorem 5.1. *Under Assumption 3, the disease-free equilibrium of system (1) is locally stable if $R_0^D < 1$ and unstable if $R_0^D > 1$.*

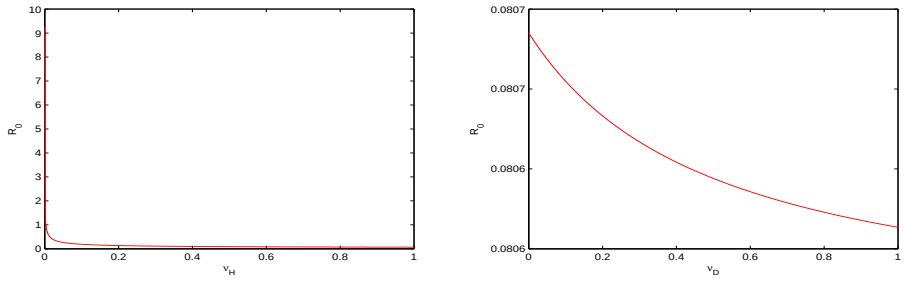
We further analyze the human-only system

$$\begin{cases}\frac{dS_H}{dt} = \lambda_H - \delta_H S_H,\\ \frac{dE_H}{dt} = -(\delta_H+\gamma_H)E_H,\\ \frac{dI_H}{dt} = \gamma_H E_H - (\delta_H+\nu_H)I_H,\\ \frac{dR_H}{dt} = \nu_H I_H - \delta_H R_H.\end{cases} \tag{11}$$

It follows that the disease-free equilibrium $(S_H^0, 0, 0, 0)$ is the unique equilibrium of system (11) and it is always stable. This presents an ideal situation that we can protect humans from the sandflies and thus eliminate the disease in humans.

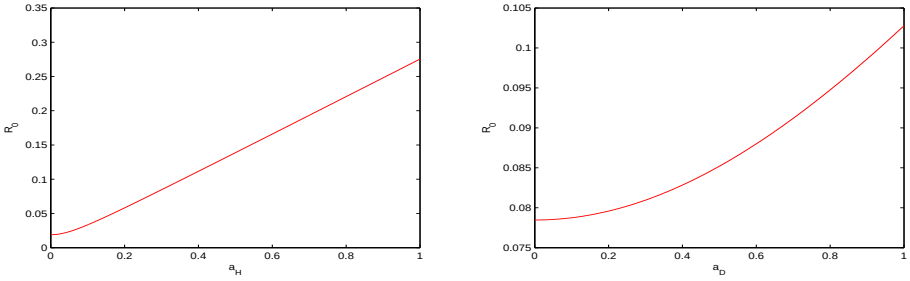
6. **Sensitivity analysis.** In this section, we present our sensitivity analysis to show how the basic reproduction number changes in terms of various values of parameters and to find out which parameters have more influence on the transmission of VL. The parameter values we use in the simulations are given in Table 2.

Firstly, we analyze the change of $\tilde{R}_0$ with respect to the parameters, shown in Figures 6 - 9. From the figures, we can see that if we ignore the vertical transmission from mother dogs to newborn dogs, that is, under Assumption 1, the transmission between humans and sandflies is more important than that between dogs and sandflies. $\tilde{R}_0$ decreases as the biting rates decrease, or probabilities of transmissions decrease. Increasing vaccination rate of dogs ν or culling rate of exposed and infective dogs c can also reduce $\tilde{R}_0$.



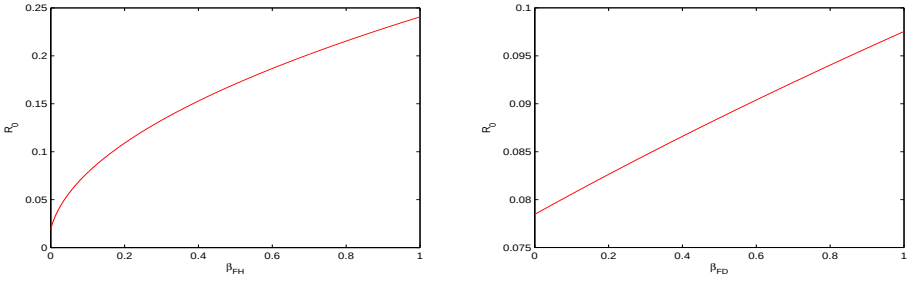
(a) (b)

FIGURE 5. The relationship between the basic reproduction number $\tilde{R}_0$ without vertical transmission and (a) recovery rate of humans ν_H; (b) recovery rate of dogs ν_D.



(a) (b)

FIGURE 6. The relationship between the basic reproduction number $\tilde{R}_0$ without vertical transmission and (a) bitting rate by sandflies on humans a_H; (b) bitting rate by sandflies on dogs a_D.



(a) (b)

FIGURE 7. The relationship between the basic reproduction number $\tilde{R}_0$ without vertical transmission and (a) probability of transmission from sandflies to humans β_{FH}; (b) probability of transmission from sandflies to dogs β_{FD}.

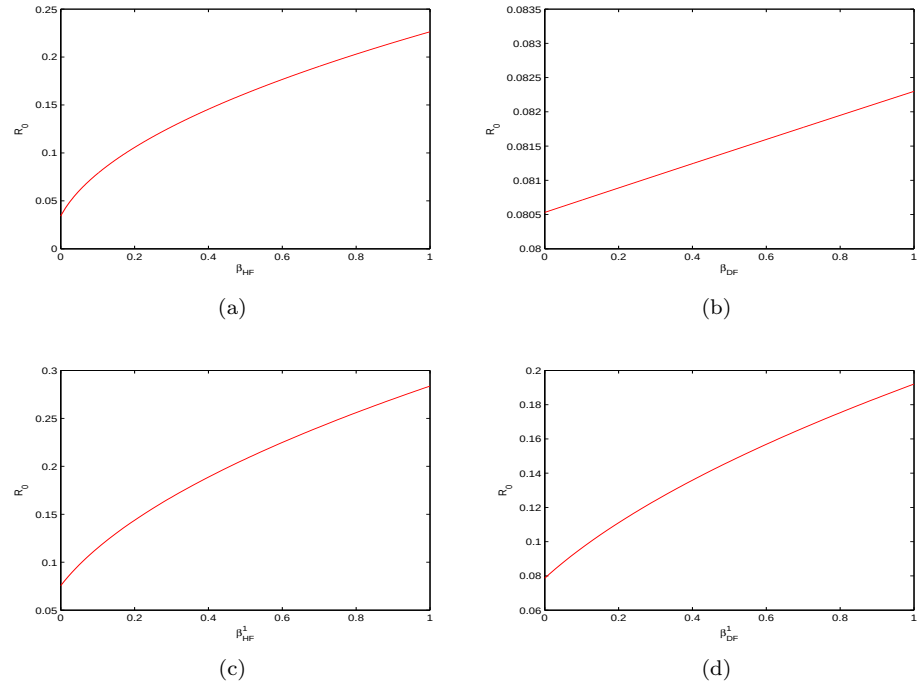


FIGURE 8. The relationship between the basic reproduction number $\tilde{R}_0$ without vertical transmission and (a) probability of transmission from infectious humans to sandflies β_{HF}; (b) probability of transmission from exposed humans to sandfliesβ'_{HF}; (c) probability of transmission from infectious dogs to sandflies β_{DF}; (d) probability of transmission from exposed dogs to sandflies β'_{DF}.

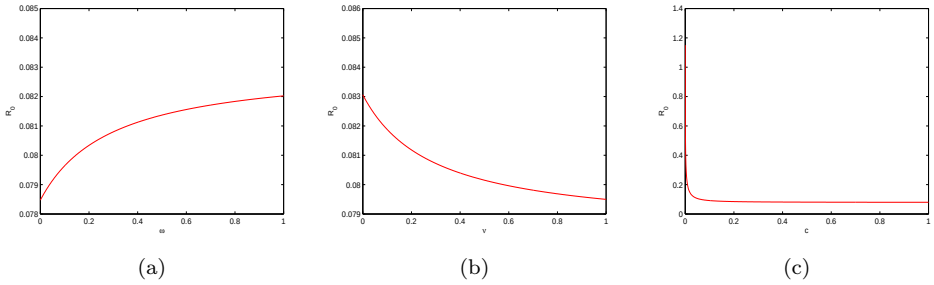


FIGURE 9. The relationship between the basic reproduction number $\tilde{R}_0$ without vertical transmission and (a) the loss rate of vaccination in dogs ω; (b) vaccination rate of dogs ν; and (c) culling rate of exposed and infective dogs c.

TABLE 2. Parameter values

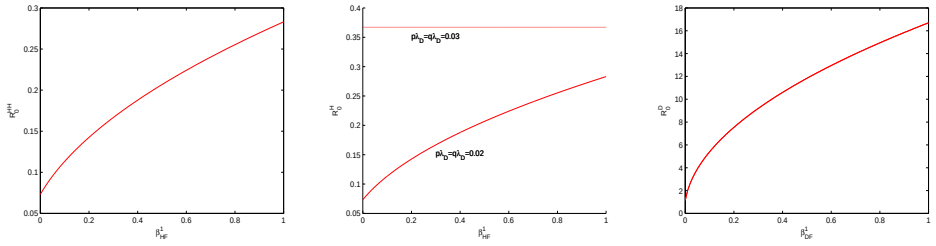
Parameter	values	References	Parameter	values	References
λ_D	8	[9, 22]	λ_H	2 million	[29]
$1/\delta_D$	599 days	[7]	$1/\delta_F$	14 days	[14]
$1/\delta_H$	73 years	[31]	β_{FD}	50%	[12]
β'_{DF}	$0 \sim 70\%$	assumed	β_{DF}	70%	[12]
β_{FH}	50%	[12]	β'_{HF}	$0 \sim 70\%$	assumed
β_{HF}	70%	[12]	p	32%	[3]
q	32%	[3]	a_D	0.1 per day	[12]
a_H	0.1 per day	[12]	$1/\gamma_D$	10 days	[25]
$1/\gamma_F$	6 days	[25]	$1/\gamma_H$	60 days	[25]
c	0.69	[15]	ν	0.165	[22]
ω	1/1095	assumed	ν_D	0.083	[15]
ν_H	0.12	[12]			

Then we compare the situations under Assumption 3 and Assumption 2. From Figures 10(a), 11(a) and 12(a), R_0^{HH} increases as any of β'_{HF}, β_{HF} and β_{FH} increases. Figures 10(b), 11(b) and 12(b) show that R_0^{HH} changes in terms of β'_{HF}, β_{HF} and β_{FH} with various $p\lambda_D$ and $q\lambda_D$. The simulation results show that even the transmission between dogs and sandflies is blocked, the parameters of dogs affect the basic reproduction number when $p\lambda_D$ and $q\lambda_D$ are sufficiently large. Note that in Figures 10(b) and 11(b), when $p\lambda_D = q\lambda_D = 0.03$, R_0^H changes slightly even when β'_{HF} and β_{HF} change from 0 to 1. Thus, when the vertical transmission of dogs is large, the influence of the change of transmission has no distinction between humans and sandflies on the basic reproduction number is not obvious.

Furthermore, comparing sub-figure (b) and (c) from Figure 10 to Figure 12, we can observe that the basic reproduction number increases faster in (c) than in (b). Thus, when we consider the vertical transmission from mother dogs to newborn dogs, the transmission between dogs and sandflies are more important than the transmission between humans and flies. This is totally different from the case under Assumption 1.

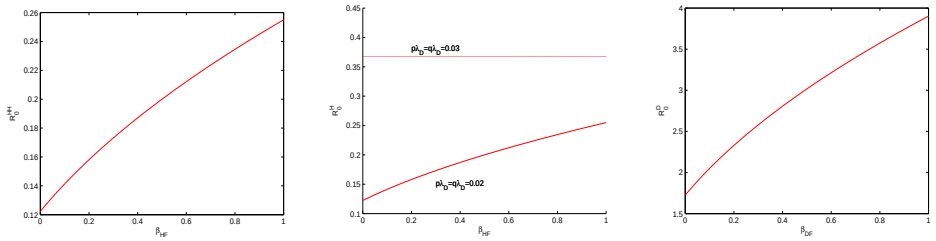
Finally, we focus on the parameters for dogs. From Figure 13, the basic reproduction number increases as the birth rate for dogs λ_D increases, which decreases as any of culling rate c, vaccination rate ν, and recovery rate ν_D increases. R_0^D decreases most quickly in Figure 13(b). Thus, if Leishmaniasis is suddenly endemic in dogs, the most effective method to control the disease is culling infected dogs. However, based on humanitarianism, we suggest to cure infectious dogs and vaccine susceptible dogs, which also help to control the disease. The observations from Figure 13(c) and (d) showed that the vaccination plays a more important role than cure from the perspective of disease spread.

We choose the sample size $n = 1500$. In Figure 14, we give the partial rank correlation coefficient (PRCC) of the basic reproduction number with blocking dog-sandfly transmission R_0^H with respect to our parameter ranges. We first note the effect of death rate of dogs δ_D, death rate of sandflies δ_F, recovery rate of humans ν_H and culling rate of exposed and infectious dogs c: as they increase, we obtain a smaller R_0^H. To increase δ_F, the DDT was the first insecticide used against phlebotomine sandflies in many countries including Brazil. To increase ν_H, more effective treatments on infective humans are needed. Increasing δ_D and c is not commendatory because it remains highly questionable. On the other hand, as λ_D, $a_H\beta_{FH}$, $a_H\beta_{HF}$, $a_H\beta'_{HF}$, p and q increase, we have a larger R_0^H. It is interesting



(a) (b) (c)

FIGURE 10. The relationship between (a) the basic reproduction numbers R_0^{HH} of human-sandfly transmission for sub-system (7) and the probability of transmission from exposed humans to sandflies β'_{HF}; (b) the basic reproduction number R_0^H with blocking dog-sandfly transmission and the probability of transmission from exposed humans to sandflies β'_{HF}; (c) the basic reproduction number R_0^D and probability of transmission from exposed dogs to sandflies β'_{DF}.

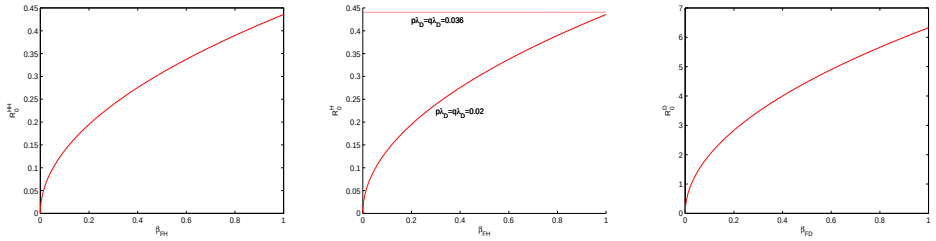


(a) (b) (c)

FIGURE 11. The relationship between (a) the basic reproduction number R_0^{HH} of human-sandfly transmission for sub-system (7) and ((a) and (b)) probability of transmission from infectious humans to sandflies β_{HF}; (b) the basic reproduction number R_0^H with blocking dog-sandfly transmission and probability of transmission from infectious humans to sandflies β_{HF}; (c) the basic reproduction number R_0^D and probability of transmission from infectious dogs to sandflies β_{DF}.

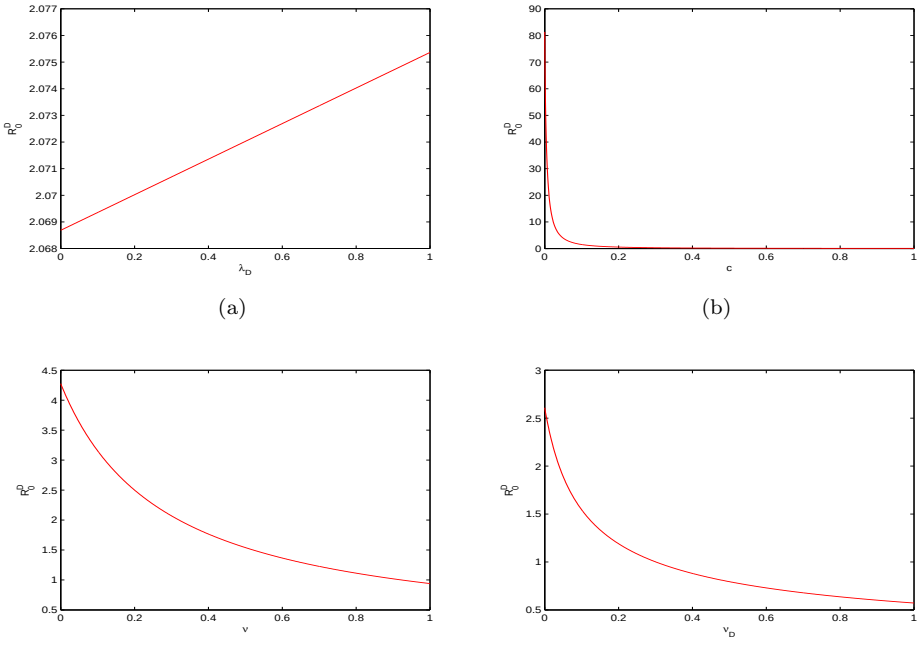
that compared with q, p has more influences on R_0^H. Compared with $a_H\beta_{HF}$, $a_H\beta'_{HF}$ influences more on R_0^H. It reminds us that the transmission from exposed humans and exposed dogs is more important.

In Figure 15, we present the PRCC for the basic reproduction number with blocking human-sandfly transmission R_0^D. The results of λ_D, δ_D, δ_F, p, q and c are similar to Figure 14. However, $a_D\beta_{FD}$, $a_D\beta_{DF}$, $a_D\beta'_{DF}$ and ν are absent in Figure 14. As $a_D\beta_{FD}$, $a_D\beta_{DF}$ and $a_D\beta'_{DF}$ increase, R_0^D increases. As ν increases, R_0^D decreases, while it has no effect on R_0^H. Thus, when transmission between dogs and



(a) (b) (c)

FIGURE 12. The relationship between (a) the basic reproduction number R_0^{HH} of human-sandfly transmission for sub-system (7) and probability of transmission from infectious sandflies to humans β_{FH}; (b) the basic reproduction number R_0^H with blocking dog-sandfly transmission R_0^H and probability of transmission from infectious sandflies to humans β_{FH}; (c) the basic reproduction number R_0^D and probability of transmission from infectious sandflies to dogs β_{FD}.



(a) (b) (c) (d)

FIGURE 13. The relationship between the basic reproduction number with blocking the human-sandfly transmission R_0^D and (a) recruitment rate of susceptible dogs λ_D; (b) culling rate of exposed and infective dogs c; (c) vaccination rate of dogs ν (c), recovery rate of dogs ν_D.

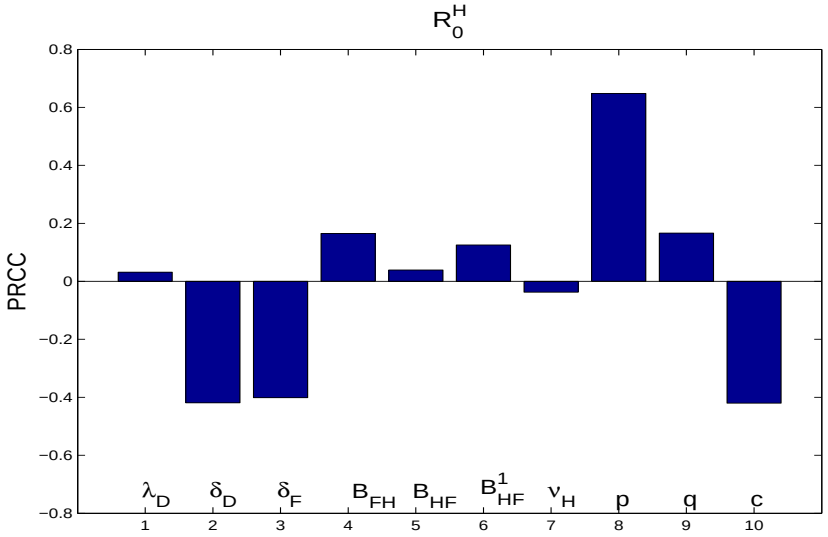


FIGURE 14. Partial rank correlation coefficients (PRCC) calculated using parameter ranges from Latin Hypercube Sampling with respect to the basic reproduction number with blocking dog-sandfly transmission R_0^H,where $B_{FH} = a_H\beta_{FH}$, $B_{HF} = a_H\beta_{HF}$, $B^1_{HF} = a_H\beta'_{HF}$.

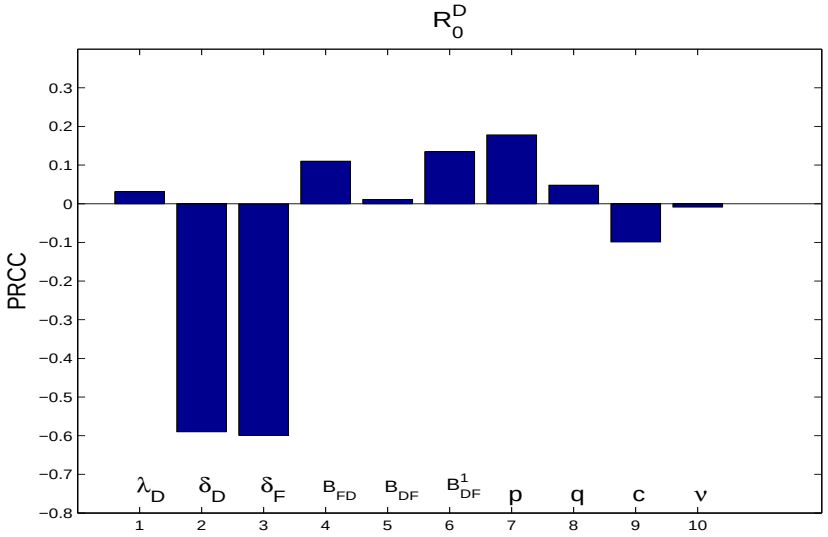


FIGURE 15. Partial rank correlation coefficients (PRCC) calculated using parameter ranges from Latin Hypercube Sampling with respect to the basic reproduction number with blocking human-sandfly transmission R_0^D, where $B_{FD} = a_D\beta_{FD}$, $B_{DF} = a_D\beta_{DF}$, $B^1_{DF} = a_D\beta'_{DF}$.

sandflies exists, more vaccination on dogs helps to control VL. However, vaccination on dogs does not help to control VL if there is only transmission within dogs.

7. **Discussion.** Dogs infected with *L. infantum* have a long asymptomatic period during which they are parasitic and able to transmit to sandflies ([3]). We hypothesize that this period of latency remarks conversion from a low transmission to a high transmission state, influenced by factors that comprise the health status of dogs, including morbid infections, nutritional status, and pregnancy. Similar factors are involved in human susceptibility to clinical diseases ([19]). Understanding the interplay between comorbidities and immune control of visceral leishmaniasis is critical for modeling parasitemia and transmission of VL, to either vector or vertical transmission, with dog reservoir populations. Moreover, within the United States, there is no evidence of vector-borne transmission of VL, vertical transmission has maintained *L. infantm* infection within a subset of dogs for at least three decades ([2]).

A mathematical model for visceral leishmaniasis transmission with dogs, sandflies and humans was developed in this paper to investigate how to prevent the disease transmission. We did not try to use our model to simulates the VL data in Brazil and China mentioned in Section 1. Instead, we tried to understand the transmission dynamics of VL and to seek effective prevention and control measures by analyzing the model. The calculation and sensitivity analysis of the basic reproduction number indicates that the vertical transmission of dogs affects the spread of VL. The analysis in Section 3 shows that the basic reproduction number with vertical transmission within dogs is obviously greater than that without vertical transmission. When the dog-sandfly transmission is blocked, VL could still become endemic among dogs even without the vectors. Furthermore, it is shown in the sensitivity analysis that when the vertical transmission of dogs is large, the change of transmission between humans and sandflies (β'_{HF} and β_{HF}) does not have a distinct influence on the basic reproduction number. Note that the partial rank correlation coefficient shows that the vertical transmission from exposed dogs affects the basic reproduction number greater than that from infective dogs. It suggests that we must pay enough attention to the asymptomatic dog populations.

Our sensitivity analysis shows that increasing either $a_D\beta_{HF}$, $a_D\beta'_{HF}$, $a_D\beta_{FH}$, $a_D\beta_{DF}$, $a_D\beta'_{DF}$ or $a_D\beta_{FD}$ will increase the basic production number. It accords with the fact that prevention of leishmaniasis requires blocking a step in the parasite's life cycle. Insecticide-impregnated dog collars, for example, can protect dogs from the bites of the vectors for several weeks. However, these are more expensive.

The model developed by Dye in [7] indicates that a canine vaccine would be a potent tool for decreasing both the human and canine incidence of leishmaniasis. Our sensitivity analysis also shows that increasing canine vaccination rate can reduce the basic reproduction number. There are two vaccines commercially available for prevention of canine leishmaniasis, with unclear efficacy. Although the basic reproduction number may decrease as a result of increasing c, the culling of seropositive dogs is not recommended. One fact is that the true number of dogs that need to be killed in order to decrease the incidence of VL in humans is unknown. Moreover, it is not only expensive but also difficult to implement the selective elimination of seropositive dogs, particularly in developing countries.

In conclusion, to control the visceral leishmaniasis, it is better to control the vertical transmission in dogs especially in the asymptomatic dogs, increase vaccination rate in dogs, and give more treatments to infective dogs.

L. infantum/HIV co-infection is another challenge for public health in many countries. It has been proven that *L. infantum*/HIV co-infected patients might be highly infectious to phlebotomine sandflies ([20]). There is also evidence for sexual transmission of VL ([21]). These complicate the transmission dynamics of LV and deserve further investigations.

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E-mail address: lanzou@163.com
E-mail address: j.chen@math.miami.edu
E-mail address: ruan@math.miami.edu