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Mathematical Models for the Transmission Dynamics of Bovine Schistosomiasis with Contaminated Environment

Solomon Kadaleka (1725190)



UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

A thesis submitted to the School of Computer Science and Applied Mathematics, Faculty of Science, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

Johannesburg, August 2020.

Declaration

I, **Solomon Kadaleka**, declare that this thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



Signature:

17TH day of AUGUST 20 20 at WITS.

Acknowledgements

"Unless the Lord builds a house, the work of the builders is wasted". Truly, without God the Almighty, this work would not have been a success. Honor and glory be unto Him.

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Dedication

To the Almighty God, my parents Grandwell and Dorothy Kadaleka Phiri, and my children Praise, Dorcas, and Solomon Kadaleka Jr.

Abstract

Schistosomiasis is a chronically debilitating infection of humans and animals, caused by different species of blood flukes. The main purpose of this thesis is to gain some insights into the transmission dynamics of the disease by exploring the role of contaminated environment. We first propose and rigorously analyze a generic deterministic mathematical model with snail and bovine hosts as a system of non-linear ordinary differential equations. Second, we extend our generic model to incorporate humans and control measures, namely treatment of humans and bovines and molluscicide of the contaminated environment.

The basic reproduction number R_0 of the two proposed models is computed and used to theoretically investigate the existence and stability of the models' steady states. By constructing a suitable Lyapunov function, we prove the global stability of the endemic equilibria. Sensitivity analysis is performed to determine the relative importance of model parameters to disease transmission. The basic reproduction number is most sensitive to model parameters biased towards the contaminated: the bovine recruitment rate, the fecal output parameter, the snail-Miracidia effective contact rate and the cercariae to miracidia survival probability. Pontrayagin's Maximum Principle is used for the optimal control analysis in order to determine the strategies which yield optimal results in controlling the spread of schistosomiasis.

Analytical results are supported with numerical simulation using Matlab, Maple and Mathematica software. Numerical simulations indicate that molluscicide proves to be more effective in containing the spread of the disease in humans and bovines, however a combined application of treatment of infected bovines and humans and molluscicide will be most effective in controlling the spread of schistosomiasis. Finally, uncertainty analysis on the non-dimensional system parameters is graphically represented using the Latin Hypercube Sampling and Partial Rank Correlation Coefficient techniques.

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List of Publications

Parts of this thesis have been submitted to ISI Journals in the form of the following research papers:

1. Solomon Kadaleka, Shirley Abelman, Jean M. Tchuenche – A Mathematical Model of the Transmission Dynamics of Bovine Schistosomiasis with Contaminated Environment.

2. Solomon Kadaleka, Shirley Abelman, Jean M. Tchuenche – A Human-Bovine Schistosomiasis Model with Treatment and Molluscicide.

3. Solomon Kadaleka, Shirley Abelman, Peter Mwamtobe, Jean M. Tchuenche – Optimal Control of a Human-Bovine Schistosomiasis Model.

Chapter 1

Introduction

1.1 General Introduction

Schistosomiasis is a snail-borne infection caused primarily by flatworms technically known as blood flukes. It remains one of the most common tropical and sub-tropical parasitic infections, particularly in much of the developing world [49]. The prevalence levels are high due to increase in population and displacement, migration, competing priorities in the health sector and development projects in water resources such as large dams and irrigation systems [17], [28].

The disease affects humans, domestic and wild animals. The disease-causing species are of the genus Schistosoma, which include *S. mansoni*, *S. japonicum*, *S. haematobium*, *S. mekongi* and *S. intercalatum*[56]. The main species are *S. mansoni*, which is transmitted by Biomphalaria snails, *S. haematobium*, transmitted by Bulinus snails and finally *S. japonicum*, transmitted by Onchomelina snails [56].

Schistosomisis primarily affects the poor segments of a population. This is due to the fact that the poor population has no access to safe drinking water and adequate sanitation [52]. The infection is endemic mainly in rural populations where most domestic and social activities in rivers and water accumulations, are carried out and these provide habitat for the disease for snails. Also there is a great risk of schistosomiasis transmission and prevalence rates in areas affected by environmental changes, leading to a disorderly urbanisation process. This gives rise to unsanitary environments which favour the establishment and maintenance of parasite reservoirs [36].

The life cycle of the schistosomes is quite complex. They go through an intermediate snail host to complete their life cycle, that is, from eggs, to miracidia, to cercariae and finally to adult worms [22]. The female schistosomes produce hundreds to thousands of eggs per day and each ovum contains a ciliated miracidium larva, which secretes proteolytic enzymes that help the eggs to migrate into the bladder, for *S. haematobium*,

or the intestines, in the case of other parasitic species [38]. Then the eggs are excreted in urine or faeces. Figure (1.1) below, from Ding *et al.*, [26], shows a complex life cycle of a schistosome, where the parasite development depends on both definitive and intermediate hosts. Once excreted the eggs can remain viable for up to 7 days. They release miracidium upon contact with water [21], where they search for an intermediate snail host, guided by light and chemical stimuli. After the miracidium penetrate the snail, they multiply asexually in cercariae larvae with embryonic suckers and a bifurcated tail. Four to six weeks after the infection, the cercariae start to leave the snail and then seek the skin of a suitable definitive host. Each infected snail can shed thousands of cercariae on a daily basis for months. When the cercariae find a host, they penetrate the skin and migrate to the blood via the lungs to the liver, where they transform into young worms. They mature within 4-6 weeks and mate, leading to the restart of the cycle [38].

1.2 Risk Factors

Several risk factors for example, poverty, lack of education and inadequate environmental sanitation affect transmission of schistosomiasis. Rural and slum dwellers in tropical and sub-tropical countries are the most affected [46], the majority of whom are children, women and farmers. Approximately 530 million cattle are at greater risk of contracting the disease in endemic regions. Infected animals in Africa and the Middle East exceed 165 million [48], causing vast losses as a result of high mortality and morbidity from severe infection [27].

It is also worth noting that human and animal schistosomiasis are dependent on environmental factors which include moisture, rainfall, temperature, water bodies such as swamps, streams, marshes and dams and also snail intermediate hosts [70]. The likelihood of increase in the impact of schistosomiasis is high due to intensified animal husbandry and conservation of water which create favourable conditions for schistosome transmission [45].

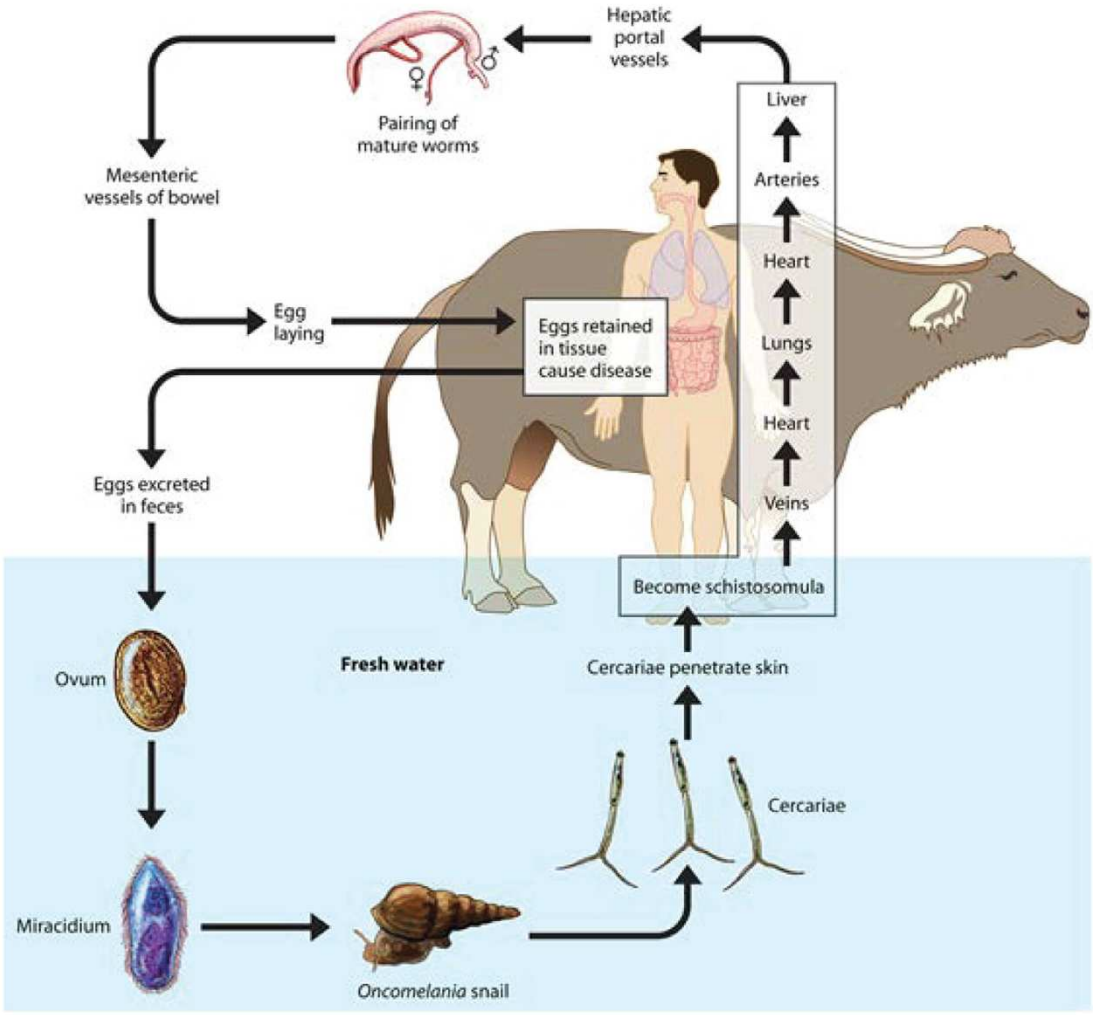


Figure 1.1: Diagram of a life cycle of a Schistosome [26].

1.3 Prevention and Control

Considering the global public health importance of schistosomiasis and the risk that might come with it, there is a need for comprehensive control measures. Some of the prevention and control measures as outlined by the Centers for Disease Control and Prevention [14], include avoiding swimming or wading in freshwater and drinking safe water. In addition, the control methods range from environmental modification to snail host elimination, chemotherapy and chemical molluscicides even though chemical anti-schistosomal control is proved to be expensive in many developing countries [17]. However, a combined treatment for both humans and bovines dramatically reduces human prevalence for a longer period of time than only single host treatment [90].

1.4 Methodology

Being one of the major ways of improving livelihood standards in the tropical and subtropical regions of the world, livestock productivity is limited by bovine schistosomiasis [57]. As such, it is one of the endemic diseases deserving attention since it causes significant economic losses within the affected regions. Though much work has been done on human schistosomiasis, to the best of our knowledge, mathematical models that have so far considered disease dynamics in bovines, particularly cattle, with due respect to the economic value they have in the regions in question, are rare. It is from this perspective that this study intends to devise mathematical models that can be used to understand schistosomiasis dynamics in bovines with regard to the role that the contaminated environment plays. Mathematical modeling is often used as a useful and viable tool for experimentation in the case where field and laboratory data are not available. Together with computational techniques, they form an essential basis for the synthesis of information as a way of understanding the patterns in epidemiology and also developing and weighing the evidence so that the correct decision is made to public health policy [82]. Deterministic compartmental mathematical models are formulated as a system of ordinary differential equations which describe the interaction between bovines, and cattle in particular, and the pathogens with biological effects such as reinfection and shedding included.

Theoretical mathematical analyses and a number of computational simulations are then performed to determine key parameters that drive bovine schistosomiasis transmission dynamics and effects of control strategies. Then, the models are qualitatively analysed in order to determine the possibility of existence and stability of the endemic and disease-free equilibria. Global stability is then determined using the Lyapunov function method.

The basic reproduction number, R_0, is computed using the next generation operator method. This is a fundamental parameter governing the spread of disease and is interpreted in relation to the results from the deterministic models. Then sensitivity analysis of the models in order to identify key parameters that drive the dynamics of the sys-

tem is carried out by analysing the model parameters using the Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) techniques. Pontrayagin's Maximum Principle is used for the optimal control analysis in order to determine the strategies which yield optimal results in controlling the spread of schistosomiasis.

Finally, computing software, Matlab, Maple and Mathematica are used to carry out the model simulations and plot relevant graphs.

1.5 Outline of the Thesis

Chapter 1 outlines the general introduction, statement of the problem, research questions and objectives as well as the research methodology. Chapter 2 places much emphasis on the literature review of mathematical models of schistosomiasis. In particular, we include studies that have looked into issues of socio-economic impact of the epidemic in the society, transmission dynamics that exist between humans and bovines, control strategies that have been put in place to control or eradicate the disease and lastly, those studies that have to do with optimal control analysis of the epidemic. In Chapter 3, we formulate the basic bovine schistosomiasis model using a system of non-linear ordinary differential equations that account for three bovine populations, namely susceptible bovines, exposed bovines and infected bovines. There are also three snail populations: susceptible, exposed and infected and a single pathogen population, in the form of the contaminated environment. The basic reproduction number, R_0, of the model system is derived. The existence and stability analysis of the model equilibrium points, that is, the disease-free and endemic steady states, are carried out. In the case of the endemic steady state, a suitable Lyapunov function is used for the proof of its global stability. In the same chapter, sensitivity analysis of the model parameters and numerical model simulations are presented. In Chapter 4, we extend the model in Chapter 3, to include humans and at the same time, incorporating therapeutic control strategies of treatment for humans and bovines and molluscicide the contaminated environment. Humans are included in the model since studies show that bovine infection prevalence is usually associated with human infection risk [11]. The aim therefore is to examine the trans-

mission dynamics of schistosomiasis in humans and bovines while still considering the role of the contami-nated environment. Like the basic model in Chapter 3, we carry out the analytical and numerical analyses of the human-bovine model. Since intervention strategies are incorporated, optimal control analysis is applied to determine the most desirable combination of strategies in combating the disease. Numerical simulations on the three control strategies, namely treatment for humans, treatment for bovines and molluscicide of the contaminated environment are also investigated. Finally, in Chapter 5, the thesis is concluded and summarized while outlining areas of possible further research.

Chapter 2

Literature Review

Livestock production is one of the principal means of achieving improved living standards in many regions of the developing world [83]. The direct impact of schistosomiasis leads to enormous annual economic losses and inhibition of socio-economic development due to low production and income of those people infected [39]. In Sub-Saharan Africa, in particular, livestock is most important to the economy of the nations and living standards of the rural masses [42]. Animal health and productivity are greatly affected by schistosomiasis infections, so much so that there is need to pay particular attention to the diagnosis which is essential in gaining complete knowledge of the infection [29]. The zoonotic nature of *Schistosomiasis japonica* has made the control too complex, and has provided a unique opportunity to develop a transmission vaccine targeting bovines to assist in the prevention of human infection and disease. Consequently, with or without field and laboratory data, mathematical models prove useful and have been developed to theoretically investigate control options targeting the different transmission pathways of the infection by incorporating control strategies such as bovine vaccination, mass human chemotherapy and molluscicides, which in some cases have led to the elimination of the disease [37]. This is possible in a case where the referred pathways of schistosomiasis in bovines is looked into and thoroughly explained. So far, there has been an emphasis on control strategies which focus on intermediate hosts in order to break the cycle of the disease transmission [61]. On the other hand, Inobaya et al., [43] propose that despite human and bovine schistosomiasis vaccines still being in the developmental stages, the approach that can lead to sustainability and future elimination of the disease, is by integrated control that would target the life cycle. The World Health Organization also has its recommendation that since it is difficult to avoid contact with infected water, especially by people in the endemic regions most of whom are fish and rice farmers, then preventive chemotherapy would lessen the occurrence and severity of the infection [89].

However, although most methods used in the control of schistosomiasis have become successful, they have been proven to have limitations among which are reinfection which

has not been prevented and returning to baseline values of the infection [62].

2.1 Economic Impact of Schistosomiasis Epidemic.

One of the major problems of livestock development in the tropics is parasitism, among which, schistosomiasis happens to be the most prevalent trematode infection [3]. As Bont and Vercruysse [8] put it, schistosome infections that occur in livestock such as cattle, receive little recognition of their veterinary significance, except for occasional reports of field outbreaks. The epidemic has exerted great health, social and financial burden on peoples' economic welfare and the affected countries in general. It has negatively affected child development and agricultural productivity, the reason being the poverty of most sub-Saharan Africa inhabitants [2]. This is also observed in Hotez [41] and Lengeler [52], that the schistosomiasis occurrence is confined to the tropics and subtropics areas because in these regions there are many poor segments of a population, who most often are marginalized and their voices are usually not heard to establish the schistosomiasis epidemic within a national political agenda.

Countries which have managed to successfully eradicate the disease are doing well on the economic front, such as Japan and Tunisia, while others like Brazil and China are taking steps to eliminate the disease [84].

2.2 The Human-Bovine Schistosomiasis Transmission

There has been a debate by some authors whether schistosomiasis is maintained by humans, animals or both of them, so as, to consider the new control strategies. Furthermore, it is pointed out that for bovines, few studies have been considered on their natural or experimental infection as such there is a need to increase and widen the studies regarding the bovines' role in the schistosomiasis epidemic [63].

According to Chen [15], it was found that snails play a more important role in the transmission of schistosomiasis in bovines than in humans. Hence it was proposed that there should be an emphasis on the comprehensive approaches that will include

environmental factors as a way of breaking the cycle in the cattle-snail transmission. In a study by Ishikawa [44], researchers found that the resurgence of the schistosomiasis epidemic had very little probability due to mass treatment and successful control of the snails. It is also important to note what the key hosts and schistosomiasis transmission pathways are, since the control strategies would be more effective when they are properly targeted.

Pathogens which transmit the infections in multiple hosts pose the greatest challenge in controlling and eliminating the disease epidemic that occurs [10]. Such pathogens are believed to possess the adaptability in switching hosts and transmission pathways. These pathogens can switch hosts and transmission modes through hybridization which usually occurs due to global changes and the migration of humans and bovines [88].

As schistosomiasis poses a serious health problem in most developing countries, several mathematical studies have been carried out on its transmission dynamics in humans, ignoring the fact that the disease also affects bovines. Humans and bovines very often even end up sharing the same water reservoirs [32]. However, many studies have given priority to the dynamics of human schistosomiasis and other helminth infections so that refinements to such models, such as reservoir hosts, host migration, seasonal heterogeneity, acquired immunity and stochastic effects are viable [30].

2.3 Schistosomiasis and the Water Environment

Being a parasitic and water-related disease, spatial spread of schistosomiasis showed connectivity to human mobility, water-mediated snail dispersal and hydrological movement of schistosome larvae [19]. Human mobility determines human exposure to environmental fresh waters on the assumption that it drives potential water contact patterns. On the other hand, pathogens spread along waterways through the processes of snail dispersal and larval transport, thereby resulting in the provision of an environmental route for the spread of the schistosomiasis epidemic.

The infection is endemic mainly in rural populations where most domestic and social

activities are carried out in rivers and water accumulations and which provide shelter for snails from the disease. Also there is greatest risk of schistosomiasis transmission and prevalence rates in areas affected by environmental changes, which lead to a disorderly urbanisation process, which in turn gives rise to unsanitary environments that favour the establishment and maintenance of infection transmission [36]. Also, complex water reservoir systems, with high densities of hosts and snail populations, have made it difficult to control the schistosomiasis epidemic, so that there is a need for mathematical modeling of the disease which can assist in examining current control strategies and if necessary, develop new ones [15]. So far, studies have shown that there is a relationship between occurrences of schistosomiasis and environmental factors, with special emphasis on patterns that exist between at-risk populations and contaminated water accumulations [36]. Hence, the environmental aspect in the transmission dynamics of bovine schistosomiasis is very important and should not be ignored.

2.4 Schistosomiasis Control

Schistosomiasis has remained complex to humans because of its parasitic adjustment to multiple hosts. The persistence of the infection in a locality has much depended on a cycle involving humans and some mammalian definite hosts, flatworms, and particular intermediate snail hosts [4]. By formulating a mathematical model of schistosomiasis transmission dynamics involving humans and intermediate snail hosts, together with additional mammalian host and a competitor snail species, it was found that control strategies such as chemotherapy alone may be ineffective in eradicating schistosomiasis in the case where long-lived mammal hosts such as water buffaloes acquire and also transmit the disease. Hence the acquiring and transmission of the disease in bovines such as cattle, water buffaloes should be investigated and appropriate intervention strategies designed.

So far, there has been emphasis only on models for African schistosomiasis, that is, S. *mansoni* and S. *haematobium*, yet the transmission models applied to schistosoma *japonicum*, which involve animal reservoirs during its transmission cycle, are very rare,

if non-existent [90]. Despite that bovines such as water buffaloes are perceived not to be an important component of the S.*japonicum* transmission cycle that affects humans, estimates of infection prevalence in bovines are still large, implying that their effect in the transmission cannot be ruled out [75]. Worthwhile to note is also the fact that once bovines like cattle are slaughtered through backyard systems, their stomach and intestinal contents including the blood and washed material are dumped into nearby water reservoirs and subsequently, eggs of schistosoma from such animals, have easy access to enter the snail intermediate hosts [57].

Complexity of river systems, numerous lakes, high population densities of hosts and snails have made the control of schistosomiasis very difficult [15]. As such, it was strongly suggested that a more comprehensive approach is needed which should take into consideration environmental factors. Also cattle-snail schistosomiasis transmission played an important role in the sustainability of the infection than that of human-snail transmission, hence the suggestion of prioritizing approaches that would break cattle-snail transmission cycle. Traditional strategies such as therapeutic measures, health education, snail control have been proposed in the past [80]. Since vector reservoir plays a significant role in the transmission dynamics of the disease and that there is strong relationship between occurrences of schistosomiasis and environmental factors such as contaminated water reservoirs, this work aims to incorporate contaminated environment into a schistosomiasis transmission model to gain theoretical insights into persistence of the disease in tropical and sub-tropical regions. The robustness of our model results highlights the importance environmental factors play on the disease transmission and are key to mitigate the disease transmission.

2.5 Optimal Control Analysis

In a malaria-schistosomiasis co-infection model in Okosun [72], optimal control analysis was considered. Treatment for each disease showed that the control strategies were different in each case, as treatment for malaria had no impact in reducing schistosomiasis and the same applied to treatment of schistosomiasis on the control of malaria. The

results then indicated that in the co-infection model, when control strategy was applied to one particular disease, it does not necessarily imply it will also have consequences on the other. From this perspective, one would wish to investigate whether treating bovine schistosomiasis can have an impact on controlling human schistosomiasis and vice versa.

A multi-host schistosomiasis model proposed by Ding et al., [25] concluded that the prevalence of human schistosomiasis could be reduced whenever the treatment of humans and eradication rates of bovines was improved [25]. With optimal control strategy unsurprisingly outperforming the constant controls, it is worthwhile to investigate how optimal control strategy impacts the mitigation of the disease prevalence of the infected bovines considering a potential drastic decrease in the snail population.

2.6 Summary

In this chapter, we presented a nearly exhaustive review of the literature of mathematical models of schistosomiasis transmission dynamics and their potential economic impact, the interplay between the schistosomiasis and the water reservoir, the control measures that have been adopted and their optimal control. In the next chapter we develop a deterministic mathematical model describing the transmission dynamics of schistosomiasis in bovines with contaminated water environment where the agents of infection among snails and bovines namely miracidia and cercariae live.

Chapter 3

The Basic Bovine Schistosomiasis Model

3.1 Model Formulation

A deterministic model describing the transmission dynamics of schistosomiasis in bovines with miracidia and cercariae, both in the water environment, as agents of infection among snails and bovines, respectively is formulated. The total bovine population (N_b), is divided into three sub-classes. The susceptible bovines S_b, are those at the risk of contracting the infection upon being in contact with cercariae in water. The exposed bovines E_b, are those having the cercariae in their bodies, whose eggs are yet to be shed into the water. Infected bovines I_b, are those having the cercariae in their body system and can shed eggs into the water which will hatch into miracidia. The snail population, (N_s), is divided into those that are susceptible (S_s), the exposed (E_s) and the infected (I_s). C_e denotes the concentration of miradia and cercariae in water contributed by bovines and snails at the rates $\varepsilon_b p_b$ and $\varepsilon_s p_s$, respectively. ε_b and ε_s represent the rate of shedding of miracidia and cercariae, while p_b and p_s denote the probabilities that miracidia and cercariae shed by infected bovines and snails survive to cercariae and adult schistosomes, respectively. Bovines are recruited at a constant rate Π_b and snails at a rate Π_s, which is the natural birth rate in the case of snails. All the recruited bovines are susceptible and they acquire schistosomiasis infection at the rate

$$\lambda_b = \frac{c_b m_b \sigma_b}{N_b} C_e + \frac{\beta_b a_c}{N_b} I_s,$$

where c_b represents the contact rate between the bovines and cercariae, σ_b is the probability of disease transmission, a_c denotes the attacking efficiency of cercariae in the bovines and β_b is the infection rate from infected snails to susceptible bovine population. Naturally, bovines show low infection rates under experimental conditions, and due to their large size and longevity, they are a potential reservoir for the maintenance and dissemination of schistosomiasis [63]. We assume the bovine body mass to be m_b.

Similarly, the force of infection for snails is

$$\lambda_s = \frac{c_s f_0 \sigma_s}{N_b} C_e + \frac{\beta_s a_m}{N_b} I_b,$$

where c_s denotes the effective contact rate for snails with miracidia, f_0 the faecal output by the bovines, σ_s is the probability of disease transmission, β_s is the infection rate from infected bovines to susceptible snails and a_m represents the attacking efficiency of miracidia. The bovines and snails die naturally at the rates μ_b and μ_s, respectively. Since susceptible bovines and snails become infected only through exposure and contact with pathogens in infested water, it is therefore assumed that these exposed bovines and snails progress to the infectious classes at the rates γ_b and γ_s, respectively. Furthermore, under natural conditions, there exists temporary acquired immunity to schistosoma infection in bovines, which is of great importance in the regulation of the infection intensity [86]. The infectious bovines are then assumed to recover due to such immunity at the rate η, after which they become susceptible again. Bovines die due to the disease at the rate ν. Also, infected snails do not recover from schistosomiasis due their short lifespan compared to that of bovines [22]. Miracidia and cercariae leave the pathogen class C_e, at the rate $d_{mc} = d_m + d_c$, where d_m is the natural death rate for miracidia while d_c denotes the natural death rate for cercariae.

The above assumptions and the model flowchart lead to the following set of deterministic non-linear ordinary differential equations that describe the transmission dynamics of the

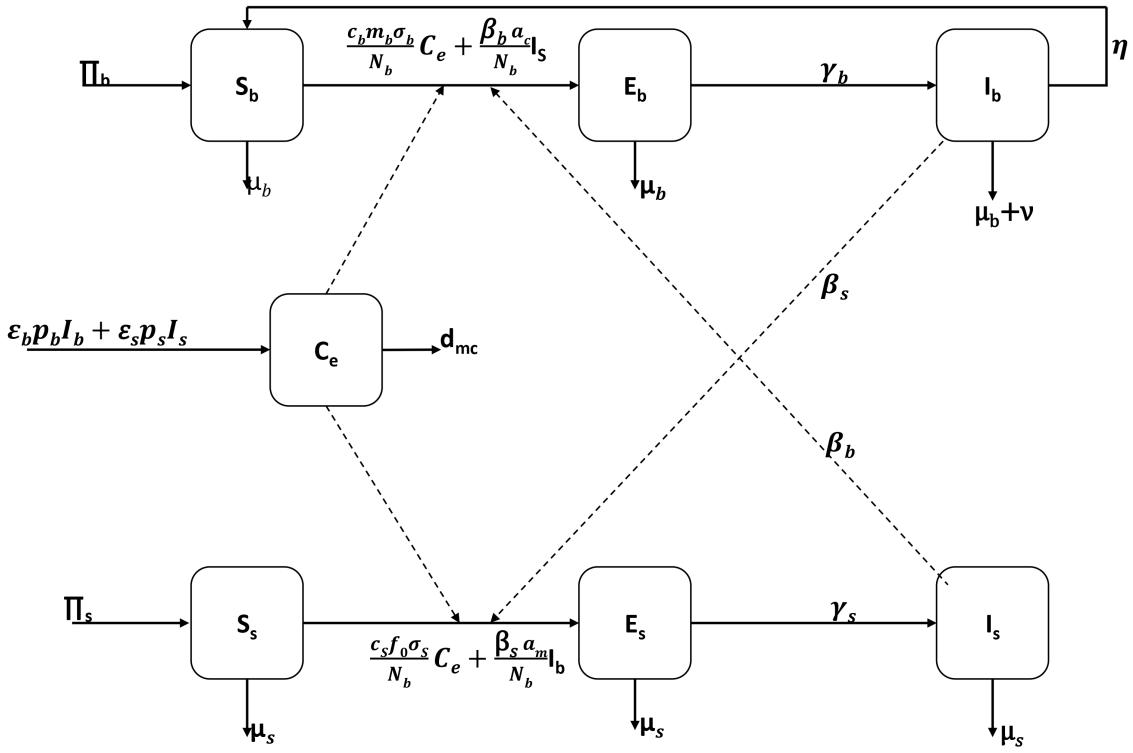


Figure 3.1: The flow diagram for bovine schistosomiasis infection. A dashed line links an infectious class to the route of infection that it causes in a different population

disease;

$$\begin{aligned}
\frac{dS_b}{dt} &= \Pi_b - \lambda_b S_b - \mu_b S_b + \eta I_b, \\
\frac{dE_b}{dt} &= \lambda_b S_b - (\mu_b + \gamma_b) E_b, \\
\frac{dI_b}{dt} &= \gamma_b E_b - (\mu_b + \nu + \eta) I_b, \\
\frac{dS_s}{dt} &= \Pi_s - \lambda_s S_s - \mu_s S_s, \\
\frac{dE_s}{dt} &= \lambda_s S_s - (\mu_s + \gamma_s) E_s, \\
\frac{dI_s}{dt} &= \gamma_s E_s - \mu_s I_s, \\
\frac{dC_e}{dt} &= (\varepsilon_b p_b I_b + \varepsilon_s p_s I_s) - d_{mc} C_e,
\end{aligned} \tag{3.1}$$

where $\lambda_b = \dfrac{c_b m_b \sigma_b}{N_b} C_e + \dfrac{\beta_b a_c}{N_b} I_s$ and $\lambda_s = \dfrac{c_s f_0 \sigma_s}{N_b} C_e + \dfrac{\beta_s a_m}{N_b} I_b$.

The description of the state variables and parameters used in the model (3.1) is summarized in the table below.

Variable	Description
S_b, E_b, I_b	Susceptible, exposed and infected bovine classes.
S_s, E_s, I_s	Susceptible, exposed and infected snail classes.
C_e	Concentration of miracidia and cercariae in water
N_b, N_s	Total population for bovines and snails.

Parameter	Description
Π_b	Natural birth rate of bovines
Π_s	Natural birth rate for snails
γ_b	Rate of disease progression from the exposed to the infected bovine class
γ_s	Rate of disease progression from the exposed snail class to the infected snail class
η	Recovery rate for bovine due to natural immunity
μ_b, μ_s	Natural mortality rate for bovine and snails
ν	Disease induced rate in infected bovines
$\varepsilon_b, \varepsilon_s$	Shedding rate of miracidia and cercariae by infected bovines and snails
σ_b	Probability of disease transmission for bovines
σ_s	Probability of disease transmission for snails
p_b	Probability that miracidia shed by infected bovines survive to cercariae
p_s	Probability that cercariae shed by infected snails survive
c_b	Contact rate between bovines and cercariae
c_s	Effective contact rate for snails with miracidia
f_0	Faecal output by bovines
m_b	Bovine body mass
a_m, a_c	Attacking efficiency of miracidia and cercariae in snails and bovines
β_b	Infection rate from infected snails to susceptible bovine population
β_s	Infection rate from infected bovines to susceptible snails
d_{mc}	Natural death rate for miracidia and cercariae

3.2 Qualitative Analysis of the Model

3.2.1 Model Analysis

In this section, we investigate the invariant region and positivity of the model system (3.1). We also examine the existence of equilibrium points and their stability. The basic reproduction number R_0, a fundamental parameter governing the spread of bovine schistosomiasis is derived.

3.2.2 Invariant Region

The model (3.1) under consideration monitors a bovine population. Hence we assume that all the state variables are positive for all time $t \geq 0$ and that the model solutions remain positive for all time $t \geq 0$. The total bovine population is given by

$$N_b(t) = S_b(t) + E_b(t) + I_b(t).$$

Similarly, the total snail population is given by

$$N_s(t) = S_s(t) + E_s(t) + I_s(t).$$

The bovine schistosomiasis transmission model will be analysed in a suitable feasible region given by

$$\Omega = \left\{(S_b, E_b, I_b, S_s, E_s, I_s, C_e) \in \mathbb{R}_+^7\right\} \tag{3.2}$$

We then assume that the dynamics of the system (3.1) without infection are asymptotically stable, that is,

$$\frac{dN_b}{dt} \leq \Pi_b - \mu_b N_b. \tag{3.3}$$

Similarly

$$\frac{dN_s}{dt} \leq \Pi_s - \mu_s N_s. \tag{3.4}$$

To show that the region Ω is positively invariant, the model must satisfy the condition that all its state variables are non-negative for all time. This implies that for all time $t \geq 0$, the solutions of the model (3.1) remain positive with positive initial value.

Applying Birkhoff and Rota's Theorem [6] on the differential inequality (3.3), we obtain

$$\frac{dN_b}{\Pi_b - \mu_b N_b} \leq dt \tag{3.5}$$

Integrating inequality (3.5) on both sides with respect to t and applying the initial condition

$N_b(0) = N_{b0}$,

$$N_b(t) \leq \frac{\Pi_b}{\mu_b} - \frac{(\Pi_b - \mu_b N_{b0})}{\mu_b} e^{-\mu_b t}. \tag{3.6}$$

As $t \to \infty$ in inequality (3.6) the population size N_b approaches

$$0 \leq N_b \leq \frac{\Pi_b}{\mu_b} \text{ implying } N_b \to \frac{\Pi_b}{\mu_b}. \tag{3.7}$$

Therefore, the feasible solution set of the bovine population of the system (3.1) enters the region

$$\Omega_b = \left\{ (S_b, E_b, I_b) \in \mathbb{R}^3_+, N_b(t) \leq \frac{\Pi_b}{\mu_b} \right\}. \tag{3.8}$$

Following the same approach above, the feasible solution set of the snail population of the system (3.1) enters the region

$$\Omega_s = \left\{ (S_s, E_s, I_s) \in \mathbb{R}^3_+, N_s(t) \leq \frac{\Pi_s}{\mu_s} \right\}. \tag{3.9}$$

The feasible solution set of the schistosome population of the model system (3.1) enters the region

$$\Omega_c = \left\{ C_e \in \mathbb{R}_+, N_c \leq \frac{\varepsilon_b p_b \Pi_b \mu_s + \varepsilon_s p_s \Pi_s \mu_b}{\mu_b \mu_s d_{mc}} \right\}. \tag{3.10}$$

This implies that the feasible solution set of model (3.1) which enters the region Ω and remains inside it, is

$$\Omega = \left\{ (S_b, E_b, I_b, S_s, E_s, I_s, C_e) \in \mathbb{R}^7_+ : S_b, E_b, I_b, S_s, E_s, I_s, C_e \geq 0; N_b \leq \frac{\Pi_b}{\mu_b}; \right.$$
$$\left. N_s \leq \frac{\Pi_s}{\mu_s}; N_c \leq \frac{\Pi^*}{d_{mc}} \right\},$$

where $\Pi^* = \dfrac{\varepsilon_b p_b \Pi_b}{\mu_b} + \dfrac{\varepsilon_s p_s \Pi_s}{\mu_s}$.

Thus the system (3.1) is biologically meaningful and its feasible solution set is positively invariant under the flow induced by the model (3.1).

3.2.3 Positivity of Solutions

Lemma 1 *Let the initial conditions for the model system (3.1) be*

$$S_{b0}, E_{b0}, I_{b0}, S_{s0}, E_{s0}, I_{s0}, C_{e0} \geq 0 \in \Omega.$$

Then the solution set $\{S_b(t), E_b(t), I_b(t), S_s(t), E_s(t), I_s(t), C_e(t)\}$ *of the model system (3.1) is positive* $\forall t \geq 0$.

Proof *Let* $S_b(t), E_b(t), I_b(t), S_s(t), E_s(t), I_s(t), C_e(t) \geq 0, \forall t \geq 0$. *From the first equation of model (3.1) we have*

$$\frac{dS_b}{dt} = \Pi_b - \lambda_b S_b - \mu_b S_b + \eta I_b \geq -(\lambda_b + \mu_b) S_b. \tag{3.11}$$

Integrating (3.11) with respect to t gives

$$\ln |S_b| \geq -\int (\lambda_b + \mu_b) dt + C,$$

$$\Rightarrow S_b(t) \geq D e^{-\int (\lambda_b + \mu_b) dt} \geq S_{b0} e^{-\int (\lambda_b + \mu_b) dt} \geq 0, \tag{3.12}$$

where $D = e^C$ *is a constant.*

Following the same method, the remaining state variables can be shown to be positive. Hence, the solution set for the model system (3.1) is positive $\forall t > 0$.

3.2.4 Existence and Stability of the Model Equilibrium Points

To obtain steady-state solutions, we set the left-hand sides of the model system (3.1) equal to zero, that is,

$$\begin{aligned}
0 &= \Pi_b - \lambda_b S_b - \mu_b S_b + \eta I_b, \\
0 &= \lambda_b S_b - (\mu_b + \gamma_b) E_b, \\
0 &= \gamma_b E_b - (\mu_b + \nu + \eta) I_b, \\
0 &= \Pi_s - \lambda_s S_s - \mu_s S_s, \\
0 &= \lambda_s S_s - (\mu_s + \gamma_s) E_s, \\
0 &= \gamma_s E_s - \mu_s I_s, \\
0 &= (\varepsilon_b p_b I_b + \varepsilon_s p_s I_s) - d_{mc} C_e.
\end{aligned} \tag{3.13}$$

The population of both bovines and snails will not be extinct since the recruitment rates Π_b and Π_s are positive nonzero constants. Thus, there exists no such trivial equilibrium point such that all seven model variables are zero. That is

$$(S_b^0, E_b^0, I_b^0, S_s^0, E_s^0, I_s^0, C_e^0) = (0, 0, 0, 0, 0, 0, 0)$$

does not exist.

3.2.5 Disease-Free Equilibrium and Computation of the Basic Reproduction Number

In the absence of bovine schistosomiasis, the model system (3.1) has a disease-free equilibrium, which is usually denoted by E_0. The bovine and snail populations that are either exposed or infected are referred to as the diseased classes. In this case, the diseased classes include E_b, I_b, E_s and I_s. However, in the absence of the disease, we have $E_b^0 = I_b^0 = E_s^0 = I_s^0 = C_e^0 = 0$. Hence, the disease-free equilibrium of the bovine schistosomiasis model (3.1) is given by

$$E_0 = (S_b^0, E_b^0, I_b^0, S_s^0, E_s^0, I_s^0, C_e^0) = \left(\frac{\Pi_b}{\mu_b}, 0, 0, \frac{\Pi_s}{\mu_s}, 0, 0, 0\right).$$

Determining the stability of E_0 is governed by the basic reproduction number which will be calculated using the next generation operator approach [85].

Let

1. $F_i(x)$ be the rate of appearance of a new infection in compartment i.
2. $V_i^+(x)$ be the transfer of bovines into compartment i by all means.
3. $V_i^-(x)$ be the rate of transfer of bovines out of compartment i. Then each function $(F_i, V_i^+,$ and $V_i^-)$ is assumed to be continuously differentiable at least twice with respect to each variable and $V_i = V_i^+ - V_i^-$.
4. x_0 be the disease-free equilibrium point.

Then, FV^{-1} is the next generation matrix for the model reproduction number, $R_0 = \gamma_s(FV^{-1})$, where $F = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right]$ and $V = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]$ with $i \geq 1$, for the number of compartments, and $1 \leq j \leq m$ for the infected compartments only [24]. Hence the basic reproduction number R_0 is given by $\gamma_s(A)$, which denotes the spectral radius, that is the largest eigenvalue of a matrix A.

F and V are $m \times m$ matrices, where m represents the number of infected classes. The entries in each of the matrices F and V are such that the (i, j) entry of F is the rate at which an infected bovine in compartment j produces new infections in compartment i while the (j, k) entry of V^{-1} is considered to be the average time an infected bovine spends in compartment j during its lifetime, on the assumption that the population remains near the disease-free equilibrium where reinfection is prevented. The expected number of new infections in compartment i produced by the infected bovine originally introduced into compartment k is thus given by the (i, k) entry of the product FV^{-1}.

The basic reproduction number R_0 sets the threshold in the study of a disease whereby its size can determine whether the disease will persist or die out. A value of unity indicates that the generation of secondary cases is sufficient to maintain the infection within the bovine population while R_0 less than unity, implies that each bovine produces, on average, less than one new infected bovine and hence the disease could potentially die out. If the value of R_0 is greater than unity, then each infectious bovine produces more than one new infected bovine during its infectious period leading to the disease invasion of the population, a sign of an epidemic occurrence.

Rewriting the model (3.1), starting with the infectious classes E_b, I_b, E_s, I_s, and using

the next-generation approach, we have

$$\begin{aligned}
\frac{dE_b}{dt} &= \lambda_b S_b - (\mu_b + \gamma_b)E_b, \\
\frac{dI_b}{dt} &= \gamma_b E_b - (\mu_b + \nu + \eta)I_b, \\
\frac{dE_s}{dt} &= \lambda_s S_s - (\mu_s + \gamma_s)E_s, \\
\frac{dI_s}{dt} &= \gamma_s E_s - \mu_s I_s, \qquad . \\
\frac{dC_e}{dt} &= (\varepsilon_b p_b I_b + \varepsilon_s p_s I_s) - d_{mc} C_e, \\
\frac{S_b}{dt} &= \Pi_b - \lambda_b S_b - \mu_b S_b + \eta I_b, \\
\frac{dS_s}{dt} &= \Pi_s - \lambda_s S_s - \mu_s S_s.
\end{aligned} \tag{3.14}$$

From the system (3.14), we define F_i and V_i as

$$F_i = \begin{pmatrix} \lambda_b S_b \\ 0 \\ \lambda_s S_s \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} \left(\frac{c_b m_b \sigma_b}{N_b} C_e + \frac{\beta_b a_c}{N_b} I_s\right) S_b \\ 0 \\ \left(\frac{c_s f_0 \sigma_s}{N_b} C_e + \frac{\beta_s a_m}{N_b} I_b\right) S_s \\ 0 \\ 0 \end{pmatrix}, \tag{3.15}$$

and

$$V_i = \begin{pmatrix} (\mu_b + \gamma_b)E_b \\ (\mu_b + \nu + \eta)I_b - \gamma_b E_b \\ (\mu_s + \gamma_s)E_s \\ \mu_s I_s - \gamma_s E_s \\ d_{mc} C_e - (\varepsilon_b p_b I_b + \varepsilon_s p_s I_s) \end{pmatrix}, \tag{3.16}$$

which represent the rate of appearance of new infection in classes E_b and E_s and also the transfer of bovines within the system compartments, respectively.

The Jacobian matrix of F, evaluated at the disease-free equilibrium E_0 is given by

$$F = \begin{pmatrix} 0 & 0 & 0 & \beta_b a_c & c_b m_b \sigma_b \\ 0 & 0 & 0 & 0 & 0 \\ 0 & \dfrac{\beta_s a_m \mu_b \Pi_s}{\mu_s \Pi_b} & 0 & 0 & \dfrac{c_s f_0 \sigma_s \mu_b \Pi_s}{\mu_s \Pi_b} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{3.17}$$

while that of V is given by

$$V = \begin{pmatrix} \mu_b + \gamma_b & 0 & 0 & 0 & 0 \\ -\gamma_b & \mu_b + \nu + \eta & 0 & 0 & 0 \\ 0 & 0 & \mu_s + \gamma_s & 0 & 0 \\ 0 & 0 & -\gamma_s & \mu_s & 0 \\ 0 & -\varepsilon_b p_b & 0 & -\varepsilon_s p_s & d_{mc} \end{pmatrix}. \tag{3.18}$$

The matrix inverse of V is given by

$$V^{-1} = \begin{pmatrix} \dfrac{1}{\mu_b + \gamma_b} & 0 & 0 & 0 & 0 \\ \dfrac{\gamma_b}{(\mu_b + \gamma_b)(\mu_b + \nu + \eta)} & \dfrac{1}{\mu_b + \nu + \eta} & 0 & 0 & 0 \\ 0 & 0 & \dfrac{1}{\mu_s + \gamma_s} & 0 & 0 \\ 0 & 0 & \dfrac{\gamma_s}{(\mu_s + \gamma_s)\mu_s} & \dfrac{1}{\mu_s} & 0 \\ \dfrac{\varepsilon_b p_b \gamma_b}{(\mu_b + \nu + \eta)(\mu_b + \gamma_b) d_{mc}} & \dfrac{\varepsilon_b p_b}{(\mu_b + \nu + \eta) d_{mc}} & \dfrac{\varepsilon_s p_s \gamma_s}{\mu_s (\mu_s + \gamma_s) d_{mc}} & \dfrac{\varepsilon_s p_s}{\mu_s d_{mc}} & \dfrac{1}{d_{mc}} \end{pmatrix}. \tag{3.19}$$

We now compute the product FV^{-1} which gives

$$FV^{-1} = \begin{pmatrix} a_{11} & a_{12} & a_{13} & a_{14} & a_{15} \\ 0 & 0 & 0 & 0 & 0 \\ a_{31} & a_{32} & a_{33} & a_{34} & a_{35} \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{3.20}$$

where

$$\begin{aligned}
a_{11} &= \frac{c_b m_b \sigma_b \mu_b \varepsilon_b p_b \gamma_b}{\Pi_b(\mu_b+\nu+\eta)(\mu_b+\gamma_b)d_{mc}},\\
a_{12} &= \frac{c_b m_b \sigma_b \mu_b \varepsilon_b p_b}{\Pi_b(\mu_b+\nu+\eta)d_{mc}},\\
a_{13} &= \frac{\gamma_s(\varepsilon_s c_b m_b \mu_b p_s \sigma_b + \beta_b \Pi_b a_c d_{mc})}{\Pi_b \mu_s(\mu_s+\gamma_s)d_{mc}},\\
a_{14} &= \frac{\varepsilon_s c_b m_b \mu_b p_s \sigma_b + \beta_b \Pi_b a_c d_{mc}}{\Pi_b \mu_s d_{mc}},\\
a_{15} &= \frac{c_b m_b \sigma_b \mu_b}{\Pi_b d_{mc}},\\
a_{31} &= \frac{\gamma_b \mu_b(\varepsilon_b c_s f_0 \mu_s p_b \sigma_s + \beta_s \Pi_s a_m d_{mc})}{\mu_s \Pi_b(\mu_b+\gamma_b)(\mu_b+\nu+\eta)d_{mc}},\\
a_{32} &= \frac{\mu_b(\varepsilon_b c_s f_0 \mu_s p_b \sigma_s + \beta_s \Pi_s a_m d_{mc})}{\mu_s \Pi_b(\mu_b+\nu+\eta)d_{mc}},\\
a_{33} &= \frac{c_s f_0 \sigma_s \mu_b \varepsilon_s p_s \gamma_s}{\Pi_b \mu_s(\mu_s+\gamma_s)d_{mc}},\\
a_{34} &= \frac{c_s f_0 \sigma_s \mu_b \varepsilon_s p_s}{\Pi_b \mu_s d_{mc}},\\
a_{35} &= \frac{c_s f_0 \sigma_s \mu_b}{\Pi_b d_{mc}}.
\end{aligned} \tag{3.21}$$

The eigenvalues of FV^{-1} are computed using the equation

$$det(\lambda I - FV^{-1}) = 0,$$

which gives

$$det(\lambda I - FV^{-1}) = \begin{vmatrix} \lambda - a_{11} & -a_{12} & -a_{13} & -a_{14} & -a_{15} \\ 0 & \lambda & 0 & 0 & 0 \\ -a_{31} & -a_{32} & \lambda - a_{33} & -a_{34} & -a_{35} \\ 0 & 0 & 0 & \lambda & 0 \\ 0 & 0 & 0 & 0 & \lambda \end{vmatrix} = 0. \tag{3.22}$$

Thus, the eigenvalues of FV^{-1} are

$$\lambda_1 = \lambda_2 = \lambda_3 = 0,$$

$$\lambda_4 = \frac{1}{2}a_{33} + \frac{1}{2}a_{11} + \frac{1}{2}\sqrt{a_{11}^2 - 2a_{11}a_{33} + 4a_{13}a_{31} + a_{33}^2},$$

$$\lambda_5 = \frac{1}{2}a_{33} + \frac{1}{2}a_{11} - \frac{1}{2}\sqrt{a_{11}^2 - 2a_{11}a_{33} + 4a_{13}a_{31} + a_{33}^2}.$$

The basic reproduction number R_0 of the model is the dominant eigenvalue which in this case is λ_4. Hence, the basic reproduction number is given by

$$R_0 = \frac{1}{2}a_{33} + \frac{1}{2}a_{11} + \frac{1}{2}\sqrt{a_{11}^2 - 2a_{11}a_{33} + 4a_{13}a_{31} + a_{33}^2}. \tag{3.23}$$

The basic reproduction number for the model measures the average number of secondary infections produced by one infectious bovine that enters an entirely susceptible bovine population. The term under the square root represents the geometric mean of the number of bovine infections produced by one infectious bovine.

The basic reproduction number of the model can be re-written as

$$R_0 = \frac{1}{2}\left(R_{01} + R_{02}\right) + \frac{1}{2}\sqrt{\left(R_{01} - R_{02}\right)^2 + 4R_{03}R_{04}},$$

where

$R_{01} = \dfrac{c_b m_b \sigma_b \mu_b \varepsilon_b p_b \gamma_b}{\Pi_b(\mu_b + \nu + \eta)(\mu_b + \gamma_b)d_{mc}}$ represents the number of new infections that result in bovines upon interacting with the contaminated environment;
$R_{02} = \dfrac{c_s f_0 \sigma_s \mu_b \varepsilon_s p_s \gamma_s}{\Pi_b \mu_s(\mu_s + \gamma_s)d_{mc}}$ accounts for new infections occurring due to the interaction between snails and contaminated environment;

$R_{03} = \dfrac{\gamma_s(\varepsilon_s c_b m_b \mu_b p_s \sigma_b + \beta_b \Pi_b a_c d_{mc})}{\Pi_b \mu_s(\mu_s + \gamma_s)d_{mc}}$ represents the transmission from the infected snails to the susceptible bovines; and
$R_{04} = \dfrac{\gamma_b \mu_b(\varepsilon_b c_s f_0 \mu_s p_b \sigma_s + \beta_s \Pi_s a_m d_{mc})}{\mu_s \Pi_b(\mu_b + \gamma_b)(\mu_b + \nu + \eta)d_{mc}}$ represents the transmission from the infected bovines to susceptible snails.

We also explain the terms in R_0 in the following way:
$\dfrac{1}{\mu_b + \gamma_b}$ is the time average a bovine spends in an exposed class, E_b,
$\dfrac{1}{\mu_s + \gamma_s}$ is the time average a snail spends in an exposed class E_s.
$\dfrac{1}{d_{mc}}$, $\dfrac{1}{\mu_s}$, $\dfrac{1}{\mu_b + \nu + \eta}$ denote the infectious life span of cercariae and miracidia, snails and bovines, respectively.

From Driessche [85], the local stability of the disease-free equilibrium point E_0, is summarised in Theorem (1).

Theorem 1 *The disease-free equilibrium E_0 exists for all R_0, and is locally asymptotically stable for $R_0 < 1$ and unstable otherwise.*

3.2.6 Global Stability of the Disease-Free Equilibrium E_0

Global stability of the disease-free equilibrium will be determined by subdividing the system (3.1) into subsystems of susceptible bovines and snails, denoted by

$$X = (S_b, S_s),$$

and infectious bovines and snails, denoted by

$$Y = (E_b, I_b, E_s, I_s, C_e).$$

To guarantee the global stability, we rewrite the model (3.1) in the form

$$\begin{aligned} \frac{dX}{dt} &= F(X, Y) \\ \frac{dY}{dt} &= G(X, Y) \end{aligned} \tag{3.24}$$

where $X \in \mathbb{R}^2_+$, $Y \in \mathbb{R}^5_+$.

The disease-free equilibrium is then denoted by $E_0 = (X_0, \mathbf{0})$, where $X_0 = \left(\frac{\Pi_b}{\mu_b}, \frac{\Pi_s}{\mu_s}\right)$ is a globally asymptotically stable equilibrium for the reduced system

$$\frac{dX}{dt} = F(X, \mathbf{0}).$$

That is,

$$\begin{aligned} \frac{dS_b}{dt} &= \Pi_b - \mu_b S_b, \\ \frac{dS_s}{dt} &= \Pi_s - \mu_s S_s, \end{aligned} \tag{3.25}$$

with $\mathbf{0} \in \mathbb{R}^5$, a zero vector.

Integrating the first equation of (3.25) with respect to t, we obtain

$$S_b(t) = \frac{\Pi_b}{\mu_b} + \left(S_{b0} - \frac{\Pi_b}{\mu_b}\right) e^{-\mu_b t}. \tag{3.26}$$

As $t \to \infty$, in (3.26), $S_b(t) \to \dfrac{\Pi_b}{\mu_b}$.

Similarly, integrating the second equation of (3.25) with respect to t, we obtain

$$S_s(t) = \frac{\Pi_s}{\mu_s} + \left(S_{s0} - \frac{\Pi_s}{\mu_s}\right) e^{-\mu_s t}, \tag{3.27}$$

which approaches $\dfrac{\Pi_s}{\mu_s}$ as $t \to \infty$.

However, the following conditions $H1$ and $H2$ should be satisfied for the global stability of a disease-free equilibrium:
$H1 : X_0 = \left(\dfrac{\Pi_b}{\mu_s}, \dfrac{\Pi_s}{\mu_s}\right)$ is a globally asymptotically stable for $\dfrac{dX}{dt} = F(X_0, \mathbf{0})$.
$H2 : G(X,Y) = A^{\star}Y - \hat{G}(X,Y)$, where $\hat{G}(X,Y) \geq 0$ for $(X,Y) \in \Omega$, such that

$$A^{\star} = D_Y G(X, \mathbf{0}) = \begin{pmatrix} -(\mu_b + \gamma_b) & 0 & 0 & \beta_b a_c & c_b m_b \sigma_b \\ \gamma_b & -(\mu_b + \nu + \eta) & 0 & 0 & 0 \\ 0 & \dfrac{\beta_s a_m \mu_b \Pi_s}{\mu_s \Pi_b} & -(\mu_s + \gamma_s) & 0 & \dfrac{c_s f_0 \sigma_s \mu_b \Pi_s}{\mu_s \Pi_b} \\ 0 & 0 & \gamma_s & -\mu_s & 0 \\ 0 & \varepsilon_b p_b & 0 & \varepsilon_s p_s & -d_{mc} \end{pmatrix}, \tag{3.28}$$

and

$$\hat{G}(X,Y) = \begin{pmatrix} (\beta_b a_c I_s + c_b m_b \sigma_b C_e)\left(1 - \dfrac{S_b}{N_b}\right) \\ 0 \\ (c_s f_0 \sigma_s C_e + \beta_s a_m I_b)\left(\dfrac{\mu_b \Pi_s}{\mu_s \Pi_b} - \dfrac{S_s}{N_b}\right) \\ 0 \\ 0 \end{pmatrix}. \tag{3.29}$$

At the disease-free equilibrium, the total bovine population is assumed to be $N_b = \dfrac{\Pi_b}{\mu_b}$ while that of the snail population is $N_s = \dfrac{\Pi_s}{\mu_s}$. As such

$$(c_s f_0 \sigma_s C_e + \beta_s a_m I_b)\left(\frac{\mu_b \Pi_s}{\mu_s \Pi_b} - \frac{S_s}{N_b}\right) \in \hat{G}(X,Y) \geq 0 \in \Omega.$$

Since conditions $H1$ and $H2$ are satisfied, the disease-free equilibrium E_0, is globally asymptotically stable.

3.3 Stability of the Endemic Equilibrium

We determine the stability of the endemic equilibrium by computing the eigenvalues of the Jacobian matrix of the system (3.1), which are then evaluated at the endemic equilibrium. However, due to the mathematical complexity for the system (3.1), we employ bifurcation analysis at the disease-free equilibrium using the Center Manifold Theory [13].

Theorem 2 *Consider the general system of ordinary differential equations with a parameter* ϕ

$$\frac{dx}{dt} = f(x, \phi), f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n \text{ and } f \in \mathbb{C}^2(\mathbb{R}^n \times \mathbb{R}) \tag{3.30}$$

where 0 is an equilibrium point of the system, that is, $f(0, \phi) \equiv 0 \ \forall \phi$ *and*

(A1) $A = D_x f(0,0) = \left[\frac{\partial f_i}{\partial x_j}(0,0)\right]$ *is the linearization matrix of the system around the equilibrium 0 with* ϕ *evaluated at 0;*

(A2) Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;

(A3) Matrix A has a right eigenvector w and a left eigenvector v corresponding to the zero eigenvalue.

Let f_k *be the kth component of f and*

$$\begin{aligned} a &= \sum_{k,i,j=1}^{n} v_k w_i w_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(0,0), \\ b &= \sum_{k,i=1}^{n} v_k w_i \frac{\partial^2 f_k}{\partial x_i \partial \phi}(0,0). \end{aligned} \tag{3.31}$$

The local dynamics of system (3.1) around 0 are totally governed by the signs of a and b.

(i) $a > 0$, $b > 0$. *When* $\phi < 0$ *with* $|\phi| << 1$, *0 is locally asymptotically stable, and there exists a positive unstable equilibrium; when* $0 < \phi << 1$, *0 is unstable and there exists a negative and locally asymptotically stable equilibrium;*

(ii) $a < 0,\ b < 0$. *When* $\phi < 0$ *with* $|\phi| << 1$, *0 is unstable; when* $0 < \phi << 1$, *0 is locally asymptotically stable, and there exists a positive unstable equilibrium;*

(iii) $a > 0,\ b < 0$. *When* $\phi < 0$ *with* $|\phi| << 1$, *0 is unstable, and there exists a locally asymptotically stable negative equilibrium; when* $0 < \phi << 1$, *0 is stable, and a positive unstable equilibrium appears;*

(iv) $a < 0,\ b > 0$. *When* ϕ *changes from negative to positive, 0 changes its stability from stable to unstable. Correspondingly a negative unstable equilibrium becomes positive and locally asymptotically stable.*

Particularly if $a > 0$ *and* $b > 0$, *then a backward bifurcation occurs at* $\phi = 0$.

Consider the model system (3.1) and let

$$x_1 = S_b,\ x_2 = E_b,\ x_3 = I_b,\ x_4 = S_s,\ x_5 = E_s,\ x_6 = I_s \text{ and } x_7 = C_e.$$

Also let N_b and N_s be given by $\sum_{i=1}^{3} x_i$ and $\sum_{i=4}^{6} x_i$, respectively.

We then write the model system (3.1) as

$$\frac{d\mathbf{X}}{dt} = f(\mathbf{X}),$$

where $\mathbf{X} = (x_1, x_2, x_3, x_4, x_5, x_6, x_7)^T$.

Thus,

$\frac{d\mathbf{X}}{dt} = (f_1, f_2, f_3, f_4, f_5, f_6, f_7)^T$ is given as follows:

$$\begin{aligned}
\frac{dx_1}{dt} &= f_1 = \Pi_b - (\lambda_b + \mu_b)x_1 + \eta x_3, \\
\frac{dx_2}{dt} &= f_2 = \lambda_b x_1 - (\mu_b + \gamma_b)x_2, \\
\frac{dx_3}{dt} &= f_3 = \gamma_b x_2 - (\mu_b + \nu + \eta)x_3, \\
\frac{dx_4}{dt} &= f_4 = \Pi_s - (\lambda_s + \mu_s)x_4, \\
\frac{dx_5}{dt} &= f_5 = \lambda_s x_4 - (\mu_s + \gamma_s)x_5, \\
\frac{dx_6}{dt} &= f_6 = \gamma_s x_5 - \mu_s x_6, \\
\frac{dx_7}{dt} &= f_7 = (\varepsilon_b p_b x_3 + \varepsilon_s p_s x_6) - d_{mc} x_7,
\end{aligned} \tag{3.32}$$

where

$$\lambda_b = \frac{1}{\sum_{i=1}^{3} x_i}(c_b m_b \sigma_b x_7 + \beta_b a_c x_6),$$

$$\lambda_s = \frac{1}{\sum_{i=1}^{3} x_i}\left(c_s f_0 \sigma_s x_7 + \beta_s a_m x_3\right).$$

Let us consider the basic reproduction number to be unity, that is, $R_0 = 1$. This implies that the chosen bifurcation parameter $c_b = c_b^*$ is given by

$$c_b^* = \frac{K_3 K_4 - 1}{K_2\left(K_1 K_3 K_4 - K_4 K_5 K_7 - K_4 K_6 K_7 - K_1\right)},$$

where

$$
\begin{aligned}
K_1 &= m_b\sigma_b\mu_b\varepsilon_b p_b\gamma_b,\\
K_2 &= \frac{1}{\Pi_b(\mu_b+\nu+\eta)(\mu_b+\gamma_b)d_{mc}},\\
K_3 &= c_s f_0\sigma_s\mu_b\varepsilon_s p_s\gamma_s,\\
K_4 &= \frac{1}{\Pi_b\mu_s(\mu_s+\gamma_s)d_{mc}},\\
K_5 &= \gamma_s\varepsilon_s m_b\mu_b p_s\sigma_b,\\
K_6 &= \gamma_s\beta_b\Pi_b a_c d_{mc},\\
K_7 &= \frac{\gamma_b\mu_b\varepsilon_b c_s f_0\mu_s p_b\sigma_s+\gamma_b\beta_s\Pi_s a_m d_{mc}}{\mu_s}.
\end{aligned}
$$

The Jacobian matrix of the system (3.1), at E_0 with $c_b = c_b^*$ is given by

$$
J(E_0,c_b^*)=\begin{bmatrix}
-\mu_b & 0 & \eta & 0 & 0 & -\beta_b a_c & -c_b^* m_b\sigma_b\\
0 & -(\mu_b+\gamma_b) & 0 & 0 & 0 & \beta_b a_c & c_b^* m_b\sigma_b\\
0 & \gamma_b & -(\mu_b+\nu+\eta) & 0 & 0 & 0 & 0\\
0 & 0 & -\dfrac{\beta_s a_m\Pi_s\mu_b}{\Pi_b\mu_s} & -\mu_s & 0 & 0 & -\dfrac{c_s f_0\sigma_s\Pi_s\mu_b}{\Pi_b\mu_s}\\
0 & 0 & \dfrac{\beta_s a_m\Pi_s\mu_b}{\Pi_b\mu_s} & 0 & -(\mu_s+\gamma_s) & 0 & \dfrac{c_s f_0\sigma_s\Pi_s\mu_b}{\Pi_b\mu_s}\\
0 & 0 & 0 & 0 & \gamma_s & -\mu_s & 0\\
0 & 0 & \varepsilon_b p_b & 0 & 0 & \varepsilon_s p_s & -d_{mc}
\end{bmatrix}.
$$

$J(E_0,c_b^*)$ of the linearised system has a simple zero eigenvalue and that all other eigenvalues have negative real parts.

As such, we analyze the system dynamics around $c_b = c_b^*$, using the Center Manifold theory.

Let $\mathbf{w} = (w_1, w_2, w_3, w_4, w_5, w_6, w_7)$ be the right eigenvector associated with the simple zero eigenvalue. This is calculated by multiplying it with the Jacobian matrix $J(E_0,c_b^*)$

and equating to zero. We obtain

$$\begin{aligned}
w_1 &= \frac{\eta w_3 - \beta_b a_c w_6 - c_b^* m_b \sigma_b w_7}{\mu_b}, \\
w_2 &= \frac{\beta_b a_c w_6 + c_b^* m_b \sigma_b w_7}{(\mu_b + \gamma_b)}, \\
w_3 &> 0, \\
w_4 &= -\frac{1}{\Pi_b \mu_s^2} \left(\beta_s a_m \Pi_s \mu_b w_3 + \mu_b c_s f_0 \sigma_s \Pi_s w_7 \right), \\
w_5 &= \frac{1}{\mu_s \Pi_b (\mu_s + \gamma_s)} \left(\beta_s a_m \Pi_s \mu_b w_3 + \mu_b c_s f_0 \sigma_s \Pi_s w_7 \right), \\
w_6 &> 0, \\
w_7 &= \frac{\varepsilon_b p_b w_3 + \varepsilon_s p_s w_6}{d_{mc}}.
\end{aligned} \tag{3.33}$$

In a similar way, the left eigenvector of $J(E_0, c_b^*)$ denoted by $\mathbf{v} = (v_1, v_2, v_3, v_4, v_5, v_6, v_7)$ is calculated by transposing $J(E_0, c_b^*)$ first and multiplying by $\mathbf{v}$, then equating to zero. This gives

$$\begin{aligned}
v_1 &= 0, \\
v_2 &> 0, \\
v_3 &= \frac{1}{(\mu_b + \nu + \eta)} \left(\frac{\beta_s a_m \Pi_s \mu_b}{\Pi_b \mu_s} v_5 + \varepsilon_b p_b v_7 \right), \\
v_4 &= 0, \\
v_5 &> 0, \\
v_6 &= \frac{1}{\mu_s} \left(\beta_b a_c v_2 + \varepsilon_s p_s v_7 \right), \\
v_7 &= \frac{1}{d_{mc}} \left(c_b m_b \sigma_b v_2 + \frac{c_s f_0 \sigma_s \Pi_s \mu_b}{\Pi_b \mu_s} v_5 \right).
\end{aligned} \tag{3.34}$$

3.3.1 Computations of a and b

Since $v_1 = 0 = v_4$, the associated non-zero partial derivatives of f_1 and f_4 will not be considered. Hence, for the system (3.1), the associated non-zero second order partial

derivatives, evaluated at E_0 are given by:

$$\begin{aligned} a &= v_2 \sum_{i,j=1}^{7} w_i w_j \frac{\partial^2 f_2}{\partial x_i \partial x_j}(0,0) + v_3 \sum_{i,j=1}^{7} w_i w_j \frac{\partial^2 f_3}{\partial x_i \partial x_j}(0,0) + v_5 \sum_{i,j=1}^{7} w_i w_j \frac{\partial^2 f_5}{\partial x_i \partial x_j}(0,0) \\ &+ v_6 \sum_{i,j=1}^{7} w_i w_j \frac{\partial^2 f_6}{\partial x_i \partial x_j}(0,0) + v_7 \sum_{i,j=1}^{7} w_i w_j \frac{\partial^2 f_7}{\partial x_i \partial x_j}(0,0), \end{aligned}$$

$$\begin{aligned} b &= v_2 \sum_{i=1}^{7} w_i \frac{\partial^2 f_2}{\partial x_i \partial c_b^*}(0,0) + v_3 \sum_{i=1}^{7} w_i \frac{\partial^2 f_3}{\partial x_i \partial c_b^*}(0,0) + v_5 \sum_{i=1}^{7} w_i \frac{\partial^2 f_5}{\partial x_i \partial c_b^*}(0,0) \\ &+ v_6 \sum_{i=1}^{7} w_i \frac{\partial^2 f_6}{\partial x_i \partial c_b^*}(0,0) + v_7 \sum_{i=1}^{7} w_i \frac{\partial^2 f_7}{\partial x_i \partial c_b^*}(0,0). \end{aligned}$$

Considering the non zero partial derivatives associated with the bifurcation coefficients a and b, we obtain

$$\begin{aligned} a &= -\frac{2\beta_b a_c \mu_b}{\Pi_b}\left(v_2 w_2 w_6 + v_2 w_3 w_6\right) - \frac{2c_b^* m_b \sigma_b \mu_b}{\Pi_b}\left(v_2 w_2 w_7 + v_2 w_3 w_7\right) \\ &- \frac{\beta_s a_m \Pi_s \mu_b^2}{\Pi_b^2 \mu_s}\left(2v_3 w_1 w_3 + 2v_3 w_2 w_3 + 2v_3 w_3 w_3\right) \\ &- \frac{c_s f_0 \sigma_s \Pi_s \mu_b^2}{\Pi_b^2 \mu_s}\left(2v_3 w_1 w_7 + 2v_3 w_2 w_7 + 2v_3 w_3 w_7\right) \\ &+ \frac{\beta_s a_m \mu_b}{\Pi_b}\left(2v_3 w_3 w_4\right) + \frac{c_s f_0 \sigma_s \mu_b}{\Pi_b}\left(2v_3 w_4 w_7\right). \\ b &= v_2 w_7 m_b \sigma_b \end{aligned}$$

From equation (3.33), we note that $w_4 < 0$, which implies that $a < 0$. Also since $w_2, w_7 > 0$, we have $b > 0$. This means the model system (3.1) exhibits a forward bifurcation at the the basic reproduction $R_0 = 1$. Hence the endemic equilibrium point E^* is locally asymptotically stable.

3.4 Global Stability of the Endemic Equilibrium Point

In the presence of the disease, the model (3.1) has an endemic equilibrium, given by

$$E^* = \left(S_b^*, E_b^*, I_b^*, S_s^*, E_s^*, I_s^*, C_e^*\right).$$

Theorem 3 *The endemic equilibrium point E^*, of model (3.1) is globally asymptotically*

stable if $R_0 > 1$.

Proof *Global stability of the endemic equilibrium point will be carried out by considering a suitable Lyapunov function. In this case we consider the function*

$$\begin{aligned} L(S_b, E_b, I_b, S_s, E_s, I_s, C_e) &= \left(S_b - S_b^* - S_b^* \ln \frac{S_b}{S_b^*}\right) + \left(E_b - E_b^* - E_b^* \ln \frac{E_b}{E_b^*}\right) \\ &+ \left(I_b - I_b^* - I_b^* \ln \frac{I_b}{I_b^*}\right) + \left(S_s - S_s^* - S_s^* \ln \frac{S_s}{S_s^*}\right) \\ &+ \left(E_s - E_s^* - E_s^* \ln \frac{E_s}{E_s^*}\right) + \left(I_s - I_s^* - I_s^* \ln \frac{I_s}{I_s^*}\right) \\ &+ \left(C_e - C_e^* - C_e^* \ln \frac{C_e}{C_e^*}\right). \end{aligned} \tag{3.35}$$

Given that

$$E^* = (S_b^*, E_b^*, I_b^*, S_s^*, E_s^*, I_s^*, C_e^*),$$

the derivative of L *with respect to time* t*, is given by*

$$\begin{aligned} \frac{dL}{dt} &= \left(1 - \frac{S_b^*}{S_b}\right)\frac{dS_b}{dt} + \left(1 - \frac{E_b^*}{E_b}\right)\frac{dE_b}{dt} + \left(1 - \frac{I_b^*}{I_b}\right)\frac{dI_b}{dt} + \left(1 - \frac{S_s^*}{S_s}\right)\frac{dS_s}{dt} \\ &+ \left(1 - \frac{E_s^*}{E_s}\right)\frac{dE_s}{dt} + \left(1 - \frac{I_s^*}{I_s}\right)\frac{dI_s}{dt} + \left(1 - \frac{C_e^*}{C_e}\right)\frac{dC_e}{dt} \\ &= \left(1 - \frac{S_b^*}{S_b}\right)(\Pi_b - (\lambda_b + \mu_b)S_b + \eta I_b) + (\lambda_b S_b - (\mu_b + \gamma_b)E_b) \\ &+ \left(1 - \frac{I_b^*}{I_b}\right)(\gamma_b E_b - (\mu_b + \nu + \eta)I_b) + \left(1 - \frac{S_s^*}{S_s}\right)(\Pi_s - (\lambda_s + \mu_s)S_s) \\ &+ \left(1 - \frac{E_s^*}{E_s}\right)(\lambda_s S_s - (\mu_s + \gamma_s)E_s) + \left(1 - \frac{I_s^*}{I_s}\right)(\gamma_s E_s - \mu_s I_s) \\ &+ \left(1 - \frac{C_e^*}{C_e}\right)(\varepsilon_b p_b I_b + \varepsilon_s p_s I_s - d_{mc} C_e). \end{aligned} \tag{3.36}$$

At the endemic equilibrium point E^**, we have*

$\Pi_b = (\lambda_b^* + \mu_b)S_b^* - \eta I_b^*,\ \mu_b + \gamma_b = \dfrac{\lambda_b^* S_b^*}{E_b^*},\ \mu_b + \nu + \eta = \dfrac{\gamma_b E_b^*}{I_b^*},\ \Pi_s = (\lambda_s^* + \mu_s)S_s^*,$
$\mu_s + \gamma_s = \dfrac{\lambda_s^* S_s^*}{E_s^*},\ \mu_s = \dfrac{\gamma_s E_s^*}{I_s^*},\ d_{mc} = \dfrac{\varepsilon_b p_b I_b^* + \varepsilon_s p_s I_s^*}{C_e^*}.$

Hence,

$$\begin{aligned}
\frac{dL}{dt} &= \mu_b S_b^* \left(2 - \frac{S_b}{S_b^*} - \frac{S_b^*}{S_b}\right) - \eta I_b^* \left(1 - \frac{I_b}{I_b^*} - \frac{S_b^*}{S_b} + \frac{S_b^* I_b}{S_b I_b^*}\right) \\
&+ A_1 C_e^* S_b^* \left(1 - \frac{S_b^*}{S_b} + \frac{C_e}{C_e^*}\right) + A_2 I_s^* S_b^* \left(1 - \frac{E_b}{E_b^*} + \frac{S_b^*}{S_b} - \frac{E_b^* S_b}{E_b S_b^*}\right) \\
&- A_1 C_e^* S_b^* \left(\frac{E_b}{E_b^*}\right) - \gamma_b E_b^* \left(1 - \frac{I_b}{I_b^*} + \frac{E_b}{E_b^*} - \frac{I_b^* E_b}{I_b E_b^*}\right) \\
&+ \mu_s S_s^* \left(2 - \frac{S_s}{S_s^*} - \frac{S_s^*}{S_s}\right) + B_1 C_e^* S_s^* \left(1 - \frac{S_s^*}{S_s} + \frac{C_e}{C_e^*}\right) \qquad (3.37) \\
&+ B_2 I_b^* S_s^* \left(1 - \frac{E_s}{E_s^*} + \frac{E_b}{E_b^*} - \frac{E_s^* S_s}{E_s S_s^*}\right) - B_1 C_e^* S_s^* \left(\frac{E_s}{E_s^*}\right) \\
&- \gamma_s E_s^* \left(1 - \frac{I_s}{I_s^*} + \frac{E_s}{E_s^*} - \frac{I_s^* E_s}{I_s E_s^*}\right) \\
&+ \varepsilon_b p_b I_b^* \left(1 - \frac{C_e}{C_e^*} + \frac{I_b}{I_b^*} - \frac{C_e^* I_b}{C_e I_b^*}\right) + \varepsilon_s p_s I_s^* \left(1 - \frac{C_e}{C_e^*} + \frac{I_s}{I_s^*} - \frac{C_e^* I_b}{C_e I_s^*}\right),
\end{aligned}$$

where $A_1 = \dfrac{\mu_b c_b m_b \sigma_b}{\Pi_b}, A_2 = \dfrac{\mu_b \beta_b a_c}{\Pi_b}, B_1 = \dfrac{\mu_b c_s f_0 \sigma_s}{\Pi_b}, B_2 = \dfrac{\mu_b \beta_s a_m}{\Pi_b}.$

We can then rewrite equation (3.37) as

$$\begin{aligned}
\frac{dL}{dt} &= \mu_b S_b^* \left(2 - \frac{S_b}{S_b^*} - \frac{S_b^*}{S_b}\right) + \mu_s S_s^* \left(2 - \frac{S_s}{S_s^*} - \frac{S_s^*}{S_s}\right) \\
&\quad - A_1 C_e^* S_b^* \left(\frac{E_b}{E_b^*}\right) - B_1 C_e^* S_s^* \left(\frac{E_s}{E_s^*}\right) \qquad (3.38) \\
&\quad + H(S_b, E_b, I_b, S_s, E_s, I_s, C_e),
\end{aligned}$$

where

$$\begin{aligned}
H &= -\eta I_b^* \left(1 - \frac{I_b}{I_b^*} - \frac{S_b^*}{S_b} + \frac{S_b^* I_b}{S_b I_b^*}\right) + A_1 C_e^* S_b^* \left(1 - \frac{S_b^*}{S_b} + \frac{C_e}{C_e^*}\right) \\
&\quad + A_2 I_s^* S_b^* \left(1 - \frac{E_b}{E_b^*} + \frac{S_b^*}{S_b} - \frac{E_b^* S_b}{E_b S_b^*}\right) - \gamma_b E_b^* \left(1 - \frac{I_b}{I_b^*} + \frac{E_b}{E_b^*} - \frac{I_b^* E_b}{I_b E_b^*}\right) \\
&\quad + B_1 C_e^* S_s^* \left(1 - \frac{S_s^*}{S_s} + \frac{C_e}{C_e^*}\right) + B_2 I_b^* S_s^* \left(1 - \frac{E_s}{E_s^*} + \frac{E_b}{E_b^*} - \frac{E_s^* S_s}{E_s S_s^*}\right) \qquad (3.39) \\
&\quad - \gamma_s E_s^* \left(1 - \frac{I_s}{I_s^*} + \frac{E_s}{E_s^*} - \frac{I_s^* E_s}{I_s E_s^*}\right) \\
&\quad + \varepsilon_b p_b I_b^* \left(1 - \frac{C_e}{C_e^*} + \frac{I_b}{I_b^*} - \frac{C_e^* I_b}{C_e I_b^*}\right) + \varepsilon_s p_s I_s^* \left(1 - \frac{C_e}{C_e^*} + \frac{I_s}{I_s^*} - \frac{C_e^* I_b}{C_e I_s^*}\right).
\end{aligned}$$

Since the arithmetic mean is greater than or equal to the geometric mean, we have

$$2 - \frac{S_b}{S_b^*} - \frac{S_b^*}{S_b} \leq 0 \text{ and } 2 - \frac{S_s}{S_s^*} - \frac{S_s^*}{S_s} \leq 0.$$

Furthermore, as H is non-positive, that is, $H \leq 0$, for $S_b, E_b, I_b, S_s, E_s, I_s, C_e \geq 0$, then $\frac{dL}{dt} \leq 0$ whenever $S_b = S_b^*,\ E_b = E_b^*,\ I_b = I_b^*,\ S_s = S_s^*,\ E_s = E_s^*,\ I_s = I_s^*,\ C_e = C_e^*$ [18, 65]. Therefore, the largest compact invariant set in

$$\left\{(S_b, E_b, I_b, S_s, E_s, I_s, C_e) \in \Omega;\ \frac{dL}{dt} = 0\right\},$$

is the singleton E^*, where E^* is the endemic equilibrium. LaSalle's invariant principle [51] then implies

$$\begin{aligned}
&\lim_{t\to\infty} S_b(t) = S_b^*, \quad \lim_{t\to\infty} E_b(t) = E_b^*, \quad \lim_{t\to\infty} I_b(t) = I_b^*, \\
&\lim_{t\to\infty} S_s(t) = S_s^*, \quad \lim_{t\to\infty} E_s(t) = E_s^*, \quad \lim_{t\to\infty} I_s(t) = I_s^*, \\
&\lim_{t\to\infty} C_e(t) = C_e^*.
\end{aligned} \tag{3.40}$$

Hence, E^* is globally asymptotically stable in the interior of Ω.

3.5 Numerical Simulations

To support the model theoretical results, model (3.1) will be simulated using the Runge-Kutta integration scheme. The model parameter values used in the simulations are given in Table (3.1) and the initial values in Table (3.2). Some of the values have been obtained from the literature while others were assumed within realistic range for the purpose of illustration.

Table 3.1: Model Parameter Values

Description	**Symbol**	**Value**	**Source**
Natural birth rate for bovines	Π_b	$0.000458\ day^{-1}$	[93]
Natural birth rate for snails	Π_s	$0.01 - 2.25\ day^{-1}$	[55]
Disease progression rate in bovines	γ_b	$0.406\ day^{-1}$	[20]
Disease progression rate in snails	γ_s	$0.105\ day^{-1}$	Assumed
Recovery rate for bovine	η	$0.00183\ day^{-1}$	[93]
Natural mortality rate for bovines	μ_b	$0.000392\ day^{-1}$	[93]
Natural mortality rate for snails	μ_s	$0.0063 - 0.033\ day^{-1}$	[94]
Disease induced rate in infected bovines	ν	$0.0039\ day^{-1}$	[31]
Shedding rate of miracidia by bovines	ε_b	$0.00232\ day^{-1}$	[58]
Shedding rate of cercariae by snails	ε_s	$2.6\ day^{-1}$	[58]
Bovine body mass	m_b	500	Assumed
Probability of transmission in bovines	σ_b	0.406×10^{-8}	[34]
Probability of transmission in snails	σ_s	0.615	[58]
Miracidia to cercariae survival probability	p_b	0.00232	[58]

3.5.1 Sensitivity Analysis

Sensitivity analysis is a measure of the relative change in a model variable when a particular parameter changes [69]. We carry out the sensitivity analysis in order to determine which model parameter of the model system (3.1) has the greatest effect on the basic reproduction number, R_0. We follow the approach in Chitnis [16] by calculating the normalized forward sensitivity index of a variable, ϕ, that depends differentiably on

Table 3.1: Model Parameter Values (Continued)

Description	**Symbol**	**Value**	**Source**
Cercariae to miracidia survival probability	p_s	0.0026	[58]
Bovine-Cercariae contact rate	c_b	$0.033 - 0.133$	[31]
Snails-Miracidia effective contact rate	c_s	$0 - 1$	[26]
Faecal output by bovines	f_0	190 gram day^{-1}	[93]
Attacking efficiency of miracidia	a_m	0.01	Assumed
Attacking efficiency of cercariae	a_c	0.02	Assumed
Infection rate from infected snails to bovines	β_b	0.0426	[34]
Infection rate from infected bovines to snails	β_s	0.1224	[34]
Natural death rate for miracidia and cercariae	d_{mc}	3	[91]

Table 3.2: Model Initial Values

Variable	**Description**	**Initial Value**
S_b	Susceptible bovines	74000
E_b	Exposed bovines	45000
I_b	Infectious bovines	0
S_s	Susceptible snails	92000
E_s	Exposed snails	60000
I_s	Infectious snails	0
C_e	Contaminated environment	7890

parameter p, using the formula

$$\Upsilon_p^{\phi} = \frac{\partial \phi}{\partial p} \times \frac{p}{\phi}.$$

The resulting sensitivity indices of the basic reproduction number, R_0, are then presented in Table (3.3) below. From Table (3.3), the natural birth rate for bovines, Π_b, is one of the most sensitive parameters of the basic reproduction number R_0. It has a

Table 3.3: Sensitivity Indices for Model Parameters

Description	**Symbol**	**Sensitivity Index**
Natural birth rate for bovines	Π_b	-0.9997
Natural birth rate for snails	Π_s	0.00024
Disease progression rate in bovines	γ_b	2.388×10^{-7}
Disease progression rate in snails	γ_s	0.0566
Recovery rate for bovine	η	-0.000074
Natural mortality rate for bovines	μ_b	0.9997
Natural mortality rate for snails	μ_s	-0.0566
Disease induced rate in infected bovines	ν	-0.00016
Shedding rate of miracidia by bovines	ε_b	0.0000092
Shedding rate of cercariae by snails	ε_s	0.9995
Bovine body mass	m_b	4.87286×10^{-13}
Probability of transmission in bovines	σ_b	4.873×10^{-13}
Probability of transmission in snails	σ_s	0.9995
Miracidia to cercariae survival probability	p_b	0.0000092
Cercariae to miracidia survival probability	p_s	0.9995
Bovine-Cercariae contact rate	c_b	4.873×10^{-13}
Snails-Miracidia effective contact rate	c_s	0.9995
Faecal output by bovines	f_0	0.9995
Attacking efficiency of miracidia	a_m	0.000238
Attacking efficiency of cercariae	a_c	0.000247
Infection rate from infected snails to bovines	β_b	0.000247
Infection rate from infected bovines to snails	β_s	0.000238
Natural death rate for miracidia and cercariae	d_{mc}	-0.9995

negative index, indicating that any increase (decrease) of Π_b, say by 10%, will decrease (increase) R_0 by 9.997%. Consider the basic reproduction number in equation (3.23).

With an increase in the natural birth rate for bovines, we observe new infections in snails and bovines, R_{01} and R_{02}, respectively, being reduced as well. This also applies to the transmission from infected snails to susceptible bovines, R_{03} and the transmission from infected bovines to susceptible snails, R_{04}. The basic reproduction number, R_0 is also reduced as a result of a decrease in new infections and transmission between bovines and snails. Another most sensitive parameter is f_0, the faecal output. As f_0 is decreased, there is low shedding of the miracidia by bovines which in turn leads to reduced infection of snails. A decrease in f_0 tends to reduce new infections in bovines and snails, as observed in R_{01} and R_{02}. It also reduces transmission from infected bovines to susceptible snails. The effective contact rate, c_s, also significantly increases or reduces new infections in snails. From the basic reproduction number, R_0, we note that reducing the contact rate, c_s, which implies reduced shedding rate of cercariae, ε_s, by snails, results in reduced reproduction number. When the chances of survival from cercariae to miracidia, p_s, are high, the occurrence of new infections in snails also increases which then leads to high transmission probability of infection in snails, σ_s. As such, due to increase in p_s and σ_s, the basic reproduction number also increases.

We also note that the natural death rate of bovines, μ_b, plays a significant role in either increasing or decreasing the basic reproduction number. This also applies to the natural mortality rate for miracidia and cercariae, d_{mc}. However, while μ_b is positively sensitive, d_{mc}, on the other hand, is observed to be negatively sensitive, so much so that as we increase the mortality rate of cercariae and miracidia, R_{01}, R_{02}, R_{03} and R_{04}, all decrease, which results in a decrease in R_0. Other parameters such as γ_s, m_b, σ_b and c_b have been shown using their indexes, to be insignificant in the transmission dynamics of schistosomiasis infection.

3.5.2 Numerical Simulations on the Bovine Schistosomiasis Model

With the use of parameter values in Table (3.1), numerical simulations of the model are provided under this section. In the case where $R_0 = 0.0237 < 1$, where the disease-free equilibrium is both locally and globally asymptotically stable (Theorem (1)). We also note that $R_{01} = 2.41 \times 10^{-11}$, $R_{02} = 0.0090$, $R_{03} = 0.1276$, and $R_{04} = 0.0027$. This satisfies the local and global stability of the disease-free equilibrium. Since $R_{01} < R_{04} < R_{02} < R_{03}$, it then shows that transmission from infected snails to susceptible bovines is more pronounced compared to the other transmissions in the system. In Figure 3.2(a), since there is no intervention at this particular time, there is a decrease in the long run, of susceptible bovines. Also, when more miracidia are shed from bovines leading to many snails being exposed, then there is a rapid decrease of the susceptible snail population (Figure 3.2(d)). As an evident result we note the increase in infectious snails (Figure 3.2(f)). Since more bovines are exposed to the cercariae, the outcome is that most of them proceed to the infectious class (Figure 3.2(c)), where they either die due to the disease or they recover and are exposed again.

Figure 3.2(b) depicts the dynamics of the exposed bovines which tend to decrease very rapidly and this could be due to several factors:- progression to the infected class, natural death rate coupled with death from the disease. Finally, as for those in the exposed snail class, E_s, we note that the contaminated environment plays a crucial role, since the contact rate that exists between miracidia, shed by infectious bovines, and the snails

themselves make it more possible for the snails to proceed to the infectious class, as shown in Figure 3.2(e).

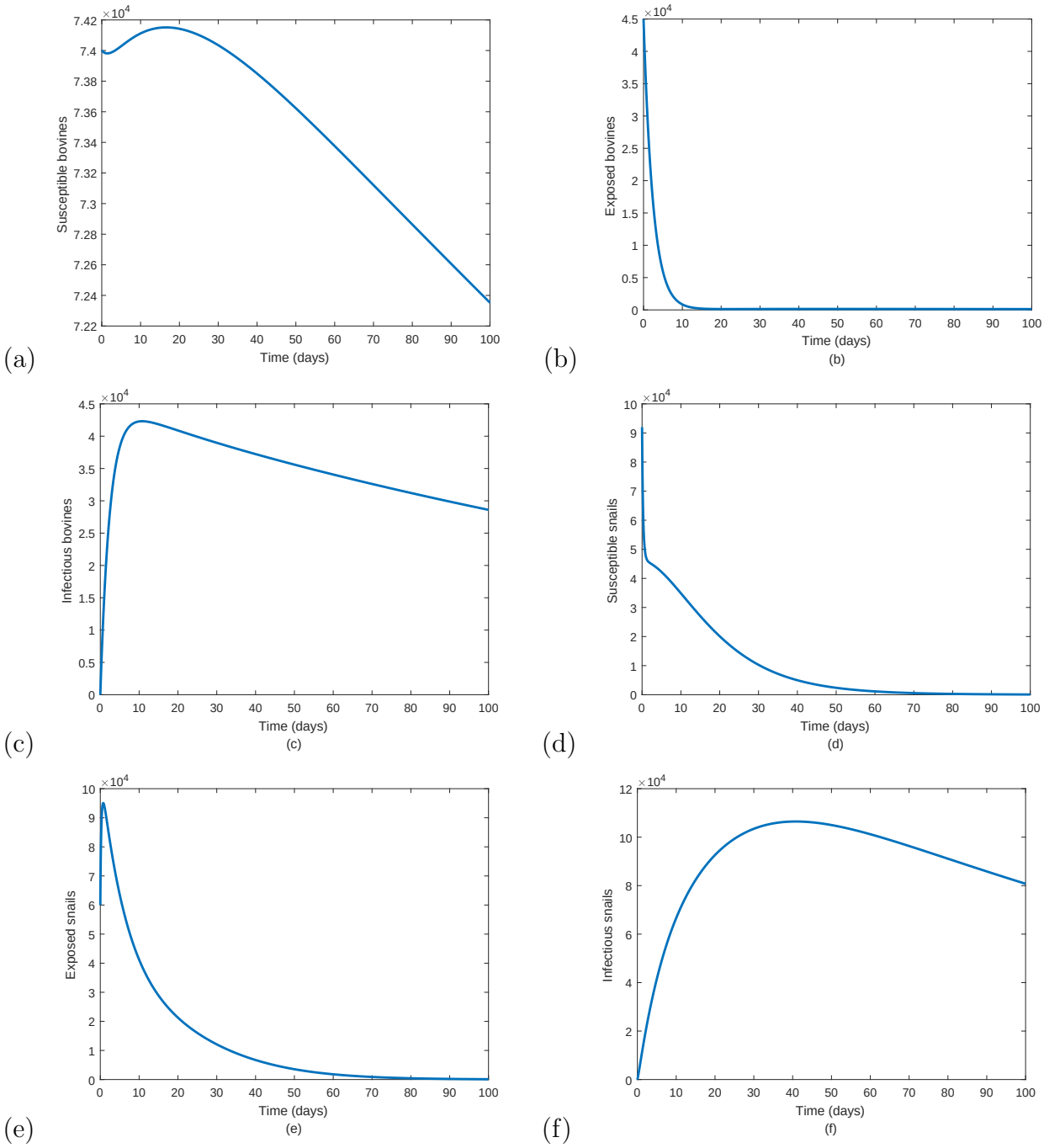


Figure 3.2: Dynamics of (a) Susceptible bovine population, (b) Exposed bovines, (c) Infectious bovines, (d) Susceptible snails, (e) Exposed snails, (f) Infectious snails. The parameter values are as given in Table (3.1) and the initial values of the state variables are; $S_b = 74000, E_b = 45000, I_b = 0, S_s = 92000, E_s = 60000, I_s = 0$.

Next, we explore the the effect of some of the most sensitive model parameters on the schistosomiasis dynamics. Figure 3.3(a) depicts the effects of varying the effective

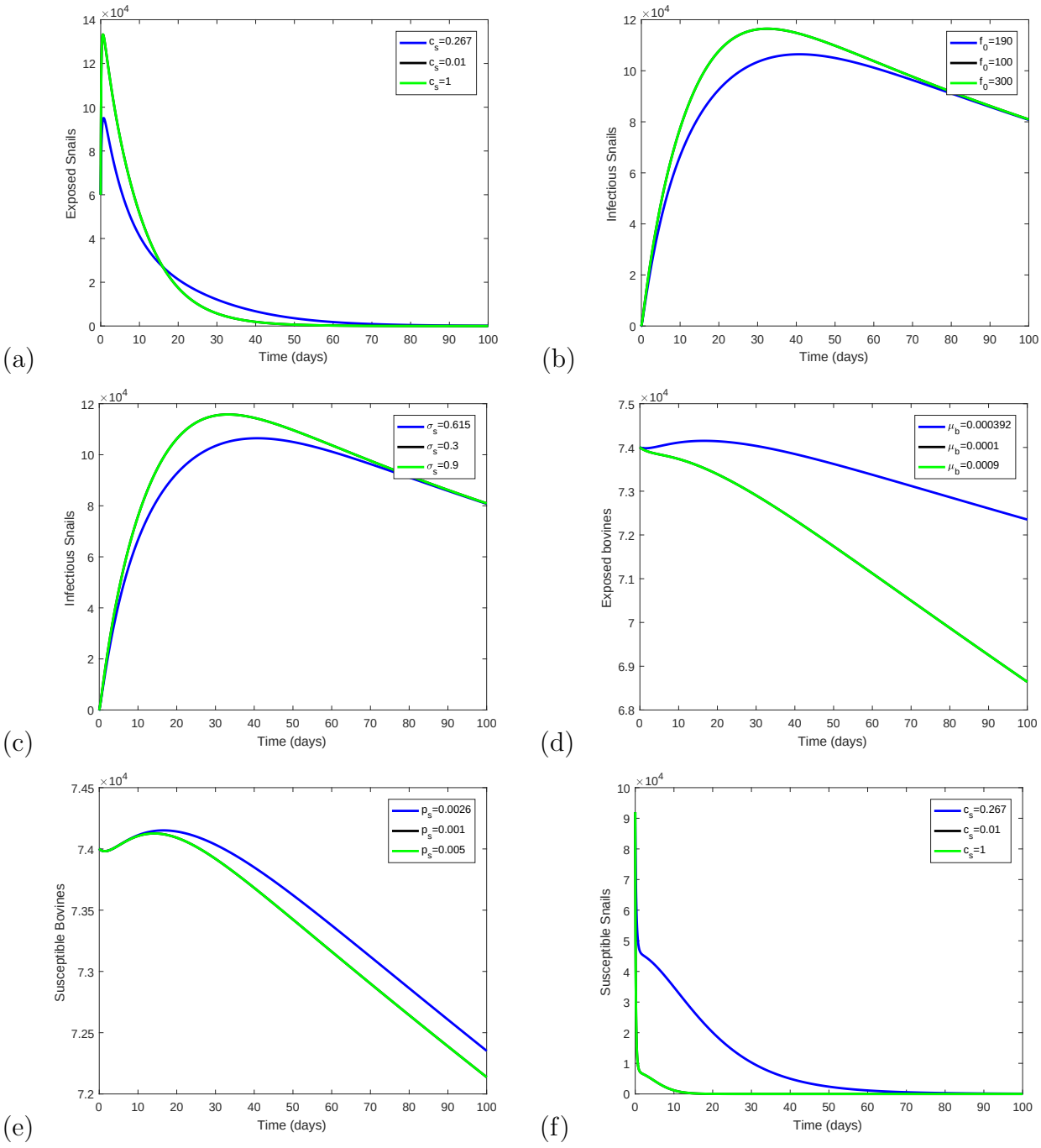


Figure 3.3: Graphs showing the effect of varying sensitive parameters in the transmission dynamics of bovine schistosomiasis for various populations.

contact rate for snails with miracidia. As the contact rate increases, there is initially a sharp increase in the number of snails, mainly due to large amounts of faecal output, f_0, from bovines that contain the miracidia. Then later, the number reaches a peak after

which it decreases exponentially. This also holds when the contact ratio is decreased.

As the faecal output, f_0, from the bovines increases, there is an increase in the number of snails infected (Figure 3.3(b)). This can be due to the fact that in the sub-Saharan regions, in particular, bovines are taken to the water reservoirs to drink; hence they produce waste which contains miracidia, which infect snails in the process. The more the faecal output, the more the snails are infected.

Figure 3.3(c) and Figure 3.3(b) have similar shapes, that is the probability of disease transmission for snails, σ_s and the faecal output f_0 produced a similar effect on the population of infectious snails. As f_0 increases, so is the probability that the snails will become infected. When the natural mortality rate for bovines is high, the number of bovines exposed decreases in the long run (Figure 3.3(d)), which implies that few will be in contact with the contaminated environment. Hence cercariae find it difficult to find secondary hosts due to shortage of bovines. This then limits the survival probability of cercariae to miracidia as many die before finding their bovines' secondary hosts. Furthermore, in Figure 3.3(e), increase in survival probability for cercariae, p_s negatively impacts (decreases) the susceptible bovine population. It is noted that once these cercariae survive, it requires few well cared for bovines to produce enough faecal output which is normally the medium for the cercariae.
On the other hand, in Figure 3.3(f), increasing snails-miracidia effective contact rate, c_s, leads to a large decrease in susceptible snails.

3.5.3 Effects of Varying Sensitive Parameters on the Basic Reproduction Number, R_0

We run the system by varying some of the key parameters in the model as described in Table (3.3). Figure 3.4(a) shows that the basic reproduction number R_0 increases when μ_b increases while it decreases as the bovines recruitment rate, Π_b increases. This supports the sensitivity results in Table (3.3) on the behaviour of the reproduction numbers in relation to μ_b and Π_b. However, from the graph we note that maximizing the herd of bovines while keeping the natural mortality to low levels reduces the schistosomiasis.

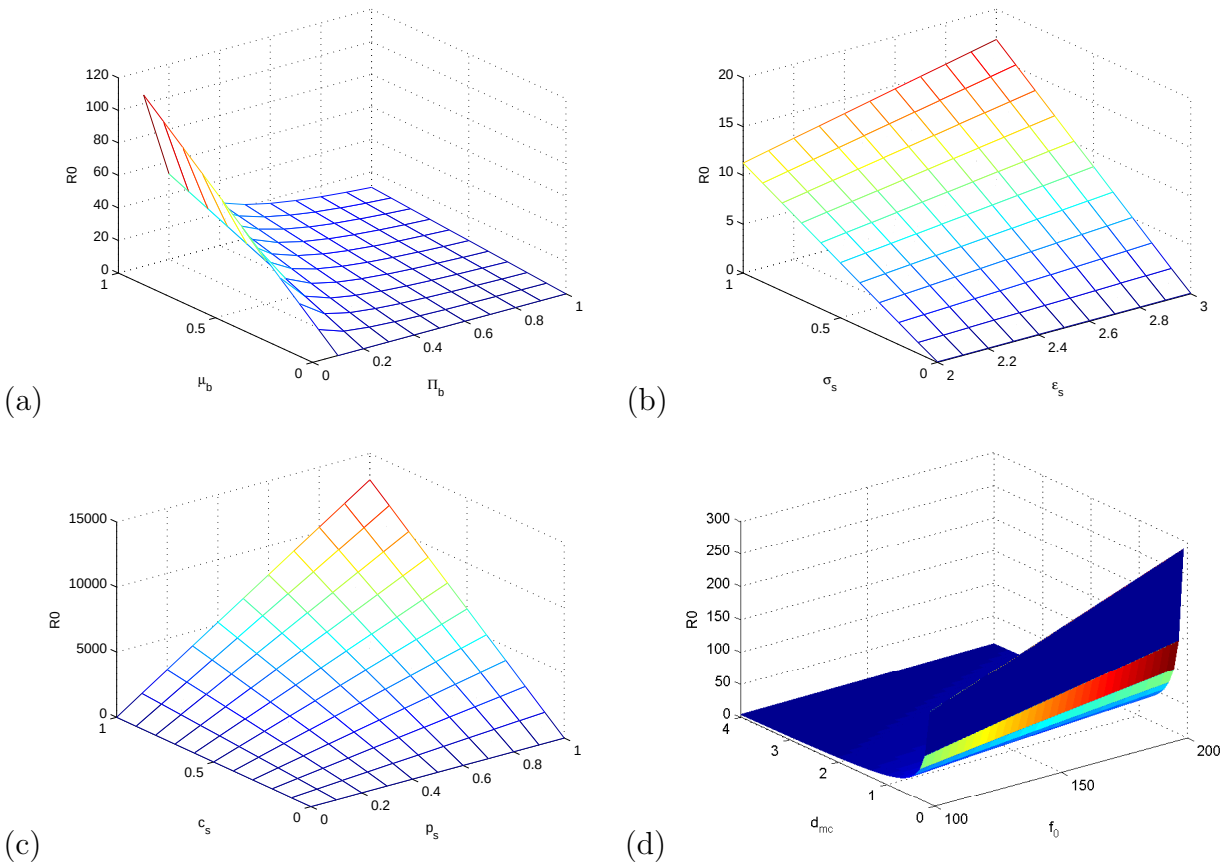


Figure 3.4: Three-dimensional plots of R_0
against the key parameters. Fixed parameter values are given in Table (3.1).

On the other hand, from Figure 3.4(b), we observe that increase in the shedding rate of cercariae by snails increases the probability of disease transmission in snails. Hence the reproduction number also increases.

In Figure 3.4(c), once the snails-miracidia effective contact rate increases, there is a high chance that these miracidia can reproduce asexually thereby making it possible for cercariae to survive to miracidia once more, upon finding bovine secondary hosts. The outcome is that there are more bovine schistosomiasis cases as seen from the increasing reproduction number. Finally, as expected, Figure 3.4(d) shows that high mortality rate of cercariae and miracidia tends to reduce the disease epidemic, while more faecal output leads to an increase in R_0, possibly because the more waste secreted by bovines, the more pathogens are carried through them.

3.6 Summary

In this chapter, we described and developed a proposed robust deterministic mathematical model of the transmission dynamics of schistosomiasis accounting for the contaminated water reservoir. The system of non-linear ordinary differential equations was then rigorously analysed theoretically. The model was biologically well-posed in a positively invariant region. The basic reproduction number which represents the number of secondary infections generated by a single infectious case in a totally susceptible population was computed. Local and global stability of both the disease-free and endemic equilibria were investigated. Sensitivity analysis to determine the relative importance of model parameters to disease transmission was performed. To support the qualitative analysis, numerical simulations were provided. The next chapter will be extended to include control measures such as treatment of bovines and humans and molluciciding of the contaminated environment/water reservoir.

Chapter 4

The Human-Bovine Schistosomiasis Model with Treatment and Mollusciciding

4.1 Introduction

We now extend our proposed bovine schistosomiasis transmission model by including human host. As the contaminated environment plays a crucial role in the transmission dynamics of bovine schistosomiasis, the disease also persists in humans. Furthermore, the measures which are targeted to bovines besides the humans are said to be vital in eliminating the transmission of the disease [93].

Several measures have so far been considered in the control of schistosomiasis. In the absence of effective vaccine for both human and bovine schistosomiasis, it has been found necessary that some interventions should target the water-related stages of the schistosome life cycle [77]. Moreover, human and bovine treatment has proved to be of short-term benefit [90]. There is also a strong suggestion to break the bovine-snail transmission cycle by employing a more comprehensive strategy that will include the environmental factors [15]. This is in agreement with the model discussed in our Chapter 3, which shows that the contaminated environment plays an important role in the transmission of the disease, so that including some control measures is viable.

Evaluation of schistosomiasis control strategies such as the combination of therapeutic measures for humans and bovines and snail control could offer better outcomes than singly applying these control options [54]. Also, some strategies like mass extermination of snails though not practical, could be very controversial and extremely costly. Thus, the World Health Organization recommends prioritizing therapeutic measures such as the use of praziquantel-based control instead of environmental modification. Due to flooding, many new snail areas emerge thereby making the control of the disease difficult, even if continuous praziquantel-based control is applied. Thus, human treatment alone is not sufficient to control the disease [96]. Other potential control measures include

restriction of bovines to fenced areas, mechanisation of agriculture, improved water supply and sanitation. But such measures increase economic burden and social impact [79].

Culling can also be thought of as one of the control strategies. This can be in the form of killing the infectious bovines. However, for one reason or another, culling animals has been criticized on animal rights grounds, that for whatever reason, killing animals is an indication of cruelty and being unethical. In fact culling can have the counter-productive outcome of increasing or fueling the epidemic as it increases human-bovine contacts [81]. Therefore, control strategies against schistosomiasis should rather be directed to the parasite or the snails instead of slaughtering animals [57].

From the above brief overview of the potential schistosomiasis control strategies that have so far been put in place, we then develop and rigorously analyse a mathematical model of the transmission dynamics of bovines schistosomiasis with human host, contaminated environment and snails. Since the contaminated environment tends to play a crucial role in the transmission dynamics of the disease, we include treatment of humans and bovines and molluscicide of the environment.

4.2 Model Formulation

Based on the model developed in Chen [15] and the basic model in Chapter 3 above, we propose a deterministic mathematical model that describes the schistosomiasis transmission dynamics in humans, bovines and snails with the inclusion of the contaminated environment that harbours the cercariae and miracidia as infection agents.

The proposed compartmental model has nine separate epidemiological classes: susceptible humans, S_H, who upon contact with the cercariae from the contaminated environment, move to the infected class I_H. These have the cercariae in their body system and are able to shed eggs into the water reservoir. The infectious individuals are then treated and progress to the treated class, T_H. Classes for bovines include, S_B, those having a risk of contracting the infection when in contact with cercariae in the water

reservoir. They also become infectious and move to infected bovine class, I_B. They are then subjected to treatment and move to the treated class, T_B. Then there is S_S, the susceptible snail population and I_S, the infected snail class. Finally, we have C_E, denoting the contaminated environment in which there is concentration of miracidia and cercariae.

The model assumes constant recruitment rates for humans, bovines and snails of Π_h, Π_b and Π_s, respectively. These rates are as a result of natural births or immigration of mature humans, bovines and snails. The force of infection for humans as they make contact with the contaminated environment is given by β_{sh}, while for bovines it is denoted by β_{sb}. Humans, bovines and contaminated environment contribute to the infection transmission in snails at the rates β_{hs}, β_{bs} and β_{cs}, respectively.

The infected snails shed cercariae at the rate ε_s and the cercariae develop into schistosomulae with survival probability of p_s. t_1 and t_2 denote the rates at which infected humans and bovines progress to the treated classes, respectively. The fraction of humans treated is $\kappa \in [0, 1]$ and the effectiveness of such human treatment is assumed to be $\tau \in (0, 1]$. The fraction of bovines treated is denoted by υ and ψ denotes the effectiveness of the treatment. As they receive treatment, humans recover at the rate r_h while bovines recover at the rate r_b. However, they might become susceptible again after recovery. Humans die naturally at a rate μ_h or die due to the disease at a rate d_h. Similarly, the natural mortality rate of bovines is given by μ_b and die due to infection at the rate d_b. The snails on the other hand, die naturally at a rate μ_s. In addition to treatment, we have also included molluscicide as a control measure. As such, we assume the fraction of the area to be subjected to molluscicides as c, where $0 \leq c \leq 1$. Furthermore, the effectiveness of molluscicide is assumed to be $q \in (0, 1]$. Since cercariae and miracidia have a short lifespan, they die naturally at the rate μ_c.

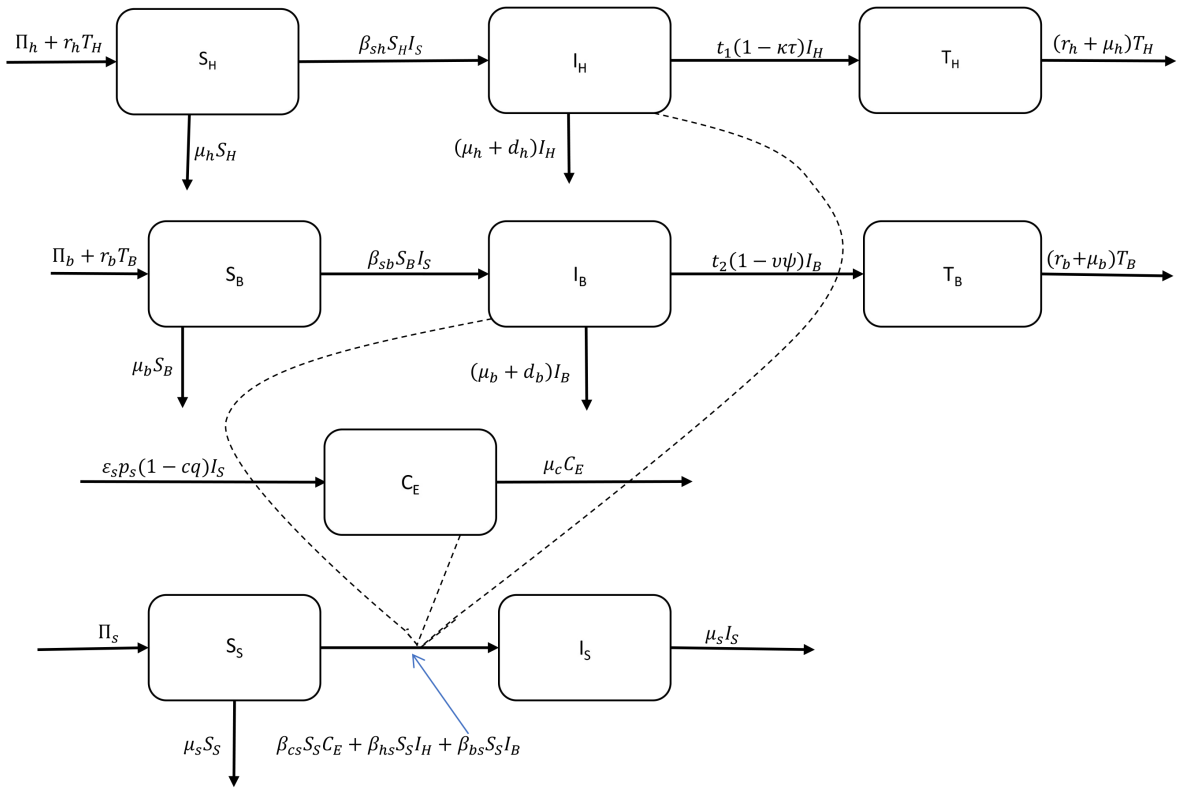


Figure 4.1: The model flow diagram of schistosomiasis transmission between humans, bovines and snails with contaminated environment

We consider a population dynamic model, as such, it is assumed that all variables and model parameters are non-negative. Hence the following system of non-linear ordinary differential equations governs the model:

$$\begin{aligned}
\frac{dS_H}{dt} &= \Pi_h - \beta_{sh} S_H I_S + r_h T_H - \mu_h S_H, \\
\frac{dI_H}{dt} &= \beta_{sh} S_H I_S - (t_1(1-\kappa\tau) + \mu_h + d_h) I_H, \\
\frac{dT_H}{dt} &= t_1(1-\kappa\tau) I_H - (r_h + \mu_h) T_H, \\
\frac{dS_B}{dt} &= \Pi_b - \beta_{sb} S_B I_S + r_b T_B - \mu_b S_B, \\
\frac{dI_B}{dt} &= \beta_{sb} S_B I_S - (t_2(1-\upsilon\psi) + \mu_b + d_b) I_B, \\
\frac{dT_B}{dt} &= t_2(1-\upsilon\psi) I_B - (r_b + \mu_b) T_B, \\
\frac{dS_S}{dt} &= \Pi_s - (\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - \mu_s S_S, \\
\frac{dI_S}{dt} &= (\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - \mu_s I_S, \\
\frac{dC_E}{dt} &= \varepsilon_s p_s (1-cq) I_S - \mu_c C_E.
\end{aligned} \tag{4.1}$$

The state variables and parameters are described in the tables below.

Table 4.1: Description of State Variables

Variable	Description
S_H	Susceptible humans
I_H	Infected humans
T_H	Treated humans
S_B	Susceptible bovines
I_B	Infected bovines
T_B	Treated bovines
S_S	Susceptible snails
I_S	Infected snails
C_E	Contaminated environment

4.3 Model Analysis

4.3.1 Feasible Region

Let the total human, bovine and snail populations at time t, be denoted by $N_H(t),\ N_B(t)$ and $N_S(t)$, respectively. Then we have

$$\begin{aligned} N_H(t) &= S_H(t) + I_H(t) + T_H(t), \\ N_B(t) &= S_B(t) + I_B(t) + T_B(t), \\ N_S(t) &= S_S(t) + I_S(t). \end{aligned} \tag{4.2}$$

We then assume that the transmission dynamics of the system (4.1) are asymptotically stable without infection. As such, we prove that the model system (4.1) is well-posed in the invariant and attracting region

$$\mathbb{D} = \left\{ (S_H, I_H, T_H, S_B, I_B, T_B, S_S, I_S, C_E) \in \mathbb{R}_+^9 : S_H, I_H, T_H, S_B, I_B, T_B, S_S, I_S, C_E \geq 0 \right\}.$$

From the system (4.1), we have

$$\begin{aligned} \frac{dN_H}{dt} &= \Pi_h - \mu_h \left(S_H + I_H + T_H\right) - d_h I_H, \\ &\leq \Pi_h - \mu_h N_H. \end{aligned} \tag{4.3}$$

Table 4.2: Description of Model Parameters

Parameter	Description
$\Pi_h,\ \Pi_b,\ \Pi_s$	Recruitment rate for humans, bovines, snails, respectively
β_{sh}	Transmission rate from infected snails to humans
$\mu_h,\ \mu_b,\ \mu_s$	Natural mortality rate of humans, bovines, snails, respectively
β_{sb}	Transmission rate from infected snails to bovines
t_1	Disease progression rate from infected to treated human classes
κ	Fraction of humans treated
τ	Effectiveness of treatment in humans
d_h	Disease induced deaths in infected humans
r_h	Recovery rate of humans
t_2	Disease progression rate from infected to treated bovine classes
υ	Fraction of bovines treated
ψ	Effectiveness of treatment in bovines
d_b	Disease induced deaths in infected bovines
ε_s	Snails shedding rate of cercariae
p_s	Probability that cercariae shed by snails survive
c	Fraction of the contaminated environment sprayed by molluscicides
q	Effectiveness of molluscicide
μ_c	Mortality rate of miracidia and cercariae
β_{cs}	Transmission rate from the contaminated environment to snails
β_{hs}	Transmission rate from infected humans to snails
β_{bs}	Transmission rate from infected bovines to snails

Similarly

$$\frac{dN_B}{dt} = \Pi_b - \mu_b N_B - d_b I_B, \rightarrow \frac{dN_B}{dt} \leq \Pi_b - \mu_b N_B. \tag{4.4}$$

And lastly,

$$\frac{dN_S}{dt} \leq \Pi_s - \mu_s N_S. \tag{4.5}$$

Applying Birkhoff and Rota's Theorem [6] to (4.3), gives

$$\frac{dN_H}{\Pi_h - \mu_s N_H} \leq dt. \tag{4.6}$$

Upon integrating both sides of (4.6) with respect to t and applying the initial condition $N_H(0) = N_{H0}$, we obtain

$$N_H(t) \leq \frac{\Pi_h}{\mu_h} - \frac{(\Pi_h - \mu_h N_{H0})\, e^{-\mu_h t}}{\mu_h}, \tag{4.7}$$

which leads to

$$0 \leq N_H \leq \frac{\Pi_h}{\mu_h} \text{ as } t \to \infty.$$

Using the same approach on equations (4.4) and (4.5), we obtain

$$0 \leq N_B \leq \frac{\Pi_b}{\mu_b} \text{ and } 0 \leq N_S \leq \frac{\Pi_s}{\mu_s}, \tag{4.8}$$

respectively, as $t \to \infty$.

Considering the ninth equation of system (4.1), and using the boundedness of I_S, that is, letting

$$M = max\left\{N_S(0), \frac{\Pi_s}{\mu_s}\right\} \text{ and } I_S \leq M,$$

then

$$\frac{dC_E}{dt} = \varepsilon_s p_s (1 - cq) I_S - \mu_c C_E \leq M \varepsilon_s p_s (1 - cq) - \mu_c C_E. \tag{4.9}$$

Hence

$$\frac{dC_E}{dt} \leq Q - \mu_c C_E, \tag{4.10}$$

where $Q = M\varepsilon_s p_s(1 - cq)$. Likewise, with $C_E(0) = C_{E0}$, we obtain

$$0 \leq C_E \leq \frac{Q}{\mu_c}.$$

Thus, the solution of model system (4.1) will enter and remain in the positive invariant region $\mathcal{D}$, where

$$\begin{aligned} \mathcal{D} \;=\; & \Big\{(S_H, I_H, T_H, S_B, I_B, T_B, S_S, I_S, C_E) \in \mathbb{R}^9_+ : S_H, I_H, T_H, S_B, I_B, T_B, S_S, I_S, C_E \geq 0; \\ & N_H \leq \frac{\Pi_h}{\mu_h}, N_B \leq \frac{\Pi_b}{\mu_b}, N_S \leq \frac{\Pi_s}{\mu_s}, C_E \leq \frac{Q}{\mu_c}\Big\}. \end{aligned}$$

4.3.2 Positivity of State Variables

For the model system (4.1) to be biologically/epidemiologically meaningful, we prove that the corresponding solution set remains non-negative for all time $t > 0$.

Theorem 4 *Let the initial values* $S_H(0) > 0, I_H(0) \geq 0, T_H(0) \geq 0,$
$S_B(0) > 0, I_B(0) \geq 0, T_B(0) \geq 0, S_S(0) > 0, I_S(0) \geq 0, C_E(0) > 0$. *Then the solutions* $(S_H, I_H, T_H, S_B, I_B, T_B, S_S, I_S, C_E)$ *of the model system (4.1) are positive for all* $t > 0$.

Proof *From the first equation of the system (4.1), it follows that*

$$\frac{dS_H}{dt} = \Pi_h - \beta_{sh} S_H I_S + r_h T_H - \mu_h S_H \geq -\beta_{sh} S_H I_S - \mu_h S_H,$$

which implies that

$$\frac{dS_H}{dt} \geq -(\beta_{sh} I_S + \mu_h) S_H. \tag{4.11}$$

Let $\hat{t} = sup\Big\{t > 0 : S_H > 0, I_H > 0, T_H > 0, S_B > 0, I_B > 0, T_B > 0, S_S > 0,$
$I_S > 0, C_E > 0\Big\} \in \Big[0, t\Big]$, *and* $\hat{t} > 0$, *then solving the differential inequality (4.11) gives*

$$\frac{d}{dt}\left[S_H(t) e^{\int_0^t \beta_{sh} I_S(u)du + \mu_h t}\right] \geq e^{\int_0^t \beta_{sh} I_S(u)du + \mu_h t}. \tag{4.12}$$

Hence,

$$S_H(\hat{t}) e^{\int_0^{\hat{t}} \beta_{sh} I_S(u)du + \mu_h \hat{t}} - S_H(0) \geq \int_0^{\hat{t}} e^{\int_0^l \beta_{sh} I_S(z)dz + \mu_h l} dl, \tag{4.13}$$

so that

$$S_H(\hat{t}) \geq S_H(0) e^{-\left(\int_0^{\hat{t}} \beta_{sh} I_S(u)du + \mu_h \hat{t}\right)} + e^{-\left(\int_0^{\hat{t}} \beta_{sh} I_S(u)du + \mu_h \hat{t}\right)} \left[\int_0^{\hat{t}} e^{\int_0^l \beta_{sh} I_S(z)dz + \mu_h l} dl\right] > 0. \tag{4.14}$$

This implies S_H *is positive for all* $t > 0$.

From the second equation, we have

$$\frac{dI_H}{dt} = \beta_{sh} S_H I_S - (t_1(1 - \kappa\tau) + \mu_h + d_h) I_H.$$

This implies

$$\frac{dI_H}{dt} \geq -(t_1(1 - \kappa\tau) + \mu_h + dh) I_H.$$

Solving the differential inequality gives

$$\ln|I_H| \geq -\int (t_1(1-\kappa\tau)+\mu_h+d_h)dt+\hat{r},$$

where $\hat{r}$ *is a constant of integration. So we obtain*

$$I_H(t) \geq I_H(0)e^{-\int (t_1(1-\kappa\tau)+\mu_h+d_h)dt} \geq 0,$$

which also shows that I_H *is positive for all* $t>0$.

In a similar way, the rest of the state variables can be shown to be positive for all $t>0$. *Thus the solution set for the model system (4.1) is positive for all* $t>0$.

4.3.3 The Disease-Free Equilibrium

The model (4.1) has a disease-free equilibrium which is obtained by setting the infectious classes equal to zero. That is, $I_H = T_H = I_B = T_B = I_S = C_E = 0$.

Therefore the disease-free equilibrium of the model (4.1) is given by

$$E_0^* = \Big(\frac{\Pi_h}{\mu_h}, 0, 0, \frac{\Pi_b}{\mu_b}, 0, 0, \frac{\Pi_s}{\mu_s}, 0, 0\Big).$$

We then establish the stability of E_0^* using the next-generation operator method [85]. With this approach, we obtain

$$F_i = \begin{pmatrix} \beta_{sh}S_H I_S \\ 0 \\ \beta_{sb}S_B I_S \\ 0 \\ \Big(\beta_{cs}C_E + \beta_{hs}I_H + \beta_{bs}I_B\Big)S_S \\ 0 \end{pmatrix}, \tag{4.15}$$

$$V_i = \begin{pmatrix} \Big(t_1(1-\kappa\tau)+\mu_h+d_h\Big)I_H \\ (r_h+\mu_h)T_H - t_1(1-\kappa\tau)I_H \\ (t_2(1-\upsilon\psi)+\mu_b+d_b)I_B \\ (r_b+\mu_b)T_B - t_2(1-\upsilon\psi)I_B \\ \mu_s I_S \\ \mu_c C_E - \varepsilon_s p_s(1-cq)I_S \end{pmatrix}, \tag{4.16}$$

from which we have the matrices F(which shows the rate of new infections) and V(for the transition terms), given by

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & \frac{\beta_{sh}\Pi_h}{\mu_h} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{\beta_{sb}\Pi_b}{\mu_b} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_{hs}\Pi_s}{\mu_s} & 0 & \frac{\beta_{bs}\Pi_s}{\mu_s} & 0 & 0 & \frac{\beta_{cs}\Pi_s}{\mu_s} \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{4.17}$$

and

$$V = \begin{pmatrix} t_1(1-\kappa\tau)+\mu_h+d_h & 0 & 0 & 0 & 0 & 0 \\ -t_1(1-\kappa\tau) & r_h+\mu_h & 0 & 0 & 0 & 0 \\ 0 & 0 & t_2(1-\upsilon\psi)+\mu_b+d_b & 0 & 0 & 0 \\ 0 & 0 & -t_2(1-\upsilon\psi) & r_b+\mu_b & 0 & 0 \\ 0 & 0 & 0 & 0 & \mu_s & 0 \\ 0 & 0 & 0 & 0 & -\varepsilon_s p_s(1-cq) & \mu_c \end{pmatrix}. \tag{4.18}$$

Multiplying F and the matrix inverse of V gives

$$FV^{-1} = \begin{pmatrix} 0 & 0 & 0 & 0 & m_{15} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & m_{35} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ m_{51} & 0 & m_{53} & 0 & m_{55} & m_{56} \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{4.19}$$

where

$$m_{15} = \frac{\beta_{sh}\Pi_h}{\mu_h\mu_s},\ m_{35} = \frac{\beta_{sb}\Pi_b}{\mu_b\mu_s},\ m_{51} = \frac{\beta_{hs}\Pi_s}{\mu_s(t_1(1-\kappa\tau)+\mu_h+d_h)},$$
$$m_{53} = \frac{\beta_{bs}\Pi_s}{\mu_s(t_2(1-\upsilon\psi)+\mu_b+d_b)},\ m_{55} = \frac{\beta_{cs}\Pi_s\varepsilon_s p_s(1-cq)}{\mu_s^2\mu_c},\ m_{56} = \frac{\beta_{cs}\Pi_s}{\mu_s\mu_c}.$$

The reproduction number, R_0, is then determined by computing the spectral radius of FV^{-1}, which happens to be the largest eigenvalue. In this case

$$R_0 = \frac{1}{2}m_{55} + \frac{1}{2}\sqrt{4m_{15}m_{51} + 4m_{35}m_{53} + m_{55}^2},$$

where $\frac{\Pi_h}{\mu_h}$, $\frac{\Pi_b}{\mu_b}$ and $\frac{\Pi_s}{\mu_s}$ represent the number of susceptible humans, bovines and snails, respectively. The contribution of humans, bovines and contaminated environment to the transmission of snail infection is given by $\frac{\beta_{hs}\Pi_s}{\mu_s}$, $\frac{\beta_{bs}\Pi_s}{\mu_s}$ and $\frac{\beta_{cs}\Pi_s}{\mu_s}$, respectively. The mean lifespan of humans is $\frac{1}{t_1(1-\kappa\tau)+\mu_h+d_h}$, and for bovines it is $\frac{1}{t_2(1-\upsilon\psi)+\mu_b+d_b}$. The snails have a lifespan of $\frac{1}{\mu_s}$ while that of cercariae and miracidia is $\frac{1}{\mu_c}$.
Hence

$$m_{55} = \frac{\beta_{cs}\Pi_s\varepsilon_s p_s(1-cq)}{\mu_s^2\mu_c}$$

shows the occurrence of new infections of snails upon contact with the contaminated environment. While

$$m_{15}m_{51} = \frac{\beta_{sh}\beta_{hs}\Pi_h\Pi_s}{\mu_s^2\mu_h(t_1(1-\kappa\tau)+\mu_h+d_h)}$$

denotes the average number of infected humans caused by a single infected snail. Lastly,

$$m_{35}m_{53} = \frac{\beta_{sb}\beta_{bs}\Pi_b\Pi_s}{\mu_s^2\mu_b(t_2(1-\upsilon\psi)+\mu_b+d_b)}$$

is the average number of infected bovines as a result of one infected snail.

4.3.4 Local Stability of the Disease-Free Equilibrium

For mathematical tractability [23], consider there is no disease, that is the disease-induced death rates and miracidia and cercariae parameters are all set to zero.

Since $d_h,\ d_b = 0$, we assume that our populations of humans, bovines and snails reach their limiting values $N_H \equiv \frac{\Pi_h}{\mu_h}$, $N_B \equiv \frac{\Pi_b}{\mu_b}$ and $N_S \equiv \frac{\Pi_s}{\mu_s}$. Hence by eliminating the equations for $\frac{dS_H}{dt}$, $\frac{dS_B}{dt}$ and $\frac{dS_S}{dt}$ from the model (4.1), we obtain the equivalent limiting

system:

$$\begin{aligned}
\frac{dI_H}{dt} &= \beta_{sh} S_H I_S - (t_1(1-\kappa\tau) + \mu_h) I_H, \\
\frac{dT_H}{dt} &= t_1(1-\kappa\tau) I_H - (r_h + \mu_h) T_H, \\
\frac{dI_B}{dt} &= \beta_{sb} S_B I_S - (t_2(1-\upsilon\psi) + \mu_b) I_B, \\
\frac{dT_B}{dt} &= t_2(1-\upsilon\psi) I_B - (r_b + \mu_b) T_B, \\
\frac{dI_S}{dt} &= (\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - \mu_s I_S, \\
\frac{dC_E}{dt} &= \varepsilon_s p_s (1-cq) I_S - \mu_c C_E,
\end{aligned} \tag{4.20}$$

defined on $\mathcal{D}_0 = \left\{ I_H, T_H, I_B, T_B, I_S, C_E \right\} \in \mathbb{R}_+^6; I_H \leq \frac{\Pi_h}{\mu_h}, T_H \leq \frac{\Pi_h}{\mu_h}, I_B \leq \frac{\Pi_b}{\mu_b}, T_B \leq \frac{\Pi_b}{\mu_b}, I_S \leq \frac{\Pi_s}{\mu_s}, C_E \geq 0 \right\}$.

Theorem 5 *The disease-free equilibrium for the limiting system (4.20) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof *The Jacobian matrix of (4.20) is*

$$J_0 = \begin{pmatrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{pmatrix}, \tag{4.21}$$

where

$$J_{11} = \begin{pmatrix} -(t_1(1-\kappa\tau) + \mu_h) & 0 \\ t_1(1-\kappa\tau) & -(r_h + \mu_h) \end{pmatrix},$$

$$J_{12} = \begin{pmatrix} 0 & 0 & \frac{\beta_{sh}\Pi_h}{\mu_h} & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

$$J_{21} = \begin{pmatrix} 0 & 0 \\ 0 & 0 \\ \frac{\beta_{hs}\Pi_s}{\mu_s} & 0 \\ 0 & 0 \end{pmatrix},$$

$$J_{22} = \begin{pmatrix} -(t_2(1-\upsilon\psi)+\mu_b) & 0 & \frac{\beta_{sb}\Pi_s}{\mu_s} & 0 \\ t_2(1-\upsilon\psi) & -(r_b+\mu_b) & 0 & 0 \\ \frac{\beta_{bs}\Pi_s}{\mu_s} & 0 & -\mu_s & \frac{\beta_{cs}\Pi_s}{\mu_s} \\ 0 & 0 & \varepsilon_s p_s(1-cq) & -\mu_c \end{pmatrix}.$$

Considering the transformation

$$J_{s0} = D \cdot J_0 \cdot D$$

where,

$$D = \begin{pmatrix} -1 & 0 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix},$$

then, we note that the matrices J_0 and J_{s0} are similar. J_0 and D are both Metzler matrices, as such J_{s0} is also a Metzler matrix. From F and V matrices of the system (4.1),with $d_h = d_b = 0$, J_{s0} can be written in the form $J_{s0} = F - V$.

We also note that $F \geq 0$ and that the matrix

$$J_{22} - J_{21}J_{11}^{-1}J_{12} = \begin{pmatrix} -(t_2(1-\upsilon\psi)+\mu_b) & 0 & \frac{beta_{sb}\Pi_s}{\mu_s} & 0 \\ t_2(1-\upsilon\psi) & -(r_b+\mu_b) & 0 & 0 \\ \frac{\beta_{bs}\Pi_s}{\mu_s} & 0 & -\mu_s - \frac{\beta_{hs}\beta_{sh}\Pi_s\Pi_h}{\mu_s\mu_h(\kappa\tau t_1 - \mu_h - t_1)} & \frac{\beta_{cs}\Pi_s}{\mu_s} \\ 0 & 0 & \varepsilon_s p_s(1-cq) & -\mu_c \end{pmatrix},$$

is a regular splitting with a diagonal negative matrix [47].

Hence the following result.

Theorem 6 (Varga Theorem) *Let $J_0 = F - V$ be a regular splitting of a real Metzler matrix, where $F \geq 0$ and V a Metzler stable matrix, then the spectral radius $\rho(FV^{-1}) \leq 1$.*

Thus, we deduce that the disease-free equilibrium E_0 is locally asymptotically stable if $R_0 < 1$ and unstable when $R_0 > 1$.

4.3.5 Global Stability of Disease-Free Equilibrium

To prove this we employ the second generation approach as described by Castillo-Chavez *et al* [12]. This is achieved by rewriting the model (4.1) in the form

$$\begin{aligned} \frac{dX}{dt} &= F(X,Y), \\ \frac{dY}{dt} &= G(X,Y),\ G(X,\mathbf{0}) = 0, \end{aligned}$$

where $X \in \mathbb{R}^m$ represents the number of uninfected individuals, that is, $\mathcal{R}^m$ is a row vector consisting of m uninfected state variable components and $Y \in \mathbb{R}^n$ denotes the number of infected population,that is, $\mathcal{R}^n$ is a row vector consisting of n infected state variable components and the disease-free equilibrium $E_0 = (X^*, \mathbf{0})$, such that $X^* = \left(\frac{\Pi_h}{\mu_h}, \frac{\Pi_b}{\mu_b}, \frac{\Pi_s}{\mu_s}\right)$ and $\mathbf{0}$ is a zero vector. Global stability of the disease-free equilibrium is guaranteed by the following conditions:

(H1) For $\frac{dX}{dt} = F(X, \mathbf{0})$, X^* is globally asymptotically stable.

(H2) $G(X,Y) = A^*Y - \hat{G}(X,Y)$, $\hat{G}(X,Y) \geq 0$ for $(X,Y) \in \mathcal{D}$, for which $A^* = D_Y(X^*, \mathbf{0})$ is an M-matrix, that is, A^* has non-negative off diagonal entries. $\mathcal{D}$ denotes the feasible region. In the case of model system (4.1), we have $X = (S_H, S_B, S_S)$, while the infectious populations are given by $Y = (I_H, T_H, I_B, T_B, I_S, C_E)$.

This gives us the vector-valued functions

$$F(X,Y) = \begin{pmatrix} \Pi_h - \beta_{sh} S_H I_S + r_h T_H - \mu_h S_H \\ \Pi_b - \beta_{sb} S_B I_S + r_b T_B - \mu_b S_B \\ \Pi_s - (\beta_{hs} I_H + \beta_{bs} I_B + \beta_{cs} C_E) S_S - \mu_s S_S \end{pmatrix}, \tag{4.22}$$

$$G(X,Y) = \begin{pmatrix} \beta_{sh} S_H I_S - (t_1(1-\kappa\tau) + \mu_h + d_h) I_H \\ t_1(1-\kappa\tau) I_H - (r_h + \mu_h) T_H \\ \beta_{sb} S_B I_S - (t_2(1-\upsilon\psi) + \mu_b + d_b) I_B \\ t_2(1-\upsilon\psi) I_B - (r_b + \mu_b) T_B \\ (\beta_{hs} I_H + \beta_{bs} I_B + \beta_{cs} C_E) S_S - \mu_s I_S \\ \varepsilon_s p_s (1-cq) I_S - \mu_c C_E \end{pmatrix}. \tag{4.23}$$

At the disease-free equilibrium, $E_0 = (X^*, \mathbf{0})$, there is global asymptotic stability, for the reduced system

$$\frac{dX}{dt} = F(X, \mathbf{0}),$$

from which we have

$$\begin{aligned} \frac{dS_H}{dt} &= \Pi_h - \mu_h S_H, \\ \frac{dS_B}{dt} &= \Pi_b - \mu_b S_B, \\ \frac{dS_S}{dt} &= \Pi_s - \mu_s S_S, \end{aligned} \tag{4.24}$$

Solving the first equation by integration, we obtain

$$S_H(t) = \frac{\Pi_h}{\mu_h} + \left(S_H(0) - \frac{\Pi_h}{\mu_h} \right) e^{-\mu_h t},$$

whose limiting value is given by $S_H(t) \longrightarrow \dfrac{\Pi_h}{\mu_h}$ with $S_H(0)$ the initial human population.

In a similar way, integrating the second and third equations of (4.24), we obtain

$$S_B(t) = \frac{\Pi_b}{\mu_b} + \left(S_B(0) - \frac{\Pi_b}{\mu_b} \right) e^{-\mu_b t},$$

$$S_S(t) = \frac{\Pi_s}{\mu_s} + \left(S_S(0) - \frac{\Pi_s}{\mu_s} \right) e^{-\mu_s t},$$

respectively.

As $t \longrightarrow \infty$, $S_B(t)$ and $S_S(t)$ approach $\dfrac{\Pi_b}{\mu_b}$ and $\dfrac{\Pi_s}{\mu_s}$, respectively.

Hence, the reduced system $\dfrac{dX^*}{dt} = F(X^*, \mathbf{0})$ has a globally asymptotically stable equilibrium point $X_0 = \left(\dfrac{\Pi_h}{\mu_h}, \dfrac{\Pi_b}{\mu_b}, \dfrac{\Pi_s}{\mu_s} \right)$ and

$$G(X,Y) = A^* Y - \hat{G}(X,Y),\ \hat{G}(X,Y) \geq 0$$

for $(X, Y) \in \mathcal{D}$. We obtain the matrix A^* as

$$\begin{pmatrix} a_{11}^* & 0 & 0 & 0 & \frac{\beta_{sh}\Pi_h}{\mu_h} & 0 \\ t_1(1-\kappa\tau) & -(r_h+\mu_h) & 0 & 0 & 0 & 0 \\ 0 & 0 & a_{33}^* & 0 & \frac{\beta_{sb}\Pi_b}{\mu_b} & 0 \\ 0 & 0 & t_2(1-\upsilon\psi) & -(r_b+\mu_b) & 0 & 0 \\ \frac{\beta_{hs}\Pi_s}{\mu_s} & 0 & \frac{\beta_{bs}\Pi_s}{\mu_s} & 0 & -\mu_s & \frac{\beta_{cs}\Pi_s}{\mu_s} \\ 0 & 0 & 0 & 0 & \varepsilon_s p_s(1-cq) & -\mu_c \end{pmatrix}, \quad (4.25)$$

where $a_{11}^* = -(t_1(1-\kappa\tau) + \mu_h + dh), a_{33}^* = -(t_2(1-\upsilon\psi) + \mu_b + d_b)$ and

$$\hat{G}(X,Y) = \begin{pmatrix} \frac{\beta_{sh}\Pi_h I_S}{\mu_h}\left(1 - \frac{S_H}{N_H}\right) \\ 0 \\ \frac{\beta_{sb}\Pi_b I_S}{\mu_b}\left(1 - \frac{S_B}{N_B}\right) \\ 0 \\ \frac{\Pi_s}{\mu_s}(\beta_{hs}I_H + \beta_{bs}I_B + \beta_{cs}C_E)\left(1 - \frac{S_S}{N_S}\right) \\ 0 \end{pmatrix}, \quad (4.26)$$

with $N_H = S_H + I_H + T_H, N_B = S_B + I_B + T_B, N_S = S_S + I_S$.

Thus $\hat{G}(X, Y) \geq 0$, thereby completing the proof for both conditions H1 and H2, leading to the global stability of E_0 of the model system (4.1).

4.3.6 Local Stability of the Endemic Equilibrium E^*

We investigate the local stability of the endemic equilibrium of the model (4.1) by using the limiting system (4.20) in which the total populations of humans, bovines and snails have reached their limit levels, that is,

$$N_H \longrightarrow N_H^*,\ N_B \longrightarrow N_B^*,\ N_S \longrightarrow N_S^*,$$

where

$$N_H^* = \frac{\Pi_h}{\mu_h},\ N_B^* = \frac{\Pi_b}{\mu_b}.\ N_S^* = \frac{\Pi_s}{\mu_s}.$$

Focussing on the domain $\mathcal{D}_0 = \{I_H, T_H, I_B, T_B, I_S, C_E\}$, we clearly note that the model system (4.1) is asymptotic to the limiting system (4.20). Hence dynamics of the model system (4.1) and the limiting system (4.20) are qualitatively equivalent.

The variation matrix of the system (4.20) at the endemic equilibrium point

$$E^* = \left(I_H^*, T_H^*, I_B^*, T_B^*, C_E^*\right),$$

is given by

$$J(E^*) = \begin{pmatrix} J_{11}(E^*) & J_{12}(E^*) \\ J_{21}(E^*) & J_{22}(E^*) \end{pmatrix},$$

where

$$J_{11}(E^*) = \begin{pmatrix} -(t_1(1-\kappa\tau)+\mu_h) & 0 & 0 \\ t_1(1-\kappa\tau) & -(r_h+\mu_h) & 0 \\ 0 & 0 & -(t_2(1-\upsilon\psi)+\mu_b) \end{pmatrix},$$

$$J_{12}(E^*) = \begin{pmatrix} 0 & \beta_{sh}S_H^* & 0 \\ 0 & 0 & 0 \\ 0 & \beta_{sb}S_B^* & 0 \end{pmatrix},$$

$$J_{21}(E^*) = \begin{pmatrix} 0 & 0 & t_2(1-\upsilon\psi) \\ \beta_{hs}S_S^* & 0 & \beta_{bs}S_S^* \\ 0 & 0 & 0 \end{pmatrix},$$

and

$$J_{22}(E^*) = \begin{pmatrix} -(r_b+\mu_b) & 0 & 0 \\ 0 & -\mu_s & \beta_{cs}S_S^* \\ 0 & \varepsilon_s p_s(1-cq) & -\mu_c \end{pmatrix}.$$

Lemma 2 (Kamgang and Sallet[47], Proposition 3.1) *Let* $M = \begin{pmatrix} A & B \\ C & D \end{pmatrix}$, *with* A *and* D *square matrices.* M *is Metzler stable if and only if matrices* A *and* $D - CA^{-1}B$ *are Metzler stable.*

Using Lemma (2), we prove the following Theorem.

Theorem 7 *If $R_0 > 1$, then the positive endemic equilibrium E^* of the limiting system (4.20) is locally asymptotically stable.*

Proof *$J(E^*)$ is a stable Metzler matrix where*

$$A = J_{11}(E^*),\ B = J_{12}(E^*),\ C = J_{21}(E^*),\ D = J_{22}(E^*).$$

Computing $D - CA^{-1}B$, we obtain

$$D - CA^{-1}B = \begin{pmatrix} M_{11} & M_{12} & M_{13} \\ M_{21} & M_{22} & M_{23} \\ M_{31} & M_{32} & M_{33} \end{pmatrix},$$

where

$$\begin{aligned}
M_{11} &= -(r_b + \mu_b), \\
M_{12} &= \frac{t_2(1-\upsilon\psi)\beta_{sb}S_B^*}{t_2(1-\upsilon\psi)+\mu_b}, \\
M_{13} &= 0, \\
M_{21} &= 0, \\
M_{22} &= -\mu_s + \frac{\beta_{hs}\beta_{sh}S_H^*S_S^*}{t_1(1-\kappa\tau)+\mu_h} + \frac{\beta_{bs}\beta_{sb}S_B^*S_S^*}{t_2(1-\upsilon\psi)+\mu_b}, \\
M_{23} &= \beta_{cs}S_S^*, \\
M_{31} &= 0, \\
M_{32} &= \varepsilon_s p_s(1-cq), \\
M_{33} &= -\mu_c.
\end{aligned}$$

$D - CA^{-1}B$ is a stable Metzler matrix if and only if

$$\begin{aligned}\Gamma \;:=\;& \mu_c\beta_{hs}\beta_{sh}(r_b+\mu_b)(t_2(1-\upsilon\psi)+\mu_b)S_H^*S_S^* \\ & +\mu_c\beta_{bs}\beta_{sb}(r_b+\mu_b)(t_1(1-\kappa\tau)+\mu_h)S_B^*S_S^* \\ & -\mu_s\mu_c(r_b+\mu_b)(t_1(1-\kappa\tau)+\mu_h)(t_2(1-\upsilon\psi)+\mu_b) \\ & -\beta_{cs}\varepsilon_s p_s(1-cq)(r_b+\mu_b)(t_1(1-\kappa\tau)+\mu_h)(t_2(1-\upsilon\psi)+\mu_b)S_S^* > 0.\end{aligned}$$

The endemic equilibrium point of the limiting system is obtained by equating the equations of system (4.20) to zero. Thus we have

$$\begin{aligned}
\beta_{sh}S_H^*I_S^* &= (t_1(1-\kappa\tau)+\mu_h)I_H^*,\\
(r_h+\mu_h)T_H^* &= t_1(1-\kappa\tau)I_H^*,\\
\beta_{sb}S_B^*I_S^* &= (t_2(1-\upsilon\psi)+\mu_b)I_B^*,\\
(r_b+\mu_b)T_B^* &= t_2(1-\upsilon\psi)I_B^*,\\
(\beta_{cs}C_E^*+\beta_{hs}I_H^*+\beta_{bs}I_B^*)S_S^* &= \mu_sI_S^*,\\
\mu_cC_E^* &= \varepsilon_sp_s(1-cq)I_S^*.
\end{aligned} \tag{4.27}$$

Hence,

$$\begin{aligned}
\Gamma &= \mu_c(r_b+\mu_b)S_S^*\Big[\beta_{hs}\beta_{sh}(t_2(1-\upsilon\psi)+\mu_b)S_H^*+\beta_{bs}\beta_{sb}(t_1(1-\kappa\tau)+\mu_h)S_B^*\Big]\\
&- (r_b+\mu_b)(t_1(1-\kappa\tau)+\mu_h)(t_2(1-\upsilon\psi)+\mu_b)S_S^*\Big(\mu_c\mu_s+\beta_{cs}\varepsilon_sp_s(1-cq)\Big),\\
&= (r_b+\mu_b)S_S^*\Big[\mu_c\beta_{hs}\beta_{sh}(t_2(1-\upsilon\psi)+\mu_b)S_H^*+\mu_c\beta_{bs}\beta_{sb}(t_1(1-\kappa\tau)+\mu_h)S_B^*\\
&- (t_1(1-\kappa\tau)+\mu_h)(t_2(1-\upsilon\psi)+\mu_b)(\mu_c\mu_s+\beta_{cs}\varepsilon_sp_s(1-cq))\Big],\\
&> (r_b+\mu_b)S_S^*\Big[\mu_c\beta_{hs}\beta_{sh}(t_2(1-\upsilon\psi)+\mu_b)S_H^*+\mu_c\beta_{bs}\beta_{sb}(t_1(1-\kappa\tau)+\mu_h)S_B^*\Big],\\
&= (r_b+\mu_b)\frac{\mu_c\mu_sI_S^*}{A_1}\Big[\mu_c\beta_{hs}\beta_{sh}(t_2(1-\upsilon\psi)+\mu_b)S_H^*+\mu_c\beta_{bs}\beta_{sb}(t_1(1-\kappa\tau)+\mu_h)S_B^*\Big],\\
&> 0,
\end{aligned}$$

where

$$A_1=\beta_{cs}\varepsilon_sp_s(1-cq)I_S^*+\mu_c\beta_{hs}I_H^*+\mu_c\beta_{bs}I_B^*.$$

Thus $J(E^*)$ is a stable Metzler matrix and there exists a unique locally asymptotically stable endemic equilibrium.

4.3.7 Global Stability of Endemic Equilibrium E^*

We prove the global stability of E^* using the Lyapunov function approach described in Pedro [73] and McCluskey [60]. Let

$$\begin{aligned} R &= \Big(S_H - S_H^* - S_H^* \ln \frac{S_H}{S_H^*}\Big) + n_1\Big(I_H - I_H^* - I_H^* \ln \frac{I_H}{I_H^*}\Big) + n_2\Big(T_H - T_H^* - T_H^* \ln \frac{T_H}{T_H^*}\Big) \\ &+\Big(S_B - S_B^* - S_B^* \ln \frac{S_B}{S_B^*}\Big) + n_3\Big(I_B - I_B^* - I_B^* \ln \frac{I_B}{I_B^*}\Big) + n_4\Big(T_B - T_B^* - T_B^* \ln \frac{T_B}{T_B^*}\Big) \\ &+\Big(S_S - S_S^* - S_S^* \ln \frac{S_S}{S_S^*}\Big) + n_5\Big(I_S - I_S^* - I_S^* \ln \frac{I_S}{I_S^*}\Big) + n_6\Big(C_E - C_E^* - C_E^* \ln \frac{C_E}{C_E^*}\Big), \end{aligned} \tag{4.28}$$

where the real numbers $n_1, n_2, n_3, n_4, n_5, n_6 > 0$.

Differentiating R with respect to time t, we obtain

$$
\begin{aligned}
R' &= \left(1-\frac{S_H^*}{S_H}\right)S_H' + n_1\left(1-\frac{I_H^*}{I_H}\right)I_H' + n_2\left(1-\frac{T_H^*}{T_H}\right)T_H' + \left(1-\frac{S_B^*}{S_B}\right)S_B' \\
&+ n_3\left(1-\frac{I_B^*}{I_B}\right)I_B' + n_4\left(1-\frac{T_B^*}{T_B}\right)T_B' + \left(1-\frac{S_S^*}{S_S}\right)S_S' + n_5\left(1-\frac{I_S^*}{I_S}\right)I_S' \\
&+ n_6\left(1-\frac{C_E^*}{C_E}\right)C_E', \\
&= \left(1-\frac{S_H^*}{S_H}\right)\left[\Pi_h - \beta_{sh}S_H I_S + r_h T_H - \mu_h S_H\right] \\
&+ n_1\left(1-\frac{I_H^*}{I_H}\right)\left[\beta_{sh}S_H I_S - (t_1(1-\kappa\tau)+\mu_h+d_h)I_H\right] \\
&+ n_2\left(1-\frac{T_H^*}{T_H}\right)\left[t_1(1-\kappa\tau)I_H - (r_h+\mu_h)T_H\right] \\
&+ \left(1-\frac{S_B^*}{S_B}\right)\left[\Pi_b - \beta_{sb}S_B I_S + r_b T_B - \mu_b S_B\right] \\
&+ n_3\left(1-\frac{I_B^*}{I_B}\right)\left[\beta_{sb}S_B I_S - (t_2(1-\upsilon\psi)+\mu_b+d_b)I_B\right] \\
&+ n_4\left(1-\frac{T_B^*}{T_B}\right)\left[t_2(1-\upsilon\psi)I_B - (r_b+\mu_b)T_B\right] \\
&+ \left(1-\frac{S_S^*}{S_S}\right)\left[\Pi_s - (\beta_{cs}C_E + \beta_{hs}I_H + \beta_{bs}I_B)S_S - \mu_s S_S\right] \\
&+ n_5\left(1-\frac{I_S^*}{I_S}\right)\left[(\beta_{cs}C_E + \beta_{hs}I_H + \beta_{bs}I_B)S_S - \mu_s I_S\right] \\
&+ n_6\left(1-\frac{C_E^*}{C_E}\right)\left[\varepsilon_s p_s(1-cq)I_S - \mu_c C_E\right].
\end{aligned}
\tag{4.29}
$$

Equating each of the equations in system (4.1) to zero, let

$\Pi_h = \beta_{sh}S_H^* I_S^* - r_h T_H^* + \mu_h S_H^*,\ (t_1(1-\kappa\tau)+\mu_h+d_h) = \dfrac{\beta_{sh}S_H^* I_S^*}{I_H^*},$

$r_h + \mu_h = \dfrac{t_1(1-\kappa\tau)I_H^*}{T_H^*},\ \Pi_b = \beta_{sb}S_B^* I_S^* - r_b T_B^* + \mu_b S_B^*,$

$(t_2(1-\upsilon\psi)+\mu_b+d_b) = \dfrac{\beta_{sb}S_B^* I_S^*}{I_B^*},\ r_b+\mu_b = \dfrac{t_2(1-\upsilon\psi)I_B^*}{T_B^*},$

$\Pi_s = (\beta_{cs}C_E^* + \beta_{hs}I_H^* + \beta_{bs}I_B^*)S_S^* + \mu_s S_S^*,\ \mu_s = \dfrac{(\beta_{cs}C_E^* + \beta_{hs}I_H^* + \beta_{bs}I_B^*)S_S^*}{I_S^*},$

$\mu_c = \dfrac{\varepsilon_s p_s(1-cq)I_S^*}{C_E^*},$

which upon substituting into (4.29), we obtain the following:

$$\begin{aligned}
\frac{dR}{dt} &= -\mu_h S_H\left(1-\frac{S_H^*}{S_H}\right)^2+\beta_{sh}S_H^*I_H^*\left(1-\frac{S_H^*}{S_H}\right)\left(1-\frac{S_HI_S}{S_H^*I_S^*}\right)\\
&-r_hT_H^*\left(1-\frac{S_H^*}{S_H}\right)\left(1-\frac{T_H}{T_H^*}\right)-n_1\beta_{sh}S_H^*I_S^*\left(1-\frac{I_H^*}{I_H}\right)\left(\frac{I_H}{I_H^*}-\frac{S_HI_S}{S_H^*I_S^*}\right)\\
&-n_2t_1(1-\kappa\tau)I_H^*\left(1-\frac{T_H^*}{T_H}\right)\left(\frac{T_H}{T_H^*}-\frac{I_H}{I_H^*}\right)-\mu_bS_B\left(1-\frac{S_B^*}{S_B}\right)^2\\
&+\beta_{sb}S_B^*I_S^*\left(1-\frac{S_B^*}{S_B}\right)\left(1-\frac{S_BI_S}{S_B^*I_S^*}\right)-n_3\beta_{sb}S_B^*I_S^*\left(1-\frac{I_B^*}{I_B}\right)\left(\frac{I_B}{I_B^*}-\frac{S_BI_S}{S_B^*I_S^*}\right)\\
&-n_4t_2(1-\upsilon\psi)I_B^*\left(1-\frac{T_B^*}{T_B}\right)\left(\frac{T_B}{T_B^*}-\frac{I_B}{I_B^*}\right)-\mu_sS_S\left(1-\frac{S_S^*}{S_S}\right)^2\\
&+\beta_{cs}C_E^*S_S^*\left(1-\frac{S_S^*}{S_S}\right)\left(1-\frac{C_ES_S}{C_E^*S_S^*}\right)+\beta_{hs}I_H^*S_S^*\left(1-\frac{S_S^*}{S_S}\right)\left(1-\frac{I_HS_S}{I_H^*S_S^*}\right)\\
&+\beta_{bs}I_B^*S_S^*\left(1-\frac{S_S^*}{S_S}\right)\left(1-\frac{I_BS_S}{I_B^*S_S^*}\right)-n_5\beta_{cs}C_E^*S_S^*\left(1-\frac{I_S^*}{I_S}\right)\left(\frac{I_S}{I_S^*}-\frac{C_ES_S}{C_E^*S_S^*}\right)\\
&-n_5\beta_{hs}I_H^*S_S^*\left(1-\frac{I_S^*}{I_S}\right)\left(\frac{I_S}{I_S^*}-\frac{I_HS_S}{I_H^*S_S^*}\right)-n_5\beta_{bs}I_B^*S_S^*\left(1-\frac{I_S^*}{I_S}\right)\left(\frac{I_S}{I_S^*}-\frac{I_BS_S}{I_B^*S_S^*}\right)\\
&-n_6\varepsilon_sp_s(1-cq)I_S^*\left(1-\frac{C_E^*}{C_E}\right)\left(\frac{C_E}{C_E^*}-\frac{I_S}{I_S^*}\right)-r_bT_B^*\left(1-\frac{S_B^*}{S_B}\right)\left(1-\frac{T_B}{T_B^*}\right).
\end{aligned}\tag{4.30}$$

This can be rewritten in the form

$$\begin{aligned}
\frac{dR}{dt} &= -\mu_h S_H\left(1-\frac{S_H^*}{S_H}\right)^2-\mu_b S_B\left(1-\frac{S_B^*}{S_B}\right)^2-\mu_s S_S\left(1-\frac{S_S^*}{S_S}\right)^2\\
&\quad+\beta_{sh}S_H^*I_H^*\left[1-\frac{S_HI_S}{S_H^*I_S^*}-\frac{S_H^*}{S_H}+\frac{I_S}{I_S^*}\right]-r_hT_H^*\left[1-\frac{T_H}{T_H^*}-\frac{S_H^*}{S_H}+\frac{S_H^*T_H}{S_HT_H^*}\right]\\
&\quad-n_1\beta_{sh}S_H^*I_S^*\left[\frac{I_H}{I_H^*}-\frac{S_HI_S}{S_H^*I_S^*}-1+\frac{I_H^*S_HI_S}{I_HS_H^*I_S^*}\right]\\
&\quad-n_2t_1(1-\kappa\tau)I_H^*\left[\frac{T_H}{T_H^*}-\frac{I_H}{I_H^*}-1+\frac{T_H^*I_H}{T_HI_H^*}\right]\\
&\quad+\beta_{sb}S_B^*I_S^*\left[1-\frac{S_BI_S}{S_B^*I_S^*}-\frac{S_B^*}{S_B}+\frac{I_S}{I_S^*}\right]-r_bT_B^*\left[1-\frac{T_B}{T_B^*}-\frac{S_B^*}{S_B}+\frac{S_B^*T_B}{S_BT_B^*}\right]\\
&\quad-n_3\beta_{sb}S_B^*I_S^*\left[\frac{I_B}{I_B^*}-\frac{S_BI_S}{S_B^*I_S^*}-1+\frac{I_B^*S_BI_S}{I_BS_B^*I_S^*}\right]\\
&\quad-n_4t_2(1-\upsilon\psi)I_B^*\left[\frac{T_B}{T_B^*}-\frac{I_B}{I_B^*}-1+\frac{T_B^*I_B}{T_BI_B^*}\right]\\
&\quad+\beta_{cs}C_E^*S_S^*\left[1-\frac{C_ES_S}{C_E^*S_S^*}-\frac{S_S^*}{S_S}+\frac{C_E}{C_E^*}\right]\\
&\quad+\beta_{hs}I_H^*S_S^*\left[1-\frac{I_HS_S}{I_H^*S_S^*}-\frac{S_S^*}{S_S}+\frac{I_H}{I_H^*}\right]\\
&\quad+\beta_{bs}I_B^*S_S^*\left[1-\frac{I_BS_S}{I_B^*S_S^*}-\frac{S_S^*}{S_S}+\frac{I_B}{I_B^*}\right]\\
&\quad-n_5\beta_{cs}C_E^*S_S^*\left[\frac{I_S}{I_S^*}-\frac{C_ES_S}{C_E^*S_S^*}-1+\frac{I_S^*C_ES_S}{I_SC_E^*S_S^*}\right]\\
&\quad-n_5\beta_{hs}I_H^*S_S^*\left[\frac{I_S}{I_S^*}-\frac{I_HS_S}{I_H^*S_S^*}-1+\frac{I_S^*I_HS_S}{I_SI_H^*S_S^*}\right]\\
&\quad-n_5\beta_{bs}I_B^*S_S^*\left[\frac{I_S}{I_S^*}-\frac{I_BS_S}{I_B^*S_S^*}-1+\frac{I_S^*I_BS_S}{I_SI_B^*S_S^*}\right]\\
&\quad-n_6\varepsilon_sp_s(1-cq)I_S^*\left[\frac{C_E}{C_E^*}-\frac{I_S}{I_S^*}-1+\frac{C_E^*I_S}{C_EI_S^*}\right],\\
&= -\mu_h S_H\left(1-\frac{S_H^*}{S_H}\right)^2-\mu_b S_B\left(1-\frac{S_B^*}{S_B}\right)^2-\mu_s S_S\left(1-\frac{S_S^*}{S_S}\right)^2\\
&\quad+\Upsilon(S_H,I_H,T_H,S_B,I_B,T_B,S_S,I_S,C_E).
\end{aligned}\tag{4.31}$$

Introducing new variables $x_1 = \frac{S_H}{S_H^*},\ x_2 = \frac{I_H}{I_H^*},\ x_3 = \frac{T_H}{T_H^*},\ x_4 = \frac{S_B}{S_B^*},$
$x_5 = \frac{I_B}{I_B^*},\ x_6 = \frac{T_B}{T_B^*},\ x_7 = \frac{S_S}{S_S^*},\ x_8 = \frac{I_S}{I_S^*},\ x_9 = \frac{C_E}{C_E^*}$ in Υ and simplifying we have

$$
\begin{aligned}
\Upsilon \;=\; & \beta_{sh}S_H^*I_H^* - r_hT_H^* + n_1\beta_{sh}S_H^*I_S^* + n_2t_1(1-\kappa\tau)I_H^* + \beta_{sb}S_B * I_S^* - r_bT_B^* \\
& + n_3\beta_{sb}S_B^*I_S^* + n_4t_2(1-\upsilon\psi)I_B^* + \beta_{cs}C_E^*S_S^* + \beta_{hs}I_H^*S_S^* + \beta_{bs}I_B^*S_S^* \\
& + n_5\beta_{cs}C_E^*S_S^* + n_5\beta_{hs}I_H^*S_S^* + n_5\beta_{bs}I_B^*S_S^* + n_6\varepsilon_s p_s(1-cq)I_S^* \\
& + x_2(\beta_{hs}I_H^*S_S^* - n_2t_1(1-\kappa\tau)I_H^* - n_1\beta_{sh}S_H^*I_S^*) \\
& + x_3(r_hT_H^* - n_2t_1(1-\kappa\tau)I_H^*) + x_6(r_bT_B^* - n_4t_2(1-\upsilon\psi)I_B^*) \\
& + x_5(\beta_{bs}I_B^*S_S^* + n_4t_2(1-\upsilon\psi)I_B^* - n_3\beta_{sb}S_B^*I_S^*) \\
& + x_8(\beta_{sh}S_H^*I_H^* + \beta_{sb}S_B^*I_S^* + n_6\varepsilon_s p_s(1-cq)I_S^* - n_5\beta_{cs}C_E^*S_S^*) \\
& + x_8(-n_5\beta_{bs}I_B^*S_S^* - n_5\beta_{hs}I_H^*S_S^*) \\
& + x_9(\beta_{cs}C_E^*S_S^* - n_6\varepsilon_s p_s(1-cq)I_S^*) + x_1x_8(n_1\beta_{sh}S_H^*I_S^* - \beta_{sh}S_H^*I_H^*) \\
& + x_4x_8(n_3\beta_{sb}S_B^*I_S^* - \beta_{sb}S_B^*I_S^*) + x_7x_9(n_5\beta_{cs}C_E^*S_S^* - \beta_{cs}C_E^*S_S^*) \\
& + x_2x_7(n_5\beta_{hs}I_H^*S_S^* - \beta_{hs}I_H^*S_S^*) + x_5x_7(n_5\beta_{bs}I_B^*S_S^* - \beta_{bs}I_B^*S_S^*) \\
& \frac{1}{x_1}(r_hT_H^* - \beta_{sh}S_H^*I_H^*) + \frac{1}{x_4}(r_bT_B^* - \beta_{sb}S_B^*I_S^*) - \Big(\frac{x_3}{x_1}\Big)r_hT_H^* \\
& + \frac{1}{x_7}\Big(-\beta_{cs}C_E^*S_S^* - \beta_{hs}I_H^*S_S^* - \beta_{bs}I_B^*S_S^*\Big) - n_1\beta_{sh}S_H^*I_S^*\Big(\frac{x_1x_8}{x_2}\Big) \\
& - n_2t_1(1-\kappa\tau)I_H^*\Big(\frac{x_2}{x_3}\Big) - n_3\beta_{sb}S_B^*I_S^*\Big(\frac{x_4x_8}{x_5}\Big) - \Big(\frac{x_6}{x_4}\Big)r_bT_B^* \\
& - n_4t_2(1-\upsilon\psi)I_B^*\Big(\frac{x_5}{x_6}\Big) - n_5\beta_{cs}C_E^*S_S^*\Big(\frac{x_7x_9}{x_8}\Big) - n_5\beta_{hs}I_H^*S_S^*\Big(\frac{x_2x_7}{x_8}\Big) \\
& - n_5\beta_{bs}I_B^*S_S^*\Big(\frac{x_5x_7}{x_8}\Big) - n_6\varepsilon_s p_s(1-cq)I_S^*\Big(\frac{x_8}{x_9}\Big).
\end{aligned}
\tag{4.32}
$$

We then determine $n_1, n_2, n_3, n_4, n_5, n_6$ the coefficients of
$x_3, x_6, x_9, x_1x_8, x_4x_8, x_7x_9, x_2x_7$ and x_5x_7 by solving the following set of non-linear equations:

$$\begin{aligned}
r_hT_H^* - n_2t_1(1-\kappa\tau)I_H^* &= 0,\\
r_bT_B^* - n_4t_2(1-\upsilon\psi)I_B^* &= 0,\\
\beta_{cs}C_E^*S_S^* - n_6\varepsilon_s p_s(1-cq)I_S^* &= 0,\\
n_1\beta_{sh}S_H^*I_S^* - \beta_{sh}S_H^*I_H^* &= 0,\\
n_3\beta_{sb}S_B^*I_S^* - \beta_{sb}S_B^*I_S^* &= 0,\\
n_5\beta_{hs}I_H^*S_S^* - \beta_{hs}I_H^*S_S^* &= 0,\\
n_5\beta_{cs}C_E^*S_S^* - \beta_{cs}C_E^*S_S^* &= 0,\\
n_5\beta_{bs}I_B^*S_S^* - \beta_{bs}I_B^*S_S^* &= 0.
\end{aligned} \tag{4.33}$$

The solution to the system (4.33) is given by

$$n_1 = \frac{\beta_{sh}S_H^*I_H^*}{\beta_{sh}S_H^*I_S^*},\ n_2 = \frac{r_hT_H^*}{t_1(1-\kappa\tau)I_H^*},\ n_3 = 1,\ n_4 = \frac{r_bT_B^*}{t_2(1-\upsilon\psi)I_B^*},\ n_5 = 1,\ n_6 = \frac{\beta_{cs}C_E^*S_S^*}{\varepsilon_s p_s(1-cq)I_S^*}.$$

Substituting into (4.32), $\Upsilon(x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8, x_9)$ becomes

$$\begin{aligned}
\Upsilon &= \beta_{sb}S_B^*I_S^*\Big(2 - \frac{1}{x_4} - \frac{x_4x_8}{x_5}\Big) + \beta_{hs}I_H^*S_S^*\Big(2 - \frac{1}{x_7} - \frac{x_7x_2}{x_8}\Big)\\
&+\beta_{bs}I_B^*S_S^*\Big(2 - \frac{1}{x_7} - \frac{x_7x_5}{x_8}\Big) + \beta_{cs}C_E^*S_S^*\Big(2 - \frac{1}{x_7} - \frac{x_7x_9}{x_8}\Big)\\
&+\beta_{sh}S_H^*I_S^*\Big(2 - \frac{1}{x_1} - \frac{x_1x_8}{x_2}\Big) + n_1^*\beta_{cs}C_E^*S_S^*\Big(1 - \frac{x_8}{x_9}\Big)\\
&+n_2^*\beta_{bs}I_B^*S_S^*\Big(1 - \frac{x_8}{x_5}\Big) + n_3^*\beta_{hs}I_H^*S_S^*\Big(1 - \frac{x_8}{x_2}\Big)\\
&+n_4^*\beta_{sb}S_B^*I_S^*\left(1 - \frac{x_5}{x_8}\right) + n_5^*\beta_{sh}S_H^*I_S^*\left(1 - \frac{x_2}{x_8}\right)\\
&n_6^*r_hT_H^*\Big(1 - \frac{1}{x_3} - \frac{x_3}{x_1x_2} + \frac{1}{x_1x_2}\Big) + n_7^*r_bT_B^*\Big(1 - \frac{1}{x_6} - \frac{x_6}{x_4x_5} + \frac{1}{x_4x_5}\Big).
\end{aligned} \tag{4.34}$$

Let $n_1^* = n_2^* = n_3^* = n_4^* = n_5^* = 1$, equation (4.34) reduces to

$$\begin{aligned}\Upsilon &= \beta_{sb}S_B^*I_S^*\Big(3-\frac{1}{x_4}-\frac{x_5}{x_8}-\frac{x_4x_8}{x_5}\Big)+\beta_{hs}I_H^*S_S^*\Big(3-\frac{1}{x_7}-\frac{x_8}{x_2}-\frac{x_7x_2}{x_8}\Big)\\ &+\beta_{bs}I_B^*S_S^*\Big(3-\frac{1}{x_7}-\frac{x_8}{x_5}-\frac{x_7x_5}{x_8}\Big)+\beta_{cs}C_E^*S_S^*\Big(3-\frac{1}{x_7}-\frac{x_8}{x_9}-\frac{x_7x_9}{x_8}\Big)\\ &+\beta_{sh}S_H^*I_S^*\Big(3-\frac{1}{x_1}-\frac{x_2}{x_8}-\frac{x_1x_8}{x_2}\Big)+n_6^*r_hT_H^*\Big(1-\frac{1}{x_3}-\frac{x_3}{x_1x_2}+\frac{1}{x_1x_2}\Big)\\ &+n_7^*r_bT_B^*\Big(1-\frac{1}{x_6}-\frac{x_6}{x_4x_5}+\frac{1}{x_4x_5}\Big).\end{aligned} \tag{4.35}$$

However, by the geometric mean inequality we note that
$\Big(3-\frac{1}{x_4}-\frac{x_5}{x_8}-\frac{x_4x_8}{x_5}\Big)\leq 0,\ \Big(3-\frac{1}{x_7}-\frac{x_8}{x_5}-\frac{x_7x_5}{x_8}\Big)\leq 0,\ \Big(3-\frac{1}{x_7}-\frac{x_8}{x_9}-\frac{x_7x_9}{x_8}\Big)\leq 0,$
$\Big(3-\frac{1}{x_1}-\frac{x_2}{x_8}-\frac{x_1x_8}{x_2}\Big)\leq 0,\ \Big(3-\frac{1}{x_7}-\frac{x_8}{x_2}-\frac{x_7x_2}{x_8}\Big)\leq 0.$
After some tedious algebraic manipulations, similar conclusions on the remaining terms can be drawn by replacing the constants n_6^* and n_7^*. This implies that

$$\begin{aligned}R' &= -\mu_hS_H\Big(1-\frac{S_H^*}{S_H}\Big)^2-\mu_bS_B\Big(1-\frac{S_B^*}{S_B}\Big)^2-\mu_sS_S\Big(1-\frac{S_S^*}{S_S}\Big)^2\\ &+\Upsilon(S_H,I_H,T_H,S_B,I_B,T_B,S_S,I_S,C_E)\leq 0.\end{aligned}$$

Also, $R'=0$ if and only if $S_H=S_H^*, I_H=I_H^*, T_H=T_H^*$,
$S_B=S_B^*, I_B=I_B^*, T_B=T_B^*, S_S=S_S^*, I_S=I_S^*, C_E=C_E^*$. Hence,
$R(S_H,I_H,T_H,S_B,I_B,T_B,S_S,I_S,C_E)$ satisfies the conditions for the Lyapunov's stability theorem.
Furthermore, the largest compact set in $\Big\{(S_H,I_H,T_H,S_B,I_B,T_B,S_S,I_S,C_E)\in\mathcal{D}: R'=0\Big\}$ is the singleton $\Big\{E^*\Big\}$, [51], thereby proving the result that the steady state $(S_H^*,I_H^*,T_H^*,S_B^*,I_B^*,T_B^*,S_S^*,I_S^*,C_E^*)$ is globally asymptotically stable in $\mathcal{D}$.

Since analytical results show that the model disease-free and endemic equilibria are globally asymptotically stable, this precludes the model to exhibit the phenomenon of backward bifurcation (that is the co-existence of a stable disease-free equilibrium with a stable endemic equilibrium), the public health implication of this epidemiological situation being that although necessary, having the basic reproduction number less than unity, it is not sufficient for disease elimination [66, 67]. For this reason, we do not carry out a bifurcation theory analysis.

4.4 Numerical Simulations

Numerical simulations of our proposed human-bovine schistosomiasis model with treatment and molluscicide are presented to support the theoretical analysis and results. Since, we have considered treatment for both humans and bovines and molluscicide as our control strategies, their effects will also be investigated by simulation using a set of parameter values given in Table (4.3). The units of all the model parameter values are per day. We initially set the population sizes as follows:

Table 4.3: Model Parameter Values

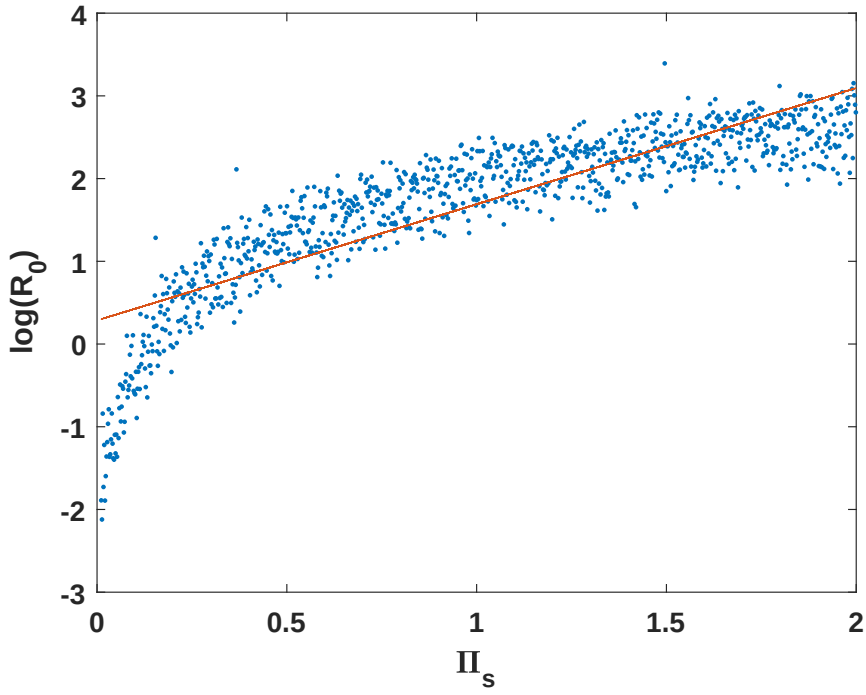
Parameter	**Value**	**Source**	**Parameter**	**Value**	**Source**
Π_h	0.3914	Estimate	Π_b	0.25	[25]
Π_s	0.45	[4]	r_h	0.2546	[25]
r_b	0.76	Estimate	β_{sh}	2.58×10^{-5}	Assumed
β_{sb}	0.000056	[25]	β_{hs}	3.12×10^{-13}	Assumed
β_{bs}	0.0000056	[25]	β_{cs}	0.615	[58]
t_1	0.03	[23]	t_2	0.25	[31]
μ_h	0.0000384	[31]	μ_b	0.35	[31]
μ_s	0.00569	[78]	μ_c	3	[23]
d_h	0.0039	[35]	d_b	0.46	[23]
ε_s	2.6	[58]	p_s	0.00232	[58]
κ	0.0075	[25]	τ	0.67	[18]
υ	0.35	Estimate	ψ	0.78	Assumed
c	0.56	Estimate	q	0.87	Assumed

$S_H = 8000,\ I_H = 50,\ T_H = 30,\ S_B = 74000,\ I_B = 10,\ T_B = 450, S_S = 92000,$ $I_S = 200,\ C_E = 7890$. First we perform sensitivity analysis on the model parameter values to investigate the relative importance of different factors that influence the transmission dynamics and control of the disease [76]. Mostly, we use the parameter values from published literature. However, there is no guarantee in their accuracy and absolute

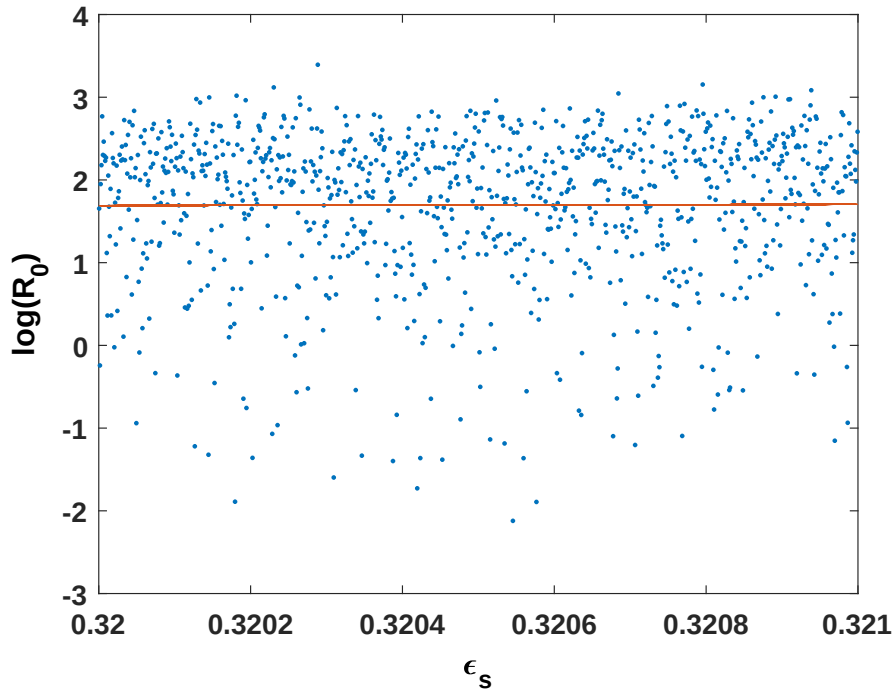
certainty. Because erroneous parameter estimation and uncertainty in the exact parameter values shroud them in uncertainty [5], identifying influential model parameters by conducting sampling and global sensitivity analysis to determine those parameters that have a substantial influence on the model output is important. We use the Latin hypercube sampling-partial rank correlation coefficient approach to characterize the statistical contribution of each parameter to the reproduction numbers [7, 40, 92] via MatLab software, and investigate the existence of the relationships between each of the parameters and their attack number with the aid of Sampling and sensitivity analyses tool SaSAT [40]. While correlation provides a measure of the strength of a linear association between an input and an output, the partial rank correlation coefficient (PRCC) is a robust sensitivity measure for non-linear but monotonic relationships, thus an efficient and reliable sampling-based sensitivity analysis method that provides a measure of monotonicity between parameters and model output after removing the linear effects of all parameters except the parameter of interest (so that little to no correlation exists between the inputs)[59]. We then evaluate the partial rank correlation coefficient (PRCC) of the parameters by performing 1000 simulations for every run. This is carried out in relation to the basic reproduction number, where scatter plots are constructed on a log 10 scale against each parameter [40].

The parameters having negative PRCCs reduce the epidemic whenever their numerical values are increased. On the other hand, those with positive PRCCs contribute to the spread of the disease once they are increased.

From Figure 4.2(a) and Figure 4.2(b), the model parameters Π_s and ε_s have positive PRCCs. That is, there is a strong correlation of the recruitment rate for snails, Π_s, and the schistosomiasis infection, which means that as more and more snails are reproduced, there is a high probability of contact between the pathogens and the snails (Figure 4.2(a)). This being the case, the large snail population will shed more cercariae, at an increased rate ε_s, within a specified time period, Figure 4.2(b). Despite the short life span of cercariae, of course many will die without contacting humans and bovines, but the chance is still high that those remaining, due to their large numbers, will still survive.



(a)



(b)

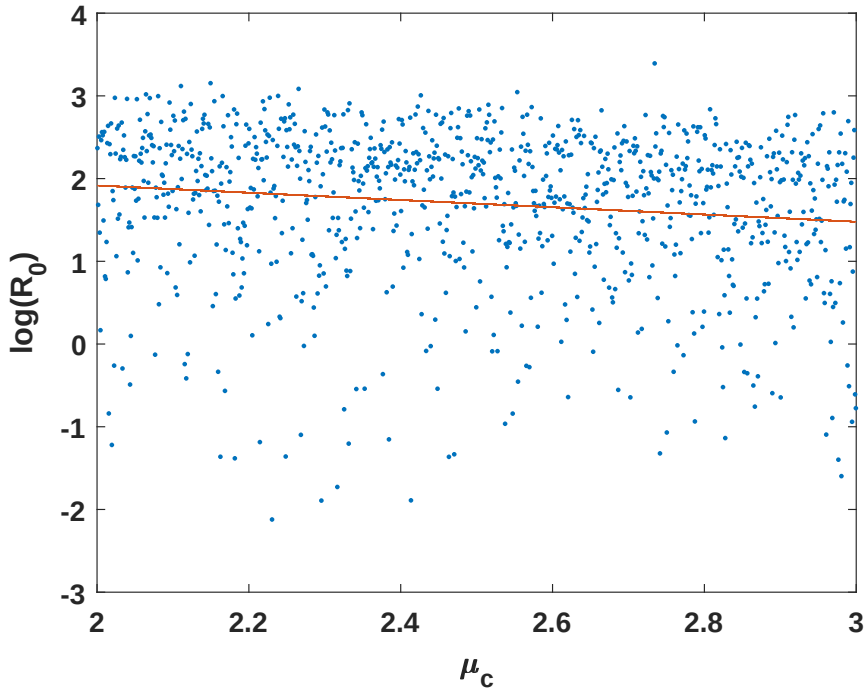
Figure 4.2: Scatter plots of parameters with positive PRCCs. In each case, the fitting line has a positive slope, 1.4045 and 14.7250 for Π_s and ε_s, respectively, an indication that there is a positive correlation between the basic reproduction number and the respective parameter.

On the other hand, $\mu_s,\ \mu_c,\ c$ and q display negative PRCCs. For illustration, we only display the graphs for μ_c and c in Figure (4.3). High mortality rates for miracidia and cercariae will likely reduce the basic reproduction number, R_0, thereby contributing to the potential containment of the disease (Figure 4.3(a)). A similar scenario occurs when the environment is molluscicided, since many snails will die leading to a reduced primary host population. As a result, this drastically reduces the pathogen population, thereby reducing the reproduction number as well (Figure 4.3(b)). Foremost, is the fact that the contaminated environment has been shown to play a crucial role in the dynamics of human-bovine schistosomiasis. This role is observed through a strong link that exists between the most sensitive parameters and the environment itself. As such, it is worthwhile to note that the strategies targeting the environment will be of great significance in controlling or eradicating the disease.

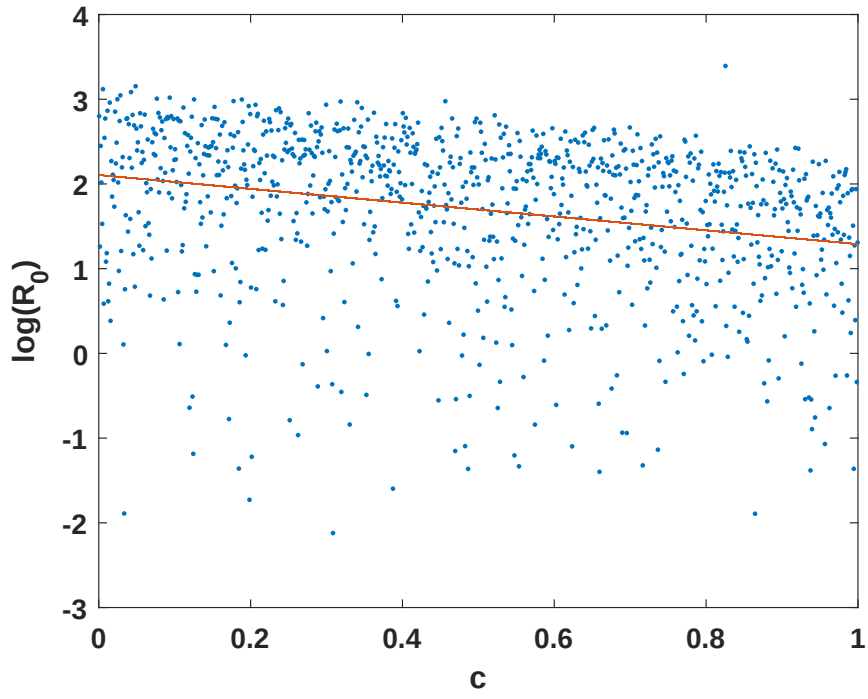
4.4.1 Convergence of Equilibrium Points

In Figure 4.4(a), it is shown that as the susceptible population increases, the infected humans decrease. This also happens in Figure 4.4(b), where an increase in the susceptible human population leads to a decrease in the treated individuals. The infected and treated human populations decrease to zero with different initial values. In both cases, we note that the population curves converge to some point which happens to be the disease-free equilibrium. After the convergence, we further observe the global stability of the steady state as described in section (4.3.3).

In the same way, Figure 4.5(a) and Figure 4.5(b) show the existence of the endemic equilibrium point. As the susceptible population and transmission rate from the contaminated environment to snails, β_{cs}, increase, we note that the basic reproduction number $R_0 = 2.2894 > 1$, which implies that the disease does not die out. The state variables also happen to converge to some steady state endemic equilibrium. This is observed in Figure 4.5(a) and Figure 4.5(b), as all the classes $S_H,\ I_H$ and T_H are positive, showing that the disease persists in the population. Irrespective of the starting initial values of the state variables, the respective solution curves tend to converge to a globally stable endemic equilibrium, which is in line with the endemic steady state



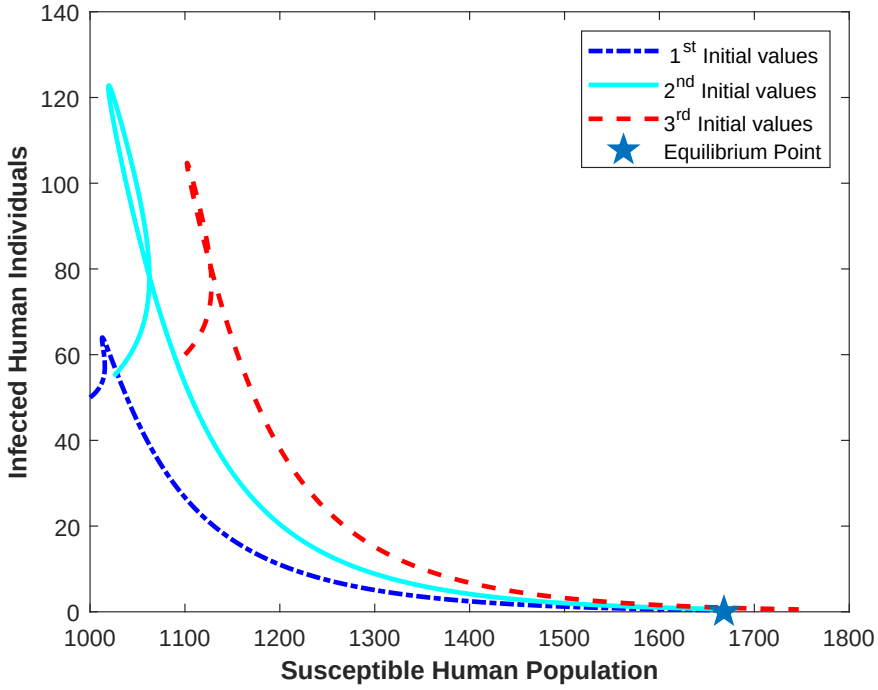
(a)



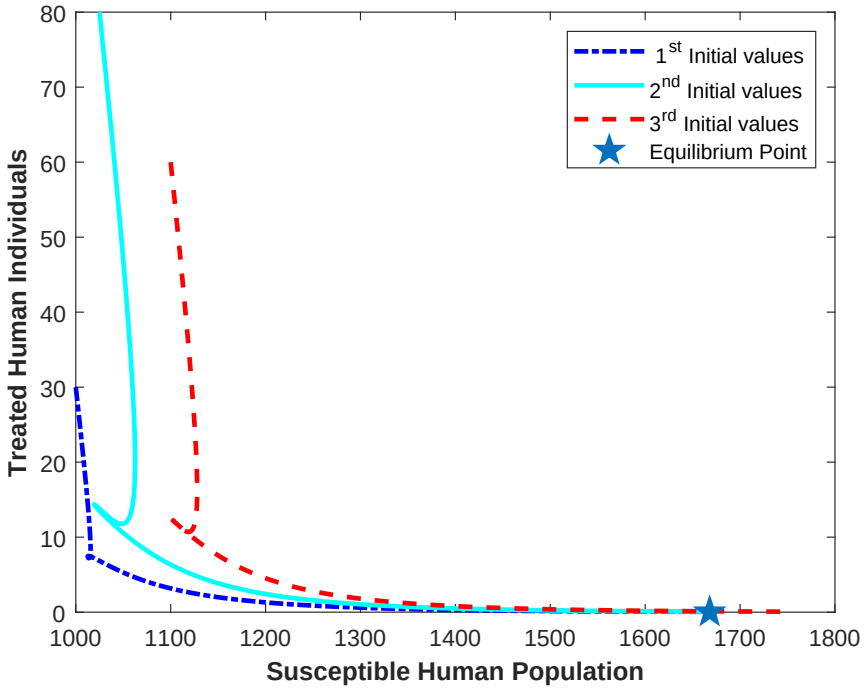
(b)

Figure 4.3: Scatter plots of parameters with negative PRCCs. In each case, the fitting line has a negative slope, -0.4384 and -0.8157 for μ_c and c, respectively, an indication that there is a negative correlation between the basic reproduction number and the parameter.

analysis described in Theorem (7) in section (4.3.6).

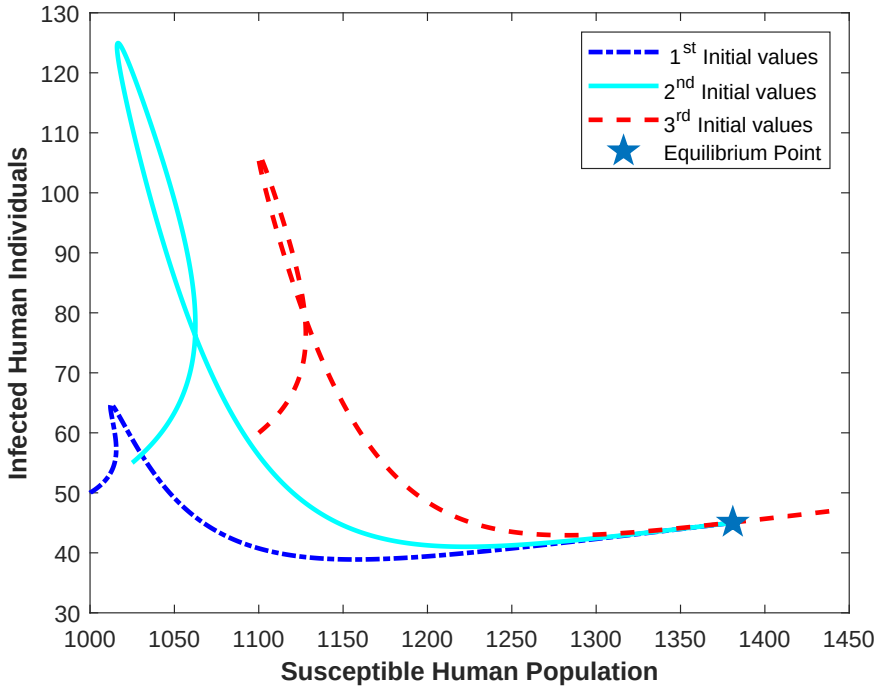


(a)

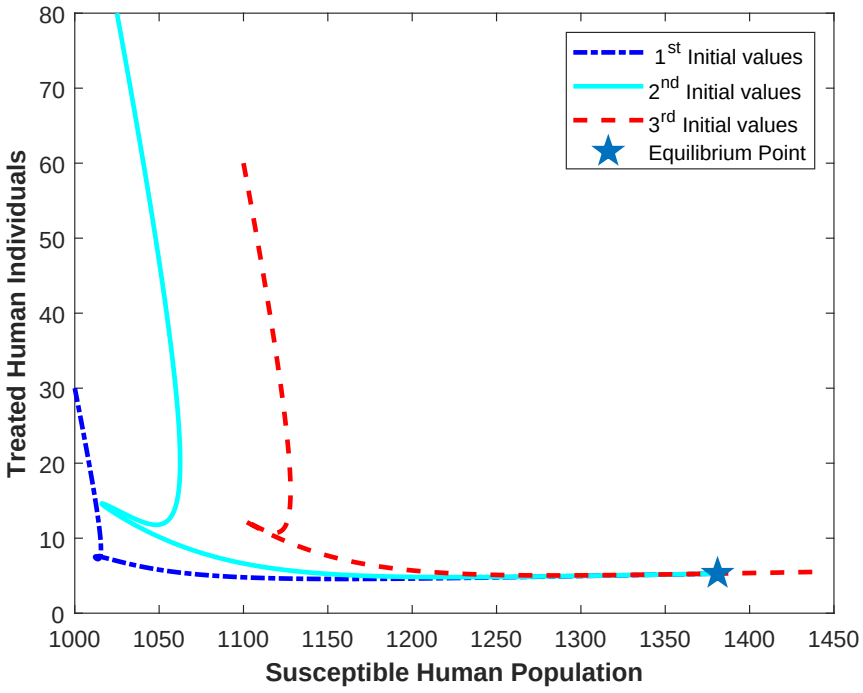


(b)

Figure 4.4: Phase plane portraits of (a) $S_H I_H-$plane and (b) $S_H T_H-$plane for $\beta_{cs} = 0.0615$ and varying initial conditions. The rest of the parameter values are given in Table (4.3). The basic reproduction number, $R_0 = 0.8989 < 1$.



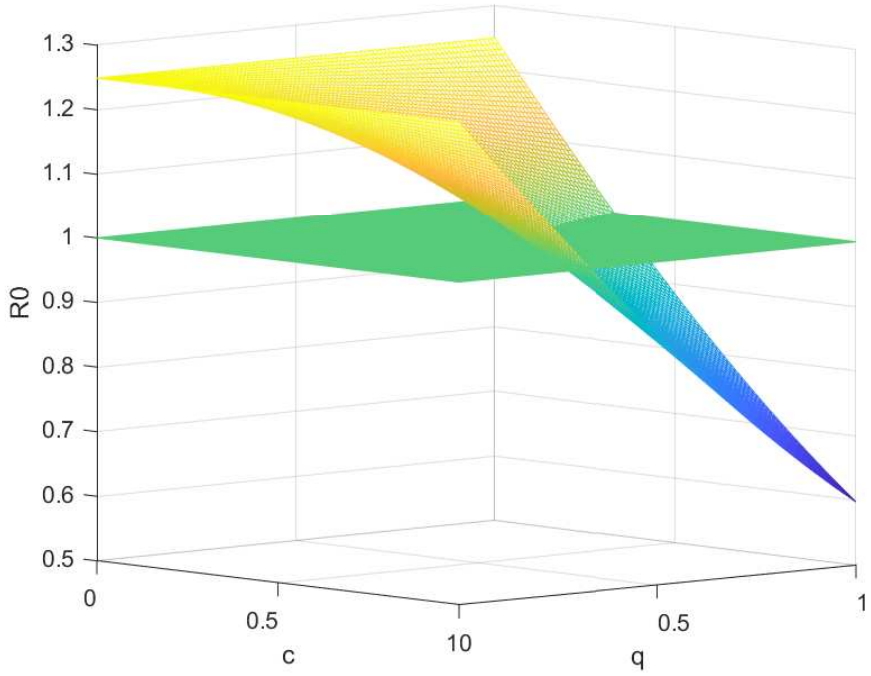
(a)



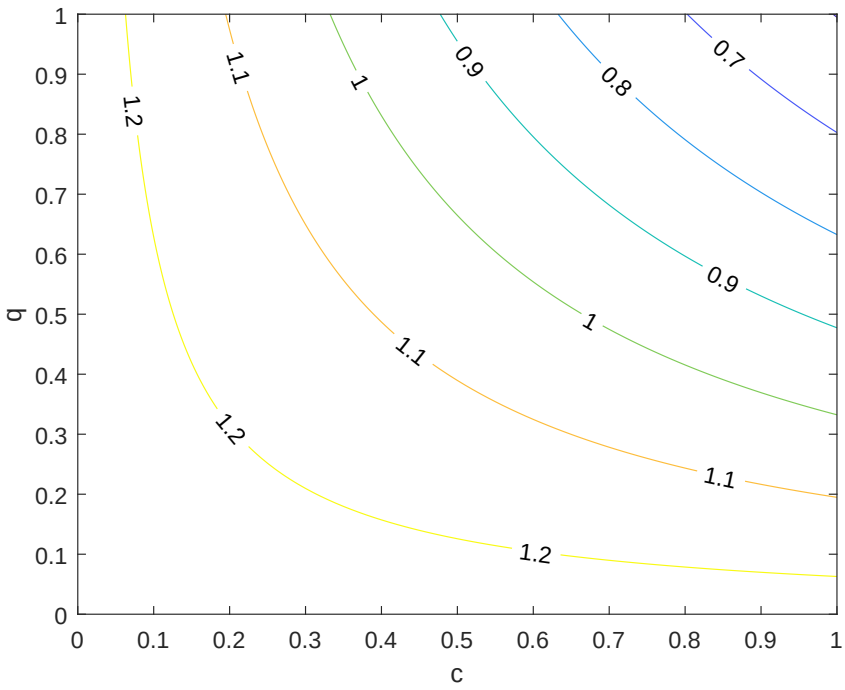
(b)

Figure 4.5: Phase plane portraits of (a) $S_H I_H-$plane and (b) $S_H T_H-$plane for $\beta_{cs} = 0.2615$ and varying initial conditions. The rest of the parameter values are given in Table (4.3). The basic reproduction number, $R_0 = 2.2894 > 1$.

4.4



(a)



(b)

Figure 4.6: Three-dimensional and contour plots of c and q against R_0. Other parameter values are fixed as shown in Table (4.3) while c and q vary.

As c and q both increase, the basic reproduction number decreases. This is clearly observed in the corresponding contour plot of Figure 4.6(b). The contours decrease in value far away to the right along the line $c = q$, an indication that both parameters are increasing while the basic reproduction number keeps decreasing. This is contrary

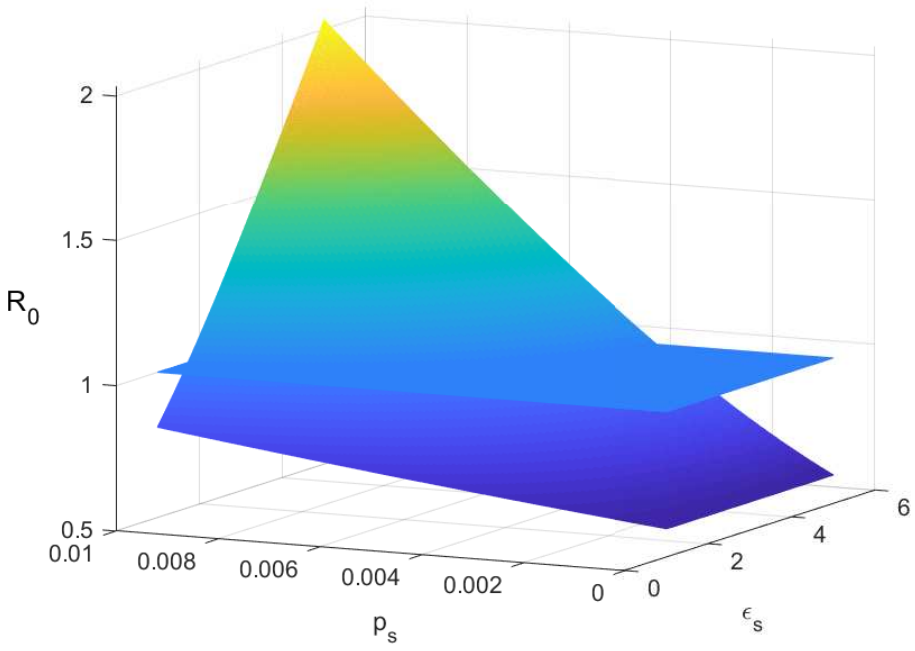
to the situation when c and q are becoming smaller and smaller, whereas R_0 is seen to be increasing. Furthermore, in the same Figure 4.6(a), we note the graph to be on both sides of the $R_0 = 1$ plane, implying that some values of c and q give $R_0 < 1$, when the disease will die out and $R_0 > 1$, when the disease will persist. This implies that molluscicide has a bigger impact regarding the control of schistosomiasis. The more the fraction of the contaminated environment is molluscicided, the more the snail population dies out. This decrease in the snail population then leads to a low survival rate p_s of cercariae and also little shedding of cercariae by the snail hosts. As such, the disease dies out. Furthermore, Figure (4.6) depicts a situation where molluscicide is effective in mitigating the cercariae population in the environment.

4.4.3 Effects of p_s and ε_s on R_0

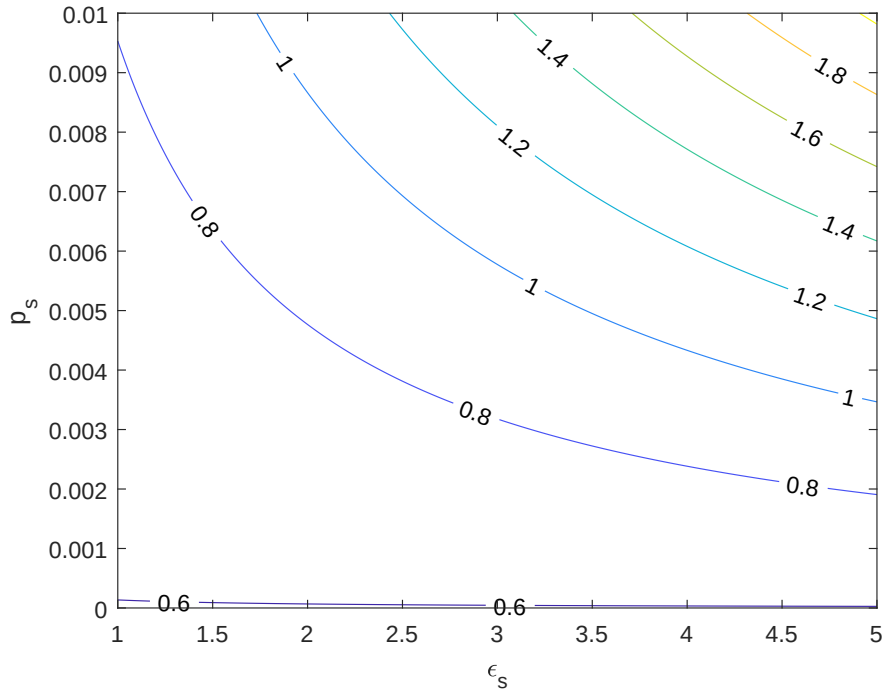
Figure 4.7(a) and Figure 4.7(b) show that an increase in ε_s and p_s, leads to an increase in the reproduction number. This increase in the reproduction number is mainly due to having too many snails in the contaminated environment. These snails in large numbers have the capability to shed many cercariae at rate ε_s. This can be controlled by mechanisms such as molluscicide as explained in Figure (4.6).

4.4.4 Effects of Π_s and β_{cs}

Like p_s and ε_s, the recruitment rate for snails Π_s, and the transmission rate from the contaminated environment to snails β_{cs}, in Figure 4.8(a) and Figure 4.8(b), tend to increase the reproduction number R_0, whenever they both increase. The reason behind the reproduction number increase is that as more and more snails are recruited into the contaminated environment, there is more room for the pathogens to find these primary snail hosts, thereby increasing the chances of transmission between the pathogens and the snails themselves. We also note from Figure (4.8) that the basic reproduction number decreases rapidly when both Π_s and β_{cs} become smaller.



(a)

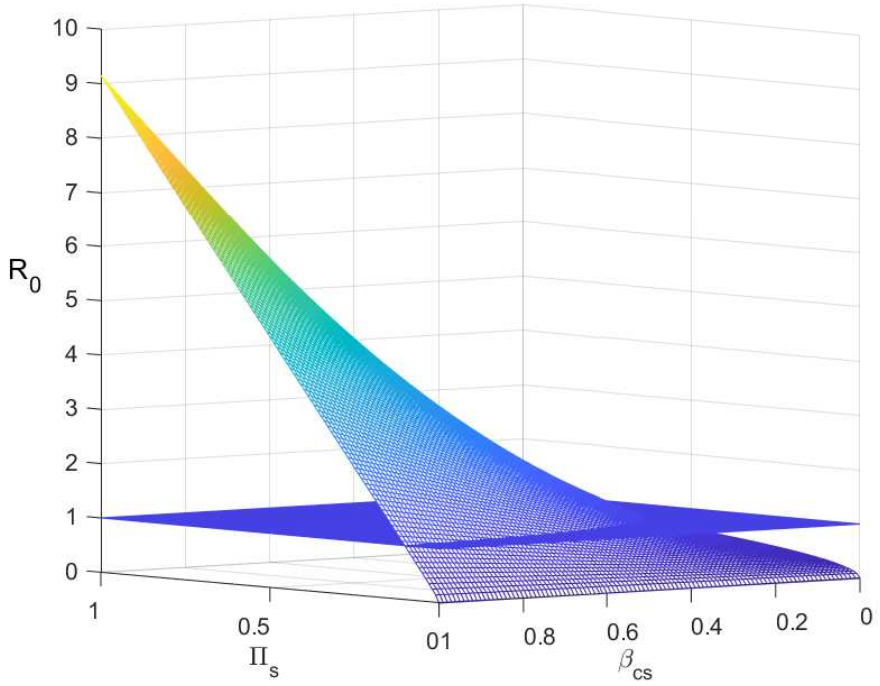


(b)

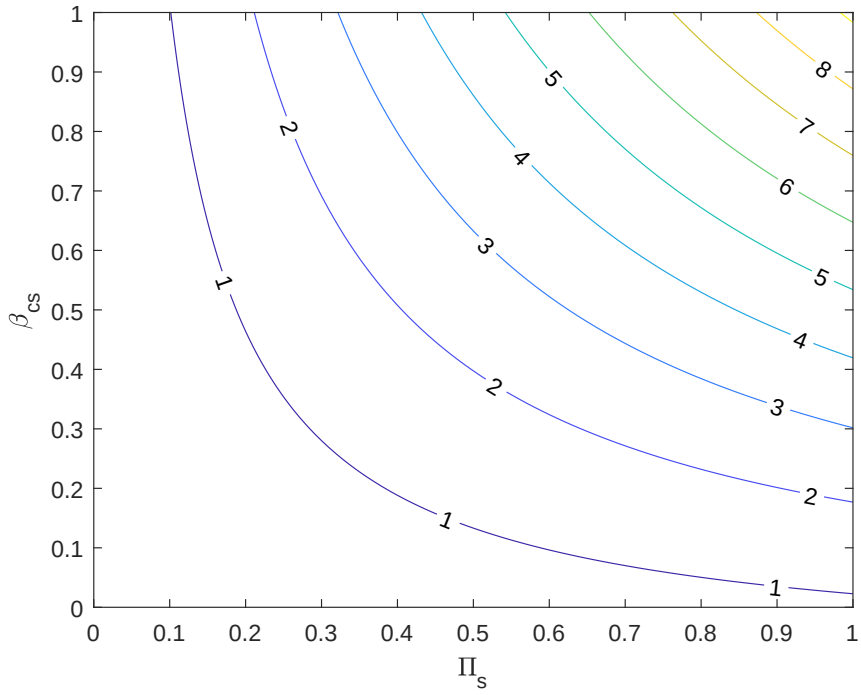
Figure 4.7: Plots showing the effect of ε_s and p_s on the basic reproduction number R_0, varying ε_s and p_s, while keeping other parameter values constant.

4.5 Optimal Control Analysis

In this section, we investigate the impact of implementing the intervention strategies while minimizing the total cost. Particularly, we look at the formulation of the optimal



(a)



(b)

Figure 4.8: Three-dimensional and contour plots for the recruitment rate for snails, Π_s, and transmission rate from contaminated environment and snails, β_{cs}, against the basic reproduction number R_0.

control model for schistosomiasis, taking into account treatment for humans and bovines and mollusciciding. In a study conducted by Molehin [64], it was stipulated that the

control of schistosomiasis has been centred mainly on the mass drug administration of praziquantel (PZQ), which is the only drug currently available for treatment. However, the prevalence and transmission of schistosomiasis has remained largely unchecked due to the fact that praziquantel is ineffective against juvenile schistosomes and does not prevent re-infection and the emergence of PZQ-resistant parasites. Furthermore, other control measures such as sanitation and hygiene programs had little to no impact which indicates severe inadequacy of such measures to interrupt the transmission. Hence, we assume the set of control variables

$$(u_1(t), u_2(t), u_3(t)),$$

where $u_1(t)$ represents the treatment of the infected humans, $u_2(t)$ the treatment of the infected bovines and lastly $u_3(t)$ denoting the molluscicide of snails in the contaminated environment, with $u_1,\ u_2$ and u_3 belonging to the interval $[0, T]$. We then examine an optimal control problem, whose objective cost function given by

$$\nabla = \{(u_1, u_2, u_3) : [0, T] \to \mathbb{R}^3 | u_i(t) \text{ is Lebesgue measurable on } \left[0, \nabla_i\right], i = 1, 2, 3\},$$

subject to the system (4.1) and suitable initial conditions. $\nabla_i,\ i = 1, 2, 3$ is represented as the upper bound of the control functions, where $(u_1, u_2, u_3) \in \mathbb{R}^3$ are between 0 and 1. The optimal system is then developed to meet the necessary conditions satisfying Pontryagin's Maximum Principle, which determines optimal control of the schistosomiasis infection. As such, we choose an optimal control u_1^*, u_2^*, u_3^* satisfying

$$\nabla(u_1^*, u_2^*, u_3^*) = \min \nabla(u_1, u_2, u_3),$$

where

$$\nabla = \{(u_1, u_2, u_3) | 0 \leq u_i \leq 1, i = 1, 2, 3\}.$$

Consequently, to minimize the number of schistosomiasis infected humans and bovines as well as the number of snails in the contaminated environment and the cost that will be incurred in the treatment and molluscicide process, we consider the objective optimal control function given by

$$\nabla(u_1, u_2, u_3) = \int_0^T (C_1 I_H + C_2 I_B + C_3 N_S + \frac{1}{2}(D_1 u_1^2 + D_2 u_2^2 + D_3 u_3^2))dt, \qquad (4.36)$$

subject to the system (4.1), where T is the final time, $C_1,\ C_2,$ and C_3 are positive constants denoting the weights that balance off the infected humans and bovines and the total snail population, respectively. D_1 and D_2 represent the positive weighting constants for treatment of humans and bovines, respectively, while D_3 denotes the positive weighting constant for molluscicide of snails in the contaminated environment. The objective function considers the whole population of snails since molluscicide could affect all of them. On the other hand, infected humans and bovines have been included because treatment is applied to these classes. We also assume that the relation between costs and their respective control functions, that is, treatment in both humans and bovines, including molluscicide in snails, happens to be non-linear, and so we opt for a quadratic control function [9]. The components $\frac{1}{2}D_1u_1^2,\ \frac{1}{2}D_2u_2^2$ and $\frac{1}{2}D_3u_3^2$ in the objective function represent the cost associated with treatment of infected humans, bovines and molluscicide in the contaminated environment, respectively.

So, we aim to minimize the number of infected humans, I_H, bovines, I_B and the general snail population, $N_S = S_S + I_S$, while seeking the minimum cost of controls $u_1(t),\ u_2(t)$ and $u_3(t)$. This is achieved by determining optimal control $u_1^*(t),\ u_2^*(t)$ and $u_3^*(t)$ such that

$$\nabla(u_1^*, u_2^*, u_3^*) = \min_{(u_1,u_2,u_3)\in\nabla} \nabla\big(u_1(t), u_2(t), u_3(t)\big), \tag{4.37}$$

subject to the following system;

$$
\begin{aligned}
\frac{dS_H}{dt} &= \Pi_h - \beta_{sh} S_H I_S + r_h T_H - \mu_h S_H, \\
\frac{dI_H}{dt} &= \beta_{sh} S_H I_S - (t_1(1-\kappa\tau) + \mu_h + d_h + u_1(t)) I_H, \\
\frac{dT_H}{dt} &= (t_1(1-\kappa\tau) + u_1(t)) I_H - (r_h + \mu_h) T_H, \\
\frac{dS_B}{dt} &= \Pi_b - \beta_{sb} S_B I_S + r_b T_B - \mu_b S_B, \\
\frac{dI_B}{dt} &= \beta_{sb} S_B I_S - (t_2(1-\upsilon\psi) + \mu_b + d_b + u_2(t)) I_B, \\
\frac{dT_B}{dt} &= (t_2(1-\upsilon\psi) + u_2(t)) I_B - (r_b + \mu_b) T_B, \\
\frac{dS_S}{dt} &= \Pi_s - (\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - (\mu_s + u_3(t)) S_S, \\
\frac{dI_S}{dt} &= (\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - (\mu_s + u_3(t)) I_S, \\
\frac{dC_E}{dt} &= \varepsilon_s p_s (1-cq) I_S - \mu_c C_E.
\end{aligned}
\tag{4.38}
$$

We use the method in Fleming [33] to develop the optimal system for which the necessary conditions that must be satisfied by an optimal control and its corresponding states are derived (Theorem 5.1, Pontryagin's Principle) in Fleming [33]. As a way of converting the state system (4.1) and objective function (4.36) into a pointwise minimized problem, we define the Hamiltonian function H, for the optimal control system (4.1) as

$$
\begin{aligned}
H(t, Q, U, \Lambda) &= L + \lambda_{sh}\frac{dS_H}{dt} + \lambda_{ih}\frac{dI_H}{dt} + \lambda_{th}\frac{dT_H}{dt} + \lambda_{sb}\frac{dS_B}{dt} + \lambda_{ib}\frac{dI_B}{dt} \\
&\quad + \lambda_{tb}\frac{dT_B}{dt} + \lambda_{ss}\frac{dS_S}{dt} + \lambda_{is}\frac{dI_S}{dt} + \lambda_{ce}\frac{dC_E}{dt},
\end{aligned}
\tag{4.39}
$$

where L is the Lagrangian of the control problem. That is,

$$
L = C_1 I_H + C_2 I_B + C_3 N_S + \frac{1}{2}\big(D_1 u_1^2 + D_2 u_2^2 + D_3 u_3^2\big).
$$

The minimum value can be achieved through the definition of the Hamiltonian, H, consisting of the integrand of L and the inner product of the vector of adjoint variables

$$
\Lambda = \Big(\lambda_{sh}, \lambda_{ih}, \lambda_{th}, \lambda_{sb}, \lambda_{ib}, \lambda_{tb}, \lambda_{ss}, \lambda_{is}, \lambda_{ce}\Big),
$$

and the derivatives of

$$Q = \Big(S_H(t), I_H(t), T_H(t), S_B(t), I_B(t), T_B(t), S_S(t), I_S(t), C_E(t)\Big),$$

given by

$$\left(\frac{dS_H}{dt}, \frac{dI_H}{dt}, \frac{dT_H}{dt}, \frac{dS_B}{dt}, \frac{dI_B}{dt}, \frac{dT_B}{dt}, \frac{dS_S}{dt}, \frac{dI_S}{dt}, \frac{dC_E}{dt}\right).$$

Hence

$$\begin{aligned} H &= C_1 I_H + C_2 I_B + C_3 N_S + \frac{1}{2}\Big(D_1 u_1^2 + D_2 u_2^2 + D_3 u_3^2\Big) \\ &+\lambda_{sh}\Big(\Pi_h - \beta_{sh} S_H I_S + r_h T_H - \mu_h S_H\Big) \\ &+\lambda_{ih}\Big(\beta_{sh} S_H I_S - (t_1(1-\kappa\tau) + \mu_h + d_h + u_1(t)) I_H\Big) \\ &+\lambda_{th}\Big((t_1(1-\kappa\tau) + u_1(t)) I_H - (r_h + \mu_h) T_H\Big) \\ &+\lambda_{sb}\Big(\Pi_b - \beta_{sb} S_B I_S + r_b T_B - \mu_b S_B\Big) \\ &+\lambda_{ib}\Big(\beta_{sb} S_B I_S - (t_2(1-\upsilon\psi) + \mu_b + d_b + u_2(t)) I_B\Big) \\ &+\lambda_{tb}\Big((t_2(1-\upsilon\psi) + u_2(t)) I_B - (r_b + \mu_b) T_B\Big) \\ &+\lambda_{ss}\Big(\Pi_s - (\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - (\mu_s + u_3(t)) S_S\Big) \\ &+\lambda_{is}\Big(\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) S_S - (\mu_s + u_3(t)) I_S\Big) \\ &+\lambda_{ce}\Big(\varepsilon_s p_s (1-cq) I_S - \mu_c C_E\Big). \end{aligned} \tag{4.40}$$

We then obtain a system of equations by taking the suitable partial derivatives of H with respect to the associated state variables.

Theorem 8 *Let* $\Big(Q^*, U^*\Big)$, *where*

$Q^*(t) = \Big(S_H^*(t), I_H^*(t), T_H^*(t), S_B^*(t), I_B^*(t), T_B^*(t), S_S^*(t), I_S^*(t), C_E^*(t)\Big)$, $U^* = \Big(u_1^*, u_2^*, u_3^*\Big)$, *be the optimal control solution of the state system (4.38) that minimizes* $\nabla(u_1, u_2, u_3)$ *over* U. *Then, there exists a vector function* $\Lambda = \Big(\lambda_{sh}, \lambda_{ih}, \lambda_{th}, \lambda_{sb}, \lambda_{ib}, \lambda_{tb}, \lambda_{ss}, \lambda_{is}, \lambda_{ce}\Big)$

satisfying the following

$$\begin{aligned}
-\lambda'_{sh} &= (\lambda_{ih}-\lambda_{sh})\beta_{sh}I_S-\lambda_{sh}\mu_h\\
-\lambda'_{ih} &= C_1+(\lambda_{is}-\lambda_{ss})\beta_{hs}S_S+(\lambda_{th}-\lambda_{ih})(t_1(1-\kappa\tau)+u_1(t))-\lambda_{ih}(\mu_h+d_h)\\
-\lambda'_{th} &= (\lambda_{sh}-\lambda_{th})r_h-\lambda_{th}\mu_h\\
-\lambda'_{sb} &= (\lambda_{ib}-\lambda_{sb})\beta_{sb}I_S-\lambda_{sb}\mu_b\\
-\lambda'_{ib} &= C_2+(\lambda_{is}-\lambda_{ss})\beta_{bs}S_S+(\lambda_{tb}-\lambda_{ib})(t_2(1-\upsilon\psi)+u_2(t))-\lambda_{ib}(\mu_b+d_b)\\
-\lambda'_{tb} &= (\lambda_{sb}-\lambda_{tb})r_b-\lambda_{tb}\mu_b\\
-\lambda'_{ss} &= C_3+(\lambda_{is}-\lambda_{ss})(\beta_{cs}C_E+\beta_{hs}I_H+\beta_{bs}I_B)-\lambda_{ss}(\mu_s+u_3(t))\\
-\lambda'_{is} &= C_3+(\lambda_{ih}-\lambda_{sh})\beta_{sh}S_H+(\lambda_{ib}-\lambda_{sb})\beta_{sb}S_B-\lambda_{is}(\mu_s+u_3(t))\\
&\quad +\lambda_{ce}(\varepsilon_s p_s(1-cq))\\
-\lambda'_{ce} &= (\lambda_{is}-\lambda_{ss})\beta_{cs}S_S-\lambda_{ce}\mu_c,
\end{aligned} \tag{4.41}$$

with transversality conditions

$$\lambda_{sh}(T)=\lambda_{ih}(T)=\lambda_{th}(T)=\lambda_{sb}(T)=\lambda_{ib}(T)=\lambda_{tb}(T)=\lambda_{ss}(T)=\lambda_{is}(T)=\lambda_{ce}(T)=0.$$

In addition, an optimal control $\left(u_1^*,u_2^*,u_3^*\right)$ *that minimizes* ∇ *could be obtained using the condition for optimality*

$$\begin{aligned}
u_1^* &= \max\left\{0,\min\left(1,\frac{(\lambda_{ih}-\lambda_{th})I_H}{D_1}\right)\right\},\\
u_2^* &= \max\left\{0,\min\left(1,\frac{(\lambda_{ib}-\lambda_{tb})I_B}{D_2}\right)\right\},\\
u_3^* &= \max\left\{0,\min\left(\frac{\lambda_{ss}S_S+\lambda_{is}I_S}{D_3}\right)\right\}.
\end{aligned} \tag{4.42}$$

Proof *By Pontryagin's Maximum Principle [74], we have the non-trivial vector function*

$$\lambda=\left(\lambda_{sh},\lambda_{ih},\lambda_{th},\lambda_{sb},\lambda_{ib},\lambda_{tb},\lambda_{ss},\lambda_{is},\lambda_{ce}\right)$$

satisfying the following:

$$\begin{aligned} 0 &= \frac{\partial H(t,Q,U,\lambda)}{\partial u}, \\ -\lambda' &= \frac{\partial H(t,Q,U,\lambda)}{\partial Q}, \\ \frac{dQ}{dt} &= -\frac{\partial H(t,Q,U,\lambda)}{\partial \lambda}. \end{aligned} \tag{4.43}$$

We use the differential equations governing the adjoint variables as a way of determining the adjoint equations. Hence, applying the adjoint conditions,

$$-\lambda' = \frac{\partial H}{\partial Q}$$

to the Hamiltonian function H, we obtain the adjoint equations:

$$\begin{aligned} -\frac{\lambda_{sh}}{dt} = \frac{\partial H}{\partial S_H} &= (\lambda_{ih} - \lambda_{sh})\beta_{sh} I_S - \lambda_{sh}\mu_h, \\ -\frac{\lambda_{ih}}{dt} = \frac{\partial H}{\partial I_H} &= C_1 + (\lambda_{is} - \lambda_{ss})\beta_{hs} S_S + (\lambda_{th} - \lambda_{ih})(t_1(1-\kappa\tau) + u_1(t)) - \lambda_{ih}(\mu_h + d_h), \\ -\frac{\lambda_{th}}{dt} = \frac{\partial H}{\partial T_H} &= (\lambda_{sh} - \lambda_{th})r_h - \lambda_{th}\mu_h, \\ -\frac{\lambda_{sb}}{dt} = \frac{\partial H}{\partial S_B} &= (\lambda_{ib} - \lambda_{sb})\beta_{sb} I_S - \lambda_{sb}\mu_b, \\ -\frac{\lambda_{ib}}{dt} = \frac{\partial H}{\partial I_B} &= C_2 + (\lambda_{is} - \lambda_{ss})\beta_{bs} S_S + (\lambda_{tb} - \lambda_{ib})(t_2(1-\upsilon\psi) + u_2(t)) - \lambda_{ib}(\mu_b + d_b), \\ -\frac{\lambda_{tb}}{dt} = \frac{\partial H}{\partial T_B} &= (\lambda_{sb} - \lambda_{tb})r_b - \lambda_{tb}\mu_b, \\ -\frac{\lambda_{ss}}{dt} = \frac{\partial H}{\partial S_S} &= C_3 + (\lambda_{is} - \lambda_{ss})(\beta_{cs} C_E + \beta_{hs} I_H + \beta_{bs} I_B) - \lambda_{ss}(\mu_s + u_3(t)), \\ -\frac{\lambda_{is}}{dt} = \frac{\partial H}{\partial I_S} &= C_3 + (\lambda_{ih} - \lambda_{sh})\beta_{sh} S_H + (\lambda_{ib} - \lambda_{sb})\beta_{sb} S_B - \lambda_{is}(\mu_s + u_3(t)) \\ &\quad + \lambda_{ce}(\varepsilon_s p_s (1 - cq)), \\ -\frac{\lambda_{ce}}{dt} = \frac{\partial H}{\partial C_E} &= (\lambda_{is} - \lambda_{ss})\beta_{cs} S_S - \lambda_{ce}\mu_c, \end{aligned} \tag{4.44}$$

with the transversality conditions

$$\lambda_{sh}(T) = \lambda_{ih}(T) = \lambda_{th}(T) = \lambda_{sb}(T) = \lambda_{ib}(T) = \lambda_{tb}(T) = \lambda_{ss}(T) = \lambda_{is}(T) = \lambda_{ce}(T) = 0.$$

Upon solving

$$\frac{\partial H}{\partial u_1} = 0,\ \frac{\partial H}{\partial u_2} = 0,\ \frac{\partial H}{\partial u_3} = 0,$$

then evaluating at the optimal control $U^* = (u_1^*, u_2^*, u_3^*)$ *on the interior of the control set, we have*

$$\begin{aligned} D_1 u_1^* &= \lambda_{ih} I_H - \lambda_{th} I_H, \\ D_2 u_2^* &= \lambda_{ib} I_B - \lambda_{tb} I_B, \\ D_3 u_3^* &= \lambda_{ss} S_S + \lambda_{is} I_S, \end{aligned} \tag{4.45}$$

from which we obtain

$$\begin{aligned} u_1^* &= \frac{(\lambda_{ih} - \lambda_{th}) I_H}{D_1}, \\ u_2^* &= \frac{(\lambda_{ib} - \lambda_{tb}) I_B}{D_2}, \\ u_3^* &= \frac{\lambda_{ss} S_S + \lambda_{is} I_S}{D_3}. \end{aligned} \tag{4.46}$$

Since the optimal controls are bounded, we then obtain the unique optimal control and hence we have

$$u_1^* = \begin{cases} 0 & if \quad \dfrac{(\lambda_{ih} - \lambda_{th}) I_H}{D_1} < 0, \\ \dfrac{(\lambda_{ih} - \lambda_{th}) I_H}{D_1} & if \quad 0 \le \dfrac{(\lambda_{ih} - \lambda_{th}) I_H}{D_1} \le 1, \\ 1 & if \quad \dfrac{(\lambda_{ih} - \lambda_{th}) I_H}{D_1} > 1, \end{cases}$$

$$u_2^* = \begin{cases} 0 & if \quad \dfrac{(\lambda_{ib} - \lambda_{tb}) I_B}{D_2} < 0, \\ \dfrac{(\lambda_{ib} - \lambda_{tb}) I_B}{D_2} & if \quad 0 \le \dfrac{(\lambda_{ib} - \lambda_{tb}) I_B}{D_2} \le 1, \\ 1 & if \quad \dfrac{(\lambda_{ib} - \lambda_{tb}) I_B}{D_2} > 1, \end{cases}$$

$$u_3^* = \begin{cases} 0 & if \quad \dfrac{\lambda_{ss} S_S + \lambda_{is} I_S}{D_3} < 0, \\ \dfrac{\lambda_{ss} S_S + \lambda_{is} I_S}{D_3} & if \quad 0 \le \dfrac{\lambda_{ss} S_S + \lambda_{is} I_S}{D_3} \le 1, \\ 1 & if \quad \dfrac{\lambda_{ss} S_S + \lambda_{is} I_S}{D_3} > 1. \end{cases}$$

4.5.1 Numerical Simulations of the Optimal Control Problem

In this section we investigate the effect of optimal control strategies on human-bovine schistosomiasis, which include treatment for both humans and bovines as well as molluscicide of the contaminated environment. This is carried out by solving the model system (4.38) and the adjoint system (4.44). An iterative fourth-order Runge-Kutta integration scheme is employed to solve the non-linear initial-value problem of model system (4.38) and the adjoint system (4.44). The parameter values are the same as those given in Table (4.3).

All the model parameters are from the literature and whenever parameter values such as the fraction of bovines treated, the fraction of the contaminated environment sprayed with molluscicides are not available in the literature, we assume realistic values for the purpose of illustration. We also assume, for illustrative purposes the weight factor values to be $C_1 = C_2 = C_3 = D_3 = 1, D_1 = 30, D_2 = 45$. These assumed values have been intuitively chosen as a way of theoretically investigating effects of the different control strategies involved and are used for the model simulation purposes on which there is necessarily no significant meaning attached [1, 50, 53, 68, 71]. However, based on the assumption that high cost will be associated with treatment of bovines, D_2 has been made greater than D_1 and D_3. This is due to the fact that there is a need for mass treatment with praziquantel to be widely practised for it to be effective [87]. It should also be noted that the three control strategies u_1, u_2 and u_3 are all constrained between zero and one, that is, $0 \leq u_i(t) \leq 1, i = 1, 2, 3$. For instance, if $u_1 = 0$, it implies no treatment is provided to humans, and $u_1 \neq 0$ implies there is at least some treatment provided to humans, with $u_1 = 1$ being the maximum treatment coverage level. The same is also inferred to for the other two control strategies u_2, treatment for bovines and u_3, which is molluscicide of the contaminated environment.

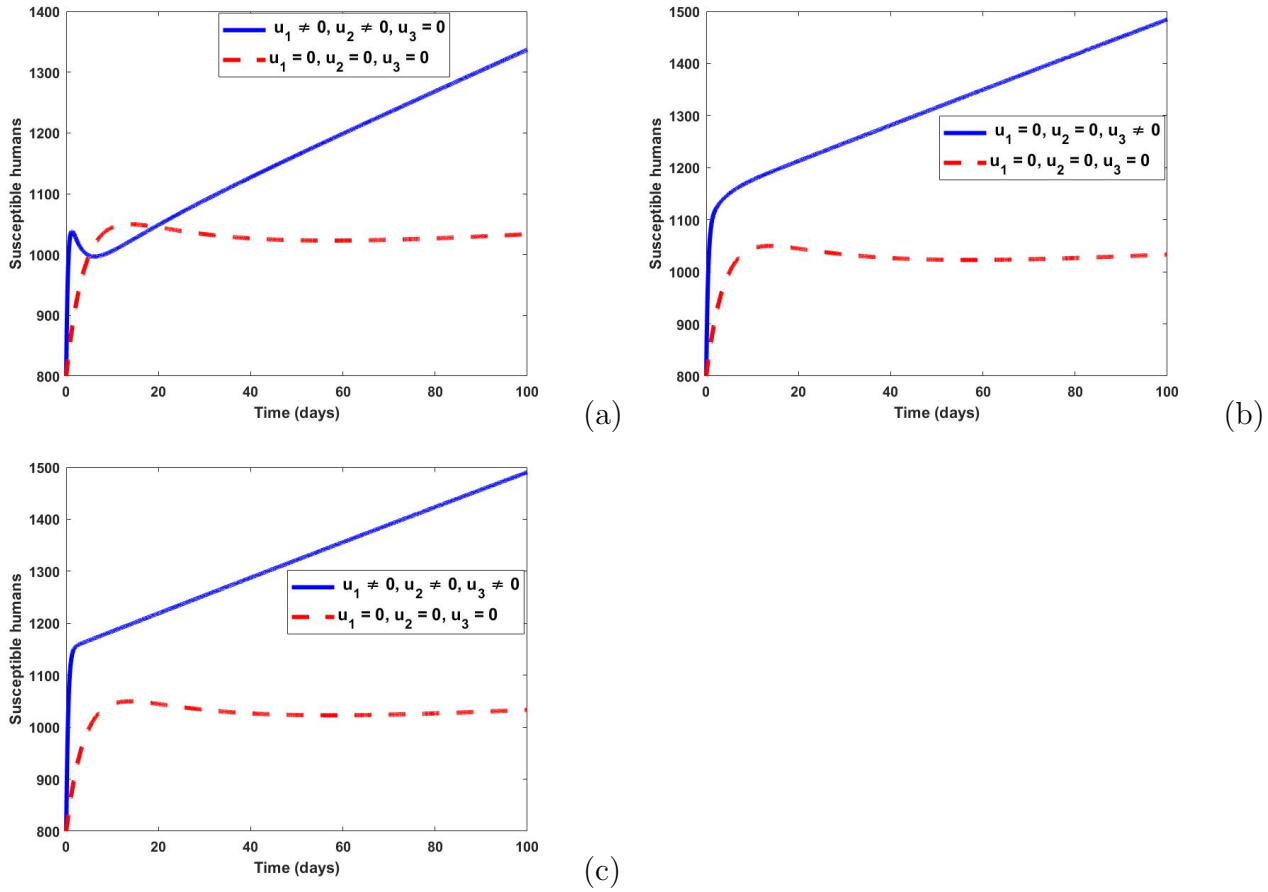


Figure 4.9: Dynamics of the susceptible human population S_H against time, with and without control strategies, u_1, u_2, u_3

Figure 4.9(a) shows the susceptible human population S_H, with only treatment of humans and bovines. When there is no treatment of humans, bovines and mollusciciding of the contaminated environment, we note as expected that the human population decreases. This decrease is a result of most humans progressing to the infectious class. In the case where u_1 and u_2 are not zero, the susceptible human population shows some reasonable increase, possibly due to the contribution of the treatment of humans, u_1. This implies that as the infectious humans, I_H, are subjected to treatment, most of them recover and move to the susceptible class again. However, this is the trend in the event u_1 and u_2 are either zero or not while u_3 is fixed to zero. Figure 4.9(b), shows that applying u_3, makes the increase greater. This also applies to the situation when all the three control strategies have been effected (Figure 4.9(c)).

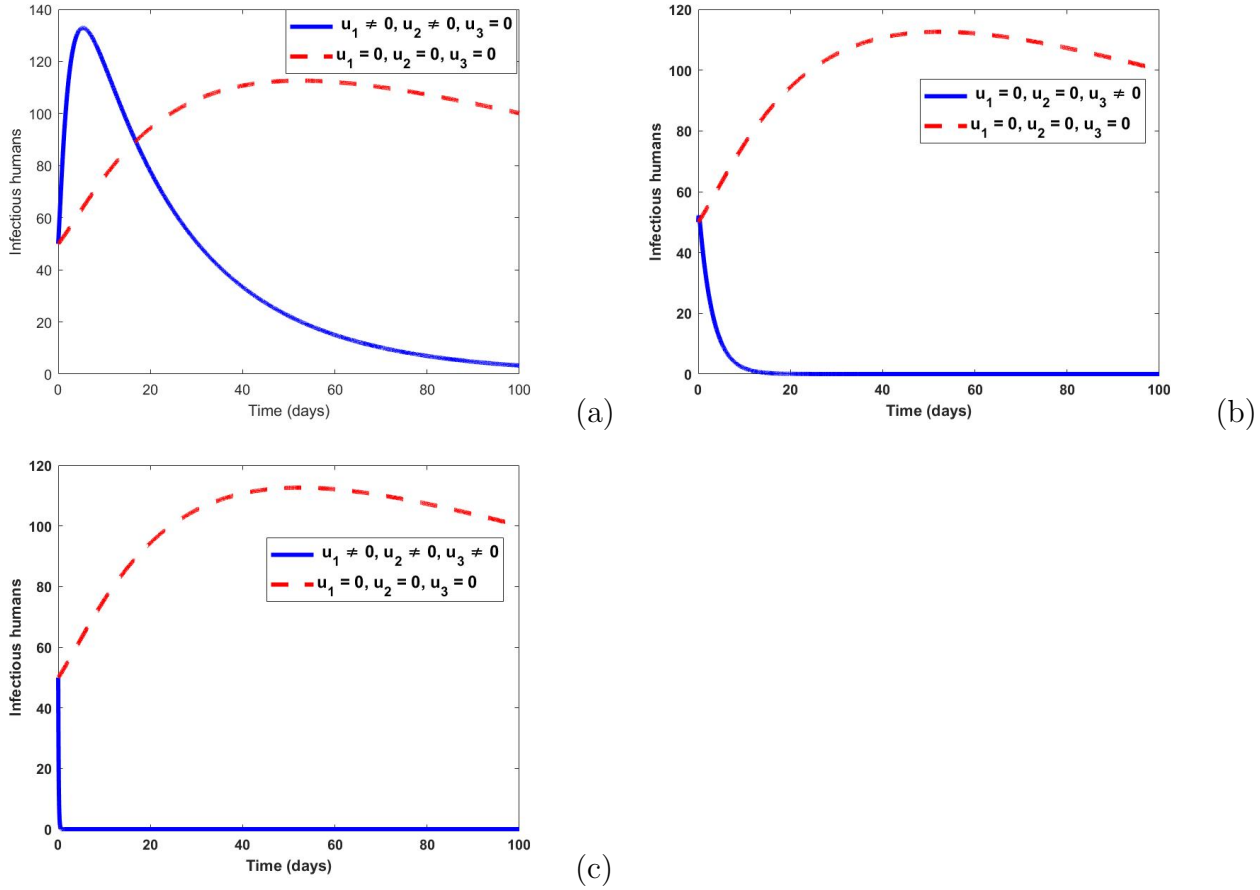


Figure 4.10: Dynamics of the infectious human population I_H against time, with and without control strategies, u_1, u_2, u_3

As the infectious humans move to the treated class T_H, the impact of treatments, u_1 and u_2 is observed in the decrease of the infected human population. Again, the situation is the same when u_3 is zero while u_1 or u_2 is either zero or not (Figure 4.10(a)). Applying molluscicide results in a sharp decrease in the infectious human population as shown in Figure 4.10(b). This also occurs when we apply all the three strategies together or u_3 together with each of the other two strategies u_1 and u_2 (Figure 4.10(c)).

The impact of treatment is also observed in the way the number of treated humans is reduced (Figure 4.11(a)). The reduction is more pronounced when molluscicide of the contaminated environment is incorporated (Figure 4.11(b)), let alone when u_3 is applied with the other two strategies, u_1 and u_2 or either of them (Figure 4.11(c)).

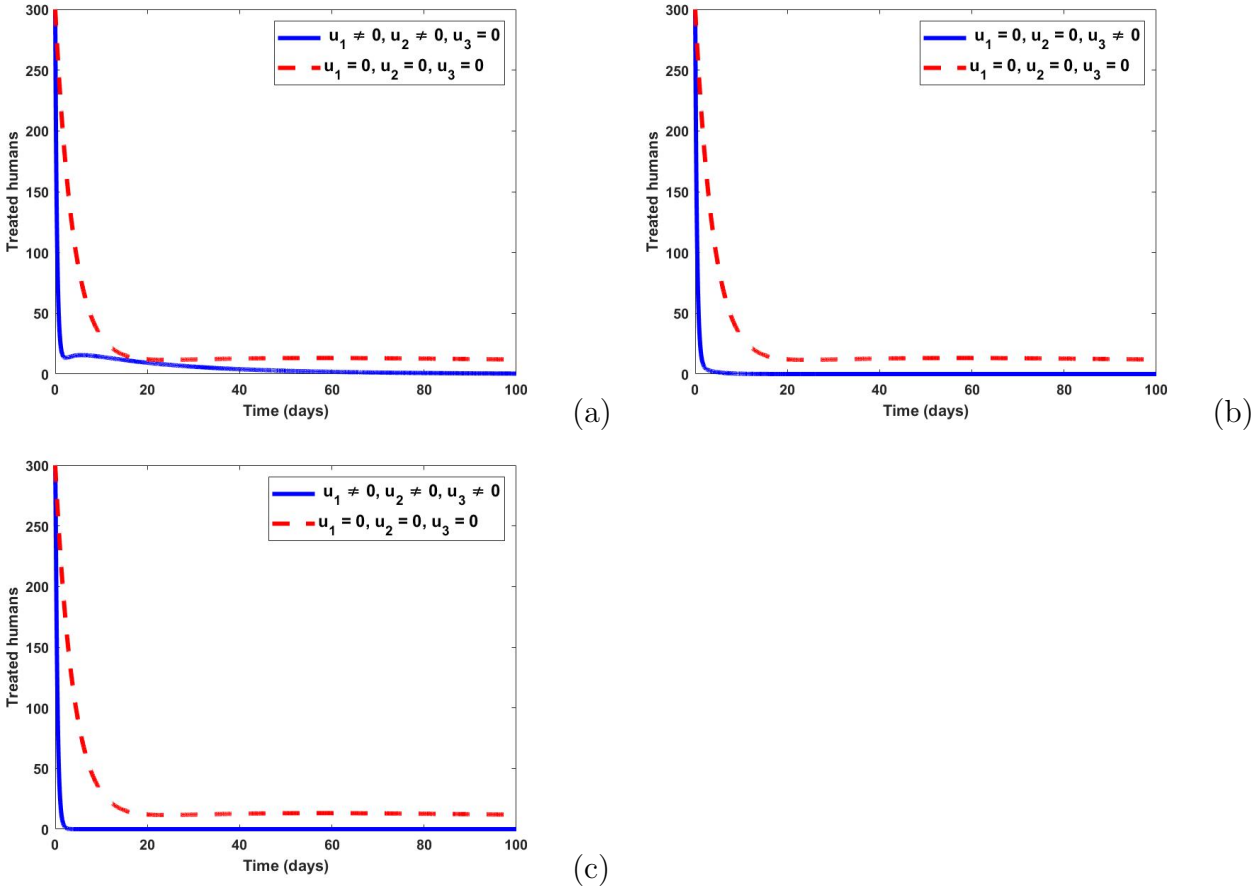


Figure 4.11: Dynamics of the treated human population T_H against time, with and without control strategies, u_1, u_2, u_3

In Figure 4.12, all the bovine population classes show a decrease. It has been observed that schistosomiasis infection in bovines, cattle in particular, is more prevalent but of low intensity. Once the bovines recover, they develop partial protection against reinfection and finally, that level of initial challenge affects immunity development [8]. This then gives us a probable cause as to why the susceptibility of bovines decreases since after recovery, most of them develop partial immunity against the disease which results in no or minimal reinfection (Figure 4.12(a)). However, with the application of u_3, most of the snails in the contaminated environment with which bovines may be in contact, die and this reduces the high prevalence of infection that usually occurs in bovines. Hence, we see a drastic drop of susceptible bovine population (Figure 4.12(b)). Furthermore, in Figure 4.12(c), the same trend persists especially when all the three strategies are applied. Numerical simulations for the remaining bovine populations follow the same

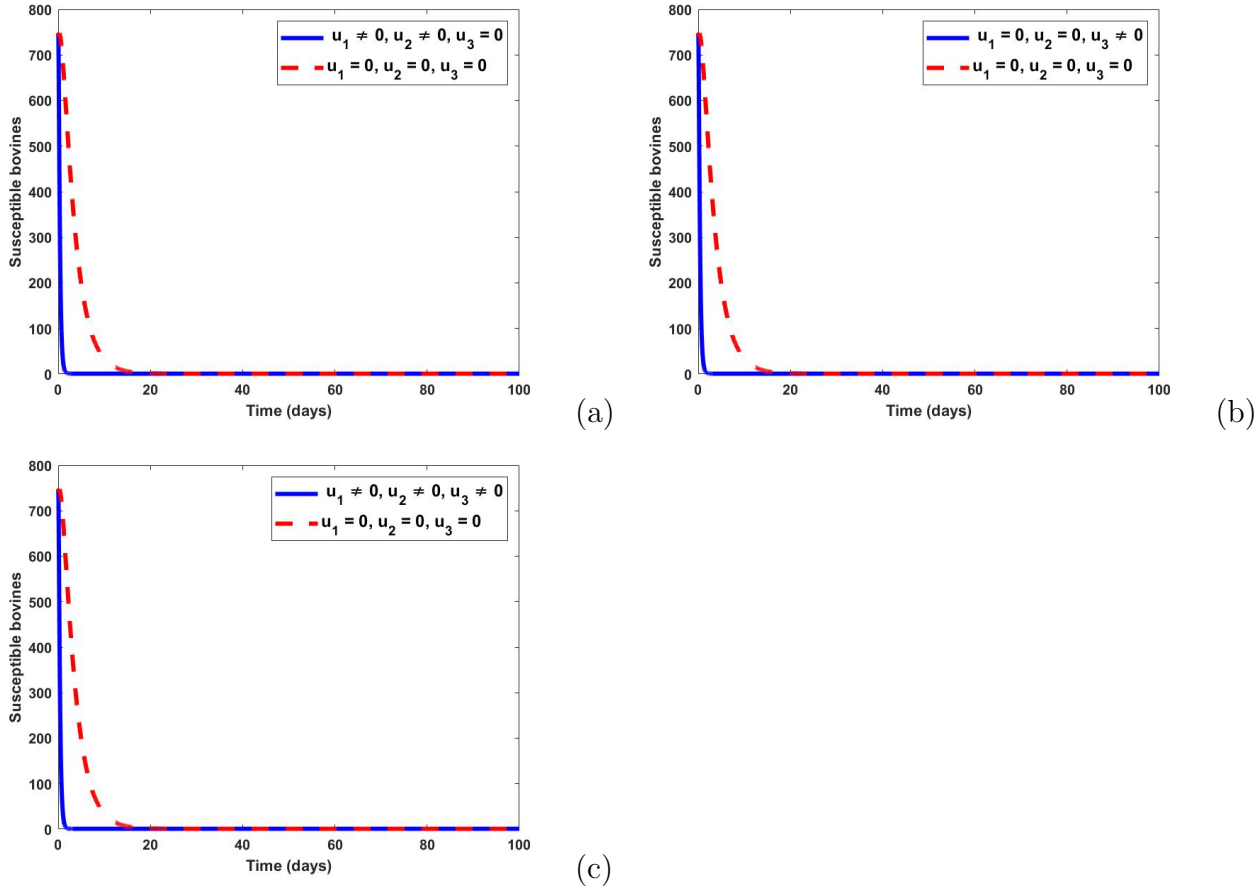


Figure 4.12: Dynamics of the susceptible bovine population S_B against time, with and without control strategies, u_1, u_2, u_3

traits as shown in the susceptible population. Although it is not clear as to whether the three strategies really have an impact on the bovine populations, as noted from the simulations, Figure 4.12, this can also be attributed to a stronger immune response in bovines [95]. Due to this immune response, we note that even in the absence of the control strategies, the bovines can still recover, though not as much as compared to when u_1, u_2 and u_3 are applied.

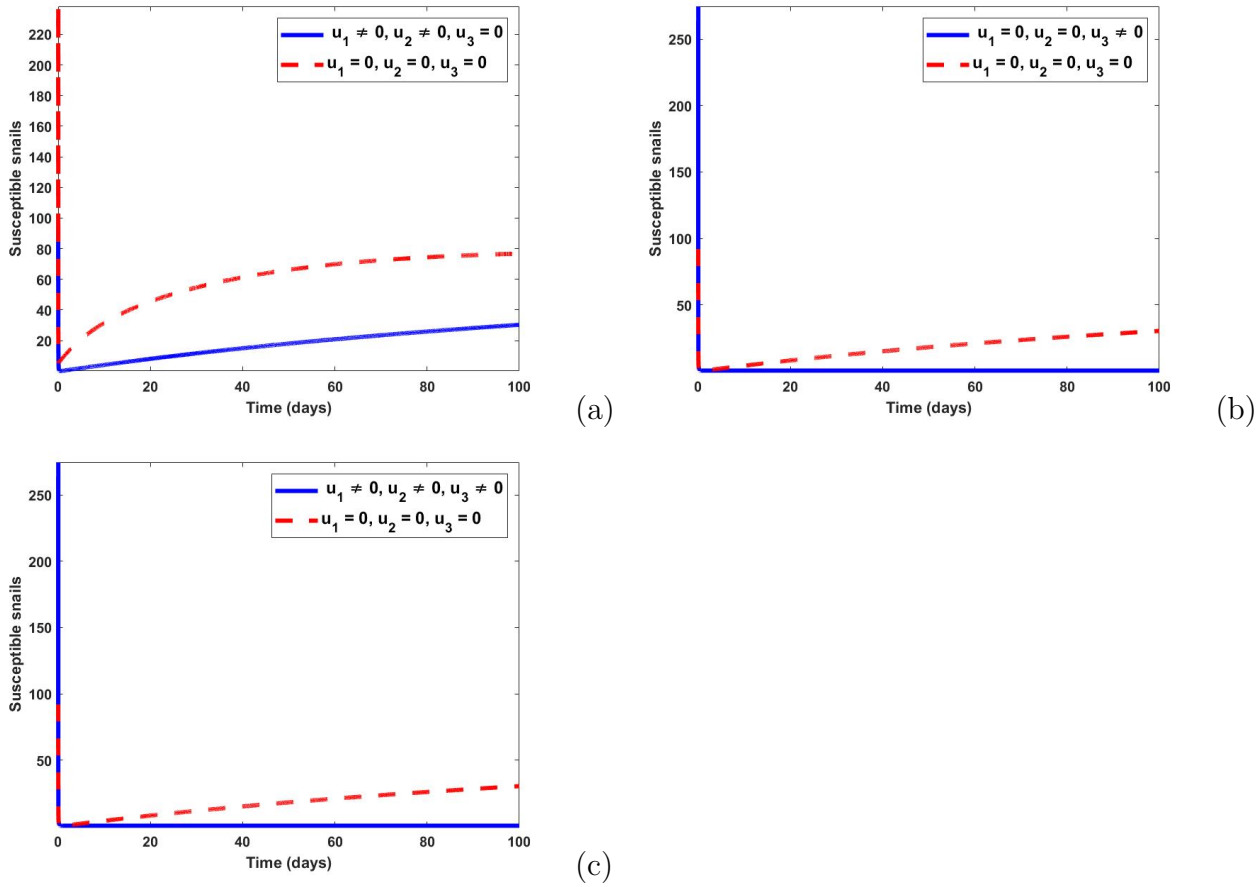


Figure 4.13: Dynamics of the susceptible snail population S_S against time, with and without control strategies, u_1, u_2, u_3

As humans and bovines are treated, the impact is also observed in the snail population (Figure 4.13 and Figure 4.14). This might be due to the fact that as the humans and bovines recover from the disease, after treatment, their ability to shed miracidia into the contaminated environment is greatly reduced, resulting in a decrease in the susceptible snail population. However, with molluscicide, there is a rapid decrease in both the susceptible and infectious snail populations. The main reason for this is that molluscicide eradicates all snails (susceptible and infected) in the contaminated environment irrespective of their disease status.

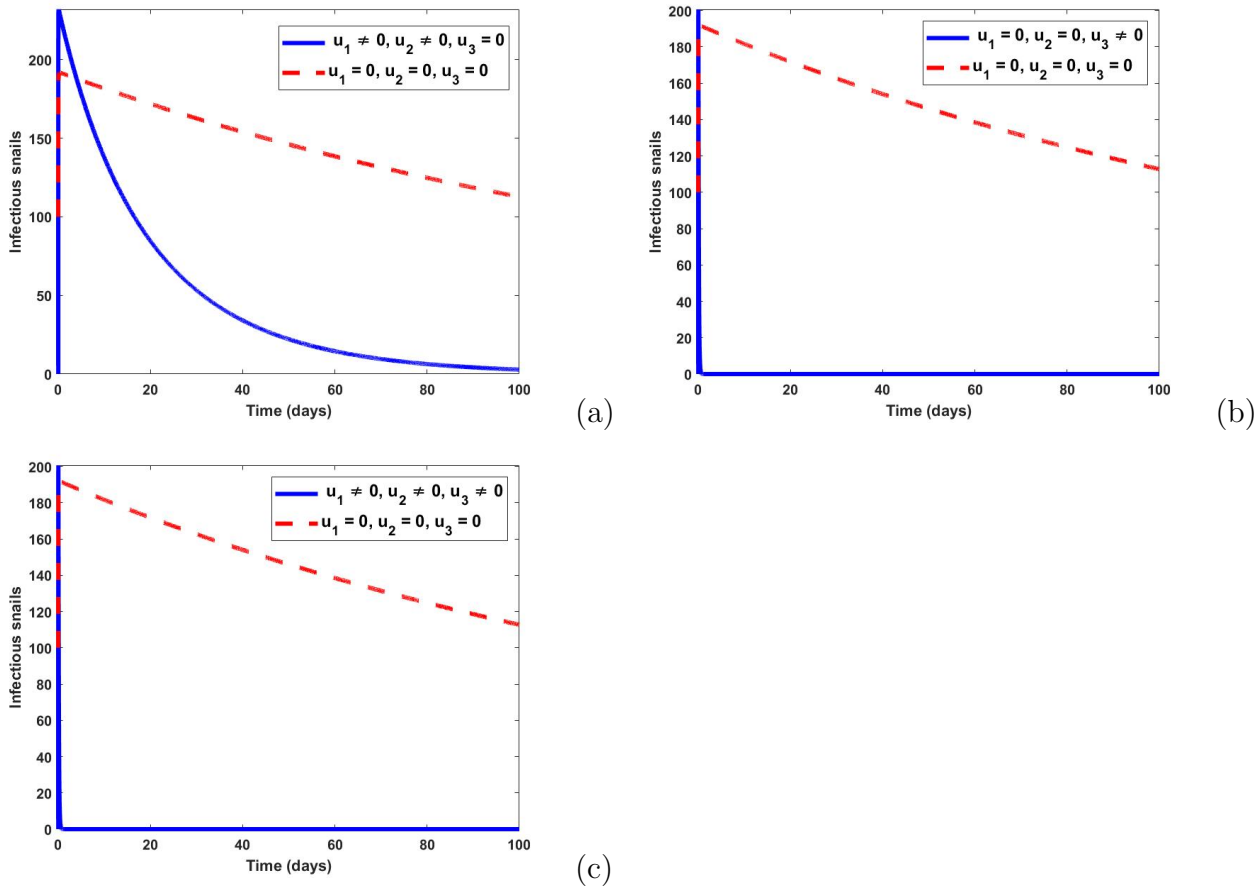


Figure 4.14: Dynamics of the infectious snail population I_S against time, with and without control strategies, u_1, u_2, u_3

4.6 Summary

In this chapter, we extended our proposed deterministic mathematical model of the transmission dynamics of schistosomiasis accounting for contaminated water reservoirs to include therapeutic measures such as treatment of bovines and humans and molluciciding of the contaminated environment. The model system of non-linear ordinary differential equations was then rigorously analysed. The model is biologically well-posed in a positively invariant region. The basic reproduction number of the extended model was computed. Global stability of the endemic equilibrium was investigated by constructing a suitable Lyapunov function. To support the theoretical results, numerical simulations were performed. Finally, where applicable, uncertainty analysis on the non-dimensional system parameters was implemented.

Chapter 5

Conclusion, Recommendations and Future Work

5.1 General Conclusion

Schistosomiasis, a snail-borne infectious disease is prevalent in tropical and sub-tropical areas of the world. The disease is transmissible to both bovines and humans. With approximately 530 million cattle susceptible to the disease and more than 165 million infected animals in Africa and the Middle East, schistosomiasis is a disease of global public health importance that has affected health, agricultural productivity, social impact and economic burden on people living in the affected often rural regions of the globe.

In Chapter 1, we presented the epidemiology of schistosomiasis, the methodology and outline of the thesis. The literature review of mathematical models of schistosomiasis transmission dynamics and its interplay with water reservoir was presented in Chapter 2.

In Chapter 3, we formulated and analysed the proposed deterministic mathematical model as a system of non-linear ordinary differential equations of the transmission dynamics of schistosomiasis accounting for the contaminated water reservoir. The model considered the transmission dynamics in the bovine populations' three sub-classes, which included susceptible bovines, S_b, exposed bovines, E_b and infected bovines, I_b. The model was then refined by incorporating the human population since the dynamics of the disease in bovines directly influence the human transmission dynamics. Using the next generation matrix approach, the basic reproduction number which represents the number of secondary infections generated by a single infectious case in a totally susceptible population was computed. Stability analysis of both the disease-free and endemic equilibria was carried out. Global stability of the endemic equilibrium was investigated by constructing a suitable Lyapunov function. The model exhibited a forward bifurcation since global stability of the model equilibria precluded the existence of a backward bifurcation, a phenomenon where a stable disease-free equilibrium co-exists with a sta-

ble endemic equilibrium, for a certain range of the associated reproduction number less than unity. Sensitivity analysis to determine the relative importance of model parameters to disease transmission was performed. Numerical simulations were undertaken to support the theoretical results. It was observed that animal reservoirs played an important role in the transmission dynamics of schistosomiasis with both bovines and human as definitive hosts [93].

The model proposed in Chapter 3 was then extended in Chapter 4 to include therapeutic measures such as treatment of bovines and humans and molluciciding of the contaminated environment. The model system of non-linear ordinary differential equations was then rigorously analysed. The model was biologically well-posed in a positively invariant region. The basic reproduction number of the extended model was computed using the next generation matrix method. The disease-free equilibrium was found to be locally asymptotically stable for $R_0 < 1$ and unstable otherwise. Global stability of the unique endemic equilibrium was investigated via the Lyapunov function approach. To mitigate the spread of the disease, the impact of control strategies such as treatment of humans and bovines and molluciciding of the contaminated water environment was investigated. Numerical simulations indicated that the contaminated environment played a crucial role in the dynamics of the schistosomiasis infection. As such, mollusciciding, which directly impacts the contaminated environment as a single control strategy was more effective compared to treatment for both bovines and humans. However, concurrently applying molluciciding and treatment of humans and bovines will yield a better outcome. The importance of the contaminated water environment was also apparent in the sensitivity analysis where the contaminated environment related parameters, such as ε_s, p_s, c, q and μ_c largely contributed towards the epidemiology of schistosomiasis. For instance, an increase in c or q leads to a significant decrease in R_0, compared to the way other parameters not linked to the environment such as κ and τ would do. Next, uncertainty analysis on the non-dimensional system parameters using the Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) in Matlab was carried out.

Optimal control theory was then applied to the extended model. Existence of the optimal control problem which satisfied the necessary conditions as provided by Pontryagin's Maximum Principle was first established. Treatment on humans and bovines as well as molluscicide of the contaminated environment was represented as $u_1(t), u_2(t)$ and $u_3(t)$, respectively. Numerical simulations of the optimal control were then carried out to validate the analytical results. It was noted that $u_3(t)$, molluciciding of the contaminated environment had greater impact on controlling the disease compared to $u_1(t)$ and $u_2(t)$, treatment of humans and bovines. Thus, continuously targeting the contaminated environment could yield better outcomes in mitigating the epidemic. However, treatment of infected humans and bovines should not be neglected as a combination of selective mass treatment and mass treatment of the reservoirs had a significant effect on reduction of the schistosomiasis prevalence [93].

5.2 Recommendations

Considering the qualitative and quantitative analysis results of the human-bovine schistosomiasis model, the following recommendations should be taken into account:

- Any effort to control the schistosomiasis infection should not ignore the contaminated environment, which has been found to play a vital role in the dynamics of the disease.
- Though almost impossible to apply or be reinforced in rural areas, humans and bovines should avoid drinking in water reservoirs.
- Since treatment is not definitive and do not prevent reinfection as treated humans or bovines are again susceptible, a schistosomiasis vaccination should be seriously considered.

5.3 Future Work

While efforts were made to incorporate several key dynamics of the disease and control, this thesis does not purport to be exhaustive. A number of limitations could be used

to extend the proposed model in future studies. For example, when considering the control strategies, our choice was too general, say, treatment of humans and bovines. It would have been ideal to specify the kind of treatment to be applied or explicitly include treated classes in the model. Also, there is a possibility of treatment resistance and treatment efficacy which were not accounted for in this thesis. Although there is no schistosomiasis vaccine, theoretically investigating the impact of a partially effective vaccine is viable pending the future development of one. Finally, since the optimal control theory has been applied on the treatment of humans and bovines and molluscicide of the contaminated environment, it would be worthwhile to evaluate the cost and cost-effectiveness of such control strategies.

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