Impact of domestic animals on prevalence of vector-borne diseases in humans

by

Md Mondal Hasan Zahid

Presented to the Faculty of the Graduate School of
The University of Texas at Arlington
in Partial fulfillment of the Requirements
for the Degree of

Doctor of Philosophy

The University of Texas at Arlington
May 2020

ACKNOWLEDGEMENTS

I would first like to thank the Almighty Allah for his blessings in my life. I would also like to thank my parents, Md Nazim Uddin Mondal and Sabiha Bilkis, for their endless efforts and contributions to my upbringing and education and for all their sacrifices to ensure my success. A special thank you goes to my wife and sons for their enormous sacrifices and support throughout my doctoral program. A big thank you goes to my elder brother, relatives, friends, and mentors for their prayers, support, and encouragement throughout my studies. I would like to express my deepest appreciation to my advisor, Dr. Christopher Kribs, for his guidance and encouragement. I am grateful to have learned from him and could not have asked for a better advisor. I would also like to thank the other members of my committee, Dr. Hristo Kojouharov, Dr. James Grover, Dr. Benito Chen, and Dr. Gaik Ambartsoumian, for their valuable feedback. Also, I would like to thank Dr. Minerva Cordero for her support to ensure the successful completion of my doctoral program. In addition, I want to thank Dr. Ricardo Gürtler for suggesting relevant articles for Chapter 2.

June 1, 2020

Impact of domestic animals on prevalence of vector-borne diseases in humans

Md Mondal Hasan Zahid

The University of Texas at Arlington

Supervising Professor: Dr. Christopher Kribs

Abstract

Vector-borne infectious diseases are one of the leading problems for public health worldwide, particularly in underdeveloped and developing countries. These diseases infect humans through the bite of infected vectors. The effect of host diversity on disease persistence, well studied in ecological literature, is examined here in a domestic setting. Some additional hosts dilute infection, while others amplify certain disease infections. Domestic animals can play an important role, as an additional host, in the disease dynamics by affecting host-pathogen interactions. However, the effect of additional hosts is not always straightforward since their presence impacts negatively by helping the vector population grow faster, and positively by reducing vector-human interactions. These facts develop a very interesting ecological question if domestic animals are helpful to human health. This study uses dynamical systems to understand disease dynamics in the presence of domestic animals, and analyses these systems qualitatively and quantitatively to understand the trade-off between these negative and positive impacts. Deterministic

population models and nonlinear ODEs are used in the development of these systems.

First, the case of Chagas disease is considered in the presence of chickens, which works here as an incompetent host. Rural customs of different placement of chickens are studied, and results showed chickens presence can reduce human infections of Chagas if they are placed at a certain distance. However, the basic reproduction number, R_0 behaves as an increasing function for up to a certain numbers of chickens, and then continues as a decreasing function of chickens. Second, visceral leishmaniasis (VL) is studied in the presence of protected dogs. As a reservoir host, dogs usually increase risk of human infections. Hence, two cases are studied here – a community without dogs, and a community with dogs protected by insecticide collars. Outcomes of this work show that community with protected dogs is better than a community without dogs in terms of human cases of VL infection. However, this reduction in infections depends on dogs' tolerance for sandfly bites. Finally, the case of Japanese encephalitis (JE) is studied in the presence of cattle. As a dead-end host, cattle help to reduce human infections of JE virus. However, in some JE prevalent areas, like India, their presence causes another human disease, leptospirosis, which spreads through the urine of infected cattle. To understand the impact of cattle in such areas, three SIR models are used. Qualitative analyses of our dynamical system and equilibria show that each disease persists when its respective basic reproduction number, $BRN > 1$. To identify the impact of cattle, total disease burdens are estimated and compared for two different scenarios – a community with cattle, and a community without cattle. These estimations show that cattle are helpful to reduce disease burden even though they cause leptospirosis infections. These three studies show that host richness by addition of domestic animals is helpful to reduce human infections of vector-borne diseases, conditionally in some cases and unconditionally in other cases.

Contents

Chapter 1

Introduction

1.1 Vector-borne diseases

Vector-borne diseases (VBDs) are one of the leading threats to the public health, specially in underdeveloped and developing countries. Humans usually get infections of these VBDs by bites of infected vectors. VBDs are responsible for more than 17% of all infectious diseases worldwide[1]. Malaria, Dengue, Chikungunya, Zika, West Nile Virus (WNV), Japanese encephalitis are well known VBDs and all these are transmitted by infected mosquitoes. There are many other VBDs which transmit by some non-mosquito vectors. Besides these well known VBDs, there are some other VBDs, like Chagas disease, leishmaniasis, schistosomiasis which affect hundreds of millions of people around the world [1]. Unfortunately, many non-mosquito transmitted vector-borne diseases have been neglected for many years and those are currently responsible for a significant portion of human infections worldwide. There are more than 700,000 deaths annually from diseases such as malaria, dengue, schistosomiasis, human African trypanosomiasis, leishmaniasis, Chagas disease, yellow fever, Japanese encephalitis and onchocerciasis [1].

1.2 Effects of additional hosts

Most vectors for VBDs get the disease producing microorganism from hosts (humans or animals) while biting to take their blood meals. Later, these infected vectors transmit the parasite either to humans or to other hosts (animals). Humans get infections through these bites; however, not all non-human hosts are infected by the bite of infected vectors. There are different types of hosts – dead-end, incompetent, competent, and reservoir. The dead-end host and incompetent host have no role in the transmission. However, there is a difference between these two – the dead-end host becomes infected by the bite of infected vector(s), whereas incompetent hosts are free of getting infections. The competent host gets infections and transmits the parasites to the vectors. The reservoir host is not only capable to transmit parasites, it also acts as a living organism where parasites can live and reproduce.

The addition of a host to a vector-host system diverts the vector population to the additional host from the focal host. This diversion either increases or decreases the disease risk based on the competency of the additional host. Thus, different hosts play different roles in the transmission of VBDs. Earlier it was believed that host richness is helpful to reduce infections of VBDs. However, recent studies show that the effect of host richness is not straightforward. In 2010, Johnson and Thieltges identified that host diversity may help to reduce human infections depending on the relative abundance of additional host(s) relative to the focal host [2]. Two years later, in 2012, Ostfeld and Keesing suggested that increases in species richness will not always decrease disease risk; indeed, in some cases diversity will cause an increase in infection risk [3]. In 2013, Miller and Huppert proved that species diversity in host populations can amplify or can dilute disease prevalence depending on vectors' preference of host [4]. They found that host diversity amplifies disease prevalence when the vector prefers the host with the highest transmission ability

and dilutes disease prevalence when the vector does not show any preference, or it prefers to bite the host with the lower transmission ability. All these studies are done from the perspective of an ecological setting.

1.3 Additional hosts in domestic setting

This dissertation shifts the context from an ecological setting to a domestic setting to answer the same question – how the presence of additional host(s) in a domestic setting affect(s) the human infections of VBDs. To answer this question, we study three different diseases in the presence of different domestic host(s).

First, we consider Chagas disease in the presence of chickens in households where chickens act like an incompetent host for the parasite *Trypanosoma cruzi (T. cruzi)*. Chagas disease spreads by the bite of infected triatomine bugs and their reproduction is limited by available sources of blood-meal. The presence of chickens distracts triatomine bugs from humans to chickens. On the other hand, chickens act as a suitable blood-meal source and help the vector population grow faster. The Chapter 2 of this dissertation aims to identify how the prevalence of Chagas disease affected by the net effect of these positive and negative impacts. In our model development, we follow the common practices among villagers to keep chickens in their houses. Based on the placement of chickens in households, we study three different cases to understand how the presence of chickens impacts the prevalence of human infections.

Second, we study visceral leishmaniasis (VL) in the presence of protected dogs (protected by insecticide-impregnated collars). Dogs are the reservoir host for the parasite of visceral leishmaniasis and hence their usual presence surely increases the disease risk

for humans. So, here we study the dynamics of VL in the presence of protected dogs to identify if the presence of these dogs is helpful to reduce human infections of VL. The presence of protected dogs helps to reduce the sandfly (vector for VL) population since the insecticide on their collars kills a fraction of the sandfly population; however, their presence increases the risk of infections because dogs are the main reservoir host for the parasite *Leishmania*.

Finally, we study the case of Japanese encephalitis (JE) in the presence of cattle in households. This study on JE virus (JEV) infections in humans is a little bit different from the other two studies of Chagas disease and VL for mainly two reasons. First, here the reproduction of the vector population (mosquitoes) is not limited by available blood-meal sources, rather by available breeding sites. Second, the presence of cattle in a domestic setting introduces another disease. Cattle are a dead-end host for the JEV and hence their presence helps to reduce JEV infections; however, their presence causes human infections of leptospirosis. Thus, the impact of cattle on human health cannot be decided just by comparing the cases of JE infection. The overall impact of cattle on disease risk in humans is to be decided by the total disease burden, resulted from these two diseases JE and leptospirosis.

1.4 Mathematical epidemiology

The modeling of infectious diseases is a widely used tool to study disease dynamics and it has been used for more than a hundred years by mathematicians, public health experts, ecologists, and by some other public health related researchers. The analysis and simulation of mathematical models help to understand the mechanism of disease spread, to predict future epidemics, to identify the impact of any disease, to identify policies to

protect human health.

In our study, we use compartmental models (SIR and SEIR) and non-linear ODEs to develop our dynamical systems to understand how the disease spreads between vector and hosts. Each of the three different studies of this dissertation conducts qualitative analysis at the beginning to understand the behavior of the disease transmission. In this process, initially, we obtain the equilibria and the basic reproduction number(s) (R_0) of our dynamical systems and then use either the corresponding Jacobian matrix directly, or the Routh-Hurwitz Criteria to find conditions on the local stability of the equilibria. Next, we analyse the global stability using either Poincaré-Bendixson Theorem, or Lyapunov function, or numerical exploration. These analyses provide an overall idea of the entire dynamical system and consequently help to understand the disease dynamics among the vector and host populations. Later, quantitative analysis is performed to estimate some threshold quantities (like R_0, the optimum number of additional hosts) of our systems. This analysis also quantifies the disease impact on human health and eventually helps to better understand the impact of domestic animals on the disease prevalence. Finally, we combine these results and use them to answer our questions in these studies. Eventually, the outcomes of these three different studies develop a detail understanding of domestic animals' role on the prevalence of vector-borne human diseases.

Chapter 2

Decoys and dilution: the impact of incompetent hosts on prevalence of Chagas disease

2.1 Introduction

2.1.1 Ecological background

Biodiversity is commonly considered a means for reduction of vector-borne zoonoses risk though it is not always true [5, 6]. Species diversity consists of two elements - species richness: number of species, and species evenness: proportional representation by each species. Adding any host to a vector-host system can reduce or can increase the disease risk. The reduction in disease risk due to the diversity in species is known as the dilution effect. The strength of dilution effect in a system depends not simply on the measures of species richness [7], it also depends on the abundance of dilution hosts relative to focal hosts [2]. The opposite effect is known as the rescue effect when the disease risk is increased. The determination of type of effect is governed by a couple of factors where the competency of the added host is one of the most important ones.

Based on the competency of additional host(s), the effect of distraction of vectors from their suitable host(s) can be broadly divided into two cases – *decoy effect* and *alternative or incompetent hosts' effect*. Decoy effect involves adding any incompetent (incapable of transmitting the disease) host whereas alternative hosts are capable of transmitting pathogens, but not as much as the focal host. The use of non-human decoys (e.g. livestock) to divert feeding mosquitoes

away from humans may reduce vector-borne infections in the short term, but the increase in successful blood meals has the potential to cause long-term increases in mosquito populations and thereby increase the risk of subsequent human exposure [5, 6].

2.1.2 Earlier works

In the last decade, many studies have investigated how biodiversity can help to reduce the incidence of infections of vector-borne zoonoses. Results from many of those studies indicate that it is more difficult than previously thought to predict the effect of biodiversity loss on the spread of vector-borne disease. In 2010, Johnson and Thieltges showed that the strength of dilution effects depends on the relative abundance of dilution hosts relative to focal hosts [2]. Two years later, in 2012, Ostfeld and Keesing suggested that increases in species richness will not always decrease disease risk; indeed, in some cases diversity will cause an increase in infection risk [3]. In 2013, Miller and Huppert tried to see the effect of host diversity on the prevalence of disease infections [4]. Their study showed the basic reproduction number, R_0, is not necessarily monotonic as a function of species diversity. Thus, the richness in host population can amplify or can dilute disease prevalence depending on vectors' preference of host. These works challenge the universally established idea that biodiversity always helps to reduce the disease risk. The challenge lies in identifying when and for what types of host–parasite interactions we are likely to find evidence of a negative relationship between diversity and disease.

This study shifts the context from sylvatic to domestic where we study the case of Chagas disease, also known as American trypanosomiasis. This is a potentially life-threatening illness caused by the protozoan parasite, *Trypanosoma cruzi* (*T. cruzi*). It is found mainly in 21 Latin American countries, where it is mostly vector-borne. The vector involved in the transmission of the parasite to humans is a triatomine bug, also known as a 'kissing bug'. An estimated 8 million people are infected worldwide, mostly in Latin America. It is estimated

that over 10,000 people die every year from clinical manifestations of Chagas disease, and more than 25 million people risk acquiring the disease [8]. Cases of Chagas disease have also been noted in the southern United States [9]. According to the World Health Organization (WHO), vector control remains the most useful method to prevent Chagas' infection in endemic areas [8].

Domestic animals play an important role in the domiciliary transmission of *T. cruzi* [10]. In 1998, Gürtler et al. investigated the influence of humans and domestic animals on household prevalence of *T. cruzi* in vector populations. Their result shows the indoor presence of chickens increases the infected vector density per house [11]. The study did not address directly the impact of presence of chickens on the prevalence of human infections. In 2007, Gürtler et al. studied the role of domestic cats and dogs in *T. cruzi* infection [12]. This study performed an entomological and sero-parasitological survey in two rural villages in Argentina. Both cats and dogs are found as epidemiologically important sources of infection for bugs and householders where dogs are nearly three times more than cats. Gürtler et al. suggested in 1998 that the preventive management of domestic animals is an essential approach to the control of Chagas disease [11]. This suggestion was implemented in 2014 where a community-based intervention was developed based on domestic animal management by De Urioste-Stone et al. and implemented in two cities in Guatemala [13]. This community intervention promoted chicken management as one of the means for reduction of Chagas disease infections.

Studies have shown that the practice, common in countries like Argentina, of bringing chickens (brooding hens) into the home for protection of eggs and chicks against predators and then leaving them outside once grown, affects domestic vector populations [14]. This study aims to identify conditions, if any, under which the presence of one common domestic animal–chickens–can reduce the vector-human interaction and eventually decrease human disease risk for Chagas. Here chickens are the additional host, which is completely unsuitable for the parasite. So, this work adds to research on species richness, specifically on the presence of an additional host. In this study, we investigate whether this inclusion of an incompetent host (decoy) dilutes or

strengthens the force of infection. Chagas disease transmission occurs primarily in rural homes in Latin America.

Usually, the presence of incompetent hosts reduces the number of encounters between the vectors and the focal host. Eventually it leads us to the perception that this reduces the disease risk. However, some earlier works, where chickens are considered to be in bedroom areas, already proved this perception wrong [10]. The practice among rural areas shows that the residence of chickens changes with time. Thus, the distance between chickens and humans is variable, rather than fixed. This fact motivates us studying the impact of the presence of chickens at varying distances from humans. In our analysis, we consider three different cases depending on the proximity of two hosts, humans and chickens. To analyze these cases, we develop models for transmission separately for each case using dynamical systems.

2.2 Model development

2.2.1 Description of cases

This work considers three different cases regarding the distance of the incompetent host (chickens) from the focal host (humans): (1) far distance case, (2) intermediate distance case, and (3) short distance case. These cases are determined by the places where chickens are kept by the villagers. Most of the year, villagers keep their chickens either in a place separated from the houses or in some part of their houses. We consider the first of these two scenarios the 'far distance case' while we consider the other the 'intermediate distance case'. However, we consider the scenario 'short distance case' when chickens are brought indoors or very close to indoors to ensure their safety at a very young age.

We begin by focusing on mean-field results rather than the range of possible variations, just to see whether the force of infection tends to be strengthened or weakened by the presence of

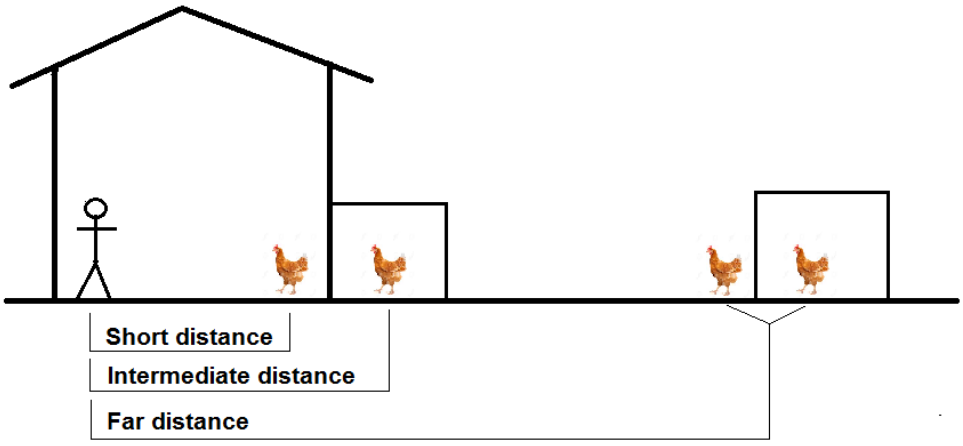


Figure 2.1: Portrayal of all the three cases

chickens. To do so, we use deterministic models (despite the small populations) since we are interested in qualitative insights. However, since stochastic effects may be significant in small populations, we will also consider a stochastic version of our model(s) to examine possible deviations from the mean.

Vectors' feeding behavior is very important in modeling vector-borne infectious diseases. In 2006, Ngwa studied the population dynamics of the mosquitos that transmit malaria to humans, incorporating the vector's feeding behavior into the model. The study divided the vector population in three categories: vectors in the breeding site, vectors moved from the breeding site to human habitat, and vectors moving from human habitat to breeding sites [36]. In a later study, Ngwa et al. further subdivided each of the three categories mentioned above into N number of sub-categories assuming that each vector has N number of gonotrophic cycles [37]. However, the triatomine vectors of Chagas disease has different behavior than mosquitos in many senses–their reproduction is independent of breeding site, they do not bite in the daytime as mosquitos do, and their movement is very limited compared to mosquitos'. Chagas vectors incline to stay near the sleeping area of the hosts, so vectors' hiding, or sleeping area is associated with specific

host populations. In our model development, we therefore base vector movement and feeding behavior on ideas in research by Gürtler et al. [10, 11].

Most people infected with Chagas disease do not know they have the disease [32, 35]. This happens as the disease is mostly asymptomatic. However, 20% - 30% of infected people may develop symptoms at a later stage (chronic stage), but it is too late to cure [31, 33, 34]. Also, people infected with Chagas disease have very limited (less than 1%) access to diagnosis and treatment [30]. Therefore, there is almost no recovery from the disease. Hence, here we consider a SI model in our work. People with Chagas disease can continue their lives without having any symptoms for 10 years or more [30]. So, we assume relatively low disease-induced death rate which allowed us to maintain a constant human population. In order to focus on the effects of the presence of incompetent hosts, we model only two host populations: primary and incompetent. The presence of other competent domestic hosts such as dogs can be incorporated by converting to a transmission-equivalent number of humans using the vectors' known feeding preferences.

2.2.2 Flow diagrams and systems

To begin with, we consider the case when chickens sleep in nests separated from the house, either a free-standing hen-house or part of barn or other building (case of far distance). Therefore, whenever bugs start to leave humans for inadequate availability of meals, they can easily and quickly find chickens as a source of their meals. However, here the vectors are unable to anticipate the presence of chickens while they are with humans.

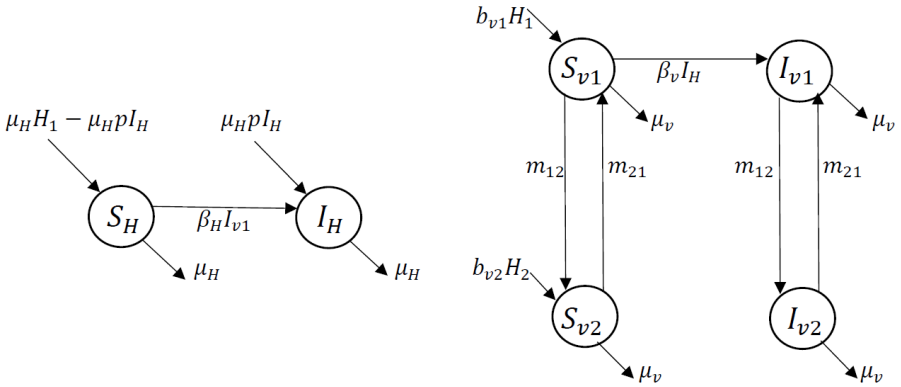


Figure 2.2: Flow diagram for 'far distance', system (2.1), where movements of vectors are independent of hosts' density.

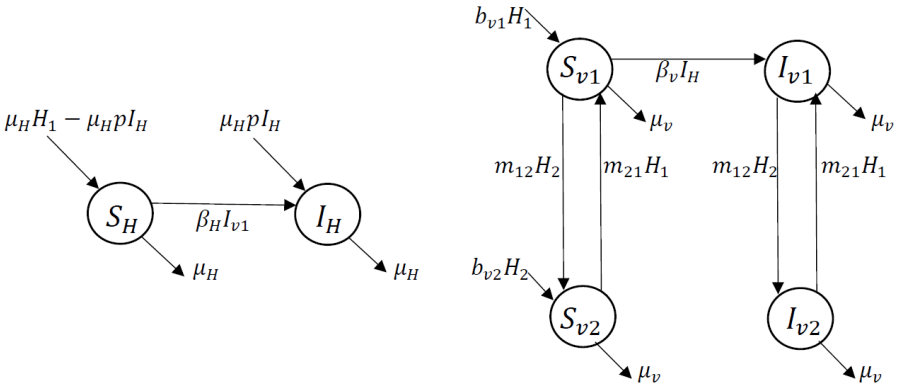


Figure 2.3: Flow diagram for 'intermediate distance', system (2.2), where movements of vectors are host density dependent.

$$
\begin{aligned}
\frac{dS_H}{dt} &= \mu_H H_1 - \mu_H p I_H - \beta_H I_{v1} S_H - \mu_H S_H \\
\frac{dI_H}{dt} &= \mu_H p I_H + \beta_H I_{v1} S_H - \mu_H I_H \\
\frac{dS_{v1}}{dt} &= b_{v1} H_1 - \beta_v I_H S_{v1} - \mu_v S_{v1} - m_{12} S_{v1} + m_{21} S_{v2} \\
\frac{dI_{v1}}{dt} &= \beta_v I_H S_{v1} - \mu_v I_{v1} - m_{12} I_{v1} + m_{21} I_{v2} \\
\frac{dS_{v2}}{dt} &= b_{v2} H_2 - \mu_v S_{v2} - m_{21} S_{v2} + m_{12} S_{v1} \\
\frac{dI_{v2}}{dt} &= m_{12} I_{v1} - m_{21} I_{v2} - \mu_v I_{v2}
\end{aligned}
\tag{2.1}
$$

$$
\begin{aligned}
\frac{dS_H}{dt} &= \mu_H H_1 - \mu_H p I_H - \beta_H I_{v1} S_H - \mu_H S_H \\
\frac{dI_H}{dt} &= \mu_H p I_H + \beta_H I_{v1} S_H - \mu_H I_H \\
\frac{dS_{v1}}{dt} &= b_{v1} H_1 - \beta_v I_H S_{v1} - \mu_v S_{v1} - m_{12} H_2 S_{v1} + m_{21} H_1 S_{v2} \\
\frac{dI_{v1}}{dt} &= \beta_v I_H S_{v1} - \mu_v I_{v1} - m_{12} H_2 I_{v1} + m_{21} H_1 I_{v2} \\
\frac{dS_{v2}}{dt} &= b_{v2} H_2 - \mu_v S_{v2} - m_{21} H_1 S_{v2} + m_{12} H_2 S_{v1} \\
\frac{dI_{v2}}{dt} &= m_{12} H_2 I_{v1} - m_{21} H_1 I_{v2} - \mu_v I_{v2}
\end{aligned}
\tag{2.2}
$$

A general compartmental model is used for describing the above mentioned idea mathematically. Here, the two hosts are humans (H_1) and chickens (H_2). Usually, some vectors are associated with humans and others are associated with chickens. However, no infections occur for the vectors (S_{v2}) who bite chickens since chickens are incompetent hosts. The per capita migration rates are independent of hosts' population density as vectors can not anticipate the presence of hosts due to the distance. Vertical transmission of T. cruzi in humans is already well documented [22, 39], and so we consider this path of transmission in our model, and assume the probability of vertical transmission (i.e., the proportion of offspring of infected mothers which are born infected due to transplacental transmission) for H_1 is p and all host demographics are at equilibrium. This is a special case (setting all the parameters related to strain I as zero) of the host switching model of [15]. All these ideas are depicted in Figure 3.1 and described by the system (2.1).

We next consider the scenario when chickens are kept a little bit closer to houses (case of intermediate distance). In this case, chickens live in a hen-house connected to the house, or in a different part of the house than the humans. Here, the proximity allows bugs staying with one host to sense the presence of other hosts and so vectors switch between hosts (humans and chickens) whenever they need. Certainly, the migration rates for vectors between hosts are determined by the availability of blood-meal sources. So, this migration between hosts is dependent on the target host's density. The model in this case is similar to the previous one, except the

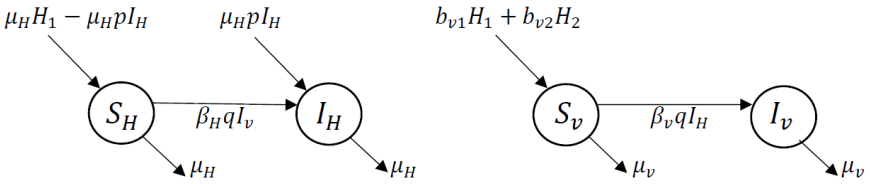


Figure 2.4: Flow diagram for 'short distance', system (2.3), where vectors don't need to migrate.

migration rates. The per capita migration rates are $m_{12}H_2$ for humans to chickens and $m_{21}H_1$ from chickens to humans. This case is visualized in Figure 2.3 and described by the system (2.2).

In the last case, chickens are brought so close to humans that vectors do not need to migrate to collect their meals (case of short distance). Now, vectors can bite and take blood meals from whomsoever they want. It is not anymore a host switching case, rather host sharing. So, all the vectors are sharing both of the host populations. Here, we assume that vectors bite humans a proportion q of the time. This case is a special case of host sharing model of [15] where all the parameters related to strain I set as zero. This model is portrayed in Figure 2.4 and represented by the system (2.3).

$$\begin{aligned}
\frac{dS_H}{dt} &= \mu_H H_1 - \beta_H q I_v S_H - \mu_H p I_H - \mu_H S_H \\
\frac{dI_H}{dt} &= \beta_H q I_v S_H + \mu_H p I_H - \mu_H I_H \\
\frac{dS_v}{dt} &= b_{v1} H_1 + b_{v2} H_2 - \beta_v q I_H S_v - \mu_v S_v \\
\frac{dI_v}{dt} &= \beta_v q I_H S_v - \mu_v I_v
\end{aligned} \tag{2.3}$$

To study the likely variation from mean-field results, we use continuous-time Markov chains (CTMC) as stochastic version of our deterministic model(s). A CTMC model has discrete populations, and discrete events occurring in continuous time as a Poisson process, with expected rates given by the deterministic rates. We use the Gillespie algorithm [38], also known as stochastic simulation algorithm (SSA), to simulate our CTMC model(s).

Table 2.1: Model variables with definition

Variable	Definition
S_H	Susceptible humans(focal host)
I_H	Infected humans
S_{v1}	Susceptible vectors associated with humans
I_{v1}	Infected vectors associated with humans
S_{v2}	Susceptible vectors associated with chickens
I_{v2}	Infected vectors associated with chickens

Table 4.1 summarizes the variables for all of our models.

2.3 Parameter estimation

While estimating parameters, we tried to take the values from the same geographical context (Argentina) to make our analysis more appropriate. Some of these parameter estimates are very rough, and we include them here primarily in order to generate illustrative qualitative trends. This study considers *Triatoma infestans* as the vector since this is the most common vector of *T. cruzi* in South America, including Argentina [16, 17, 18].

During our careful literature review, we did not find any documented data for infection rates for humans and for vectors (β_H and β_v respectively). To estimate these values we used the method from [19] which gives the following formulas for our case:

$$\beta_H = \frac{\mu_H(1-p)y_H}{(1-y_H)I_v},\ \beta_v = \frac{\mu_v y_v}{(1-y_v)I_H}$$

where y_H and y_v represent the prevalence of the disease in humans and chickens respectively. We take 27.81% (y_H) for humans [20] and 4.1% (y_v) for vectors [21], and multiply the household size and the number of bugs in a house by these prevalence values to find the value of I_H and I_v. In our literature review, we found the value 0.09 (documented as 9%) [22] for probability (proportion) of vertical transmission (p). For the human death rate, (μ_H) we take the reciprocal

Table 2.2: Estimation of average lifespan for *Triatoma infestans* while feeding only on humans and chickens (base data are taken from [16])

Feeding pattern	Stage	Duration	Lifespan by gender	Lifespan by host's	Mean lifespan
Fed on humans	Egg to Nymph V	29.2 wks	45.5 wks	46.05 wks	41.2 wks ($\frac{41.2}{52}$ year)
	Adult as male	16.3 wks			
	Egg to Nymph V	29.2 wks	46.6 wks		
	Adult as female	17.4 wks			
Fed on chickens	Egg to Nymph V	18.9 wks	34.0 wks	36.35 wks	
	Adult as male	15.1 wks			
	Egg to Nymph V	18.9 wks	38.7 wks		
	Adult as female	19.8 wks			

of their average lifespan and get $\frac{1}{77.5}$/year [23]. However, we did not find any direct documented data for vectors' death rate (μ_v). So, we used different data from the study done in 2015 by Medone et al. [16] and did our own estimation to find average lifespan for *Triatoma infestans* (Table 2.2) and finally take the reciprocal to get $\frac{52}{41.2}$/year as value for μ_v. Finally, using our own formula the infection rates are obtained as

$$\beta_H = \frac{\frac{1}{77.5}\text{/year} \times (1-0.09) \times \frac{27.81}{100}}{(1-\frac{27.81}{100}) \times (26 \times \frac{4.1}{100})\text{vector}} = 0.004\text{/vector-year},$$

$$\beta_v = \frac{\frac{52}{41.2}\text{/year} \times \frac{4.1}{100}}{(1-\frac{4.1}{100})(5 \times \frac{27.81}{100})\text{human}} = 0.041\text{/human-year}.$$

In our literature review, we did not find any documented data for vectors' birth rate per human (b_{v1}). Hence, we used the total vector population in disease free state from Table 2.4 to do back-calculation for estimating b_{v1}. Setting migration rates (m_{12} and m_{21}) as zero in N^*_{v1} for intermediate case, we get $N^*_{v1} = V_1 = \frac{b_{v1}H_1}{\mu_v}$ and eventually we get the formula:

$$b_{v1} = \frac{\mu_v V_1}{H_1}$$

Our study found documented value for household size as 5 persons [24] and for bugs per infested house as 26 (1429 bugs in 55 houses, only the domiciliary cases are considered since we are

Table 2.3: Summary of estimated model parameters

Par.	Definition	Value	Range	Units	Reference
β_H	Infection rate for human	0.004	0.0036 – 0.0046	1/vector-year	This study
β_v	Infection rate for vectors	0.041	0.0343 – 0.047	1/human-year	This study
p	Probability of vertical transmission in humans	0.09	0.00218 – 0.09	-	[22]
b_{v1}	Vectors birth rate (per human)	2.95	2.0 – 4.08	vector/human-year	This study
b_{v2}	Vectors birth rate (per chicken)	14.75	12.1 – 16.55	vector/chicken-year	This study
μ_H	Death rate for human	1/77.5	1/87.5 – 1/67.5	1/year	[23]
μ_v	Death rate for vectors	52/41.2	52/46.6 – 52/34	1/year	This study
m_{12}	migration rate from humans to chickens in (2.2)	$\frac{365}{(14\times15)}$	$\frac{365}{(14\times20)}$ – $\frac{365}{(14\times10)}$	1/chicken-year	This study
m_{21}	migration rate from chickens to humans in (2.2)	$\frac{365}{(14\times5)}$	$\frac{365}{(14\times7)}$ – $\frac{365}{(14\times4)}$	1/human-year	This study
q	proportion of time at which vectors fed on humans	1/6	-	-	[25]

looking for vectors' birth rate per human) (V_1) [10]. The vector data were taken from houses where other hosts (dogs and cats) live also. In our literature review, we got 2.0 dogs and 0.5 cats per house [24]. So, to make the value of b_{v1} truly per human we use the equivalence relation (based on the vectors' feeding pattern) among hosts done by Gürtler et al. [25] where they show one dog or cat is equivalent to 2.45 (mean of 2.3 and 2.6) humans. After doing some basic arithmetic, we found the equivalent number of persons per household is 11.125 (we use this as H_1 only for the estimation of b_{v1}, otherwise we used 5 as the value of H_1). Using this equivalent value in the above formula for b_{v1} we obtained

$$b_{v1} = \frac{(\frac{52}{41.2})/\text{year} \times 26 \text{ vector}}{11.125 \text{ human}} = 2.95 \text{ vector/human-year}.$$

Since vectors fed on chickens five times more than humans [25], we multiply the value of b_{v1} by 5 to get the value for b_{v2} which gives 14.75/chicken-year.

For estimating migration rate from chickens to humans (m_{21}), we take the time duration of vectors' last feeding to seeking a new host from [26], convert it to year, take the reciprocal of it and finally divide by household size which gives $\frac{365}{14\times5}$/human-year. For estimating the value of m_{12}, we similarly use the number of chickens/household, which is 15 [24] and get $m_{12} = \frac{365}{14\times15}$/chicken-year. For the proportion of time at which vectors fed on humans (q), we found $\frac{1}{6}$ (documented as five times more fed on chickens compare to humans) [25]. Then we decide the range of values for all model parameters (except for q since it is absent in the intermediate case) using same methods and same source of data that are used to estimate our baseline values. All the parameter estimates are summarized in Table 3.2.

2.4 Analysis

The goal of this study is to analyze the impact of the additional incompetent host on the prevalence of Chagas disease among humans. The equilibria and the basic reproduction number (R_0)

are primary indicators for such observations.

2.4.1 Equilibria and BRNs

To find the equilibria of all three dynamical systems, we set every single equation equal to zero for each model separately and solve. In this process, we find the total vector population (N^*_{v1}) from the disease-free equilibrium; those are shown in Table 2.4. However, expressions provided in Table 4 hold for both the disease-free and endemic equilibria, because all three models assume that infection does not affect vector birth or death rates. We also get the infected human population (I^*_H) from the endemic equilibrium. Even though we are interested in observing the behavior of the infected population class, we still need to know the basic reproduction number (R_0) as it plays a very important role in interpreting the behavior of any infectious disease. To find the expression for R_0 we use the next generation method [27]. The expressions for R_0 and I^*_H for all three cases are in Table 2.5.

The expressions for R_0 and I^*_H clearly manifest that I^*_H is positive in all three cases iff R_0 >1. Now, to check the impact of the presence of our incompetent host, chickens (H_2), we define I^*_H as a function of H_2 and then take the derivative of this newly defined function with respect to H_2. The expressions of these derivatives for far distance and short distance cases are given in Table 2.6. From the expressions, it is evident that these derivatives are always positive, which implies bringing chickens into the system always makes the situation worse for humans.

Table 2.4: N^*_{v1} for all three cases

Far distance	Intermediate distance	Short distance
$\frac{b_{v1}H_1+b_{v2}H_2\left(\frac{m_{21}}{m_{21}+\mu_v}\right)}{\mu_v\left(1+\frac{m_{12}}{m_{21}+\mu_v}\right)}$	$\frac{b_{v1}H_1+b_{v2}H_2\left(\frac{m_{21}H_1}{m_{21}H_1+\mu_v}\right)}{\mu_v\left(1+\frac{m_{12}H_2}{m_{21}H_1+\mu_v}\right)}$	$\frac{b_{v1}H_1+b_{v2}H_2}{\mu_v}$

Table 2.5: R_0 and I_H^* for all three cases, note N_{v1}^* is a function of H_2 in each case

Case	R_0	I_H^*
Far distance	$\frac{p}{2}+\sqrt{\frac{p^2}{4}+\frac{\beta_H\beta_v H_1 N_{v1}^*}{\mu_h\mu_v\left(1+\frac{m_{12}}{m_{21}+\mu_v}\right)}}$	$\frac{-\mu_H(1-p)\mu_v\left(1+\frac{m_{12}}{m_{21}+\mu_v}\right)+\beta_H\beta_v H_1 N_{v1}^*}{\beta_v\left[\mu_H(1-p)+\beta_H N_{v1}^*\right]}$
Intermediate distance	$\frac{p}{2}+\sqrt{\frac{p^2}{4}+\frac{\beta_H\beta_v H_1 N_{v1}^*}{\mu_H\mu_v\left(1+\frac{m_{12}H_2}{m_{21}H_1+\mu_v}\right)}}$	$\frac{-\mu_H(1-p)\mu_v\left(1+\frac{m_{12}H_2}{m_{21}H_1+\mu_v}\right)+\beta_H\beta_v H_1 N_{v1}^*}{\beta_v\left[\mu_H(1-p)+\beta_H N_{v1}^*\right]}$
Short distance	$\frac{p}{2}+\sqrt{\frac{p^2}{4}+\frac{\beta_H\beta_v H_1 q^2 N_{v1}^*}{\mu_H\mu_v}}$	$\frac{-\mu_H(1-p)\mu_v+\beta_H\beta_v H_1 q^2 N_{v1}^*}{\beta_v\left[\mu_H(1-p)q+\beta_H q^2 N_{v1}^*\right]}$

Table 2.6: Derivatives of I_H^* with respect to H_2

Far distance	$\frac{\mu_H(1-p)\beta_H\beta_v m_{21}b_{v2}H_1\left[1+\frac{\beta_v H_1}{\mu_v\left(1+\frac{m_{12}}{m_{21}+\mu_v}\right)}\right]}{\beta_v(m_{21}+\mu_v)\left(\mu_H(1-p)+\beta_H\left[\frac{b_{v2}H_2}{\mu_v\left(1+\frac{m_{12}+\mu_v}{m_{21}}\right)}+\frac{b_{v1}H_1}{\mu_v\left(1+\frac{m_{12}}{m_{21}+\mu_v}\right)}\right]\right)^2}$
Short distance	$\frac{\mu_H(1-p)\beta_H b_{v2}\mu_v(q\beta_v H_1+\mu_v)}{\beta_v[q\beta_H(b_{v1}H_1+b_{v2}H_2)+\mu_H(1-p)\mu_v]^2}$

2.4.2 Additional conditions

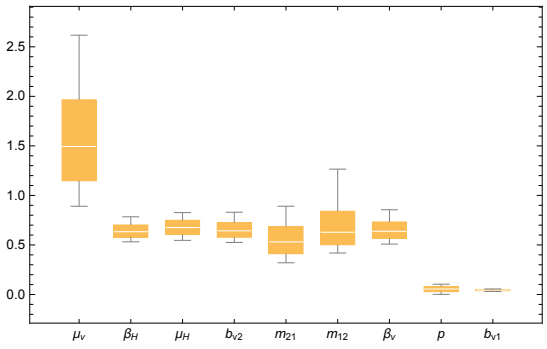
However, the consequences for the intermediate distance case are not straightforward. Here, the value of the derivative $I_H^{*'}$ (with respect to H_2) either can be positive or can be negative depending on certain conditions. In our analysis, we find housing chickens at an intermediate distance from humans can cause the prevalence of Chagas disease among humans to be slowed down only if

$$b_{v2} < \frac{m_{12}}{m_{21}}\left[\frac{\mu_H(1-p)}{\beta_H H_1}\mu_v K + b_{v1}(1+K)\right], \tag{2.4}$$

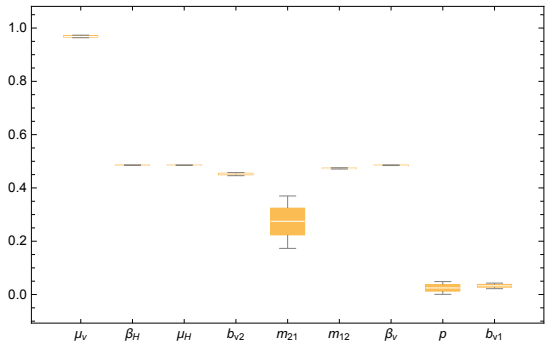
where $K = \frac{\mu_v(1+\frac{m_{12}H_2}{m_{21}H_1+\mu_v})}{\beta_v H_1(1+\frac{m_{12}H_2}{m_{21}H_1+\mu_v})^{-1}+\mu_v(1-\frac{m_{12}H_2}{m_{21}H_1+\mu_v})}$.

The above condition (2.4) on b_{v2} can only be true if

$$m_{12}H_2 < (m_{21}H_1+\mu_v)\sqrt{1+\frac{\beta_v H_1}{\mu_v}} \tag{2.5}$$

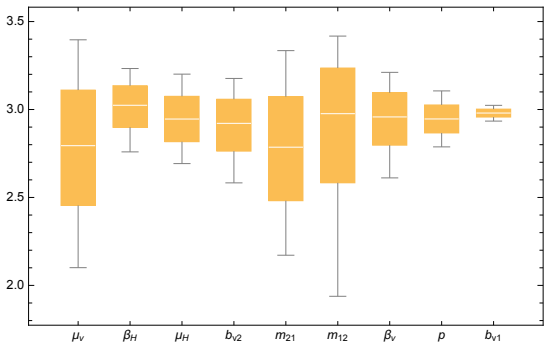


(a) Sensitivity indices for I_H^*

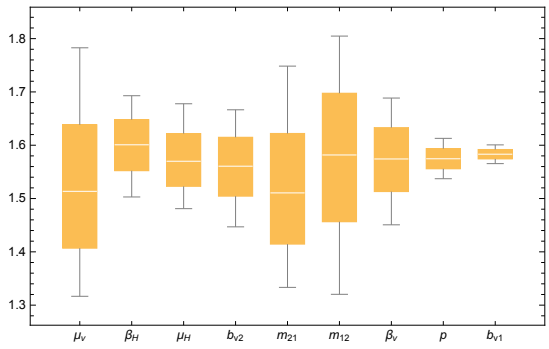


(b) Sensitivity indices for R_0

Figure 2.5: Sensitivity Analysis for all model parameters over a reasonable range



(a) uncertainty in the output of I_H^*



(b) uncertainty in the output of R_0

Figure 2.6: Uncertainty in our results while parameter values vary over a reasonable range

Here, the second addend in (2.4) is directly proportional to b_{v1}, and the first term is inversely proportional to both β_v(through K) and β_H. Thus this condition is easy to satisfy when vectors have easy access to humans (high b_{v1}) or disease transmission (β_H and β_v) is low. So, the presence of chickens is helpful in this case if the birth rate of vectors with chickens is less than a certain threshold value which is relative to the birth rate of vectors with humans and inversely proportional to the infection rate among humans.

2.4.3 Sensitivity and uncertainty analysis

A local sensitivity analysis of the potential endemic prevalence of Chagas disease (I_H^*) and R_0 was performed (Figure 2.5). Sensitivity indices for quantities were carried out for all model pa-

rameters over a reasonable estimated range (Table 3.2), and the outcomes indicate that neither quantity is highly sensitive to those model parameters which are more difficult to estimate well. Both measures I_H^* and R_0 are most sensitive to vector longevity, μ_v, which is a well known quantity. All normalized sensitivity indices for R_0 except μ_v's were less than 1/2. Remarkably, neither measure (I_H^* and R_0) is highly sensitive to vector (feeding on humans) birth rate (b_{v1}). Vector migration rates (m_{12}, m_{21}) are the only significantly influential parameters, except vector death rate (μ_v), to the measure I_H^*. These sensitivity analyses show that the parameters not known well are less influential and the most influential parameters are known well. Hence, this study will not be significantly affected even if the actual values of our estimated parameters vary significantly from our estimation.

2.4.4 Quantitative analysis

To facilitate interpretation, here we illustrate our results numerically for only the helpful case (intermediate case) in brief. At baseline (our estimated parameter values), we get $I_H^* = 2.97$ and $R_0 = 1.58$. Moreover, we estimate values of I_H^* and R_0 over the same range of value for each model parameter to identify the effect of variation in parameter values. Our results show that variation in values of vector death rate (μ_v, which is well known as noted above) and migration rates (m_{12} and m_{21}) cause some significant uncertainty in our results (Figure 2.6). For these varying parameter values, the I_H^* and R_0 range from 1.9 to 3.4, and 1.32 to 1.80 respectively. In addition to these numerical values for I_H^* and R_0, we find the condition $b_{v2} < 19.57$/chickens-year at which the presence of chickens is helpful in reducing prevalence of Chagas disease in humans.

In our analysis, we find R_0 strictly decreasing function of m_{12} and strictly increasing function of m_{21}. However, R_0 increases for up to a certain number of chickens and then start to decrease (Figure 3.2). This implies that for our parameter values the presence of chickens can

reduce the infections in humans depending on the number of this incompetent host. Now, the condition for making the presence of chickens helpful becomes easier to satisfy as migration of vectors from humans to chickens increases and it becomes difficult as migration from chickens to humans increases. However, increasing the number of chickens makes the helpfulness criterion (2.4) easier to satisfy. All the numerical values here are based on our parameter estimations which can be different with other set of parameter values. However, the qualitative result will be the same regardless of parameter values.

2.4.5 CTMC as stochastic version

We use a deterministic model to develop qualitative insights into our systems. A stochastic model such as a CTMC shows how randomness in individual behavior causes deviations from mean-field results. Here we show results from a CTMC for the intermediate distance case only since the presence of chickens in the other two cases never reduces human infections. To analyze the CTMC model, we performed 100 simulations for each value of H_2. Figure 2.8 plots the number of infected people at endemic equilibrium (I_H^*), where the solid line indicates the mean-field results for the intermediate case, and the dashed lines represent an envelope of $\pm$1SD. This figure clearly illustrates that the CTMC simulation results follow the same trend established in the deterministic model; thus, variation due to stochasticity does not oppose the answer provided by the deterministic model to the central question of this study.

Our results and analyses show that the presence of an incompetent host, in our case chickens, can reduce the prevalence of Chagas disease in humans under certain conditions only if chickens are placed at an intermediate distance from humans.

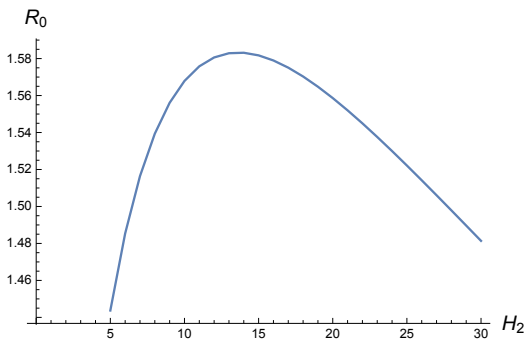


Figure 2.7: Behavior of R_0 as number of chickens (H_2) varies

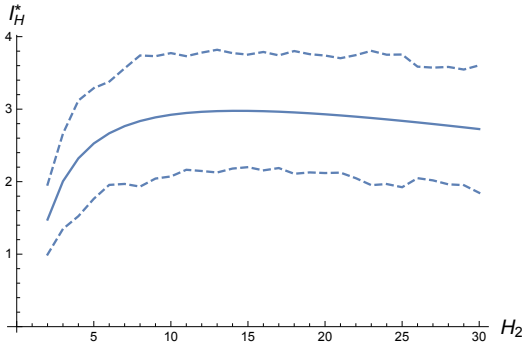
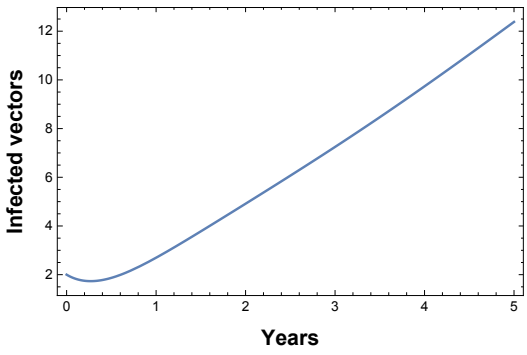
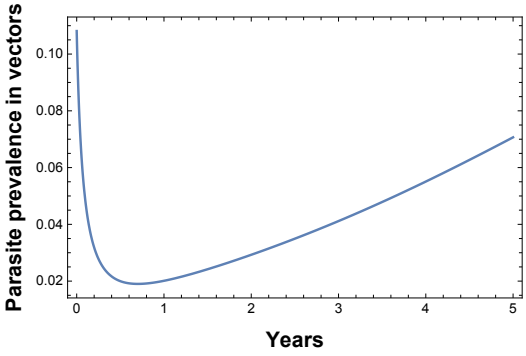


Figure 2.8: The solid curve shows the mean-field value of the endemic equilibrium; dashed curves indicate an envelope of ±1SD deviation from that value, based on simulations from the CTMC



(a)



(b)

Figure 2.9: Infections in vectors when chickens are kept indoors (Short distance case)

2.5 Discussion

This is the first study to understand how the placement of chickens in households affects the transmission of Chagas disease in humans. The case when farmers bring their chickens inside the bedrooms, or very close to bedrooms, increases the number of infections in humans. This short-distance case was studied by Gürtler et al. [11] who focused on vector infections, rather than human infections. Even though the goal of this study is completely different from theirs, we show here analogous computations for comparison. Our analysis shows that both the num-

ber, and density of infected vectors increase when chickens kept indoors, after a brief transient decrease (Figure 2.9). This result agrees with the result of [11] in terms of vector infection. The other two cases, intermediate distance and far distance, studied here are new approaches to understand the impact of chickens' presence in households.

For the far case, where vectors cannot anticipate the location of chickens, the decoy process does not help to reduce human infections. Here, vectors try to stay with humans as long as they can survive since they can't see any alternative food sources around them. So, by the time when a portion of them start to leave humans, the infections are already spread among humans at a large scale. Consequently, this case is not helpful for the purpose of controlling the prevalence of infections among humans.

In the remaining case, when chickens reside at a distance (adjacent to humans) such that vectors can detect the presence of remaining host while staying with the other, vector populations begin to migrate from humans to chickens in search of their blood-meals. The vector population with chickens will increase with time for having enough food sources and at some point they will start to move towards humans in search of new blood-meal sources. The net effect of vectors' migration from humans to chickens, and from chickens to humans will determine the effects of chickens' presence. Our results show that there are certain conditions under which human infections can be reduced. This will happen as most of the vectors will switch from humans to chickens before people in houses are infected that much.

The presence of chickens in houses can only help to reduce the prevalence of Chagas disease among humans when villagers keep their chickens at a distance which allows the vectors to anticipate the location of other hosts, but does not allow vectors to share both of the chickens and humans as their blood meal sources. Hence, it can be concluded that the decoy process, by the presence of an incompetent host, does not always help to reduce the disease prevalence among humans.

Results here offer valuable information to contribute in improving control of Chagas transmission. However, proper understanding of the outcomes of this study depends on the distance from which vectors can sense the presence of hosts. Triatomine vectors detect host by identifying the presence of factors such as, water vapor, heat, and distinctive odors from different odorants (including CO_2) [28, 29]. We found only one documented data source which says triatomine bugs can identify human presence from two meters by detecting heat [29]. Also, variation in vector migration rates between humans and chickens has significant impact on our results. Thus, research is needed to identify true threshold distance between humans and chickens to distinguish between short distance and intermediate distance cases; also, field study is required to estimate vector's migration rates between humans and chickens. As an NTD, Chagas disease has very few data on its transmission cycles. Consequently, we use relatively simple models based on available information regarding demographics and transmission mechanisms, and parametrized by few data what are available. Reliable estimations of our model parameters will better ground our quantitative results. In addition, availability of additional key rates relating to transmission will permit more detailed models.

Chapter 3

Impact of dogs with deltamethrin-impregnated collars on prevalence of visceral leishmaniasis

3.1 Introduction

The Leishmaniases are a group of diseases caused by the protozoa parasite *Leishmania* [40, 42], which is transmitted by the bites of female sandflies [42, 43]. Over 20 Leishmania species known to be infective to humans are transmitted by the bite of infected female phlebotomine sandflies. Leishmaniasis is classified as a neglected tropical disease (NTD). It is found in parts of the tropics, subtropics, and southern Europe [42]. However, the disease mainly affects poor people in Africa, Asia and Latin America [40]. There are three main types of leishmaniasis among which visceral, often known as Kala-azar, is the most serious form of the disease [40]. Regarding visceral leishmaniasis, more than 90% of all cases occur in just the six countries of India, Bangladesh, Sudan, South Sudan, Brazil, and Ethiopia [50].

Out of 200 countries and territories reporting to the World Health Organization (WHO), 77 countries are endemic for visceral leishmaniasis in 2017. In 2016, over 90% of global VL cases were reported from seven countries: Brazil, Ethiopia, India, Kenya, Somalia, South Sudan and Sudan. As of October 2018, 50 VL-endemic countries have reported 2017 data to the WHO Global Leishmaniasis programme [40]. Annually, 700,000 to 1 million new cases and 20,000 to 30,000 deaths occur [41]. Currently, this is one of the major public health concerns. Even though

human VL is spread by female sandflies, dogs are the main reservoir of the VL parasite. Thus, dogs presence in a community normally increases human VL incidence. In the last couple of decades, many clinical and mathematical studies have been conducted aiming to understand the dynamics of Zoonotic VL (ZVL). In these studies, researchers tried to find ways of controlling VL prevalence. Different strategies for controlling the incidence of VL have been considered, most notably culling dogs and putting insecticide-impregnated dog collars on dogs.

In 2002, Gavgani et al. clinically studied two possible strategies– early diagnosis and treatment, and use of deltamethrin-impregnated dog collars ($DIDC$). The presence of deltamethrin insecticide on dog collars helps to kill a portion of sandlies, and eventually reduces the disease transmission. Outcomes of the study showed that use of $DIDC$ is helpful in reducing human infection, and this strategy can replace the controversial dog culling program [46]. In addition to clinical studies, several mathematical models have also been used to study transmission and control strategies for ZVL. In 2010, ELmojtaba et al. used a modified SIR model to study the dynamics of leishmaniasis in Sudan [47]. Their study found the human treatment rate to be the key parameter in disease control since they considered humans as competent hosts. However, human treatment needs to be accompanied by control of the vector, and reservoir populations to eradicate the disease from trhe community. They suggest to maintain a distance between the hosts (humans and dogs); a similar suggestion is claimed in a later study by Zahid and Kribs [49], [Chapter 2]. Later, Ribas et al. (2013) proposed and analyzed a deterministic mathematical model in order to compare different control strategies. They showed that using $DIDC$ is better at reducing human infections [44].

In 2016, Zhao et al. studied ZVL transmission using an SEIR deterministic model [48]. In their model they incorporated hospitalization of infected humans, migration for the sandfly population, and infection-related death for sandflies. Also, they assumed that the contact rates between sandflies and hosts (dogs and humans) are independent of vector population, biting exposed dogs cannot infect sandflies, and immunity for both of the hosts, humans and dogs, is

permanent. Later, they compared three different control strategies−vaccination of dogs, use of insecticide at vector breeding sites, and personal protection. Their analysis found controlling the sandfly population to be the most effective control measure.

The next year, in 2017, Shimozako et al. used the SEIR deterministic model also to study ZVL disease dynamics. They included a delay term instead of using latent compartment for the sandfly population [45]. In this study, they estimated the basic reproduction number R_0 and analyzed the stability and sensitivity of the system, and finally made some recommendation regarding control strategies. Unlike Zhao's work, they assumed that sandflies can be infected from biting exposed dogs, and immunity gained by both of the host populations is temporary. Interestingly, they assumed that exposed dogs and humans become susceptible to VL when recovery precedes the appearance of symptoms. Their work also assumed that the rate at which vectors bite hosts is independent of host density. Outcomes of their study showed that control strategy for ZVL should be focused on sandflies and infected dogs. However, considering the ethical concerns regarding culling dogs they recommend to prioritize the control of sandfly population.

All the research related to ZVL has mainly addressed public health concerns where researchers study different control strategies. In these studies, we always find the presence of human and dog populations as hosts for sandflies, the vector of the disease. This host richness (host diversity) leads us to think about the dilution effect (reduction in disease risk resulting from species diversity). The effect of the presence of an additional host is not straightforward. It can increase, or decrease disease risk depending on varieties of factors. In 2010, Johnson and Thieltges showed that host diversity helps in reducing human infections depending on the relative abundance of additional host(s) relative to the focal host [2]. In 2013, Miller and Huppert proved that species diversity in host population can amplify or can dilute disease prevalence depending on vectors' preference of host [4]. Recently in 2019, Zahid and Kribs established that the presence of an additional host in domestic settings can help to reduce disease prevalence

in humans if the distance between two host populations remains within a certain range [49], [Chapter 2]. These works challenge the established idea that biodiversity always helps to reduce disease risk. It is always interesting to observe how the presence of other hosts, in addition to humans, influences the dynamics of vector-borne diseases, impacts disease risk and human health.

This study shifts the research question from a public health viewpoint to an ecological one. As dogs are the main reservoir for the parasite, the usual presence of dogs in a domestic, or in a community setting makes VL transmission faster ensuring more suitable blood-meal source for its vector sandflies. Hence, this paper aims to identify the impact of the presence of protected dogs (protected by putting deltamethrin-impregnated dog collars) as an additional host on the prevalence of VL in humans.

The presence of protected dogs in a community has two contradictory effects. It ensures a better blood-meal source for vector population since biting a dog is much easier for sandflies than biting a human. Thus, dog presence in a community helps sandfly population to grow faster. Moreover, dog presence increases the proportion of infected sandflies (since dogs are the main reservoir of the parasite) which eventually increases human infection risk. On the contrary, use of $DIDC$s on dogs as topical insecticide reduces the sandfly population by the lethality effect, which can result in fewer cases of VL. The net result of these two contrary effects may reduce or enhance the risk of human prevalence. The goal of this study is to understand and examine this net effect, and eventually to understand if the presence of protected dogs has any dilution effect on human risk of VL infections. To answer this question, here we consider two different settings: a setting with protected dogs, and a setting with no dogs. To analyze and understand these two different settings, in this study we use an SEIRS deterministic model.

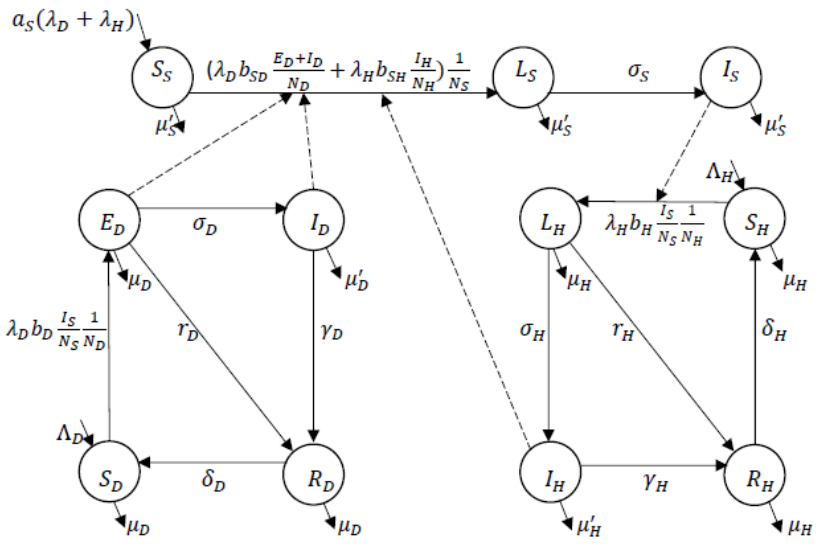


Figure 3.1: Population flow among the compartments

3.2 Model development

The SEIRS model we use here to understand the dynamics of VL incorporates three different populations: two hosts−dogs and humans, and the vector− sandflies. In our model, we do not consider the PKDL phase of leishmaniasis, because our research question is to identify the effect of insecticide dog collars on the number of human cases, which is independent of the eect of the PKDL class. We neither consider hospitalization of sick humans, nor any migration for the vectors. Based on results of an early clinical study [51], we include disease transmission from symptomatic infected humans to vectors. This inclusion makes this model different from the models formulated by Zhao et al. [48], and by Shimozako et al. [45].

Like the models proposed by [44, 45], we also assume hosts' immunity temporary. Similar to their model, we assume both of the hosts may acquire natural immunity directly from the exposed state. In contrast to [44, 45], however, we assume that exposed hosts cannot become susceptible without having any immunity. In our model, we have $\mu'_D = \mu_D + \alpha_D$ and $\mu'_H = \mu_H + \alpha_H$ where α_D and α_H represent VL-induced death rates for dogs and humans respectively. The presence of deltamethrin on the collars causes additional deaths at the rate α_S

(migration of sandflies due to presence of $DIDC$s, if any, can be included in α_S) for vectors. So, the vectors are leaving at a rate μ'_S where $\mu'_S = \mu_S + \alpha_S$.

$$
\begin{aligned}
\frac{dS_D}{dt} &= \Lambda_D - \left(\lambda_D b_D \frac{I_S}{N_S}\frac{1}{N_D} + \mu_D\right) S_D + \delta_D R_D \\
\frac{dE_D}{dt} &= \lambda_D b_D \frac{I_S}{N_S}\frac{S_D}{N_D} - (\sigma_D + r_D + \mu_D) E_D \\
\frac{dI_D}{dt} &= \sigma_D E_D - \left(\gamma_D + \mu'_D\right) I_D \\
\frac{dR_D}{dt} &= r_D E_D + \gamma_D I_D - (\delta_D + \mu_D) R_D \\
\frac{dS_H}{dt} &= \Lambda_H - \left(\lambda_H b_H \frac{I_S}{N_S}\frac{1}{N_H} + \mu_H\right) S_H + \delta_H R_H \\
\frac{dL_H}{dt} &= \lambda_H b_H \frac{I_S}{N_S}\frac{S_H}{N_H} - (\sigma_H + r_H + \mu_H) L_H \\
\frac{dI_H}{dt} &= \sigma_H L_H - \left(\gamma_H + \mu'_H\right) I_H \\
\frac{dR_H}{dt} &= r_H L_H + \gamma_H I_H - (\delta_H + \mu_H) R_H \\
\frac{dS_S}{dt} &= a_S (\lambda_D + \lambda_H) - \left(\left(\lambda_D b_{S_D}\frac{E_D + I_D}{N_D} + \lambda_H b_{S_H}\frac{I_H}{N_H}\right)\frac{1}{N_S} + \mu'_S\right) S_S \\
\frac{dL_S}{dt} &= \left(\lambda_D b_{S_D}\frac{E_D + I_D}{N_D} + \lambda_H b_{S_H}\frac{I_H}{N_H}\right)\frac{S_S}{N_S} - \left(\sigma_S + \mu'_S\right) L_S \\
\frac{dI_S}{dt} &= \sigma_S L_S - \mu'_S I_S
\end{aligned}
\tag{3.1}
$$

where $N_D = S_D + E_D + I_D + R_D$

$N_H = S_H + L_H + I_H + R_H$

$N_S = S_S + L_S + I_S$

$\lambda_D = \frac{c_D N_D}{c_D N_D + c_H N_H} \min(c_S N_S, c_D N_D + c_H N_H)$

$\lambda_H = \frac{c_H N_H}{c_D N_D + c_H N_H} \min(c_S N_S, c_D N_D + c_H N_H)$

$\mu'_D = \mu_D + \alpha_D$, $\mu'_H = \mu_H + \alpha_H$, $\mu'_S = \mu_S + \alpha_S$.

The most important factor which makes our model distinct from others' models is the encounter (biting) rate between hosts and vectors, which incorporates the notion of host irritability. The maximum number of bites per unit time a dog can tolerate is not the same as the maximum number of bites per unit time a human can tolerate. This issue of host-density dependent

Table 3.1: Model variables with definition

Variable	Definition
S_D, S_H	Susceptible dogs, Susceptible humans
L_H, L_S	Latent humans, Latent sandflies
E_D	Exposed dogs
I_D, I_H	Infected humans
S_S	Susceptible sandflies
I_S	Infected vectors
R_D, R_H	Recovered (Temporary) Dogs, Recovered (Temporary) humans

encounter rate is addressed by Blayneh et al. in 2010 [53] while modeling dynamics of West Nile Virus. However, the contact rate they used is independent of host population size. But, the sandfly biting rate is limited both by the sandfly's preferred feeding rate and by host irritability (unlike mosquitos, which are limited primarily by availability of breeding sites). So, we consider the encounter rate between sandflies and dogs $\lambda_D = \frac{c_D N_D}{c_D N_D + c_H N_H} \min(c_S N_S, c_D N_D + c_H N_H)$, and the encounter rate between sandflies and humans $\lambda_H = \frac{c_H N_H}{c_D N_D + c_H N_H} \min(c_S N_S, c_D N_D + c_H N_H)$ where c_D and c_H represent the number of bites a dog, and a human can tolerate per unit time, c_S represents the number of bites a single sandfly desires to make per unit time, and N's represent population sizes. This inclusion of the host population dependent biting rate makes our model distinct from other earlier proposed models. However, not all the bites (encounters) can transmit the disease and so we multiply the total number of encounters by b_D (or b_H or b_{SH} or b_{SD}) (Table 3.2) which represents the proportion of bites (between 0 to 1) that result new infections to dogs (or to humans or to sandflies). Finally, we have our model which is shown in Figure 3.1 and described by system (3.1). All the model variables are summarized in Table 4.1.

3.3 Parameter estimation

In 2017 the World Bank listed 207,833,831 as total population and 13.918/year as the birth rate (crude) per 1000 people for Brazil [56]. We use the total number of municipalities in Brazil, 5570 [57], to estimate the average population (37,313) in a single municipality of Brazil. Then using this average population and the birth rate we estimate the recruitment rate for humans to

get Λ_H=1.42 humans/day. To estimate the recruitment rate in the dog population, we use the results of a study performed in 2005-2008 in Vargem Grande, a neighborhood of the municipality of São Paulo, Brazil, with a population of 16,946 [58]. The study estimated 1337 and 1445 new dogs in 2006 and 2008 respectively, which gives a mean increase of 1391 dogs/year. Then we apply the ratio 2.20, of the population per municipality (estimated above) to the population of the study area of [58], which estimates an increment of 3060 dogs/year in a municipality of average population. And, we get $\Lambda_D = \frac{3060}{365}$ dogs/day=8.39 dogs/day.

Female sandflies take 3 to 5 days after their emergence to take a blood-meal, and it takes 7.67 days (mean of 6 days, 8 days, and 9 days) from blood-meal to oviposition (laying of eggs) [52]. They usually take only one blood-meal until they lay eggs, and begin feeding again after oviposition [70]. Therefore, each vector has a single bite in every 7.67 days, and thus we have $c_S = \frac{1}{7.67}$ bite/vector-day=0.13 bite/vector-day. Also, we have 10 (mean of 13, 8 and, 9) new female sandflies per egg batch [52] which gives us a_S=10 sandflies/bite.

A study in 2010 found 12 sandflies infected when 81 sandflies were fed on people with active VL infection [51], and this gives us $b_{SH} = \frac{12}{81} = 0.148$ infected sandfly/bite. Another study in 2013 showed that 35.8% of sandflies that fed on asymptomatic dogs, and 24.7% of sandflies that fed on symptomatic dogs got the infection [55]. We take the mean (30.25%) of these two estimations to get b_{SD} =0.3025 sandfly/bite. However, for b_H, b_D we take the estimations from [54] as 0.5 infected human/bite, and 0.01 infected dog/bite respectively.

In 2017, life expectancy at birth in Brazil was 76 years [56], so we take its reciprocal to estimate the natural death rate for people in Brazil which gives $\mu_H = 3.6 \times 10^{-5}$/day. In Brazil, there are four common dog breeds, and their mean lifespan is 11.875 years [59]. We take the reciprocal of the life span as death rate, and we get $\mu_D = 2.30 \times 10^{-4}$/day. To estimate the natural death rate of sandflies we take the reciprocal of their mean lifespan which is 2 weeks [60], and get μ_S =0.0174/day.

Table 3.2: Summary of model parameters

Par.	Definition	Value	Units	Reference
Λ_D	recruitment rate for dogs (by birth)	8.39	dogs/day	This study
Λ_H	recruitment rate for humans (by birth)	1.42	humans/day	This study
a_S	birth rate for sandflies	10	sandflies/bite	This study
b_D	infection to dogs from sandflies' bite	0.01	infected dog/bite	[54]
b_H	infection to humans from sandflies' bite	0.5	infected human/bite	[54]
b_{SD}	infection to sandflies from biting dogs	0.3025	infected sandfly/bite	This study
b_{SH}	infection to sandflies from biting humans	0.148	infected sandfly/bite	This study
c_D	inverse of dogs' irritability	45	bites/dog-day	This study
c_H	inverse of humans' irritability	15	bites/human-day	This study
c_S	bites a single sandfly disere	0.13	bite/sandfly-day	This study
σ_D	incubation rate	1.11×10^{-2}	1/day	This study
σ_H	incubation rate	6.85×10^{-3}	1/day	[68]
σ_S	incubation rate	0.117	1/day	This study
γ_D	recovery rate (dogs)	9.04×10^{-4}	1/day	[63]
γ_H	recovery rate (humans)	2.5×10^{-3}	1/day	[45]
δ_D	Inverse of temporary recovery period (dogs)	2.74×10^{-3}	1/day	[65]
δ_H	Inverse of temporary recovery period (humans)	5.48×10^{-4}	1/day	[65]
r_D	spontaneous recovery rate	1.1×10^{-2}	1/day	[64]
r_H	spontaneous recovery rate	8.22×10^{-3}	1/day	[63]
μ_D	natural death rate	2.30×10^{-4}	1/day	This study
μ_H	natural death rate	3.6×10^{-5}	1/day	This study
μ_S	natural death rate	0.0714	1/day	This study
α_D	disease induced death rate for dogs	1.14×10^{-3}	1/day	This study
α_H	disease induced death rate for humans	8.26×10^{-7}	1/day	This study
α_S	$DIDC$ induced death rate for sandflies	0.1995	1/day	This study

A study of ZVL cases in Bihar, India, in 2013 showed that 154 patients died among a total of 3,641 patients [61], and their average life span was 66.73 years. However, the life expectancy at birth in Bihar at that time period was 68.1 years [62]. Therefore, we take the difference of the reciprocals of these two life span and estimated lethality of ZVL as $\alpha_H = \left(\frac{1}{66.73} - \frac{1}{68.1}\right)$ /years $= 3.015 \times 10^{-4}$/years $= 8.26 \times 10^{-7}$/day. Earlier studies show that average life-span of infected dogs is two years [54, 71] which gives us $\mu'_D = \mu_D + \alpha_D = \frac{1}{2\times 365 \text{ days}} = 1.37 \times 10^{-3}$/day. This value, and already estimated value $\mu_D = 2.30 \times 10^{-4}$/day give us $\alpha_D = \mu'_D - \mu_D = 1.37 \times 10^{-3}$/day $- 2.30 \times 10^{-4} = 1.14 \times 10^{-3}$/day. To estimate the $DIDC$ induced death rate (α_S) for sandflies, we study [66] where sandflies were exposed to dogs protected (with $DIDC$). From each individual experiment, we take the number of exposed sandflies, and the number of flies that died in 20 hours duration from their exposure, and pooled data from all trials to get 5,766 and 1245 as the totals of exposed sandflies, and dead sandflies respectively. However, our estimation of sandflies' natural death rate (μ_s=0.0714/day) estimates 333 natural deaths [1] of sandflies in a span of 20 hours. The remaining deaths of 1245-333=912 sandflies are not attributable to natural mortality. These estimations, and sandflies' natural death rate 0.0714/day give us the estimation $\alpha_S = (\frac{912}{333}) \times \mu_S$=0.0714/day=0.1955/day.

A laboratory study in 2011 observed sandflies' incubation rate as 7-10 days [67]. So, here we take the reciprocal of the mean of 7 and 10 days to estimate the latent period as $\sigma_S = \frac{1}{8.5}$/day=0.117/day. Another work in the same year estimated that individuals without symptomatic VL need on average about 146 days to develop LST-positivity after a PCR-positive finding [68], and this leads us to estimate $\sigma_H = \frac{1}{146}$day$= 6.85 \times 10^{-3}$day. A review paper published in 2002 mentioned the incubation period for dogs as 2-4 months [69]. We took reciprocal of the mean of this range of 2-4 months (3 months=90 days), and estimate $\sigma_D = \frac{1}{90}$/day$= 1.11 \times 10^{-2}$/day.

All other parameter values are taken directly from earlier research studies.

[1] $5766 \times (1 - e^{-\mu_S \frac{20}{24}\text{day}}) = 5766 \times \left(1 - e^{(-0.0714/\text{day}) \times \frac{20}{24}\text{day}}\right) = 333$

3.4 Analysis

We begin with the general model where we incorporate three different populations – sandflies (the vector), and two host populations– dogs (protected with $DIDC$) and humans. Later, we consider a special case without dogs in the setting. Finally, we compare these two cases to understand the impact of the presence of protected dogs on the prevalence of VL infections in humans. The study actually aims to understand the effects of host diversity on disease transmission, and eventually on human health.

In the general model, the total number of desired bites for sandflies and the total number of bites that hosts can tolerate together may not be equal. Thus, in our analysis we consider two cases in terms of total number of possible encounters. In the first case, we assume the maximum total number of possible vector bites is less than the total possible number of bites that both hosts (humans and protected dogs) can tolerate together, that is when $c_S N_S < c_D N_D + c_H N_H$. The other scenario takes place when $c_S N_S > c_D N_D + c_H N_H$. For the initial case our calculation estimates the total vector population as $N_S(t) = N_S(0)e^{(a_S c_S - \mu'_S)t}$ (recall $\mu'_S = \mu_S + \alpha_S$) which shows that the vector population decreases with time and eventually dies out, if $a_S c_S < \mu'_S$. However, N_S increases with time under the condition $a_S c_S > \mu'_S$. If the vector population continues to grow then the base condition of the first case, that is $c_S N_S < c_D N_D + c_H N_H$, cannot be true after a certain time. Eventually, the relation between the maximum possible number of vector bites and the maximum host bite tolerance (inverse of hosts' irritability) turns into $c_S N_S > c_D N_D + c_H N_H$, which is the second case. These analyses give us two scenarios: either the vector population dies out, or the only possible case is $c_S N_S > c_D N_D + c_H N_H$ (second case). Since we are interested to understand the disease dynamics, from here our study will consider only the case of $c_S N_S > c_D N_D + c_H N_H$.

3.4.1 Equilibria and BRN

To find equilibrium points for our model we set all the equations of our system equal to zero and solve them for state variables. After performing some basic arithmetic we get the disease free equilibrium (DFE) as $S_D = \frac{\Lambda_D}{\mu_D}$, $E_D = 0, I_D = 0, R_D = 0$, $S_H = \frac{\Lambda_H}{\mu_H}$, $L_H = 0, I_H = 0, R_H = 0$, $S_S = \frac{a_S}{\mu_S}(c_D\frac{\Lambda_D}{\mu_D}+c_H\frac{\Lambda_H}{\mu_H})$, $I_S = 0, L_S = 0$. Then we use the next generation method [27] to get the basic reproduction number (BRN),

$$R_0 = \frac{2^{\frac{1}{3}}}{3}\frac{Q_{12}}{\left(Q_3+\sqrt{Q_3^2-\frac{4}{27}Q_{12}^3}\right)^{\frac{1}{3}}} + \frac{1}{2^{\frac{1}{3}}}\left(Q_3+\sqrt{Q_3^2-\frac{4}{27}Q_{12}^3}\right)^{\frac{1}{3}} \tag{3.2}$$

where

$$Q_{12} = \frac{\Lambda_D}{\mu_D}\frac{b_D c_D}{a_S K_3}\frac{b_{SD}c_D}{K_4K_6}\left(\frac{\gamma_D+\mu_D+\alpha_D}{\sigma_D}\right)+\frac{\Lambda_H}{\mu_H}\frac{b_H c_H}{a_S K_3}\frac{b_{SH}c_H}{K_5K_6}, \text{ and } Q_3 = \frac{\Lambda_D}{\mu_D}\frac{b_D c_D}{a_S K_3}\frac{b_{SD}c_D}{K_4K_6}.$$

Here Q_{12} accounts for transmission between infected vectors and infected hosts, while Q_3 accounts for transmission between infected vectors and exposed dogs. The terms are not simply added to form R_0 because the cycles overlap as exposed dogs become infected dogs later. However, when $Q_{12} = 0$, $R_0 = Q_3^{\frac{1}{3}}$, and when $Q_3 = 0$, $R_0 = \sqrt{Q_{12}}$ (see Appendix 1). In other words, in the absence of one of the two transmission cycles, R_0 measures the transmission efficiency of the other cycle. In general $R_0 \leq \sqrt{Q_{12}} + Q_3^{\frac{1}{3}}$. The K_i are given below.

Later, we obtain the following quadratic equation (in I_H) for endemic equilibrium (see Appendix 2):

$$AI_H^2 + BI_H + C = 0$$

where

$$A = \left(\frac{b_H c_H}{b_D c_D}\frac{K_4}{K_5}K_2 - K_1\right)\left[b_{SH}c_H\left(K_2+\frac{K_5K_6}{b_Hc_H}\right) - a_S\frac{K_5K_6}{b_Hc_H}c_H\frac{\alpha_H}{\mu_H}\right],$$

$$B = -\left(\frac{\Lambda_D}{\mu_D}c_D b_{SD}K_7 + \frac{\Lambda_H}{\mu_H}b_{SH}c_H\frac{b_Hc_H}{b_Dc_D}\frac{K_4}{K_5}\right)\left(K_2+\frac{K_5K_6}{b_Hc_H}\right)$$
$$-\left(\frac{b_Hc_H}{b_Dc_D}\frac{K_4}{K_5}K_2 - K_1\right)\left(\frac{\Lambda_H}{\mu_H}b_{SH}c_H - a_SK_3\frac{k_5K_6}{b_Hc_H}\right) + \frac{\Lambda_H}{\mu_H}a_S\frac{K_4K_6}{b_Dc_D}c_H\frac{\alpha_H}{\mu_H} + \frac{\Lambda_D}{\mu_D}a_S\frac{K_5K_6}{b_Hc_H}c_D\frac{\alpha_D}{\mu_D},$$

$$C = \frac{\Lambda_H}{\mu_H}\left(\frac{\Lambda_H}{\mu_H}b_{SH}c_H\frac{b_Hc_H}{b_Dc_D}\frac{K_4}{K_5} + \frac{\Lambda_D}{\mu_D}c_Db_{SD}K_7 - a_SK_3\frac{K_4K_6}{b_Dc_D}\right),$$

with

$$K_1 = \frac{\sigma_D+r_D+\mu_D}{\mu_D}\frac{\gamma_D+\mu'_D}{\sigma_D} - \frac{\delta_D}{\mu_D}\left(\frac{r_D}{\delta_D+\mu_D}\frac{\gamma_D+\mu'_D}{\sigma_D} + \frac{\gamma_D}{\delta_D+\mu_D}\right)$$

$$K_2 = \frac{\sigma_H+r_H+\mu_H}{\mu_H}\frac{\gamma_H+\mu'_H}{\sigma_H} - \frac{\delta_H}{\mu_H}\left(\frac{r_H}{\delta_H+\mu_H}\frac{\gamma_H+\mu'_H}{\sigma_H} + \frac{\gamma_H}{\delta_H+\mu_H}\right)$$

$$K_3 = c_D\frac{\Lambda_D}{\mu_D} + c_H\frac{\Lambda_H}{\mu_H}$$

$$K_4 = (\sigma_D + r_D + \mu_D)\frac{\gamma_D+\mu'_D}{\sigma_D}$$

$$K_5 = (\sigma_H + r_H + \mu_H)\frac{\gamma_H+\mu'_H}{\sigma_H}$$

$$K_6 = \frac{\sigma_S+\mu'_S}{\sigma_S}$$

$$K_7 = \frac{\gamma_D+\mu'_D}{\sigma_D} + 1$$

where $K_1, K_2 > 0$.

To understand the behavior of disease dynamics, the threshold value $BRN(R_0)$ and endemic equilibrium (EE) need to be understood, and interpreted properly. Our analysis shows $R_0 > 1$ if and only if $C > 0$ (see Appendix 3). For endemic equilibrium, we cannot establish any specific condition to ensure the positivity of EE since its analytic expression, obtained from equation (3.4.1), is very complex (recall expressions of coefficients A, B and C). Consequently, we perform numerical explorations to understand the behavior of our dynamical system, and finally conclude that the model has a unique positive endemic equilibrium whenever $R_0 > 1$ (when a second solution set exists, the other solution set is non-positive). It does not appear possible for A, B, C all to be positive together. To check the stability of our EE, we evaluate the Jacobian matrix of our dynamical system, and perform numerical explorations (see Appendix 3 for further detail), which indicate that the endemic equilibrium is unconditionally stable.

3.4.2 Special case: without dogs

Now, we consider the case of having no dogs in the scene, a special case (setting all variables and parameters related to dogs to zero) of our original model. Our analysis for this special case finds the DFE as $S_H = \frac{\Lambda_H}{\mu_H}, L_H = 0, I_H = 0, R_H = 0, S_S = \frac{a_S}{\mu_S}, L_S = 0, I_S = 0$, and BRN as $R_0 = \sqrt{\frac{b_S H b_H c_H}{a_S K_5 K'_6}}$ where $K'_6 = \frac{\sigma_S+\mu_S}{\sigma_S}$ (derived from K_6 by setting $\alpha_S = 0$). In this case

the endemic equilibrium (3.4.1) simplifies to a linear equation which thus has at most a single solution, in which we get the expression for the infected human population as

$$I_H^* = \frac{\Lambda_H}{\mu_H}\left(\frac{b_{SH}b_Hc_H - K_5K_6'a_S}{b_{SH}\left(b_Hc_HK_2 + K_5K_6'\right) - a_SK_5K_6'\frac{\alpha_H}{\mu_H}}\right)$$

which can be expressed in terms of R_0 as

$$I_H^* = \frac{\Lambda_H}{\mu_H}\left(\frac{R_0^2 - 1}{K_2R_0^2 + \frac{b_{SH}}{a_S} - \frac{\alpha_H}{\mu_H}}\right).$$

Since some algebra shows that $K_2 > \alpha_H/\mu_H$, the unique endemic equilibrium exists precisely when $R_0 > 1$.

3.4.3 Quantitative analysis

Based on our parameter estimation, we calculate R_0 and I_H^* for all three possible cases: community with dogs protected with $DIDC$, community without dogs, and community with dogs having no protective measure. We estimate I_H^* =3023, 3329, and 4677 in a population size of 39,445, respectively, for these three cases. These estimates indicate that the presence of DIDC-protected dogs is better than having no dogs, which in turn is better than having unprotected dogs (in terms of human infections of leishmaniasis). The R_0 values for these same cases are 1.47, 3.51, and 2.05 respectively. These results provide fewer human infections with a higher R_0 value for the no dog case compared to the case of unprotected dogs. Humans are spreading infections faster in the case of no dog; however, the contribution of the dog population to new infections is missing in this case. Thus, the case of no dog in the community produces fewer infections even though the R_0 value is higher compared to the case of unprotected dogs. The expression for R_0 in (3.2) helps us to understand this apparently unusual result better. One of Q_{12}'s two terms, and all of Q_3, have to do with dogs. Removing them will reduce R_0, especially

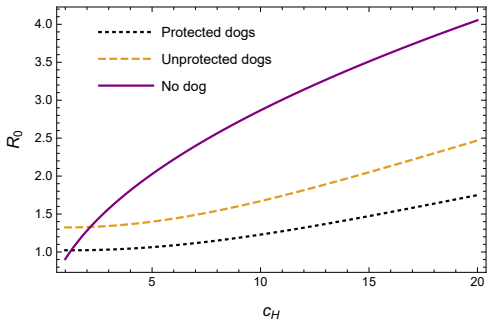


Figure 3.2: R_0 values change their order while a parameter (c_H) varies

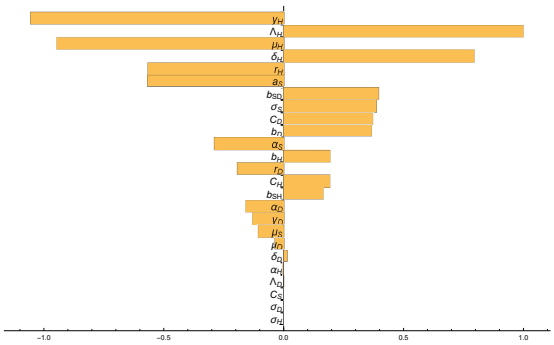
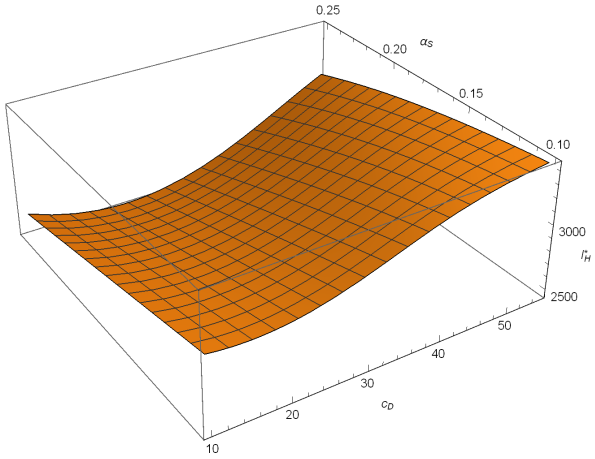
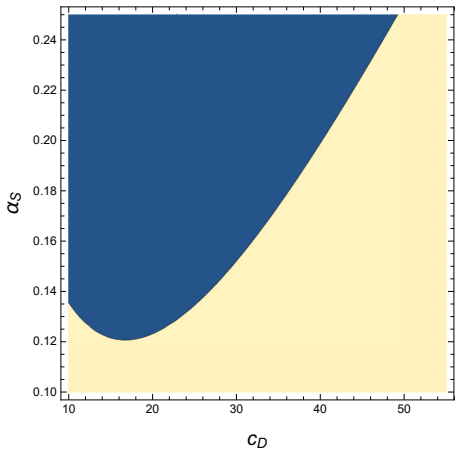


Figure 3.3: Local sensitivity analysis of I_H^* for all model parameters



(a) Human cases of VL with varied combination of efficacy of $DIDC$s and dogs' irritability (where irritability=$\frac{1}{c_D}$)



(b) Darker region represents lower infections and lighter region represents higher infections

Figure 3.4: Effect of dogs' irritability, and $DIDC$ efficacy on human infections of VL

since sandfly biting rate is asymptotically host-dependent. Figure 3.2 shows how the order of R_0 values changes for a certain parameter (c_H) range, to match the I_H^* ordering.

A local sensitivity analysis of the endemic prevalence of leishmaniasis (I_H^*), for the case of protected (with $DIDC$) dogs' presence, was performed for all of our model parameters (Figure 3.3). Among the top 6 parameters with higher normalized sensitivity indices, γ_H, r_H, and δ_H are well known [45, 63, 65]. Among the remaining three, Λ_H, and μ_H are location-specific. The remaining of the top 6 influential parameters is a_S, which is estimated using documented data

[52]. Of the parameters with normalized sensitivity indices greater than $\frac{1}{4}$, the two most of interest to this study are c_D and α_S.

Now we vary the values of c_D and α_S together to observe the contribution of dogs' irritability and the efficacy of $DIDC$ simultaneously in reducing human infections. Our analysis shows that the number of human infections increases with dogs' tolerance for bites (c_D), because this allows vectors' easy access to bite dogs which helps the sandfly population to grow. It also increases the proportion of infected sandflies, because the probability of infection to sandflies from biting dogs is higher than the probability of new infection from biting humans. The number of human infections increases also for extremely low dog tolerance, because it reduces the effects of protective collars by reducing the number of interactions between sandflies and dogs significantly. Also, humans get almost all the bites here which eventually increases human infection risk. Hence, the number of human cases of VL infections is not always proportional to dogs' tolerance to sandfly bites. Figure 3.4 clearly explains the above discussion regarding the effect of dogs' tolerance for sandfly bites, where sub-figure (b) of 3.4 represents the human cases with respect to the dog tolerance and collar's efficiency. Our analysis also shows that human infections decrease with the population size of protected dogs. However, based on our parameter estimation, we find 58% of the dog population needs to be protected with $DIDC$ to ensure the effectiveness of the presence of protected dogs in reducing human risk of VL infections.

3.5 Discussion

The model used in this study gives a new insight to the study of visceral leishmaniasis transmission among human, dog, and sandfly populations. This happens as this study considers humans as a competent host (based on earlier research [51]), in contrast to most other studies' assumption of treating humans as a dead-end host (assuming dogs as the only source of vector infections). The host-population-dependent biting rate for sandflies highlights the impact

of host biodiversity more than other models used in the earlier studies of leishmanisis. Our results show the presence of dogs with $DIDC$ (as topical insecticide) in a community produces fewer human infections compared to infections in the same community without dogs. It is also confirmed that a community without dogs is better in terms of VL infections in humans than a community containing unprotected dogs.

Zhao et al. (2016) [48] develop and analyze an SEIR model assuming hosts' recovery from infections permanent. In our model, we consider recovery for hosts as temporary which leads us to use an SEIRS model. They incorporate sandfly migration in the model which we do not. Their analysis finds the condition $R_0 < 1$ insufficient for complete control of the disease since they observe the existence of backward bifurcation under the condition $R_c < R_0 < 1$. In our study, we find only one endemic equilibrium, which precludes any possibility of the existence of backward bifurcation. Identifying which feature of their model is responsible for the backward bifurcation is prevented by the fact that their study did not provide the definition of k_3 which is present in the definition of R_c. Their model does include disease-related death, but ours includes it also and does not appear to exhibit backward bifurcation. Even though our study does not focus on optimal control policy like Zhao et al., we study the impact of presence of protected (with $DIDC$) dogs, and find this presence helpful in producing fewer human infections.

Shimozako et al. (2017) [45] assumed recovery for both hosts from VL infections is temporary, so they used an SEIRS model in studying ZVL transmission. We also use a modified SEIRS model even though we exclude their assumption that exposed hosts (dogs and humans both) can become susceptible without developing any immunity. We also do not adopt their assumption that latent, and clinically ill dogs have different probabilities of infecting sandflies. They find VL transmission completely dependent on the dog and sandfly populations. However, our study shows each of the three populations has contributions in the dynamics of VL transmission. Shimozako et al. (2017) suggests that control of VL transmission should be based on the sandfly population. Our analysis agrees with this suggestion, showing that presence of

dogs with $DIDC$ protection (which reduces sandfly population) reduces human cases of visceral leishmanisis.

Our study also draws on an ecological perspective to inform public health policy. In the literature review, we mentioned ecological studies [2, 4, 49], [Chapter 2] in which the presence of additional hosts (known as host richness) may help in reducing the human infection risk depending on some factors, such as the abundance of additional host(s) relative to the focal host, vectors' preference of host for feeding, and distance between the primary host and additional host. This study also found the presence of an additional host (dogs protected with $DIDC$) helpful in reducing human risk of VL infections. However, this reduction is independent of all three of the factors which are identified in [2, 4, 49], [Chapter 2]. We find that dogs' presence in a community does not produce fewer human infections if dogs' irritability is very high, or extremely low even after $DIDC$s are ensured on them. This ecological change helps to protect human health only if dogs' irritability ranges somewhere in the intermediate level.

Our proposed model has a few limitations in its development. In our study, we assume all dogs in a community are protected by deltamethrin-impregnated collars which may not be possible in reality. Also, we do not incorporate sandfly migration in our model. However, this migration rate can be included in our $DIDC$-induced sandfly death rate (α_S). Inclusion of this migration may have some impact on our numerical results, and also on the range of dog irritability values which are helpful. However, our qualitative results will remain the same. We have also simplified the VL cycle in humans (for instance, omitting PKDL's role as a possible reservoir) in order to focus on the role played by DIDC-protected dogs. Addressing these limitations could produce better insights into visceral leishmaniasis dynamics. Our proposed model offers a better base than other models for studying control strategies for ZVL, and VL transmission since we incorporate some real, and very important issues, like human infectivity and the role of host irritability.

Chapter 4

Impact of cattle on joint dynamics and disease burden of Japanese encephalitis and leptospirosis

4.1 Introduction

4.1.1 Japanese encephalitis

Japanese encephalitis viral disease (JE) was first documented in 1871 in Japan [72]. Japanese encephalitis (JE) is the main cause of viral encephalitis in many countries of Asia and the western Pacific. 24 countries in the WHO South-East Asia and Western Pacific regions have Japanese encephalitis virus (JEV) transmission risk, which includes more than 3 billion people [72, 73]. JEV is transmitted to humans through bites from infected mosquitoes of the Culex species (mainly *Culex tritaeniorhynchus*). The virus exists in a transmission cycle between mosquitoes, pigs and/or water birds and is transmitted to humans by infected mosquito bite. JE is predominantly found in rural and periurban settings [74, 75]. Each year there are nearly 68,000 clinical cases of JE globally, with approximately 13,600 to 20,400 deaths. JE primarily affects children. Most adults in endemic countries have natural immunity after childhood infection, but individuals of any age may be affected. Most people infected with JE do not have symptoms or have only mild symptoms. However, a small percentage of infected people develop inflammation of the brain (encephalitis), with symptoms including sudden onset of headache, high fever, disorientation, coma, tremors, and convulsions. Approximately 1 in 250 infections results in severe clinical illness. Severe disease is characterized by rapid onset of high fever,

headache, neck stiffness, disorientation, coma, seizures, spastic paralysis, and ultimately death. [72, 73]. The case fatality rate for the disease can be as high as 30% among those with disease symptoms. In addition, 20-30% of those who survive suffer permanent neuropsychiatric sequelae [74].

4.1.2 Leptospirosis

Leptospirosis is a bacterial disease that affects humans and animals. Leptospirosis is considered to be the most widespread zoonotic disease in the world [76]. It is caused by bacteria of the genus *Leptospira* [77]. The bacteria are spread through the urine of infected animals, which can get into water or soil and can survive there for weeks to months. Humans can become infected through contact with urine (or other body fluids, except saliva) from infected animals; also, through contact with water, soil, or food contaminated with the urine of infected animals [78]. In humans, leptospirosis may occur in two phases, where about 10% of infected people move to the 2nd phase [76]. The first phase causes a wide range of symptoms, some of which may be mistaken for other diseases: fever, chills, headache, muscle aches, vomiting, or diarrhea. The second phase, if it occurs, is more severe; the person may have kidney damage, liver failure, meningitis, respiratory distress, and even death [77, 79]. It is estimated that more than 1 million cases occur worldwide annually, including almost 60,000 deaths [79].

4.1.3 Earlier studies

In the last couple of decades, many ecological and field studies, along with a few mathematical ones, have been conducted to understand the dynamics of JEV transmission and to find some control measures to reduce JEV prevalence in humans. In 2001, a study used a probabilistic model of pathogen transmission to investigate various control measures for JEV transmission in humans [80]. Outcomes of the study show that a combination of control measures of similar

effect (strategies to reduce vector population, **or** strategies to reduce vector-human interactions) is more effective compared to the combination of control measures of different effects (strategy to reduce vector population and strategy to reduce human-vector interaction). In 2014, Khan et al. studied the dynamics of JEV transmission in a pig population in northwest Bangladesh [81]. This study developed an SEIR model to understand transmission dynamics in pigs, and to estimate the potential impact of pig vaccination. Their results found that the prevalence of JE in pig populations can be reduced by up to 89% when 75% of susceptible pigs are vaccinated each year. The next year, in 2015, Lord et al. performed a study to rethink JEV transmission among hosts and vectors [82]. They suggested using a mathematical model parameterized with data to quantify the relative roles of potential species in JEV transmission.

Very little research has been done, to the best of our knowledge, to understand the dynamics of leptospirosis in cattle and humans. In 2017, Chadsuthi et al. investigated the leptospirosis prevalence in livestock and humans in Thailand for 2010-2015 [83]. They tested humans, buffaloes, cattle, pigs, and analyzed collected data. Their analysis found livestock more susceptible to leptospirosis infection compared to humans. Later, in 2018, another study was done to understand the spread of leptospirosis in lambs in New Zealand. Here, researchers used a simple SI model to predict conditions under which the disease would persist in the lamb population [84]. Analysis of this study suggested that increasing the *leptospira* death rate in farms can reduce infection in livestock, and eventually in humans.

There are many countries in Asia where both JE and leptospirosis are prevalent. Taking this reality into account, this study is developed to investigate the prevalence of both diseases in humans. Cattle contribute to leptospirosis infections in humans, acting as a source of *leptospira*. However, the presence of cattle in a domestic or peridomestic setting can be considered as an additional host for JE vectors, where humans act as the primary host. Hence, the presence of cattle increases host richness in the setting, which might eventually reduce the combined burden of these two diseases for humans. Earlier studies showed that an additional host (host richness)

in a setting helps to reduce human infections of vector-borne diseases if certain conditions are maintained [2, 4, 85, 49], [Chapter 2,3]. Johnson and Thieltges in 2010 identified that host diversity may help to reduce human infections depending on the relative abundance of additional host(s) relative to the focal host [2]. In 2013, Miller and Huppert proved that species diversity in host populations can amplify or can dilute disease prevalence depending on vectors' preference of host [4]. Recently in 2020, Zahid and Kribs showed that an additional host (dog, reservoir host) in a community can help in reducing the prevalence of visceral leishmaniasis in humans depending on the additional host's irritability to vector bites [85], [Chapter 3]. In another study, the same authors established that the presence of an additional host (chicken, incompetent host) in a domestic setting might help to reduce the prevalence of Chagas disease in humans if the distance between the two host populations (humans and chickens) is maintained at a certain range [49], [Chapter 2].

The presence of cattle helps to reduce human-vector interactions by attracting mosquitoes towards them from humans. Cattle have no contribution to the transmission of JE [86] whereas they act as a source of leptospirosis infections in humans. Thus, in terms of infections, the presence of cattle has two opposite influences on human health – it helps to reduce JE prevalence in humans and contributes to leptospirosis risk in humans. The goal of this study is to understand the dynamics of both diseases in each population, and eventually to understand if the presence of cattle in a setting, where JE and leptospirosis both are prevalent, is helpful to reduce the combined burden of JE and leptospirosis in humans. To answer this question we compare two different peridomestic settings: a setting involving cattle with humans, pigs, and mosquitoes, and the other setting involving humans, pigs, and mosquitoes without cattle. To understand disease dynamics, and to compare the proposed two settings, we develop SIR models for cattle, pig and human populations, and an SI model for the mosquito population. This study estimates the total number of $DALY$s (Disability-Adjusted Life Year) generated from JEV and (in the presence of cattle) leptospirosis infections for both settings and compare them to identify the better scenario. To the best of our knowledge, this is the first work ever to consider JE and

leptospirosis infections together. More broadly, this extends the well-studied question in disease ecology of the impact of an additional host to a multi-pathogen context.

4.2 Model development

The goal of this work is to understand the dynamics of Japanese encephalitis virus (JEV) and leptospirosis infections together and to estimate the impact of cattle presence on human infections of these diseases. Therefore, we select a location for this study where both diseases are prevalent. We choose Malkangiri, the southern district of Odisha (Orissa) State in India. Malkangiri has a history of JE outbreaks since 2009 where the cases are documented as Acute Encephalitis Syndrome (AES) [87]. This AES can include infections other than JE. Studies showed that AES cases are not always cases of JE infections, they can be cases of the severe form (the 2nd phase) of leptospirosis infections [88, 89, 90]. This fact, along with the high prevalence of leptospirosis in cattle in neighbor districts [91, 92], illustrates the presence of human leptospirosis cases in our study location.

We use an SIR model to understand the dynamics of JEV among pig, mosquito, and human populations; also, to understand the dynamics of leptospirosis between cattle and human populations. JEV mainly exists in a transmission cycle between mosquitoes and pigs, and humans get the infection of JE from bites of infected mosquitoes (I_m) [72, 73]. However, infected humans do not infect feeding mosquitoes due to the lack of sufficient viremia. So, humans are dead-end hosts for JEV [72, 73, 74, 101]. Also, cattle have no role in the maintenance of JEV in nature [86]. Thus, humans and cattle have no contribution to JEV transmission. We consider total number of pig bites as $\lambda_h = \frac{b_m N_m}{k_r N_r + k_c N_c + N_h} N_h$ and total number of human bites as $\lambda_h = \frac{b_m N_m}{k_r N_r + k_c N_c + N_h} N_h$, where N_m, N_r, N_c, and N_h represent sizes of mosquito, pig, cattle and human populations respectively, $b_m N_m$ represents total mosquito bites. Here, k_r and k_c are defined based on mosquitoes' feeding preference among hosts (see Table 4.2). In our model

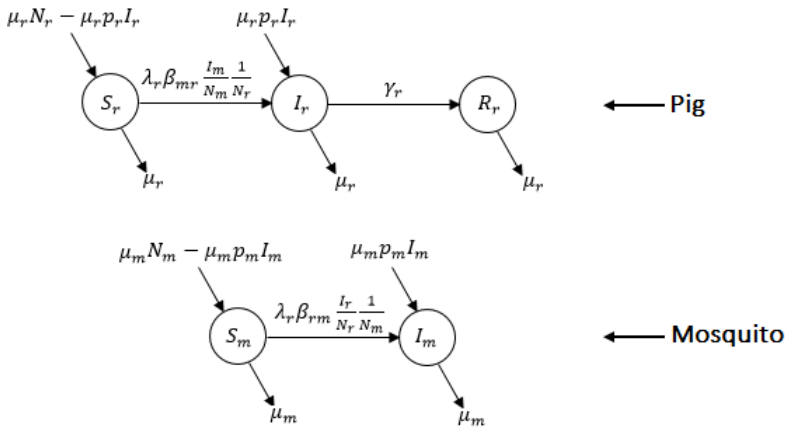


Figure 4.1: Flow diagram for pig and mosquito population

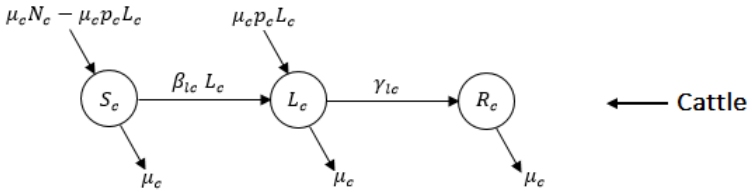


Figure 4.2: Flow diagram for cattle population

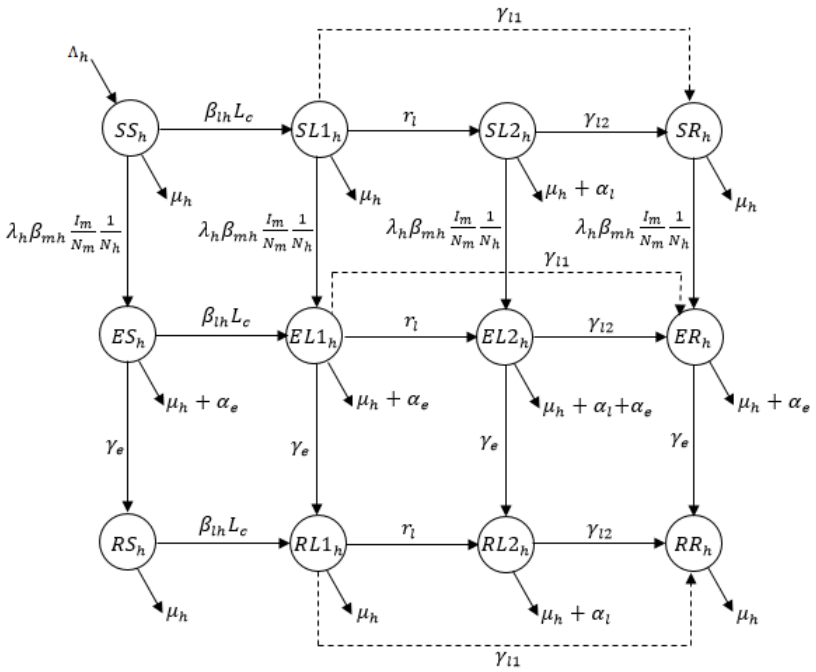


Figure 4.3: Flow diagram for human population

development, we consider the vertical transmission of JEV in pigs, and mosquitoes. All these ideas are illustrated in Figures 4.1, 4.2, and 4.3.

Leptospirosis spreads through the urine of infected cattle or pigs and is transmitted through the contact of contaminated (by the urine of infected animal) surfaces or water [78]. Here, we ignore leptospirosis infections through pigs, because people usually keep pigs in a separate place from houses. Another important reason is its population size (N_r), which is very small compared to the cattle population size (N_c). Therefore, in our model cattle are the only source of *Leptospira*, which causes the disease. Hence, cattle and humans are getting infections just due to the presence of cattle (Figure 4.2 and Figure 4.3). Here, we consider that *Leptospira* can be transmitted in cattle through vertical transmission also.

Susceptible humans get leptospirosis infections and move to $SL1_h$ from SS_h. Most leptospirosis infected humans recover from the first phase, while the remaining move to the second phase of the infection ($SL2_h$). Finally, patients from the second phase move to SR_h upon their recovery. The SR_h compartment represents people who already recovered from leptospirosis infection; however, they are still susceptible to JEV. A portion of susceptible humans get JE infections by infected mosquito bites before leptospirosis infection and move to ES_h. Some of these infected humans get leptospirosis infection before their recovery from JE and move to $EL1_H$. The remaining population of ES_h move directly to the JE recovered class (RS_h). Similar to $SL1_h$, most people from $EL1_h$ move to $EL2_h$ while others move to ER_h. Recovered people from JEV infections (RS_h) get leptospirosis infections and move to $RL1_h$. Then, similar to $SL1_h$ and $El1_h$, most of them move to RR_h after recovery from leptospirosis, while others enter the second phase of infections ($RL2_h$). Finally, people recover from $RL2_h$ and move to RR_h, which contains people who recovered from infections of both diseases.

$$
\begin{aligned}
\frac{dS_c}{dt} &= \mu_c N_c - \mu_c p_c L_c - (\beta_{lc} L_c + \mu_c) S_c \\
\frac{dL_c}{dt} &= \beta_{lc} L_c S_c + \mu_c p_c L_c - (\gamma_{lc} + \mu_c) L_c \\
\frac{dR_c}{dt} &= \gamma_{lc} L_c - \mu_c R_c \\
\frac{dS_r}{dt} &= \mu_r N_r - \mu_r p_r I_r - \lambda_r \beta_{mr} \frac{I_m}{N_m} \frac{1}{N_r} S_r - \mu_r S_r \\
\frac{dI_r}{dt} &= \lambda_r \beta_{mr} \frac{I_m}{N_m} \frac{1}{N_r} S_r + \mu_r p_r I_r - (\gamma_r + \mu_r) I_r \\
\frac{dR_r}{dt} &= \gamma_r I_r - \mu_r R_r \\
\frac{dS_m}{dt} &= \mu_m N_m - \mu_m p_m I_m - (\lambda_r \beta_{rm} \frac{I_r}{N_r} \frac{1}{N_m} S_m + \mu_m) S_m \\
\frac{dI_m}{dt} &= \lambda_r \beta_{rm} \frac{I_r}{N_r} \frac{1}{N_m} S_m + \mu_m p_m I_m - \mu_m I_m \\
\frac{dSS_h}{dt} &= \Lambda_h - \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SS_h - \beta_{lh} L_c SS_h - \mu_h SS_h \\
\frac{dES_h}{dt} &= \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SS_h - (\beta_{lh} L_c + \gamma_e) ES_h - (\mu_h + \alpha_e) ES_h \\
\frac{dRS_h}{dt} &= \gamma_e ES_h - \beta_{lh} L_c RS_h - \mu_h RS_h \\
\frac{dSL1_h}{dt} &= \beta_{lh} L_c SS_h - \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SL1_h - (\gamma_{l1} + r_l + \mu_H) SL1_h \\
\frac{dEL1_h}{dt} &= \beta_{lh} L_c ES_h + \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SL1_h - (\gamma_{l1} + \mu_h + \alpha_e + \gamma_e + r_l) EL1_h \\
\frac{dRL1_h}{dt} &= \beta_{lh} L_c RS_h + \gamma_e EL1_h - (r_l + \gamma_{l1} + \mu_H) RL1_h \\
\frac{dSL2_h}{dt} &= r_l SL1_h - \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SL2_h - (\gamma_{l2} + \alpha_l + \mu_h) SL2_h \\
\frac{dEL2_h}{dt} &= r_l EL1_h + \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SL2_h - (\gamma_{l2} + \gamma_e + \mu_h + \alpha_l + \alpha_e) EL2_h \\
\frac{dRL2_h}{dt} &= r_l RL1_h + \gamma_e EL2_h - (\gamma_{l2} + \mu_h + \alpha_l) RL2_h \\
\frac{dSR_h}{dt} &= \gamma_{l1} SL1_h + \gamma_{l2} SL2_h - \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SR_h - \mu_h SR_h \\
\frac{dER_h}{dt} &= \gamma_{l1} EL1_h + \gamma_{l2} EL2_h + \lambda_h \beta_{mh} \frac{I_m}{N_m} \frac{1}{N_h} SR_h - (\gamma_e + \alpha_e + \mu_h) ER_h \\
\frac{dRR_h}{dt} &= \gamma_{l1} RL1_h + \gamma_{l2} RL2_h + \gamma_e ER_h - \mu_h RR_h
\end{aligned}
\tag{4.1}
$$

where

$\lambda_r = \frac{b_m N_m}{k_r N_r + k_c N_c + N_h} k_r N_r$ and $\lambda_h = \frac{b_m N_m}{k_r N_r + k_c N_c + N_h} N_h$.

Table 4.1: Model variables with definition

Variable	Definition
S_c, S_p, S_m	Susceptible cattle, pigs, mosquitoes
L_c, I_r, I_m	Infected cattle, pigs, mosquitoes
R_c, R_r	Recovered cattle, pigs
SS_h	Humans susceptible to both JE and leptospirosis
ES_h	Humans infected with JE, but susceptible to leptospirosis
RS_h	Humans recovered from JE and susceptible to leptospirosis
$SL1_h$	Humans susceptible to JE, but infected with 1st phase of leptospirosis
$EL1_h$	Humans infected with JE and 1st phase of leptospirosis
$RL1_h$	Humans recovered from JE and infected with 1st phase of leptospirosis
$SL2_h$	Humans susceptible to JE, but infected with 2nd phase of leptospirosis
$EL2_h$	Humans infected with JE and 2nd phase of leptospirosis
$RL2_h$	Humans recovered from JE and infected with 2nd phase of leptospirosis
SR_h	Humans susceptible to JE, but recovered from leptospirosis
ER_h	Humans infected with JE, but susceptible to leptospirosis
RR_h	Humans recovered from both JE and leptospirosis

In our model development, we consider constant populations for cattle, pigs, and mosquitoes. For disease transmission, we choose standard incidence for JEV, because infected mosquitoes (I_m) are free to bite any individual among our host populations. On the other hand, we use mass-action incidence for *Leptospira* transmission, because the new infections depend on the availability of infected cattle (L_c). Also, we assume our cattle, pig and mosquito populations to be constant.

4.3 Parameter estimation

The World Bank recorded the life expectancy of people at birth in India in 2017 as 69.165 years [93]. Taking the reciprocal of this value we get the natural death rate for humans as $\mu_h = 3.96 \times 10^{-5}$/day. As per the 2014 census by the local health department, Malkangiri district had a population of 641,385 in 2014 with 109,483 households [94]. However, according to the World Bank data rural population in India in 2014 and 2018 was 876,035,725 and 892,321,651 respectively [95]. We use the ratio of these two populations to estimate the popula-

tion of Malkangiri district in 2018, which gives us the population as 653,309 (N_h) with 111,518 households. In our literature review, we did not find any value for the human recruitment rate. Hence, we use one of our equations (9th in the system) in a disease-free state which gives the equation $\Lambda_h = \mu_h N_h$. Then we use this equation, and our already estimated values of μ_h and N_h, to get $\Lambda_h = 25.87$ human/day.

We did not find any documented data for the size of cattle and pig populations (N_c and N_r respectively) in Malkangiri district. However, we found one documented data source which mentioned that the numbers of humans, cattle and pigs in Korkunda block of Malkangiri district in 2014 were 143,867, 80,583 (75,772+4,811), and 10,007 respectively in 29,667 households [87]. We use these numbers to estimate cattle and pigs per household, and then use our estimated number of households (111,518) to calculate numbers of total cattle and total pigs in the district in 2018, which gives $N_c = \frac{80{,}583}{29{,}667} \times 111,518 = 302,911$ and $N_r = \frac{10{,}007}{29{,}667} \times 111,518 = 37,616$. Now we need to know the feeding pattern of JEV vectors (value of k_c and k_r) to estimate λ_r and λ_h. We found a study that estimated the feeding preference for JE vectors in the southern part of India as 46.4% on cattle, 4.8% on pigs, and 1.5% on humans [96]. Using these values we have $k_c = \frac{46.4}{1.5}$ human/cattle and $k_r = \frac{4.8}{1.5}$ human/pig.

To estimate λ_r and λ_h, we also need to have the size of JEV carrier mosquito populations (N_m), along with their biting rate (b_m). A field study in rural villages of Western Yunnan Province of China was done in 2013 to estimate the abundance of mosquitoes in an Asian rural setting [97]. Researchers collected mosquitoes from two households in each of four studied villages in each month for a 12 month-study. The total collection of mosquitoes was 85,307. It is equivalent to $\frac{85{,}307}{(2\times4)\times12}$=888 mosquitoes/household. So, for our study we have a total of (111,518×888)=99,027,984 mosquitoes. Another study carried out in some villages of Malkangiri district showed that 69.1% of available mosquitoes are vectors for JEV [87]. Hence, the total number of JEV vectors we have is N_m=99,027,984×69.1%=68,428,337. We found documented data for the biting rate of JEV vectors which give b_m=0.25 bite/mosquito-day (mean of 0.2 and

Table 4.2: Summary of model parameters (TS=This study)

Par.	Definition	Value	Units	Ref.
Λ_h	recruitment rate for humans	25.87	human/day	This study
p_c	probability of vertical transmissions of leptospirosis in cattle	0	-	This study
p_r	probability of vertical transmissions of JE in pigs	0	-	This study
p_m	probability of vertical transmissions of JE in mosquitoes	0.04	-	This study
β_{lc}	infection rate of leptospirosis to cattle	9.3×10^{-8}	1/day-cattle	This study
β_{lh}	infection rate of leptospirosis to humans	9.12×10^{-12}	1/day-cattle	This study
β_{rm}	infection probability of JE to mosquito from biting pigs	0.82	mosquito/bite	[99]
β_{mr}	infection probability of JE to pigs from mosquitoes' bite	0.635	pig/bite	[99]
β_{mh}	infection probability of JE to humans from mosquitoes' bite	0.316	human/bite	[99]
γ_e	recovery rate from JE	$\frac{1}{7}$	1/day	[100]
γ_{lc}	recovery rate from leptospirosis for cattle	2.38×10^{-3}	1/day	This study
γ_{l1}	recovery rate from 1st phase of leptospirosis (humans)	$\frac{1}{10}$	1/day	[104]
γ_{l2}	recovery rate from 2nd phase of leptospirosis (humans)	$\frac{1}{14}$	1/day	[104]
r_l	transfer rate from phase 1 to phase 2 of leptospirosis	0.033	1/day	This study
γ_r	recovery rate from JE for pigs	$\frac{1}{4}$	1/day	[101]
μ_c	natural death rate for cattle	3.42×10^{-4}	1/day	This study
μ_r	natural death rate for pigs	3.91×10^{-4}	1/day	This study
μ_m	natural death rate for mosquitoes	$\frac{1}{59.8}$	1/day	[102]
μ_h	natural death rate for humans	3.96×10^{-5}	1/day	[93]
α_e	JE-induced death rate for humans	0.0383	1/day	This study
α_l	leptospirosis-induced death rate (during 2nd phase for humans	3.13×10^{-2}	1/day	This study
b_m	mosquito's biting rate	0.25	bite/mosquito-day	[98]
N_c	cattle population size of the study area	302,911	cattle	This study
N_m	mosquito population size of the study area	68,428,337	mosquitoes	This study
N_r	pig population size of the study area	37,616	pigs	This study
N_h	human population size of the study area	653,309	humans	This study
k_c	vector's feeding preference (humans over cattle)	$\frac{46.4}{1.5}$	human/cattle	This study
k_r	vector's feeding preference (humans over pigs)	$\frac{4.8}{1.5}$	human/pig	This study
λ_r	encounter rate between pigs and mosquitoes	142,102	bite (total)/day	This study
λ_h	encounter rate between humans and mosquitoes	771,250	bite (total)/day	This study

0.3) [98]. Anyway, not all mosquito bites belong to these three hosts. Also, blood-meal analysis showed that some mosquitoes bite more than one host [96]. Hence, we estimated that about 70% of mosquito bites are distributed among cattle, pig and human population. Thus, $\lambda_r = \frac{0.25\times68{,}428{,}337\times70\%}{\frac{4.8}{1.5}\times37{,}616+\frac{46.4}{1.5}\times302{,}911+653{,}309} \times (\frac{4.8}{1.5} \times 37,616)$=142,102 bite (total)/day and $\lambda_h = \frac{0.25\times68{,}428{,}337\times70\%}{\frac{4.8}{1.5}\times37{,}616+\frac{46.4}{1.5}\times302{,}911+653{,}309} \times 653,309$=771,250 bite (total)/day.

In 2000, the Indian Council of Medical Research carried out a study which found the transmission and infection rate for JEV vectors [99]. The study showed that vectors have 82% infection probability from pigs; however, the transmission probabilities of infections from mosquitoes to humans and mosquitoes to pigs are 31.6% and 63.5% respectively. Hence, we have $\beta_{rm} = 0.82$ mosquito/bite, $\beta_{\text{mr}} = 0.635$ pig/bite, and $\beta_{\text{mh}} = 0.316$ human/bite. A separate review study on the expansion of JEV carried out in 2009 which mentioned that pigs maintain enough viremia to infect mosquitoes for up to 4 days [101]. Taking the reciprocal of this value we get $\gamma_r = \frac{1}{4}$/day. For JE vectors' mortality rate, we found a study that estimated their life expectancy as 59.8 days [102], and this gives us $\gamma_m = \frac{1}{59.8}$/day. Humans' mean recovery period during the 2012 JE outbreak in Odisha was 7 days [100], which gives us $\gamma_e = \frac{1}{7}$/day. For the estimation of μ_r, we found that domestic pigs have an average lifespan of 6-10 years, but, that can be shorter due to certain problems [103]. Thus, instead of the median (8 years) of the range, we choose 7 years as the life expectancy for pig population which eventually estimated $\mu_r = \frac{1}{7\times365}$/day $= 3.91 \times 10^{-4}$/day.

A review study from 2014 mentioned the mean durations for the acute phase (1st phase, in our model) and immune phase (2nd phase, in our model) as 10 days and 14 days respectively [104]. Taking reciprocals of these values we get $\gamma_{l1} = \frac{1}{10}$ /day and $\gamma_{l2} = \frac{1}{14}$ /day. Another study in coastal south India estimated that 51 out of 202 (25.24%) leptospirosis patients move to the 2nd phase [105]. Hence, we use this result and the ratio $\frac{r_l}{\gamma_{l1}+r_l+\mu_h} = \frac{51}{202}$ to estimate the transfer rate from phase 1 to phase 2, and found $r_l = 0.033$**/day**. We found a couple of documented data for cattle recovery period of leptospirosis which are inconsistent in values [106, 107, 108].

Hence, based on those available values we choose that cattle can shed *leptospira* in their urine for 60 weeks, which gives $\gamma_{lc} = \frac{1}{60\times7}$/day $= 2.38\times10^{-3}$/day. In 2016, a different disease in cattle in Odisha state was studied which had the highest cattle age group of 6.5-7.5 years; however, they did not mention the highest or average age [109]. So, we take 8 years as the lifespan for cattle in Odisha, which gives us $\mu_c = \frac{1}{8\times365}$/day $= 3.42\times10^{-4}$/day.

We did not find enough evidence for vertical transmission of leptospirosis in cattle (p_c) and of JEV in pigs (p_r), and therefore we assume $p_c = 0$ and $p_r = 0$. However, we found 4% effective vertical transmission for JEV vectors, which gave $p_m = 0.04$ [110]. In 2016, in Malkangiri district 37 died out of 175 JE patients [94]. Using this ratio and the relation $\frac{\alpha_e}{\alpha_e+\gamma_e+\mu_h} = \frac{37}{175}$, we estimated $\alpha_e = 0.0383$/day. The case fatality rate for leptospirosis infection is 7.69% [113]. Also, we already know that about 25.24% leptospirosis cases move to the 2nd phase [105]. Hence, the case fatality rate among patients of 2nd phase is $\frac{7.69}{25.24}\times100$, which implies $\alpha_l = 3.13\times10^{-2}$/day.

During our literature review, we did not find any value for infection rates of leptospirosis in cattle and in humans (β_{lc} and β_{lh} respectively). Hence, we follow the method used in [49, 19], [Chapter 2] to estimate β_{lc} and β_{lh}which gives $\beta_{lc} = \frac{\gamma_{lc}+\mu_c}{\left(1-\left(\frac{\gamma_{lc}+\mu_c}{\mu_c}\right)y_c\right)N_c}$, $\beta_{lh} = \frac{\mu_h N_h y_h}{\left(\left(1+\frac{r_l}{\gamma_{l2}+\mu_h+\alpha_l}\right)\frac{\Lambda_h}{\gamma_{l1}+\mu_h+r_l}-y_h N_h\right)N_c y_c}$ where y_c and y_h are prevalence of leptospirosis in cattle and in humans respectively. We did not find any documented data for y_c in Malkangiri. However, we found one study from 2013 which estimated leptospirosis prevalence as 20.7% in cattle in a neighbour district of Malkangiri [92]. We choose $y_c = \frac{20.7\%}{2} = 11.35\%$ since the sample collections of this study were not random, rather were mostly from the villages with a history of abortions and other disorders. Also, we did not find documented data for leptospirosis prevalence in humans in Malkangiri. However, we found human and cattle prevalence of leptospirosis in another prevalent location of leptospirosis, northeast Thailand. We estimated leptospirosis prevalence in cattle for this area to be $\frac{34+2+58}{130+183+238} = \frac{94}{551} = 17\%$ using the data from a study published in 2016 [111]. A different study estimated 12.5 annual cases of human leptospirosis per 100,000 people [112]. We used the ratio of estimated leptospirosis prevalence in cattle for our study

area (11.35%) and of northeast Thailand (17%), and the annual cases of human leptospirosis in northeast Thailand (12.5 per 100,000) to calculate annual cases of human leptospirosis for our study area, and found $\frac{12.5\times11.35}{17} = 8.35$ cases per 100,000 people, which is equivalent to 0.00835%. Also, we have a weighted recovery period as $\frac{(10+14)\times25.24\%+10\times74.76\%}{100\%} = 13.53$ days, which gives us $\frac{365}{13.53} = 27$ as the number of generations in a year for infected people. Finally, we got $y_h = \frac{0.00835\%}{27} = 3.09 \times 10^{-6}$. Using these prevalence values and our expressions for leptospirosis infection rates, we got $\beta_{lc} = 9.66 \times 10^{-8}$/day-cattle and $\beta_{lh} = 9.11 \times 10^{-12}$/day-cattle.

4.4 Analysis

We begin with the general model where we consider the presence of cattle which includes both JE and leptospirosis diseases. Later, we consider the scenario without cattle; this special scenario has JEV infection only. Finally, we estimate total disease burdens for these two scenarios and compare them to understand the impact of cattle on disease burden in JE prevalent areas. The goal of this study is actually to understand how the presence of domestic animals, here cattle, helps to reduce disease burden.

4.4.1 Cattle system

First, we analyse the cattle system, which is decoupled from the other two subsystems – the pig-mosquito system, and the human system. We set all the equations of this system equal to zero and solve them for state variables to find equilibria values. After performing some basic algebra we get the disease free equilibrium (DFE) as $S_c = N_c, L_c = 0, R_c = 0$, and the endemic equilibrium (EE) as

$$S_c^* = \frac{\gamma_{lc} + \mu_c(1-p_c)}{\beta_{lc}}, L_c^* = \left(N_c - \frac{\gamma_{lc} + \mu_c(1-p_c)}{\beta_{lc}}\right)\frac{\mu_c}{\gamma_{lc}+\mu_c}, R_c^* = \left(N_c - \frac{\gamma_{lc} + \mu_c(1-p_c)}{\beta_{lc}}\right)\frac{\gamma_{lc}}{\gamma_{lc}+\mu_c}.$$

Then we use the next generation method [27] to obtain the basic reproduction number (BRN) which gives $R_{0l} = \frac{\beta_{lc} N_c + \mu_c p_c}{\gamma_{lc} + \mu_c}$. We find that the EE exists under the condition $R_{0l} > 1$. Here the EE is globally asymptotic stable if and only if $R_{0l} > 1$, otherwise the DFE is globally stable (see appendix 4 for details).

4.4.2 Pig-mosquito system

Before we begin our discussion on the pig-mosquito subsystem, here we consider a simplifying assumption that the two diseases do not significantly affect the magnitude of the human population, so that we can replace $N_h(t)$ by $N_h(0)$ in the denominator of λ_r and λ_h, in order to simplify the analysis. This assumption is supported by both our literature review and the later numerical analysis. As per the study [94], JEV infection causes $\frac{37}{641{,}385} \times 100,000 = 5.77$ annual deaths per 100,000 people. Also, leptospirosis infection causes $12.5 \times 7.69 = 0.96$ annual death per 100,000 people [112, 113]. These two estimations give us a total of 44 ($= \frac{653{,}309}{100{,}000} \times (5.77 + 0.96)$) annual deaths due to both diseases, which is 0.0067% of the total human population. Under this assumption, mosquito's biting rates to pigs, and humans ($\frac{\lambda_r}{N_r}$ and $\frac{\lambda_h}{N_h}$ respectively) become constants, and the vector-reservoir (pig-mosquito) subsystem is decoupled from the human subsystem. The pig-mosquito subsystem is already decoupled from the cattle subsystem. Now, following the same approaches, like the cattle system, for the pig-mosquito system, we get the DFE as $S_r = N_r, I_r = 0, R_r = 0, S_m = N_m, I_m = 0$, and the EE as

$$
\begin{aligned}
S_r^* &= \frac{\lambda_r\beta_{rm} + N_m\mu_m(1-p_m)\frac{\mu_r+\gamma_r}{\mu_r}}{\frac{\lambda_r\beta_{rm}}{N_r}\left(\frac{\lambda_r\beta_{mr}}{N_r}\frac{\mu_r+\gamma_r}{\mu_r} + (\gamma_r+\mu_r(1-p_r))\right)}(\gamma_r+\mu_r(1-p_r)),\\
I_r^* &= \frac{\frac{\lambda_r\beta_{rm}}{N_r}\lambda_r\beta_{mr} - N_m\mu_m(1-p_m)(\gamma_r+\mu_r(1-p_r))}{\frac{\lambda_r\beta_{rm}}{N_r}\left(\frac{\lambda_r\beta_{mr}}{N_r}\frac{\mu_r+\gamma_r}{\mu_r} + (\gamma_r+\mu_r(1-p_r))\right)},\\
R_r^* &= \frac{\frac{\lambda_r\beta_{rm}}{N_r}\lambda_r\beta_{mr} - N_m\mu_m(1-p_m)(\gamma_r+\mu_r(1-p_r))}{\frac{\lambda_r\beta_{rm}}{N_r}\left(\frac{\lambda_r\beta_{mr}}{N_r}\frac{\mu_r+\gamma_r}{\mu_r} + (\gamma_r+\mu_r(1-p_r))\right)}\frac{\gamma_r}{\mu_r},\\
S_m^* &= \frac{\lambda_r\beta_{mr}\frac{\mu_r+\gamma_r}{\mu_r} + N_r(\gamma_r+\mu_r(1-p_r))}{\frac{\lambda_r\beta_{mr}}{N_m}\left(\frac{\lambda_r\beta_{rm}}{N_m} + \mu_m(1-p_m)\frac{\mu_r+\gamma_r}{\mu_r}\right)}(1-p_m)\mu_m,\\
I_m^* &= \frac{\frac{\lambda_r\beta_{rm}}{N_m}\lambda_r\beta_{mr} - N_r(1-p_m)\mu_m(\gamma_r+\mu_r(1-p_r))}{\frac{\lambda_r\beta_{mr}}{N_m}\left(\frac{\lambda_r\beta_{rm}}{N_m} + \mu_m(1-p_m)\frac{\mu_r+\gamma_r}{\mu_r}\right)}.
\end{aligned}
\tag{4.2}
$$

We get the BRN for the pig-mosquito system as

$$
R_{0e} = \frac{1}{2}\left(\left(\frac{\mu_r}{\mu_r+\gamma_r}p_r + p_m\right) + \sqrt{\left(\frac{\mu_r}{\mu_r+\gamma_r}p_r - p_m\right)^2 + 4\frac{\lambda_r\beta_{mr}}{\mu_m N_m}\frac{\lambda_r\beta_{rm}}{(\mu_r+\gamma_r)N_r}}\right).
$$

Here the EE exists and is locally asymptotically stable (LAS) if and only if $R_{0e} > 1$, otherwise the DFE is LAS. Next, we develop a strong Lyapunov function to show that the DFE is globally stable when $R_{0e} < 1$ (see appendix 5 for details). Then, we analyse the stability of the EE numerically which indicates that the EE here is globally stable if and only if $R_{0e} > 1$.

4.4.3 The limiting system

The cattle subsystem and the pig-mosquito subsystem are decoupled from the human subsystem respectively by the model and the assumption that the magnitude of the human population is insignificantly affected by the effect of JE and leptospirosis. As these two subsystems go to equilibrium, the limiting system for system 4.1 is given by the human subsystem with L_c and I_m replaced by their equilibrium values (please see system (4.3)).

$$
\begin{aligned}
\frac{dSS_h}{dt} &= \Lambda_h - \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SS_h - \beta_{lh}L_c^*SS_h - \mu_h SS_h \\
\frac{dES_h}{dt} &= \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SS_h - (\beta_{lh}L_c^* + \gamma_e)ES_h - (\mu_h + \alpha_e)ES_h \\
\frac{dRS_h}{dt} &= \gamma_e ES_h - \beta_{lh}L_c^*RS_h - \mu_h RS_h \\
\frac{dSL1_h}{dt} &= \beta_{lh}L_c^*SS_h - \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SL1_h - (\gamma_{l1} + r_l + \mu_H)SL1_h \\
\frac{dEL1_h}{dt} &= \beta_{lh}L_c^*ES_h + \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SL1_h - (\gamma_{l1} + \mu_h + \alpha_e + \gamma_e + r_l)EL1_h \\
\frac{dRL1_h}{dt} &= \beta_{lh}L_c^*RS_h + \gamma_e EL1_h - (r_l + \gamma_{l1} + \mu_H)RL1_h \\
\frac{dSL2_h}{dt} &= r_l SL1_h - \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SL2_h - (\gamma_{l2} + \alpha_l + \mu_h)SL2_h \\
\frac{dEL2_h}{dt} &= r_l EL1_h + \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SL2_h - (\gamma_{l2} + \gamma_e + \mu_h + \alpha_l + \alpha_e)EL2_h \\
\frac{dRL2_h}{dt} &= r_l RL1_h + \gamma_e EL2_h - (\gamma_{l2} + \mu_h + \alpha_l)RL2_h \\
\frac{dSR_h}{dt} &= \gamma_{l1}SL1_h + \gamma_{l2}SL2_h - \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SR_h - \mu_h SR_h \\
\frac{dER_h}{dt} &= \gamma_{l1}EL1_h + \gamma_{l2}EL2_h + \beta_{mh}\frac{\lambda_{h0}}{N_h}\frac{I_m^*}{N_m}SR_h - (\gamma_e + \alpha_e + \mu_h)ER_h \\
\frac{dRR_h}{dt} &= \gamma_{l1}RL1_h + \gamma_{l2}RL2_h + \gamma_e ER_h - \mu_h RR_h
\end{aligned}
\tag{4.3}
$$

where $\lambda_{h0} = \frac{b_m N_m}{k_r N_r + k_c N_c + N_{h0}} N_h$ (here $N_{h0} = N_h(0)$). Here N_m is constant which makes the term $\frac{I_m^*}{N_m}$ to be constant and $\frac{\lambda_{h0}}{N_h}$ ($= \frac{b_m N_m}{k_r N_r + k_c N_c + N_{h0}}$=constant) is also constant. Thus, the resulting system (system (4.3)) is linear and has only one equilibrium (see equation (17) in Appendix 6) where the equilibrium values are functions of L_c^* and I_m^*. Hence, the behavior of the limiting system follows the behavior of our cattle and pig-mosquito subsystems. Now, a theorem by Horst R. Thieme [114] leads us to the fact that the behavior of the entire system is asymptotic to the behavior of the limiting system, which is linear. Eventually, the entire system is governed by the behavior of the cattle and the pig–mosquito subsystems.

4.4.4 Entire system

Next, we extend our analysis to the entire system, which includes the cattle, the pig–mosquito, and the human subsystems. We obtain the invasion reproduction number (IRN) for both diseases following the approach by Mitchell & Kribs [115]. Each of these IRNs is found to be the same as the corresponding BRNs. Thus, both of the IRNs are independent of the presence of the other disease. This result is easily comprehensible since neither of these diseases' transmissions is affected by the other. Our preceding analyses found two different values for both L_c^* and I_m^*; hence, their all possible combinations produces four different equilibria for the entire system. These four equilibria are – DFE, endemic in leptospirosis and free of JE, endemic in JE and free of leptospirosis, and endemic in both diseases respectively. So, for the entire system, we have four different scenarios – (i) $R_{0l} < 1$ and $R_{0e} < 1$ (ii) $R_{0l} > 1$ and $R_{0e} < 1$, (iii) $R_{0l} < 1$ and $R_{0e} > 1$, and (iv) $R_{0l} > 1$ and $R_{0e} > 1$.

4.4.5 Special case: no cattle

Now we consider the scenario without cattle which eliminates the possibility of leptospirosis infections in humans. Here the BRN for JE ($\mathcal{R}_{0e}$) is different compared to the BRN (R_{0e}) from from the general model since the λ_r in R_{0e} is a function of cattle population size. The absence of cattle reduces the human system to a three-dimensional system, which gives the EE for the human system as

$$SS_h^* = \frac{\Lambda_h}{\mu_h + \frac{\lambda_{h0}\beta_{mh}}{N_h}\frac{I_m^*}{N_m}}, ES_h^* = \frac{\frac{\lambda_{h0}\beta_{mh}}{N_h}\frac{I_m^*}{N_m}}{(\mu_h + \gamma_e + \alpha_e)}\left(\frac{\Lambda_h}{\mu_h + \frac{\lambda_{h0}\beta_{mh}}{N_h}\frac{I_m^*}{N_m}}\right),$$
$$RS_h^* = \frac{\frac{\lambda_{h0}\beta_{mh}}{N_h}\frac{I_m^*}{N_m}\gamma_e}{\mu_h(\mu_h + \gamma_e + \alpha_e)}\left(\frac{\Lambda_h}{\mu_h + \frac{\lambda_{h0}\beta_{mh}}{N_h}\frac{I_m^*}{N_m}}\right)$$

where $\lambda_{h0} = \frac{b_m N_m}{k_r N_r + N_{h0}} N_h$ (here $N_{h0} = N_h(0)$). This special case has DFE, and the only endemic equilibrium (EE) when $\mathcal{R}_{0e} > 1$. This EE is completely governed by I_m^* (see equation (4.2) for I_m^*).

4.4.6 Quantitative analysis

To better understand the impact of cattle, some numerical analyses are done based on our parameter estimations. Using our estimated parameter values, we find $R_{0l} = 10.35$ and $R_{0e} = 1.008$ respectively in the presence of cattle. However, our estimations in the absence of cattle found $\mathcal{R}_{0e} = 12.97$. Based on our estimated parameter values, in the presence of cattle we estimate 72 and 228 annual cases for leptospirosis and JE respectively, whereas the annual deaths are 6 and 48 respectively. In the absence of cattle, we estimate 9,407 and 1,988 number of annual cases and annual deaths due to JEV infections. Next, we perform numerical analysis to estimate total cases and the BRN of JE and leptospirosis as the average number of cattle per household varies and plot the related graphs (Figure 4.4). The Figure 4.4(a) shows that the JEV infection decreases as the number of cattle increases; however, the human leptospirosis incidence increases with the cattle; the Figure 4.4(b) illustrates that BRN for JE exponentially decreases, and for leptospirosis linearly increases as the number of average cattle increases. So, the presence of cattle has positive and negative impacts on human health.

4.4.7 Impact of cattle

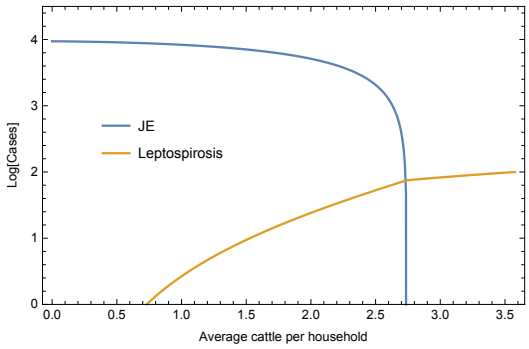
To quantify the impact of cattle on human health, we calculate the total disease burden for our two settings – with cattle and without cattle. In this calculation we follow an approach similar to the approach of the study [116] where they followed WHO guidelines [117]. To calculate the total disease burden they estimated total $DALY$ (Disability-Adjusted Life Year) where one $DALY$ means the loss of one year of healthy life. The $DALY$ is composed of YLD (Years Lost due to Disability) resulting from infections and YLL (Years of Life Lost) caused by disease-induced premature deaths which are calculated using formulas $YLD = I \times DW \times L_1$ and $YLL = D \times L_2$, where I and D represent the total number of infections (cases) and total number

of deaths respectively. Here L_1 = average duration (in years) of illness which is the reciprocal of the recovery rate for survival cases and of the death rate for non-survival cases, and L_2 = standard life expectancy at age of death (in years) = average life expectancy of the community – average age at premature death and the term DW is the disability weight for diseases which ranges from 0 (perfect health) to 1(death). It can be thought of as the proportional reduction in perfect health due to any adverse health condition caused by infections. So, the total burden of disease can be represented as the sum of YLD and YLL, which gives

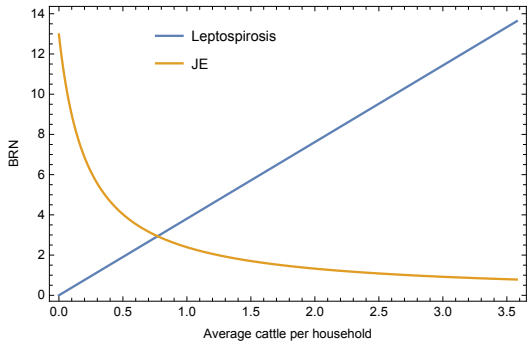
$$DALY = I \times DW \times L_1 + D \times L_2.$$

In this work, we study two different diseases, JE and leptospirosis. Hence, we will have different values of I, D, L_1, L_2 and of DW for JE, and leptospirosis. Here the quantities L_1s are the reciprocals of the γ_{l1}, γ_{l2} for the first and second phases of leptospirosis respectively, and the reciprocal of the γ_e for JE. To estimate L_2s, we need to know the average ages of infections which are 40.48 years [105] and 5 years [100] for leptospirosis and JEV infections respectively. The average age of infections and the average age of deaths are the same for leptospirosis; however, they are different for JE (5 years and 3 years respectively [100]). The values of DW differs between leptospirosis and JE; it also differs between phases of leptospirosis. Furthermore, the DW has different values for survival and non-survival. All these different values of DW are taken from the study [118] based on the severity (mild or severe) of illness and on the onward complications upon recovery. Therefore, using the above formula for $DALY$ we calculate total $DALY$s separately for JE and leptospirosis infections and add them to have total $DALY$ cause from both diseases combined.

Based on our parameter estimations, the above formula and values together calculate 4,396 $DALY$s and 157,642 $DALY$s for the setting with cattle and without cattle respectively. These results clearly show that the presence of cattle has a huge positive impact on the disease burdens in JE-prevalent areas. Next, we calculate total $DALY$s varying the average number of cattle



(a) Relation between avg cattle/household and total cases of JE and leptospirosis accumulated over a year



(b) The BRNs for leptospirosis and JE as cattle per household varies

Figure 4.4: The effect of cattle on infections and BRNs

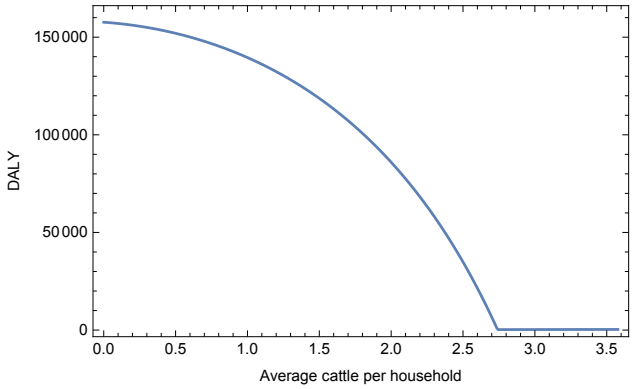


Figure 4.5: Relation between avg cattle/household and annual disease burden (in $DALY$s)

per household to understand how the variation in the average number of cattle per household changes the annual disease burden. The results of these calculations are portrayed in Figure 4.5, which evidently illustrates that the presence of cattle is unconditionally helpful in terms of the annual disease burden. However, there is an optimum value for the average number of cattle per household to ensure the minimum disease burden which is 2.75. Maintaining cattle beyond this threshold value the annual disease burden increases slowly which is generated from the infections of leptospirosis. On the other hand, keeping fewer cattle per household than the optimum number causes a sharp rise in the annual disease burden due to a significant increase in JE infections.

4.5 Discussion

To the best of our knowledge, this is the first work to understand the joint dynamics of JE and leptospirosis. Our qualitative analysis exhibits the classic threshold behavior of the system. The quantitative analysis shows that the presence of cattle reduces total disease burden even though it introduces leptospirosis. It happens because the number of JE cases is reduced by the cattle presence at a higher rate than the rate at which humans get leptospirosis infections due to the presence of cattle. Also, the case fatality rate (CFR) of JE infections is higher than the CFR of leptospirosis infections. The disability weight is higher for JE infections than for the leptospirosis infections, and the average age of JEV infections is very low compared to the average age of leptospirosis infections. Even though the presence of cattle is always helpful, there is an optimum average number of cattle per household which minimizes the annual disease burden.

Our analysis found that the presence of cattle helps to reduce the annual disease burden in JE-prevalent areas because of the vector's (mosquitoes') feeding preference. Mosquitoes prefer to bite cattle at a much higher proportion compared to the proportion to bite humans or pigs. Thus, cattle reduce mosquito-human interactions and eventually reduce human cases of JEV infections. This result is consistent with the result of an ecological study by Miller and Huppert [4] where they identified that vectors' feeding preference decides whether or not host richness is helpful to dilute disease prevalence. Also, our results found that the JE prevalence in humans decreases as the cattle population increases. This finding is consistent with the finding of another ecological study on vector-borne diseases by Johnson and Thieltges [2] where they found that the strength of the dilution effects depends on the relative abundance of the dilution host to the focal host.

This study didn't consider seasonality in its model development. Considering seasonality will provide a more accurate picture of short-term dynamics. We didn't include seasonality because the concern of our study is primarily with the overall disease burden, not with the detailed

disease dynamics. In our analysis, we assumed constant biting rates to pigs and humans which should not have any significant impact on our results since the mosquito population is not limited by the available host populations, rather by available breeding sites. We also assumed a homogeneous distribution among households and those cattle close enough to households to affect the infection risks for JEV and leptospirosis. Large cattle farms farther away from homes than pigs are, are not likely to affect those risks (except to employees). However, studies have shown that heterogeneity does affect disease risk [119, 120]. In our case, heterogeneity is the heterogeneous distribution of household cattle per household.

Chapter 5

Conclusion

In this dissertation, we shift a well studied ecological question to a domestic setting and try to find related answers. Many ecological studies have been done to study the effect of host diversity on the prevalence of vector-borne infectious diseases. Here, we study how domestic animals influence disease dynamics while acting as an additional host. The impact of domestic animals on disease prevalence is not straightforward because they have both positive and negative impacts on disease transmission. Moreover, domestic animals act differently on the disease transmission based on their role for specific pathogens and their vector. Thus, to answer our dissertation question well, we study three different cases.

The result of our study on Chagas disease in Chapter 2 is not straightforward. Our analyses found that the presence of chickens can be helpful to reduce human infections when villagers keep chickens at a place from where triatomine bugs (the vector) can anticipate the presence of the hosts. It is only helpful if the birth rate of vectors feeding on chickens (b_{v2}) is less than a certain threshold value. Our numerical analysis found this threshold value as 19.57/chicken-year. Thus, the decoy process by the presence of an incompetent host does not help unconditionally.

Our analyses in Chapter 3 show that the presence of dogs with deltamethrin-impregnated collars in a community is better than a community without dogs when a certain percent of dogs

Table 5.1: Summary of the findings of our three case studies

Case	Negative impact	Positive impact	Net effect
Chagas with chickens	Helps vectors to grow faster	distracts vectors from humans	Human infections reduced if chicken placed at a certain distance
VL with protected dogs	Helps vectors to grow faster	distracts and kills vector population	Human infections reduced based on dogs tolerance to sandfly bites
JE with cattle	cause leptospirosis infections	distracts vectors from humans	Significant reductions in total disease burden unconditionally

can be ensured to have the protected collar. The presence of protected dogs impacts positively by killing (by the insecticide on collars) a fraction of the sandfly population while impacts negatively by acting as a source of infection (since dog is a reservoir host). Thus, when a certain portion of dogs in a community has protected collars, the positive impact of having protected dogs is much higher in magnitude than the negative impact of dogs' presence.

The outcome of the study on Japanese encephalitis (JE) in the presence of cattle is a little bit different from the outcomes of our previous two studies. Here, we found that the presence of cattle in households in a JE prevalent area is always helpful in terms of disease burden even though the presence of cattle in a domestic setting introduces leptospirosis, a bacterial disease spreads by the urine of infected cattle. However, there is an optimum value for the average number of cattle per household to ensure the minimum disease burden which is 2.75. Maintaining cattle beyond this threshold value slowly increases the annual disease burden, which is generated from the infections of leptospirosis. On the other hand, keeping fewer average cattle per household than the optimum number causes a sharp rise in the annual disease burden due to a significant increase in JE infections. The outcomes of these three studies are summarized in Table 5.1.

This dissertation found that the relationship between the abundance of dilution hosts rel-

ative to focal hosts and positive impact is not always monotone which is inconsistent with the outcome of the study by Johnson & Thieltges [2]. Our work on Chagas disease in Chapter 2 identifies that the presence of an additional host, here chicken, increases disease risk when villagers keep chickens up to a certain number, and beyond that threshold number the risk of human infections begins to go down. However, our work on visceral leishmaniasis in Chapter 3 shows that the relation between the abundance of dilution host and the reduction in human infections is monotone. We also found that host richness is not always helpful to reduce infection risk which complies with the finding of the study [3]. Our analyses found that host richness is not helpful in the far distance case of Chapter 2; however, in other cases it is helpful. In addition to these two findings, we also found that the relationship between vector's feeding preference and positive impact on infection reduction is not always consistent which partially complies with the findings of Miller & Huppert [4]. In our works on Chagas in Chapter 2 and on JE in Chapter 4, we consider vectors' feeding preference in our model development. Our results in Chapter 4, where vectors mostly prefer the dead-end host cattle, comply with the findings of the study by Miller & Huppert; however, the short distance case in Chapter 2 showed that the preference of biting an additional host with no transmission ability can amplify the disease prevalence.

Each of the chapters studied here has limitations in its model development. We also used some assumptions for the purpose of the simplification of analysis. Thus, further work can be done excluding these limitations and assumptions. In our analyses, most of our model parameters are estimated in this study. So, reliable estimations of these parameters are needed to ground our qualitative results better.

Appendix

Appendix 1. Simplification of R_0 when $Q_3 = 0$

$$\begin{aligned}
\frac{2^{1/3}Q_{12}}{3\left(\sqrt{\frac{-4Q_{12}^3}{27}}\right)^{1/3}} + \frac{\left(\sqrt{\frac{-4Q_{12}^3}{27}}\right)^{1/3}}{2^{1/3}} &= \frac{Q_{12}}{\sqrt{3}\left(-Q_{12}^3\right)^{1/6}} + \frac{\left(-Q_{12}^3\right)^{1/6}}{\sqrt{3}} \\
&= \frac{Q_{12} + \left(-Q_{12}^3\right)^{1/3}}{\sqrt{3}\left(-Q_{12}^3\right)^{1/6}} \\
&= \frac{Q_{12}\left(1 + (-1)^{1/3}\right)}{\sqrt{3}\sqrt{Q_{12}}\,(-1)^{1/6}} \\
&= \frac{\sqrt{Q_{12}}\left(1 + \frac{1}{2} + i\frac{\sqrt{3}}{2}\right)}{\sqrt{3}\left(\frac{\sqrt{3}}{2} + \frac{i}{2}\right)} \\
&= \frac{\sqrt{Q_{12}}\left(\frac{3}{2} + i\frac{\sqrt{3}}{2}\right)}{\left(\frac{3}{2} + i\frac{\sqrt{3}}{2}\right)} \\
&= \sqrt{Q_{12}}
\end{aligned}$$

Appendix 2. Derivation of equation (3.4.1)

Using the value of λ_D in the 1st equation of the system (3.1) at steady state gives

$$S_D = \frac{\Lambda_D}{\mu_D} - \left[\left(\frac{\sigma_D + r_D + \mu_D}{\mu_D}\right)\left(\frac{\gamma_D + \mu'_D}{\sigma_D}\right) I_D - \frac{\delta_D}{\mu_D}\left(\frac{r_D}{\delta_D + \mu_D}\frac{\gamma_D + \mu'_D}{\sigma_D} + \frac{\gamma_D}{\delta_D + \mu_D}\right)\right] = \frac{\Lambda_D}{\mu_D} - K_1 I_D \tag{1}$$

At steady states, 3rd equation of system (3.1) gives

$$E_D = \frac{\gamma_D + \mu'_D}{\sigma_D} I_D \tag{2}$$

The value of λ_D, equation (1), equation (2), and the 2nd equation of system (3.1) at steady state gives

$$c_D b_D \frac{\Lambda_D}{\mu_D}\frac{I_S}{N_S} - K_1 c_D b_D \frac{I_S}{N_S} I_D - K_4 I_D = 0 \tag{3}$$

Similarly, 5th, 6th, and 7th equations of system (3.1) at steady states gives

$$c_H b_H \frac{\Lambda_H}{\mu_H} \frac{I_S}{N_S} - K_2 c_H b_H \frac{I_S}{N_S} I_H - K_5 I_H = 0 \tag{4}$$

The 9th equation of the system (3.1) at steady state give

$$L_S = \frac{\mu'_S}{\sigma_S} I_S \tag{5}$$

At steady state, the sum of 9th, and 10th equations of system (3.1), and equation (5) give

$$S_S = \frac{a_S(\lambda_D + \lambda_H)}{\mu'_S} - \frac{\sigma_S + \mu'_S}{\sigma_S} I_S \tag{6}$$

Now, the equation (6), and the 10th equation of system (3.1) at steady state give

$$(c_D b_{SD} K_7 I_D + c_H b_{SH} I_H) \left(1 - K_6 \frac{I_S}{N_S}\right) - K_6 \mu'_S I_S = 0 \tag{7}$$

Now, equation (3), and equation (4) respectively give

$$\frac{I_S}{N_S} = \frac{K_4}{c_D b_D} \left(\frac{\Lambda_D}{\mu_D} - K_1 I_D\right)^{-1} I_D \tag{8}$$

$$\frac{I_S}{N_S} = \frac{K_5}{c_H b_H} \left(\frac{\Lambda_H}{\mu_H} - K_1 I_H\right)^{-1} I_H \tag{9}$$

Then, using equation (8), and equation (9) we get

$$I_D = \frac{\Lambda_D}{\mu_D} \left[\frac{b_H c_H}{b_D c_D} \frac{K_4}{K_5} (\Lambda_H \mu_H - K_2 I_H) + K_1 I_H\right]^{-1} I_H \tag{10}$$

Finally, substituting the value of $\frac{I_S}{N_S}$ from (9), and I_D from (10) in equation (7) we get

$$AI_H^2 + BI_H + C = 0$$

Appendix 3. Endemic equilibrium analysis

The expression for C can be written as

$$\begin{aligned}
\frac{C}{\frac{\Lambda_H}{\mu_H}c_D b_{SD}\frac{\Lambda_D}{\mu_D}} &= K_7 + \frac{\frac{\Lambda_H}{\mu_H}}{\frac{\Lambda_D}{\mu_D}}\frac{c_H b_{SH}}{c_D b_{SD}}\frac{c_H b_H}{c_D b_D}\frac{K_4}{K_5} - \frac{1}{Q_3} \\
\frac{C}{\frac{\Lambda_H}{\mu_H}c_D b_{SD}\frac{\Lambda_D}{\mu_D}} &= K_7 + \frac{\Lambda_H}{\mu_H}\frac{b_H c_H}{a_S K_3}\frac{b_{SH}c_H}{K_5 K_6}\frac{1}{Q_3} - \frac{1}{Q_3} \\
\frac{CQ_3}{\frac{\Lambda_H}{\mu_H}c_D b_{SD}\frac{\Lambda_D}{\mu_D}} &= K_7 Q_3 + \frac{\Lambda_H}{\mu_H}\frac{b_H c_H}{a_S K_3}\frac{b_{SH}c_H}{K_5 K_6} - 1 \\
&= Q_3\left(\frac{\gamma_D+\mu_D+\alpha_D}{\sigma_D}+1\right) + \frac{\Lambda_H}{\mu_H}\frac{b_H c_H}{a_S K_3}\frac{b_{SH}c_H}{K_5 K_6} - 1 \\
&= Q_3\left(\frac{\gamma_D+\mu_D+\alpha_D}{\sigma_D}\right) + Q_3 + \frac{\Lambda_H}{\mu_H}\frac{b_H c_H}{a_S K_3}\frac{b_{SH}c_H}{K_5 K_6} - 1 \\
&= \left(\frac{\Lambda_D}{\mu_D}\frac{b_D c_D}{a_S K_3}\frac{b_{SD}c_D}{K_4 K_6}\left(\frac{\gamma_D+\mu_D+\alpha_D}{\sigma_D}\right) + \frac{\Lambda_H}{\mu_H}\frac{b_H c_H}{a_S K_3}\frac{b_{SH}c_H}{K_5 K_6}\right) + Q_3 - 1
\end{aligned}$$

$$C\,\frac{Q_3}{\frac{\Lambda_H}{\mu_H}c_D b_{SD}\frac{\Lambda_D}{\mu_D}} = Q_{12} + Q_3 - 1 \tag{11}$$

Our analysis found R_0 as a increasing function in Q_{12}, and $R_0 = 1$ if and only if $Q_{12} + Q_3 = 1$. Since $\frac{Q_3}{\frac{\Lambda_H}{\mu_H}c_D b_{SD}\frac{\Lambda_D}{\mu_D}}$ is a positive quantity, then from (11) we have $R_0 > 1$ if and only if $C > 0$.

To explore the range of solutions to equation (3.4.1) numerically, we considered all parameters except δ_H and b_{SD} to be fixed at their default values, and then considered A and C as functions of δ_H and b_{SD} respectively. We found the intervals on which A and C were positive and negative, and explored each possible combination. We found no cases in which A, B, C are all positive. Of the seven remaining combinations, only three ($A > 0, B < 0, C > 0$; $A, B < 0, C > 0$; $A < 0, B, C > 0$) led to positive solutions. The Jacobian matrix for each of these three cases gives a set of eigenvalues with negative real part, which ensures that the endemic equilibrium is locally asymptotically stable.

Appendix 4. Stability of the endemic equilibrium of the cattle system

Proposition 1: The endemic equilibrium for the cattle subsystem is locally stable if and only if $R_{0l} > 1$.

Proof: We find the Jacobian matrix of the cattle system at the EE which gives the characteristic equation

$$\left(\lambda^2 + \mu_c R_{0l}\lambda + \mu_c(\gamma_{lc} + \mu_c)(R_{0l} - 1)\right)(\lambda + \mu_c) = 0.$$

Here, $\lambda = -\mu_c$ is negative. Next, we use Routh-Hurwitz Criteria to check if the real part of remaining eigenvalues are negative. As per Routh-Hurwitz Criteria, the coefficients of λ and the constant term need to be positive to ensure the negativity of real parts of eigenvalues. Here it is evident that the coefficient of λ is always positive and the constant term is positive when $R_{0l} > 1$.

Hence, the EE for the cattle subsystem is locally stable if and only if $R_{0l} > 1$.

Proposition 2: The endemic equilibrium for the cattle subsystem is globally stable when $R_{0l} > 1$, otherwise the DFE is globally stable.

Proof: The first two equations of the cattle subsystem are

$$\begin{aligned} S_c^{'} &= \mu_c N_c - \mu_c p_c L_c - (\beta_{lc} L_c + \mu_c) S_c \\ L_c^{'} &= \beta_{lc} L_c S_c + \mu_c p_c L_c - (\gamma_{lc} + \mu_c) L_c. \end{aligned} \tag{12}$$

It is evident from the system (12) that $S_c^{'} > 0$ if $S_c = 0$ and $L_c^{'} = 0$ if $L_c = 0$, which means the system (12) is well posed. Now, the system (12) gives $S_c^{'} + L_c^{'} = (S_c + L_c)^{'} = \mu_c N_c - \mu_c S_c - (\mu_c + \gamma_{lc}) L_c$. From this relation it is evident that $(S_c + L_c)^{'} \leq 0$ if either $S_c \geq N_c$, or $L_c \geq N_c$ which shows all solutions are bounded.

Now we define $\beta(S_c, L_c) = \frac{1}{S_c L_c}$ to use Dulac's Criterion to check if the EE approaches a limit cycle. Here we assume $F(S_c, L_c) = S_c^{'}$ and $G(S_c, L_c) = L_c^{'}$ which give

$$\frac{\partial}{\partial S_c}(\beta F)+\frac{\partial}{\partial L_c}(\beta G)=-\frac{\mu_c N_c}{L_c S_c^2}+\frac{\mu_c p_c}{S_c S_c^2}=\frac{\mu_c}{S_c^2}(p_c-\frac{N_c}{L_c})\leq 0 \tag{13}$$

So, no limit cycle exists.

Hence, by Poincaré-Bendixson Theorem all solutions approach the EE when $R_{0l}>1$ which means the EE is globally stable if and only if $R_{0l}>1$, otherwise the DFE is globally stable.

Appendix 5. Stability of the endemic equilibrium of the pig-mosquito system

Proposition 3: The endemic equilibrium for the pig–mosquito subsystem is locally stable if and only if $R_{0e}>1$.

Proof: We can reduce our system to a system of three equations since pig and mosquito populations are constant. We Replace $S_r=N_r-(I_r+R_r)$ and $S_m=N_m-I_m$ in the 3rd and 5th equation of the system (4.1) and get the reduced pig-mosquito system as

$$\begin{aligned}
I_r^{'}&=\frac{dI_r}{dt}=\lambda_r\beta_{mr}\frac{I_m}{N_m}\frac{1}{N_r}(N_r-(I_r+R_r))-(\mu_r(1-p_r)+\gamma_r)\,I_r\\
R_r^{'}&=\frac{dR_r}{dt}=\gamma_r I_r-\mu_r R_r\\
I_m^{'}&=\frac{dI_m}{dt}=\lambda_r\beta_{rm}\frac{I_r}{N_r}\frac{1}{N_m}(N_m-I_m)-\mu_m(1-p_m)I_m
\end{aligned} \tag{14}$$

Next, we find the Jacobian matrix of the reduced system (14) at the EE which gives the characteristic equation

$$\lambda^3+A_1\lambda^2+A_2\lambda+A_3=0.$$

Here, $A_1=-(a_1+a_2+a_3)$, $A_2=a_1b_2-a_2b_1+a_1c_3-a_3c_1+b_2c_3$, and $A_3=a_3b_2c_1+a_2b_1c_3-a_1b_2c_3$ where $a_1=-\frac{\lambda_r\beta mr}{N_mN_r}I_m^*-(\gamma_r+\mu_r(1-p_r))$, $a_2=-\frac{\lambda_r\beta_{rm}}{N_mN_r}I_m^*$, $a_3=\frac{\lambda_r\beta_{rm}}{N_mN_r}(N_r-I_r^*-R_r^*)$, $b_1=\gamma_r$, $b_2=-\mu_r$, $c_1=\frac{\lambda_r\beta_{rm}}{N_mN_r}(N_m-I_m^*)$, $c_3=-\frac{\lambda_r\beta_{rm}}{N_mN_r}I_r^*-\mu_m(1-p_m)$.

Next, as per Routh-Hurwitz Criteria, we verify $A_1,A_2>0$ and $A_1A_2>A_3$ to check if the real parts of all eigenvalues are negative. Here, A_1 is clearly positive. Also, our analysis found

$A_2 > 0$ and $A_1 A_2 > A_3$.

Hence, the endemic equilibrium for the pig–mosquito subsystem is locally stable if and only if $R_{0e} > 1$.

Proposition 4: The DFE for the pig–mosquito subsystem is globally stable when $R_{0e} < 1$.

Proof: We define our Lyapunov function as

$$\begin{aligned} V(I_r, R_r, I_m) &= \frac{\mu_m(1-p_m)}{\frac{\lambda_r \beta_{mr}}{N_m}} I_r + I_m + \left(\frac{\mu_m \left(1-p_m\right)\left(\mu_r(1-p_r)+\gamma_r\right)}{\frac{\lambda_r \beta_{mr}}{N_m}} - \frac{\lambda_r \beta_{rm}}{N_r} \right) \frac{R_r}{\gamma_r} \\ &= \frac{\mu_m(1-p_m)}{\frac{\lambda_r \beta_{mr}}{N_m}} I_r + I_m + \frac{1}{\gamma_r} \left(\frac{1}{\mathcal{R}^2} - 1 \right) R_r \end{aligned} \tag{15}$$

which gives

$$\begin{aligned} V^{'}(I_r, R_r, I_m) &= \frac{\mu_m(1-p_m)}{\frac{\lambda_r \beta_{mr}}{N_m}} I_r^{'} + I_m^{'} + \left(\frac{\mu_m \left(1-p_m\right)\left(\mu_r(1-p_r)+\gamma_r\right)}{\frac{\lambda_r \beta_{mr}}{N_m}} - \frac{\lambda_r \beta_{rm}}{N_r} \right) \frac{R_r^{'}}{\gamma_r} \\ &= -\mu_m(1-p_m) \frac{I_r + R_r}{N_r} - \frac{\lambda_r \beta_{rm}}{N_r} \frac{I_m}{N_m} - \frac{\mu_r}{\gamma_r} \left(\frac{\mu_m \left(1-p_m\right)\left(\mu_r(1-p_r)+\gamma_r\right)}{\frac{\lambda_r \beta_{mr}}{N_m}} - \frac{\lambda_r \beta_{rm}}{N_r} \right) R_r \\ &= -\mu_m(1-p_m) \frac{I_r + R_r}{N_r} - \frac{\lambda_r \beta_{rm}}{N_r} \frac{I_m}{N_m} - \frac{\mu_r}{\gamma_r} \left(\frac{1}{\mathcal{R}^2} - 1 \right) R_r. \end{aligned} \tag{16}$$

Here we use a alternative threshold quantity $\mathcal{R}$ to understand if the function V satisfies all the conditions of a strong Lyapunov function which is defined as

$$\mathcal{R} = \sqrt{\frac{\lambda_r \beta_{rm} \lambda_r \beta_{mr}}{N_r N_m} \frac{1}{\mu_m \left(1-p_m\right)\left(\mu_r(1-p_r)+\gamma_r\right)}}$$

where $\mathcal{R} > 1$ if and only if $R_{0e} > 1$.

Now, the alternative threshold value $\mathcal{R}$, equation (15) and equation (16) easily verify that

$$V(0,0,0) = 0 \text{ and } V(I_r, R_r, I_m) > 0 \text{ for } (I_r, R_r, I_m) \neq (0,0,0) \text{ when } \mathcal{R} < 1.$$

Also, $V^{'}(0,0,0) = 0$ and $V^{'}(I_r, R_r, I_m) < 0$ for $(I_r, R_r, I_m) \neq (0,0,0)$ when $\mathcal{R} < 1$.

Hence, the DFE for the pig-mosquito system is globally stable when $R_{0e} < 1$ (since $\mathcal{R} < 1 \Leftrightarrow$ $\mathrm{R}_{0e} < 1$).

Appendix 6. Equilibrium of the limiting system

$$
\begin{aligned}
SS_h^* &= \frac{\Lambda_h}{\beta_{lh}L_c^* + \mu_h + \frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}} \\
ES_h^* &= \frac{\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}}{\beta_{lh}L_c^* + \mu_h + \gamma_e + \alpha_e} SS_h^* \\
RS_h^* &= \frac{\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}\gamma_e}{(\beta_{lh}L_c^* + \mu_h)(\beta_{lh}L_c^* + \mu_h + \gamma_e + \alpha_e)} SS_h^* \\
SL1_h^* &= \frac{\beta_{lh}L_c^*}{\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \gamma_{l1} + r_l + \mu_h} SS_h^* \\
EL1_h^* &= \frac{\beta_{lh}L_c^*\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}}{\gamma_{l1} + \gamma_e + r_l + \mu_h + \alpha_e}\left(\frac{1}{\beta_{lh}L_c^* + \gamma_e + \mu_h + \alpha_e} + \frac{1}{\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \gamma_l + r_l + \mu_h}\right) SS_h^* \\
RL1_h^* &= \frac{\beta_{lh}L_c^*\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}\gamma_e}{\gamma_{l1} + r_l + \mu_h}\left(\frac{1}{(\beta_{lh}L_c^* + \mu_h)(\beta_{lh}L_c^* + \mu_h + \gamma_e + \mu_e)} + \frac{1}{\gamma_{l1} + r_l + \mu_h + \gamma_e + \alpha_e}\right) SS_h^* \\
SL2_h^* &= \frac{r_l\beta_{lh}L_c^*}{(\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \gamma_{l2} + \alpha_l + \mu_h)(\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \gamma_{l1} + r_l + \mu_h)} SS_h^* \\
EL2_h^* &= \frac{r_l EL1_h + \frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}SL2_h}{\gamma_{l2} + \alpha_l + \gamma_e + \alpha_e + \mu_h} \\
RL2_h^* &= \frac{r_l RL1_h + \gamma_e EL2_h}{\gamma_{l2} + \alpha_l + \mu_h} \\
SR_h^* &= \frac{\beta_{lh}L_c^*\left(\gamma_{l1} + \frac{r_l\gamma_{l2}}{(\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \gamma_{l2} + \mu_h + \alpha_l)}\right)}{(\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \mu_h)(\frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m} + \gamma_{l1} + r_l + \mu_h)} SS_h^* \\
ER_h^* &= \frac{\gamma_{l1}EL1_h + \gamma_{l2}EL2_h + \frac{\lambda_h\beta_{mh}}{N_h}\frac{I_m^*}{N_m}SR_h}{\gamma_e + \alpha_e + \mu_h} \\
RR_h^* &= \frac{\gamma_{l1}RL1_h + \gamma_{l2}RL2_h + \gamma_e ER_h}{\mu_h}
\end{aligned}
\tag{17}
$$

Bibliography

[1] World Health Organization, *Vector-borne diseases*, https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases, Update date 03-02-2020, Access date 05-25-2020.

[2] P.T.J. Johnson, and D.W. Thieltges,Diversity, decoys and the dilution effect: how ecological communities affect disease risk, *The Journal of Experimental Biology*, **213** (2010), 961-970.

[3] Richard S. Ostfeld and Felicia Keesing, Effects of Host Diversity on Infectious Disease, *Annual Review of Ecology, Evolution, and Systematics*, **43** (2012), 157-182.

[4] Ezer Miller, Amit Huppert, The Effects of Host Diversity on Vector-Borne Disease: The Conditions under Which Diversity Will Amplify or Dilute the Disease Risk, *PLOS One*, **8(11): e80279** (2013), https://doi.org/10.1371/journal.pone.0080279.

[5] Allan Saul, Zooprophylaxis or zoopotentiation: the outcome of introducing animals on vector transmission is highly dependent on the mosquito mortality while searching, *Malaria Journal*, **2:32** (2003).

[6] A. Dobson, I. Cattadori, R.D. Holt, R.S. Ostfeld, F. Keesing, K. Krichbaum, J.R. Rohr, S.E. Perkins and P.J. Hudson, Sacred cows and sympathetic squirrels: the importance of biological diversity to human health, *Annual Review of Ecology, Evolution, and Systematics*, **3(6)** (2006), 714-718.

[7] K. Loguidice, S.T.K. Duerr, M.J.Newhouse, K.A. Schmidt, M.E. Killilea, And R.S. Ostfeld, Impact of host community composition on Lyme Disease risk, *Ecology*, **89(10)** (2008), 2841-2849.

[8] World Health Organization, Chagas disease (American trypanosomiasis), http://www.who.int/chagas/disease/en/, Access date: 10-22-2017

[9] Center for Disease Control and Prevention, Parasites-American Trypanosomiasis (also known as Chagas Disease), https://www.cdc.gov/parasites/chagas/gen_info/detailed.html, Access date: 10-22-2017

[10] MARIA C. Cecere, Ricardo E. Gürtler, Roberto Chuit and Joele Cohen, Effects of chickens on the prevalence of infestation and population density of Triatoma infestans in rural houses of north-west Argentina, *Medical and Veterinary Entomology*, **11** (1997), 383-388.

[11] Ricardo E. Gürtler, Joel E. Cohen, Maria C. Cecere, Marta A. Lauricella, Roberto Chuit, and Elsa L. Segura, Influence of Humans and Domestic Animals on the Household Prevalence of Trypanosoma Cruzi in Triatoma Infestans Populations in Northwest Argentina, *Am. J. Trop. Med. Hyg*, **58(6)** (1998), 748-758.

[12] R.E. Gürtler, M.C. Cecere, M.A. Lauricella, M.V. Cardinal, U. Kitron, and J.E. Cohen, Domestic dogs and cats as sources of Trypanosoma cruzi infection in rural northwestern Argentina, *Parasitology*, **134(1)** (2007), 69-82.

[13] Sandra M. De Urioste-Stone, Pamela M. Pennington, Elizabeth Pellecer, Teresa M. Aguilar, Gabriela Samayoa, Hugo D. Perdomo, Hugo Enrŕquez and José G. Juárez, Development of a community-based intervention for the control of Chagas disease based on peridomestic animal management: an eco-bio-social perspective, *Trans R Soc Trop Med Hyg*, **109** (2015), 159-167.

[14] Ricardo E. Gürtler, Maria C. Cecere, Diego P. Vazquez, Roberto Chuit, Joel E. Cohen, Host-Feeding Patterns of Domiciliary Triatoma infestans (Hemiptera: Reduviidae) in Northwest Argentina: Seasonal and Instar Variation, *Journal of Medical Entomology*, **33(1)** (1996), 15-26.

[15] Christopher M. Kribs and Christopher Mitchell, Host switching vs. host sharing in overlapping sylvatic *Trypanosoma cruzi* transmission cycle, *Journal of Biological Dynamics*, **9** (2015), 247-277.

[16] Paula Medone, Agustin Balsalrobe, Jorge E. Rabinovich, Gerardo A. Marti, Frédéric Menu, Life History Traits and Demographic Parameters of Triatoma infestans (Hemiptera: Reduviidae) Fed on Human Blood, *Polpulation Biology/Genetics*, **52(6)** (2015), 1282-1290.

[17] P. L. Marcet, T. Duffy, M. V. Cardinal, J.M. Burgos, M. A. Lauricella, M. J. Levin, U.Kitron, R. E. Gürtler and A. G. Schijman, PCR-based screening and lineage identification of Trypanosoma cruzi directly from faecal samples of triatomine bugs from northwestern Argentina, *Parasitology*, **132** (2006), 57-65.

[18] Á. Moncayo and A.C. Silveira, Current epidemiological trends of Chagas disease in Latin America and future challenges: epidemiology, surveillance, and health policies, *Academia Nacional de Medicina, Bogotá, Colombia*, **Chapter 4** (2012), 60-88.

[19] Christopher Kribs-Zaleta, Estimating Contact Process Saturation in Sylvatic Transmission of Trypanosoma cruzi in the United States, *PLOS Neglected Tropical Diseases*, **4(4):e656** (2010), doi:10.1371/journal.pntd.0000656.

[20] Patricio Diosque, Angel Marcelo Padilla, Rubén Oscar Cimino, Rubén Marino Cardozo, Olga Sanchez Negrette, Jorge Diego Marco, Rosa Zacca, Carlos Meza, Aligio Juarez, Hugo Rojo, Ricardo Rey, Rosa Milagros Corrales, Julio Rubén Naseer, And Miguel Angel Basombrío, Chagas Disease in Rural Areas of Chaco Province, Argentina: Epidemiologic Survey in Humans, Reservoirs, And Vectors, *American Journal of Tropical Medicine and Hygene*, **71(5)** (2004), 590-593.

[21] E. Gürtler, M.C. Cécere, R.M. Petersen, D.N. Rubel and N. J. Schweigmann, Chagas disease in north-west Argentina: association between Trypanosoma cruzi parasitaemia in dogs and cats and infection rates in domestic Triatoma infestans, *Transactions of the Royal Society of Tropical Medicine and Hygeine*, **87** (1993), 12-15.

[22] Olga Sánchez Negrette, María Celia Mora, Miguel Ángel Basombrío, High Prevalence of Congenital Trypanosoma cruzi Infection and Family Clustering in Salta, Argentina, *Pediatrics*, **115(6)** (2005), 668-672.

[23] Central Intelligence Agency, CIA. *The World Factbook*, Update date: November 2018, https://www.cia.gov/library/publications/the-world-factbook/geos/ar.html, Access date: 11-22-2018.

[24] Ricardo E. Gürtler, María C. Cecere, Gonzalo M. Vázquez-Prokopec, Leonardo A. Ceballos, Juan M. Gurevitz, María del Pilar Fernández, Uriel Kitron, Joel E. Cohen, Domestic Animal Hosts Strongly Influence Human-Feeding Rates of the Chagas Disease Vector Triatoma infestans in Argentina, *PLOS Neglected Tropical Diseases*, **8(5)**: e2894 (2014), doi:10.1371/journal.pntd.0002894.

[25] Ricardo E. Gürtler, Joel E. Cohen, Marcia C. Cecere and Roberto Chuit, Shifting Host Choices of the Vector of Chagas Disease, Triatoma Infestans, in Relation tothe Availability of Host in Houses in North-West Argentina, *Journal of Applied Ecology*, **34(3)** (1997), 699-715.

[26] Cleber Galvao, Dayse da Silva Rocha, Jos e Jurburg and Rodolfo Carcavallo, Início da atividade de vôo em Triatoma infestans (Klug, 1834) e T. melanosoma Martínez, Olmedo Carcavallo, 1987 (Hemiptera, Reduviidae), *Memórias do Instituto Oswaldo Cruz*, **96** (2001), 137-140.

[27] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz, On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations, *J. Math. Biol*, **28** (1990), 365–382.

[28] Claudio Ricardo Lazzari, Marcos Horácio Pereira, Marcelo Gustavo Lorenzo, Behavioural biology of Chagas disease vectors, *Mem Inst Oswaldo Cruz, Rio de Janeiro*, **108 (Suupl. I)** (2013), 34-47.

[29] Pablo G. Guerenstein, Claudio R. Lazzari, Host-seeking: How triatomines acquire and make use of information to find blood, *Acta Tropica*, **110** (2009), 148-158.

[30] DND*i*, DISEASE FACTSHEET: Chagas disease, https://www.dndi.org/wp-content/uploads/2018/12/Factsheet2018_Chagas.pdf, Access date 09-05-2019.

[31] CDC, Parasites - American Trypanosomiasis (also known as Chagas Disease), https://www.cdc.gov/parasites/chagas/disease.html, Access date 09-05-2019.

[32] JOHNS HOPKINS Medicine, Chagas Disease, https://www.hopkinsmedicine.org/health/conditions-and-diseases/chagas-disease, Access date 09-05-2019.

[33] Mayo Clinic, Chagas disease, https://www.mayoclinic.org/diseases-conditions/chagas-disease/diagnosis-treatment/drc-20356218, Access date 09-05-2019.

[34] World Health Organization, Chagas disease (American trypanosomiasis), https://www.who.int/news-room/fact-sheets/detail/chagas-disease-(american-trypanosomiasis), Access date 09-05-2019.

[35] Info CHAGAS, What you need to know about Chagas disease, http://www.infochagas.org/en/cuales-son-los-sintomas, Access date 09-05-2019.

[36] Gideon A. Ngwa, On the Population Dynamics of the Malaria Vector, *Bulletin of Mathematical Biology*, **68** (2006), 2161-2189.

[37] Gideon A. Ngwa, Terence T. Wankah, Mary Y. Fomboh-Nforba, Calsitus N. Ngonghala, Miranda I. Teboh-Ewungkem, On a Reproductive Stage-Structured Model for the Population Dynamics of the Malaria Vector, *Bulletin of Mathematical Biology*, **76** (2014), 2476–2516.

[38] D.T. Gillespie, A General Method for Numerically Simulating the stochastic time evolution of coupled chemical reactions, *The Journal of Computational Physics*, **22** (1976), 403-434.

[39] Christopher M. Kribs-Zaleta, Alternative transmission modes for Trypanosoma cruzi, *Mathematical Biosciences and Engineering*, **7** (2010), 657-673.

[40] World Health Organization, *Global Health Observatory (GHO) data* https://www.who.int/gho/neglected_diseases/leishmaniasis/en/, Access date- 01-22-2019.

[41] World Health Organization, *Leishmaniasis* https://www.who.int/news-room/fact-sheets/detail/leishmaniasis, updated- 03-14-2018, Accessed- 01-22-2019.

[42] Centers for Disease Control and Prevention, *Parasites - Leishmaniasis* https://www.cdc.gov/parasites/leishmaniasis/index.html, update date- 73-26-2018, Access date- 02-10-2019.

[43] World Health Organization, *Leishmaniasis*, https://www.who.int/leishmaniasis/disease_epidemiology/en/, Access date- 02-11-2019

[44] Laila Massad Ribas, Vera Lucia Zaher, Helio Junji Shimozako, and Eduardo Massad, Estimating the Optimal Control of Zoonotic Visceral Leishmaniasis by the Use of a Mathematical Model, *The Scientific World Journal*, http://dx.doi.org/10.1155/2013/810380 (2013).

[45] Helio Junji Shimozako, Jianhong Wu, Eduardo Massad, Mathematical modelling for Zoonotic Visceral Leishmaniasis dynamics: A new analysis considering updated parameters and notified human Brazilian data, *Infectious disease modeling*, **2** (2017), 143-160.

[46] A S Mazloumi Gavgani, M H Hodjati, H Mohite, C R Davies Effect of insecticide-impregnated dog collars on incidence of zoonotic visceral leishmaniasis in Iranian children: a matchedcluster randomised trial, *LANCET*, **360** (2002), 374-379.

[47] Ibrahim M. ELmojtaba, J.Y.T. Mugisha, Mohsin H.A. Hashim, Mathematical analysis of the dynamics of visceral leishmaniasis in the Sudan, *Applied Mathematics and Computation*, **217** (2010), 2567-2578.

[48] Songnian Zhao, Yan Kuang, Chih-Hang Wu, David Ben-Arieh, Marcelo Ramalho-Ortigao, Kaiming Bi Zoonotic visceral leishmaniasis transmission: modeling, backward bifurcation, and optimal control, *Journal of mathematical biology*, **73** (2016), 1525-1560.

[49] M.H. Zahid, C.M. Kribs, Decoys and Dilution: The Impact of Incompetent Hosts on Prevalence of Chagas Disease, *Bulletin of Mathematical Biology*, **82(41)**, (2020), https://doi.org/10.1007/s11538-020-00710-5.

[50] Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, Cano J, et al., Leishmaniasis Worldwide and Global Estimates of Its Incidence, *PLoS ONE*, **7(5):e35671** (2012), https://doi.org/10.1371/journal.pone.0035671.

[51] Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, Cano J, et al., Competence of the Human Host as a Reservoir for Leishmania Chagasi, *The Journal of Infectious Diseases*, **182** (2000), 997-1000.

[52] Phillip Lawyer, Mireille Killick-Kendrick, Tobin Rowland, Edgar Rowton, and Petr Volf, Laboratory colonization and mass rearing of phlebotomine sand flies (Diptera, Psychodidae), *Parasite*, **24(42)** (2017), https://doi.org/10.1051/parasite/2017041.

[53] Kbenesh W. Blayneh, Abba B. Gumel, Suzanne Lenhart, Tim Clayton, Backward Bifurcation and Optimal Control in Transmission Dynamics of West Nile Virus, *Bulletin of Mathematical Biology*, **72** (2010), 1006-1028.

[54] Lise Trotz-Williams, Luigi Gradoni, Disease risks for the travelling pet: Leishmaniasis, *InPractice*, **25(4)** (2003), 190-197, https://inpractice.bmj.com/content/25/4/190.

[55] Márcia Dalastra Laurenti, Claudio Nazaretian Rossi, Vânia Lúcia Ribeiro da Matta, Thaise Yumie Tomokane, Carlos Eduardo Pereira Corbett, Nágila Francinete Costa Secundino, Paulo Filemon Paulocci Pimenta, Mary Marcondes, Asymptomatic dogs are highly competent to transmit Leishmania (Leishmania) infantum chagasi to the natural vector, *Veterinary Parasitology*, **196(3-4)** (2013), 296-300.

[56] The World Bank, World Bank data, 2017, https://data.worldbank.org/country/brazil?most_recent_value_desc=true, Access date 09-01-2019

[57] Instituto Brasilerio de Geografia Estatistica (IBGE), IBGE releases population estimates of municipalities for 2017, https://agenciadenoticias.ibge.gov.br/en/agencia-press-room/2185-news-agency/releases-en/16134-ibge-releases-population-estimates-of-municipalities-for-2017, Access date 09-01-2019

[58] Rita C.M. Garcia, Marcos Amaku, Alexander W. Biondo, and Fernando Ferreira, Dog and cat population dynamics in an urban area: evaluation of a birth control strategy, *Pesquisa Veterinária Brasileira*, **38(3)** (2018), 511-518.

[59] DOGELL, Brazilian Dogs Breeds List - All Dog Breeds From Brazil, https://dogell.com/dog-breeds/origin/brazil, Access date 09-01-2019

[60] howMed, Sandfly-Characteristics, Life Cycle and Control Measures, http://howmed.net/community-medicine/sandfly-characteristics-life-cycle-and-control-measures/, Access date 09-01-2019

[61] Sarah Jervis, Lloyd A. C. Chapman, Shweta Dwivedi, Morchan Karthick, Aritra Das, Epke A. Le Rutte, Orin Courtenay, Graham F. Medley, Indranath Banerjee, Tanmay Mahapatra, Indrajit Chaudhuri, Sridhar Srikantiah, and T. Déirdre Hollingsworth, Variations in visceral leishmaniasis burden, mortality and the pathway to care within Bihar, India, *Parasites & Vectors*, **10(601)** (2017), https://dx.doi.org/10.1186/s13071-017-2530-9.

[62] UNDP, Inequality adjusted Human Development Index for India's States, 2011, https://www.undp.org/content/dam/india/docs/inequality_adjusted_human_development_index_for_indias_state1.pdf, Access date 09-02-2019

[63] Lanotte G, Rioux JA, Perieres J, Vollhardt Y., Ecology of leishmaniasis in the south of France. 10. Developmental stages and clinical characterization of canine leishmaniasis in relation to epidemiology. (author's transl), *Annales de parasitologie humaine et comparée*, **54(3)** (1979), 277-95.

[64] R. Badaro, T. C. Jones, E. M. Carvalho, D. Sampaio, S. G. Reed, A. Barral, R. Teixeira, W. D. Johnson, Jr., New Perspectives on a Subclinical Form of Visceral Leishmaniasis, *The Journal of Infectious Diseases*, **154(6)** (1986), 1003-1011.

[65] M. N. Burattini, F. A. B. Coutinho, L. F. Lopez, and E. Massad, "Modelling the dynamics of leishmaniasis considering human, animal host and vector populations, *Journal of Biological Syatems*, **6(4)** (1998), 337-56.

[66] R. Killick-Kendrick, M. Killick-Kendrick, C. Focheux, J. Derewure , M-P. Puech, and M. C. Cadiergues, Protection of dogs from bites of phlebotomine sandflies by deltamethrin collars for control of canine leishmaniasis, *Medical and Veterinary Entomology*, **11** (1997), 105-111.

[67] Stamper LW, Patrick RL, Fay MP, Lawyer PG, Elnaiem D-EA, Secundino N, et al., Infection Parameters in the Sand Fly Vector That Predict Transmission of Leishmania major , *PLoS Negl Trop Dis.*, **5(8):e1288** (2011), https://doi.org/10.1371/journal.pntd.0001288.

[68] Stauch A, Sarkar RR, Picado A, Ostyn B, Sundar S, Rijal S, et al., Visceral Leishmaniasis in the Indian Subcontinent: Modelling Epidemiology and Control , *PLoS Negl Trop Dis.*, **5(11):e1405** (2011), https://doi.org/10.1371/journal.pntd.0001405.

[69] Javier Moreno and Jorge Alvar, Canine leishmaniasis:epidemiological risk and theexperimental model , *Trends in Parasitology*, **18(9)** (2002), 399-405.

[70] European Centre for Disease Prevention and Control, Phlebotomine sand flies - Factsheet for experts, https://www.ecdc.europa.eu/en/disease-vectors/facts/phlebotomine-sand-flies, Access date 09-01-2019

[71] Javier Moreno, Jorge Alvar, Canine leishmaniasis: epidemiological risk and the experimental model, *Trends in Parasitology*, **18(9)** (2002), 399-405, https://doi.org/10.1016/S1471-4922(02)02347-4

[72] World Health Organization, *Japanese encephalitis*, https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis, Update date 05-09-2019, Access date 02-28-2020.

[73] Centers for Disease Control and Prevention, *Japanese Encephalitis*, https://www.cdc.gov/japaneseencephalitis/index.html, Update date 02-08-2019, Access date 02-23-2020.

[74] World Health Organization, *Japanese encephalitis*, https://www.who.int/immunization/diseases/japanese_encephalitis/en/, Update date 04-09-2015, Access date 02-23-2020.

[75] Centers for Disease Control and Prevention, *Japanese Encephalitis*, https://www.cdc.gov/japaneseencephalitis/transmission/index.html, **Access date- 07-02-2019**.

[76] Centers for Disease Control and Prevention, *Leptospirosis*, https://www.cdc.gov/leptospirosis/health_care_workers/index.html, Update date 01-07-2020, Access date 02-29-2020.

[77] Centers for Disease Control and Prevention, *Leptospirosis*, https://www.cdc.gov/leptospirosis/index.html, Update date 03-13-2019, Access date 02-29-2020.

[78] Centers for Disease Control and Prevention, *Leptospirosis*, https://www.cdc.gov/leptospirosis/infection/index.html, Update date 06-09-2015, Access date 02-29-2020.

[79] Centers for Disease Control and Prevention, *Leptospirosis*, https://www.cdc.gov/leptospirosis/symptoms/index.html, Update date 10-27-2017, Access date 02-29-2020.

[80] Howard S. Ginsberg, Integrated pest management and allocation of control efforts for vector-borne diseases, *Journal of vector ecology*, **26(1)** (2001), 32-38.

[81] Salah Uddin Khan, Henrik Salje, A. Hannan, Md. Atiqul Islam1, A. A. Mamun Bhuyan, Md. Ariful Islam1, M. Ziaur Rahman, Nazmun Nahar, M. Jahangir Hossain, Stephen P. Luby, Emily S. Gurley, Dynamics of Japanese Encephalitis Virus Transmission among Pigs in Northwest Bangladesh and the Potential Impact of Pig Vaccination, *PLoS Negl Trop Dis*, **8(9)**:e3166, (2014), doi:10.1371/journal.pntd.0003166.

[82] Jennifer S. Lord, Emily S. Gurley, Juliet R. C. Pulliam, Rethinking Japanese Encephalitis Virus Transmission: A Framework for Implicating Host and Vector Species, *PLOS Neglected Tropical Diseases*, **9(12)**:e0004074 (2015), doi:10.1371/journal.pntd.0004074.

[83] Sudarat Chadsuthi, Dominique J. Bicout, Anuwat Wiratsudakul, Duangjai Suwancharoen, Wimol Petkanchanapong, Charin Modchang, Wannapong Triampo6, Parntep Ratanakorn, Karine Chalvet-Monfray, Investigation on predominant Leptospira serovars and its distribu-

tion in humans and livestock in Thailand, 2010-2015, *PLoS Negl Trop Dis*, **11(2)**:e0005228, (2017), doi:10.1371/journal. pntd.0005228.

[84] A.M. Babylon, M.G. Roberts, G.C. Wake, Modelling leptospirosis in livestock, *Theoritical Population Biology*, **121**, (2018), 26-32.

[85] Mondal Hasan Zahid, Christopher M.Kribs, Impact of dogs with deltamethrin-impregnated collars on prevalence of visceral leishmaniasis, *Infectious Disease Modelling*, **5** (2020), 235-247.

[86] M.A. Ilkal, V. Dhanda, B.U. Rao, S.George, A.C. Mishra, Y. Prasanna, S. Gopalkrishna, Khorshed M. Pavri, Absence of viraemia in cattle after experimental infection with Japanese encephalitis virus, *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **82(4)** (1988), 628-631.

[87] Sonia Thankachy, Smrutidhara Dash Sudhansu Sekhar Sahu, Entomological investigation of Japanese encephalitis outbreak in Malkangiri district of Odisha state, India, *Pathogens and Global Health*, **113(5)** (2018), 246-253.

[88] Sourish Ghosh and Anirban Basu, Acute Encephalitis Syndrome in India: The Changing Scenario, *Annals of Neurosciences*, **23(3)** (2016), 131-133.

[89] SA Khan, P Dutta, J Borah, P Chowdhury, R Topno, M Baishya, J Mahanta, Leptospirosis presenting as acute encephalitis syndrome (AES) in Assam, India, *Asian Pacific Journal of Tropical Disease*, **2(2)** (2012), 151-153.

[90] Siraj A. Khan, Trishna Bora, Basanta Laskar, Abdul M. Khan, and Prafulla Dutta, Scrub Typhus Leading to Acute Encephalitis Syndrome, Assam, India, *Emerging Infectious Diseases*, **23(1)** (2017), 148-150.

[91] V Balamurugan, S Veena, S R A Thirumalesh, A Alampuri, R Sridevi, P P Sengupta, G Govindaraj, M Nagalingam, D Hemadri, M R Gajendragad and H Rahman, Distribution of serogroup specific antibodies against leptospirosis in livestock in Odisha, *Indian Journal of Animal Sciences*, **87(5)** (2017), 546-551.

[92] V Balamurugan, S Veena, S R A Thirumalesh, A Alampuri, R Sridevi, P P Sengupta, G Govindaraj, M Nagalingam, D Hemadri, M R Gajendragad and H Rahman, Seroprevalence of Bovine Leptospirosis in Odisha, India, *World Journal of Veterinary Science*, **1** (2013), 1-7.

[93] The World Bank, World Bank data, https://data.worldbank.org/indicator/SP.DYN.LE00.IN?locations=IN&most_recent_value_desc=true, Access date 04-08-2020

[94] Sudhansu Sekhar Sahu, Smrutidhara Dash, Thankachy Sonia, Subramaniam Muthukumarave, Thirumal Sankari, Kasinathan Gunasekaran, Purushothaman Jambulingam, Entomological investigation of Japanese encephalitis outbreak in Malkangiri district of Odisha state, India, *Mem Inst Oswaldo Cruz*, **113(6): e170499** (2018).

[95] The World Bank, World Bank data, https://data.worldbank.org/indicator/SP.RUR.TOTL?locations=IN&most_recent_value_desc=true, Access date 04-08-2020

[96] P. Philip Samuel, N. Arunachalam, J. Hiriyan, B. K. Tyagi, Host Feeding Pattern of Japanese Encephalitis Virus Vector Mosquitoes (Diptera: Culicidae) from Kuttanadu, Kerala, India, *Journal of Medical Entomology*, **45(5)** (2008), 927-932.

[97] H-L Zhan, Y-Z Zhang, W-H Yang, Y. Feng, RS Nasci, et al., Mosquitoes of Western Yunnan Province, China: Seasonal Abundance, Diversity, and Arbovirus Associations, *PLOS One*, **8(10)**:e77017 (2013), https://doi.org/10.1093/jmedent/45.5.927.

[98] M. H. Birley, P. K. Rajagopalan, Estimation of the Survival and Biting Rates of Culex Quinquefasciatus (Diptera: Culicidae), *Journal of Medical Entomology*, **18(3)** (1981), 181-186.

[99] Indian Council of Medical Research, Japanese encephalitis virus infection in mosquitoes and its epidemiological implications, *ICMR Bulletin*, **30(4)** (2000).

[100] Bhagirathi Dwibedia, Namita Mohapatraa, Sushil Kumar Rathorea, Maheswar Pandaa, Satya Sundar Patia, Jyotsnamayee Sabata, Bandana Thakura, Sailendra Pandaa Shantanu

Kumar Kara, An outbreak of Japanese encephalitis after two decades in Odisha, India, *Indian J Med Res*, **142(Supplement)** (2015), 30-32.

[101] Andrew F. van den Hurk, Scott A. Ritchie, John S. Mackenzie, Ecology and Geographical Expansion of Japanese Encephalitis Virus, *Annual Review of Entomology*, **54(1)** (2009), 17-35.

[102] D H Baik and C Y Joo, Epidemio-entomological survey of Japanese encephalitis in Korea, *The Korean Journal of Parasitology*, **29(1)** (1991), 67-85.

[103] Pets on Mom, *The Life Span of Domestic Pigs*, https://animals.mom.me/life-span-domestic-pigs-7920.html, Access date 05-03-2020.

[104] Suman Veerappa Budihal, Khalid Perwez, Leptospirosis Diagnosis: Competancy of Various Laboratory Tests, *Journal of Clinical and Diagnostic Research*, **8(1)** (2014), 199-202.

[105] Ramesh Holla , Bhagwan Darshan , Latika Pandey, Bhaskaran Unnikrishnan, Nithin Kumar, Rekha Thapar , Prasanna Mithra, and Vaman Kulkarni, Leptospirosis in Coastal South India: A Facility Based Study, *BioMed Research International*, https://doi.org/10.1155/2018/1759125.

[106] FC Leonard, PJ Quinn, WA Ellis, K O'Farrell, Duration of urinary excretion of leptospires by cattle naturally or experimentally infected with Leptospira interrogans serovar hardjo, *Veterinary Record*, **131(19)** (1992), 435-439.

[107] AB Thierman, Experimental leptospiral infections in pregnant cattle with organisms of the Hebdomadis serogroup, *American Journal of Veterinary Research*, **43(5)** (1982), 780-84.

[108] C.G. Mackintosh , R.B. Marshall E.S. Broughton, The use of a hardjo-pomona vaccine to prevent leptospiruria in cattle exposed to natural challenge with leptospira interrogans serovar hardjo, *New Zealand Veterinary Journal*, **28(9)** (1991), 174-77.

[109] Sangram Biswal, Dhruba Charan Nayak and Kautuk Kumar Sardar, Prevalence of ketosis in dairy cows in milk shed areas of Odisha state, India, *Veterinary World*, **9(11)** (2016), 1242-1247.

[110] Sebastian Lequime, Richard E. Paul, Louis Lambrechts, Determinants of Arbovirus Vertical Transmission in Mosquitoes, *PLOS Pathogens*, **12(5)**:e1005548 (2016), https://doi.org/10.1371/journal.ppat.1005548.

[111] Duangjai Suwancharoen, Supaluck Limlertvatee, Philaiphon Chetiyawan, Phichet Tongpan, Nongluck Sangkaew, Yaowarat Sawaddee, Kanya Inthakan and Anuwat Wiratsudakul, A nationwide survey of pathogenic leptospires in urine of cattle and buffaloes by Loop-mediated isothermal amplification (LAMP) method in Thailand, 2011-2013, *Journal of Veterinary Medical Science*, **78(9)** (2016), 1495-1500.

[112] Soawapak Hinjoy, Epidemiology of Leptospirosis from Thai National Disease Surveillance System, 2003-2012, *OSIR*, **7(2)** (2014), 1-5, http://www.osirjournal.net/index.php/osir/article/view/38.

[113] Abani Bhusan Jena, Kailash C. Mohanty and N. Devadasan, An outbreak of leptospirosis in Orissa, India: the importance of surveillance, *Tropical Medicine and International Health*, **9(9)** (2004), 1016-1021.

[114] Horst R. Thieme, Convergence results and a Poincaré -Bendixson trichotomy for asymptotically autonomous differential equations, *Journal of Mathematical Biology*, **30** (1992), 755-763.

[115] Christopher Mitchell, Christopher Kribs, Invasion reproductive numbers for periodic epidemic models, *Infectious Disease Modelling*, **4** (2019), 124-141.

[116] Mondal Hasan Zahid and Christopher M. Kribs, Ebola: Impact of hospital's admission policy in an overwhelmed scenario, *Mathematical Biosciences and Engineering*, **15(6)** (2018), 1387-1399.

[117] World Health Organization, *Japanese encephalitis*, https://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/, Access date 05-10-2020.

[118] J. A. Salomon, J. A. Haagsma, A. Davis, C. M. de Noordhout, S. Polinder, A. H. Havelaar, A. Cassini, B. Devleesschauwer, M. Kretzschmar, N. Speybroeck and C. J. L. Murray, Disability weights for the Global Burden of Disease 2013 study, *The Lancet*, **3** (2015), 712-723.

[119] A Marm Kilpatrick, Peter Daszak, Matthew J Jones, Peter P Marra and Laura D Kramer, Host heterogeneity dominates West Nile virus transmission, *Proceedings of The Royal Society B*, **273** (2006), 2327–2333.

[120] Pieter T. J. Johnson and Jason T. Hoverman, Heterogeneous hosts: how variation in host size, behaviour and immunity affects parasite aggregation, *Journal of Animal Ecology*, **83** (2014), 1103-1112.

BIOGRAPHICAL STATEMENT

Mondal Hasan Zahid was born in Dinajpur, Bangladesh, and earned a Bachelor of Science in Mathematics and a Masters of Science in Applied Mathematics at the University of Dhaka, Bangladesh in 2004 and 2006 respectively. In 2008, he joined the Public service Commission, Bangladesh as a Lecturer. After serving the nation for almost seven years, he moved to the US in August 2015 intending to earn his doctoral degree in mathematics at The University of Texas at Arlington (UTA). At UTA, he worked under the supervision of Dr. Christopher Kribs and performed his research in mathematical modeling of infectious diseases. During his doctoral program, he received a significant number of travel grants and awards to present his research at conferences in the US and around the world. He also organized a couple of mini-symposiums in national and international conferences. His research is featured in SIAM NEWS and UTA College of Science News. As a recognition of his contribution, he received the Outstanding Graduate Student Researcher award from the department of mathematics at UTA for the academic year 2019-2020.