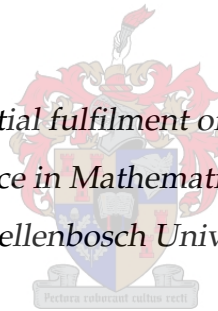


**Modeling the Economics of Insecticide and
Trypanocide-Treated Cattle Interventions against
Trypanosomiasis Disease within a Multi-host Situation**

by

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*Thesis presented in partial fulfilment of the requirements for the
degree of Master of Science in Mathematics in the Faculty of Science
at Stellenbosch University*



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March 2017

Declaration

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Abstract

Modeling the Economics of Insecticide and Trypanocide-Treated Cattle Interventions against Trypanosomiasis Disease within a Multi-host Situation

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2017

Trypanosomiasis, sleeping sickness in humans and nagana in animals, is vectored by tsetse flies (*Glossina genus*), which have acquired their infection from feeding on an infectious host. Its control or elimination is a major challenge faced by farmers in keeping their cattle herd free of the disease, in large areas of sub-Saharan Africa. We conducted an economic evaluation of two tsetse control interventions, namely: treatment of infected cattle with trypanocides known as trypanocide-treated cattle (TTC), and use of insecticide-treated cattle (ITC), as measures of controlling or eliminating the disease. The two forms of the disease considered are: (i) one caused by *Trypanosoma vivax*, affecting mainly the livestock, and (ii) one caused by *Trypanosoma brucei rhodesiense* which is present mainly in humans. A benefit-cost analysis was performed for the former, while a cost-effectiveness was carried out for the latter because of the impossibility of assigning a monetary value to the benefit of saving a human life. We adapted two models that best describe the biology of *T. vivax* infection and then extended both models to incorporate

the biology of the *T. b. rhodesiense* infection. Both the ITC and TTC Models against *T. vivax* and *T.b. rhodesiense* infections disease states (prevalence and incidence rates) were analyzed and sensitivity analysis was also conducted. The results fully support findings from established literature. The models' economic evaluation indicates that ITC intervention yields higher benefit-cost ratios and a higher cost-effectiveness ratio (CER), or number of cases prevented per dollar spent, than the TTC intervention. These results support previous findings about the comparative advantage of ITC over TTC for trypanosomiasis control and elimination using static models. We recognize, however, that the approach will only be viable when there is a sufficient density of cattle within the tsetse infested area.

Keywords: Trypanosomiasis, *T. vivax*, *T. b. rhodesiense*, Insecticide and Trypanocide-Treated Cattle, Benefit-cost and Cost-effectiveness analysis, Sensitivity analysis.

Opsomming

Modellering van die ekonomie van ingrypings teen Trypanosomiase deur Insekdoder en Trypanocide behandelde beeste in multi-gasheer omstandighede

*("Modeling the Economics of Insecticide and Trypanocide-Treated Cattle Interventions against
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Trypanosomiase, ook bekend as slaapsiekte in mense en nagana in diere, word versprei deur tsetsevlieë (*Glossina* genus), wat besmetting opdoen deur op aansteeklike gashere te voed. Die beheer of uitskakeling van die siekte is 'n groot uitdaging wat boere in groot dele van sub-Sahara Afrika in die gesig staar. Ons het 'n ekonomiese evaluering van twee tsetse beheer metodes, naamlik: behandeling van besmette beeste met trypanocides oftewel trypanocide behandelde beeste (TTC) en die toedien van insekdoders, oftewel insekdoder behandelde beeste (ITC) as bepalers van die beheer of die uitskakeling van die siekte. Die twee vorms van die siekte wat in ag geneem is, is: (i) een veroorsaak deur *Trypanosoma vivax*, wat hoofsaaklik die vee beïnvloed en (ii) een veroorsaak deur *Trypanosoma brucei rhodesiense*, wat hoofsaaklik die mens beïnvloed. 'n Voordeel-koste-

ontleding is uitgevoer vir eersgenoemde, terwyl 'n koste-effektiwiteit vir laasgenoemde uitgevoer is, aangesien 'n mens se lewe nie in geldwaarde uitgedruk kan word nie. Ons het twee modelle wat die biologie van *T. vivax* infeksie die beste beskryf uitgebrei en ook die biologie van die *T. b. rhodesiense* infeksie in beide modelle ingesluit. Beide die ITC en TTC modelle vir *T. vivax* en *T. b. rhodesiense* infeksies is ontleed en sensitiwiteits analyses is gedoen. Die prevalensie en insidensie koerse bepaal deur die modelle stem ooreen met die resultate gevind in die literatuurstudie. Ekonomiese evaluering van die modelle dui aan dat die ITC ingryping hoër voordeel-koste verhoudings oplewer en 'n hoër kostedoeltreffendheidsverhouding of aantal gevalle voorkom per dollar bestee as die TTC ingryping het. Hierdie resultate ondersteun vorige bevindings oor die vergelykende voordeel van ITC oor TTC vir tripanosomiase beheer en uitskakeling met behulp van statistiese modelle. Ons bevind egter dat die benadering slegs lewensvatbaar sal wees as daar 'n voldoende digtheid van vee binne die tsetse besmette area is.

Sleutelwoorde: Tripanosomiase, *T. vivax*, *T. b. rhodesiense*, Insekdoder en Trypanocide Behandelde Beeste, Koste-ontleding, Koste-effektiwiteit en ensitiwiteits Analises

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Dedications

This work is dedicated to my family, friends and most of all to my deceased dad (Mr. Andrew B. Jamah)—whose death during this period brought me pain, sorrow and the strength to make this work a success.

Publications

The paper below, which is an extract from this thesis will be submitted for publication:

1. A Mathematical and Economic Assessment Model of Insecticide and Trypanocide-Treated Cattle Interventions against Trypanosomiasis Disease in a Multi-host Situation.

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Chapter 1

Background of the Study

Trypanosomiasis is a neglected tropical disease under the classification of the World Health Organization (WHO). It is vectored by tsetse flies (*Glossina* spp) that occur in thirty-six (36) countries across the African Continent. The flies transmit several species of trypanosome, causing sleeping sickness in humans (Human African Trypanosomiasis or HAT) and nagana in animals (African Animal Trypanosomiasis or AAT). The disease is passed on to human hosts through bites by tsetse fly (*Glossina* genus) which have picked up the infection from human hosts or from infectious animals carrying the human form of the disease [84]. The most widely-known forms of the disease are as follows: the one caused by the parasite *Trypanosoma brucei gambiense*, which is found in West Africa and the disease form caused by *Trypanosoma brucei rhodesiense* parasite, which is found in East and Southern Africa. The latter is the more severe form of the disease. Gambiense HAT is accountable for more than 97% of all infection in humans, which can be asymptomatic for months or even years, and can become fatal if left untreated [54].

The host parasites of the disease are capable of infecting various kinds of domesticated and wild animals that might likely be the source for human infection. There has been strong evidence of clinical cases of the disease detected in domestic animals, wild animals and other species [3, 80, 81]. In most parts of Africa, cattle are the main hosts

affected because the fly prefers feeding on them, rather than on smaller animals such as goats and pigs, says [81].

Of the recommended techniques, our research will focus on the economics of insecticide and trypanocide-treated cattle as interventions against trypanosomiasis in a multi-host situation through the use of dynamical models, which has not previously been used in conducting both benefit-cost and cost-effectiveness analyses of trypanosomiasis control.

1.1 Research Questions/ Statement of the Problem

Over nearly two decades there was a gradual reduction in the activities and capacities of both tsetse-control departments and national veterinary services, thus reducing surveillance for African sleeping sickness. This led to a widespread epidemic of the diseases. It was recognized that the problem of trypanosomiasis was becoming seriously neglected on a continental scale [66].

In the early 2000s, a declaration by African governments, followed by creating a pan-African programme to deal with tsetse and trypanosomiasis, brought this issue back to the centre stage. At the same time, measures were being implemented to control the massive reappearance of HAT [66]. Getting involved in larger scale interventions, means that resource allocation and prioritization are key issues. Decision-making with regard to tsetse control strongly relied on costs and benefits of interventions data, in handling the economic aspects of the disease, and its control has generally been regarded as especially complex. Knowledge of the disease impact on cattle productivity is sparse, and is based entirely on individual, site-specific studies, thus yielding very variable results [62, 67]. Historically, the economic analysis of African trypanosomiasis began with estimates of the costs of control, progressing to studies of the impact on livestock productivity and to project-based benefit-cost studies for specific areas where disease control operations were undertaken [62].

1.2 Objectives of the Study

The traditional role of mathematical models for trypanosomiasis has been to give one an understanding of the transmission dynamics of the disease within the study population. Mathematical models [28, 34] have been used to suggest that the disease form in humans caused by the parasite *T. b. rhodesiense*, and the animal form caused by *T. vivax*, can be controlled through the use of ITC and TTC, but the benefit-cost and cost-effectiveness of these interventions has not been studied using a dynamical modeling approach. We look, not only at interventions maximizing benefits to farmers, but also their cost-effectiveness and efficiency in eradicating the human disease.

The main aim of this work is to conduct a cost evaluation for the control or elimination of the disease and to estimate the changes in economic, turnover resulting from two different tsetse control interventions:

- (i) The use of insecticide-treated cattle (ITC), whereby insecticide is applied topically to hosts, thereby increasing tsetse mortality without directly increasing parasite mortality.
- (ii) The use of injected trypanocides, which kill trypanosome species without increasing tsetse mortality.

In our modelling, we consider two trypanosome species: *T. vivax*, a trypanosome species that is highly infectious to livestock hosts, and *T. b. rhodesiense*, which infects humans.

1.3 Methods

The methods to be used are as follows:

- (i) Extend existing mathematical models that describe the two distinct control interventions.
- (ii) Use computational tools (MATLAB) in simulating and analyzing our models.

1.4 Overview of the Chapter

This chapter began with a background of the study, and is followed by three sections, namely: research questions, objectives of the study and methods of implementation. In each of these sections, we set forth a platform leading to the succeeding section. The background of the study set the stage for our research questions. The objectives of our study clearly pointed out the primary reason(s) for undertaking such a study. Following the statement of the problem section is the methods section, which outlined the tools used in the achieving of our study objectives.

Chapter 2

Review of Related Literature

The subject trypanosomiasis, which is a tropical neglected disease has a vast history and with a lengthy literature regarding its control and interventions approaches. However, this work is mainly focus on the economics of the disease control, management intervention options against the disease is discussed in-depth in this chapter and different tsetse species and demography is also highlighted in this and the preceding chapters.

The disease trypanosomiasis, depends completely on being vectored by tsetse fly, after which different stages occur in both the mammalian host and the vector. There are varieties of trypanosome species vectored by tsetse files that cause HAT and AAT across sub-Saharan Africa. The parasites multiply within mammalian hosts, and the disease is picked up the fly takes an infectious blood meal. Thereafter, within twenty-one days the parasites mature and move to the salivary glands of the fly, which is then fully infectious for a possible transmission back to vertebrate hosts during another blood meal [29]. While depredations by African Trypanosomiasis in both humans and animals were clearly identified and recognized as early as the beginning of the 20th century, concerted efforts to quantify and analyze its economic impact on African agriculture really began in the 1970s. Nevertheless, awareness of the economic dimension had been growing for some time, as techniques for dealing with trypanosomiasis were being developed and refined in the 1950s and 1960s; studies increasingly included analyses of the costs of the

control methods developed and implemented.

Interest in the economics of trypanosomiasis control grew with the Food and Agriculture Organization (FAO) and WHO including it within their agendas in the 1960s. The first studies looking openly at the economic aspects of the disease were held in the 1970s and when the FAO held a conference in 1977 on the economics of tsetse and trypanosomiasis control, establishing the subject firmly on tsetse and trypanosomiasis agenda [46]. Since the early 1970s, the socio-economic sides of the disease, alongside its control in humans and their livestock, have been studied in many locations, using and developing a wide range of techniques to gather data and use it in economic analyses [46].

2.1 Tsetse Population Dynamics, Birth Rate, Transmission Probability and its Feeding Preference

Tsetse fly, which has a completely different reproduction process, making it unique as opposed to other insects, deposits a single egg which is fertilised and kept within the uterus during pregnancy. Its reproductive rate strongly depends on the production rate of its larvae and the rate at which those larvae developed into adults through the pupa stage [27].

Tsetse population dynamic is influenced mainly by its mortality rate, which has a direct effect on the population growth of the vector [27], and an indirect effect on parasites that they transmit [59]. In 2012, it was found out that age distributions of insect and their population mortality rate can be evaluated by following the time course of survival of insects sampled in the field [8].

Methods for estimating tsetse mortality from data on ovarian dissection rely strongly on the following three major assumptions: (i) the capture likelihood is independent of the fly's age; (ii) the population of the vector under study has a stable age distribution, and lastly, (iii) adult tsetse mortality is not a function of age [79]. The proportion of a fly's blood meals taken from a host does not merely depend on its abundance, but also on the

fly's feeding preferences [48]. The transmission of the disease in a fly has been shown to be a direct consequence of an infectious blood meal from the host. The likelihood of an infection arising in tsetse from an infectious blood meal obtained from a vertebrate host varies with the complexity of the developmental cycle. There is evidence that a vector has a higher likelihood of being infected with the *T. b. rhodesiense* parasite during its first blood-meal than subsequent blood-meals compared to that of *T. vivax* and *T. congolense* [68].

2.2 Life Circle of the Disease in Tsetse and Human Host

In the vector, trypanosomes reside almost exclusively in the bloodstream and are transmitted by the bite of the tsetse fly which acquires the infection while taking a blood-meal, and returns the trypanosome to a vertebrate host in its saliva when it takes another blood meal. This means of transmission is done by inoculation, which makes this group of trypanosomes to also be considered as saliva-type or "Salivarian". Another type of trypanosomes species is the *Trypanosoma cruzi*, which is transmitted by fecal contamination and is referred to as a "Stercorarian". The range of African trypanosomiasis is determined by the range of the vector. Interestingly, only newly hatched tsetse flies are competent to transmit the disease.

The ingested form that is infectious for the fly is termed the short-stumpy bloodstream trypomastigote, which is a non-dividing form. As shown in Figure 2.1 above, following ingestion, the blood-meal is retained within the midgut, and the parasite differentiates into a procyclic form and divides by binary fission. After about two weeks some procyclics migrate from the midgut through the hemocoel eventually reaching the salivary glands. At this point they differentiate through an epimastigote stage into a metacyclic trypomastigote stage, which is a non-dividing form infectious for the mammalian host. Metacyclic trypomastigotes are found in the salivary glands approximately 20 days after the bloodmeal, and there are approximately 40,000 trypomastigotes per bite, but it takes only 400 to initiate an infection, says [23].

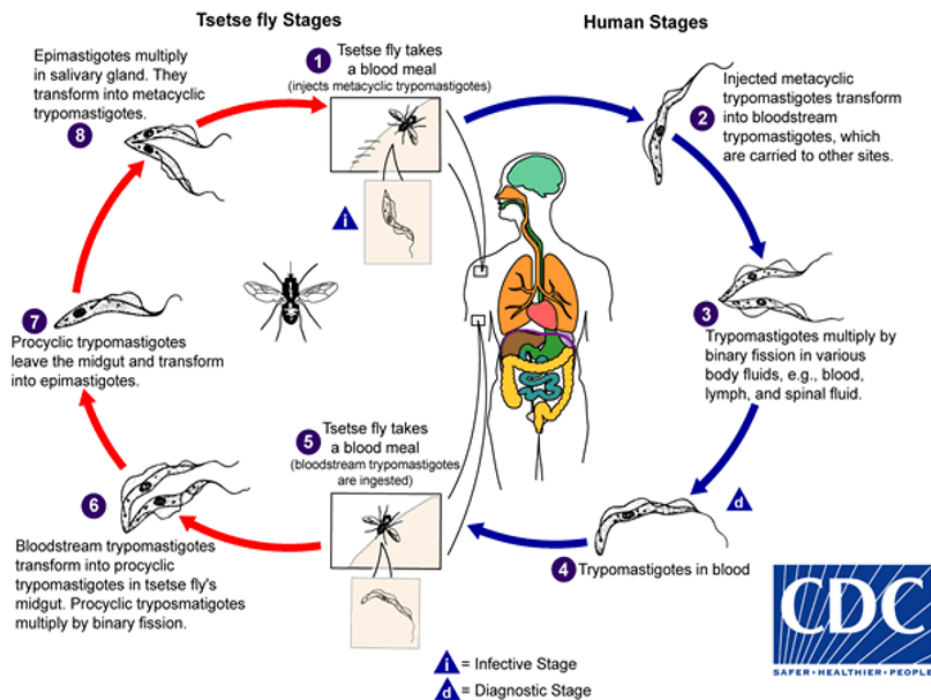


Figure 2.1: Disease life circle with tsetse and human host. Source: Adapted from [23].

2.3 Burden of the Disease in Humans and Livestock

The major burden of trypanosomiasis within the African continent is found in cattle. There are three major forms of the pathogen that cattle are subjected to, namely: *T. congolense* and *T. vivax*, and *T. b. rhodesiense* to a lesser extent. The two parasite forms discussed are: *T. vivax*, and *T. brucei*—whose two sub species are: (i) *T. brucei. brucei*, which only infects cattle and is not harmful to them and (ii) *T. b. rhodesiense*, which is the only form that causes disease in humans found in East and Southern Africa. These parasites have unequal rate of transmission, that is, the rates of transmission from vector to host are quite different than from host to vector. This results in a complex epizootiological pattern characterized in flies by low prevalence of infection of *T. congolense* and *T. b. rhodesiense*, but a higher prevalence of *T. vivax*, and in cattle, a high prevalence of *T. congolense* and *T. vivax* but a low prevalence of *T. b. rhodesiense* [32].

It has been very difficult to estimate the size of the problem posed by HAT, both on a

continental and a national or local scale. It is estimated that nearly 60 million people are exposed to the risk of trypanosomiasis infection in at least 20 countries but only around 3-4 million of those people are subject to surveillance [10, 55]. Estimates also show that there are over 10,000 cases of HAT per year, causing an estimated disease burden of 1.3 million Disability Adjusted Life Years (DALYs), and resulting in a financial loss in excess of more than \$1 billion due to the effects of the disease in both animals and humans [22, 38, 65].

Estimates of the burden of sleeping sickness based on field data have been undertaken in Southern Sudan for *T. b. gambiense* disease and in South-Eastern Uganda for *T. b. rhodesiense* disease [63]. The disease is inevitably fatal in untreated individuals, and only a proportion of those infected are treated; between 3% and 5% of these die. Thus the number of DALYs lost per infected person is very high. The total number of deaths due to sleeping sickness is estimated at about 50,000 to 100,000 persons annually, which could imply an annual burden of disease of some 2 million DALYs [10].

The nature of human to fly contact and the tendency of the disease to infect individuals in particular occupations, especially in the early stages of epidemics, are well known. This increases the disease's impact on households, since it tends to hit the main providers, which are lost to the family if they die undiagnosed. Estimates have been made, based on interviews with diagnosed patients, of the financial costs borne by their families. Payments for pre-treatment drugs, such as vitamins, plus other costs such as transport, food provided during hospitalization and treatment, amount to a figure equivalent to 12% of the annual income from their agriculture proceeds [26]. First-stage treatment dose costs are estimated at US\$107 for pentamidine at a subsidized price, as against US\$227 at full market price, and US\$114 for suramin, and for second-stage treatment the estimates are US\$257 for treatment using melarsoprol and US\$675 using eflornithine [55].

With regard to the burden of the disease in animals at risk, an estimated 50 million livestock live within a highly infected tsetse zone stretching around an area of nearly 10 million square km in sub-Saharan Africa [7, 25]. There have been several efforts to

quantify the impact of the disease in cattle. Some studies seek to find the direct impact on key cattle productivity and its monetary impact [61], while others investigate the indirect impacts of the disease constraint on livestock and crop outputs [7, 25]. Owing to the fatal nature of this disease, much research has been conducted to provide methods of eradicating the disease or minimizing its spread, particularly through managing the vector [28, 34, 76].

2.4 Tsetse Control Interventions

Over the past years, measures to control the disease have been conducted on a broad front, though with limited success; that is, areas previously clear by control measures often become reoccupied by migrating flies, thus leaving the total fly distribution remaining largely unchanged over nearly half a century [48]. *T. vivax*, *T. congolense* and *T. b. rhodesiense* trypanosomes species continue to have high prevalence in much of Africa thus making ranching difficult in many areas [48]. Control measures of the disease are generally used to restrict trypanosomiasis of livestock; nevertheless, estimating the benefits of particular control measures requires one having a knowledge of how specified reductions in the tsetse population will affect the livestock productivity parameters.

Vector control activities have been primarily aimed at controlling HAT, which have been undertaken at various times and in different localities. In the wake of these controlled activities, huge success from intervention strategies against both the vector and parasite of the disease has resulted mostly from the administering of drugs to treat the disease both in humans and livestock. This has led to a greater understanding of the biology and ecology of tsetse, and advancement in the cost-effectiveness and benefit-cost of tsetse control, and has rejuvenated much interest in the approach to disease management [2, 77].

Major Tsetse Control Intervention Strategies

There are two main strategies for the control of the disease, which are reducing the disease reservoir and controlling its vector population. The types of control interventions within these strategies are as follows:

2.4.1 Insecticide-Treated Cattle (ITC)

The risk to cattle population in most parts of the African continent is from both tsetse and tick borne diseases, which allows a single control measure to control several diseases. This has been warmly welcomed by farmers. Consequently, the use of ITC for vector control increased speedily, leading to several publications on the treatment of cattle with pyrethroids, which reduces tsetse and tick related diseases [4, 24]. Insecticide application to cattle has proven to be the most appealing technique for use by farmers, because it involves simple procedures that require no special purchase of baits. The first application of this method in Zimbabwe and West Africa contributed to a widely accepted view that pyrethroids are effective on cattle for 2-3 months [46]. More recently, work in Zimbabwe suggested that the persistence of effectiveness averaged only one month, and could be as short as five days in hot weather [75]. Since the introduction of the ITC intervention approach, which has been refined in its application because of the vector preferential feeding on larger cattle in a herd, the cost incurred by farmers in the control or elimination of the disease has been reduced. Applying restricted application of insecticides to locations on cattle where ticks accumulate reduces the amount of insecticides required, thereby reducing tsetse and trypanosomiasis and at the same time providing tick control [6]. This form of insecticide application provides financial benefits to farmers and helps to alleviate concerns about the environmental impact of insecticides used [6, 76]. Currently, a lot of studies have shown that the application of insecticide can be restricted to cattle legs and belly where most tsetse feed, which could reduce total material costs of treatment by 90% [70].

In addition, since tsetse prefer feeding on the bigger animals within a herd, those animals are the only ones that need to be treated, which further saves costs [70, 72]. The restriction of insecticide to larger cattle allows younger cattle to be exposed to ticks, which

enables them to develop natural immunity to tick-borne diseases and subsequently reduces the impact on dung fauna, which play a central role in maintaining soil fertility [17, 73, 74]. There is still a problem in that its application can only be used in areas where there is a large number of cattle, though has been suggested by modeling that insecticide is more effective even when cattle are distributed spatially [71].

2.4.2 Trypanocide-Treated Cattle (TTC)

Generally, treating cattle has been narrowed down to two main strategies, namely: (i) mass treatment—where all of the cattle are given treatment at a certain rate, and (ii) selective treatment—where only those cattle showing symptoms of illness are treated [48]. The success of a treatment relies strongly on the type of treatment that is carried out, and on the trypanocidal effect of the drug in relation to its treatment rate. In the mass treatment regime, nearly all of the cattle are considered free from disease if and only if the treatment interval is much less than the average duration of prophylaxis afforded by the drug. Regardless of the type of treatment strategy, the disease prevalence within cattle host increases speedily with the drug prophylactic effect [48].

The impact of trypanocide intervention has been demonstrated using two impact scenarios [28]. Details on those case scenarios regarding the impact of trypanocide on permutated hosts can be found in [28].

2.4.3 Traps, Targets and Bait Technology

Traps are complex three dimensional structures, which are inspected every few days if they are to be kept in good order and there is difficulty attracting some tsetse, especially *Glossina morsitans* and *Glossina austeni*. It became more cost-effective to replace traps with simple visual targets that are coated with sticky deposit, to sample *Glossina austeni* [46]. Generally, the substitution of targets for traps has been cost-effective in all parts of Africa, the general principle being that an effective trap can be readily converted into a target that is twice as effective at about half the cost. In order to use traps, there were

studies of the effect of various visual and olfactory stimuli on different types of response [46]. As the result of these studies, it was possible to design economical traps, such as the F3 and Epsilon [39]. The relative effectiveness of various trap types varied accordingly to the tsetse species to be sampled [20]. Surprisingly, it was also found out that the relative efficacy also depends on the geographical location. Thus, for *G. pallidipes* in Kenya and the Eastern province of Zambia, the Ngu trap proved about twice as effective as the Epsilon, and the reverse was true in Zimbabwe for the relative performance of the same trap [39]. Odour attractants and repellents had played a major role in perfecting the bait technology against insects. A number of attractants were identified and the approximate rate at which they are released in the odour of a large ox are as follows: acetone at 5 mg/h, butanone at 0.5 mg/h, 1-Octen-3-ol (octenol) at 0.05 mg/h, 4-methyl phenol at 0.05mg/h, 3-n-propyl phenol at 0.005 mg/h [46].

In the 1970s, the first of the new baits was developed and arose largely from empirical work with tsetse of the palpalis group found in West Africa. Biconical and pyramidal traps were some of the most effective devices, which have been widely used for surveys long ago [39]. However, these traps were not significantly cost-effective for use on their own in large-scale control operations. In addition, they performed poorly against the morsitans group, a problem which was dealt with in the late 1970s onward by a more analytical approach to bait development.

2.4.4 Tsetse Control Insecticides (Aerial Spraying)

The *Glossina pallidipes* species of vector are much more susceptible to most insecticides but their biology is unique in many ways and only chemicals with specific properties have proved suitable [46]. There is a wide range of natural and synthetic insecticides available, offering different levels of toxicity. Toxicity to the insect is obviously important and low toxicity of operators has been a key factor, particularly where tsetse control was carried out over large areas, and those applying the insecticides under arduous African bush conditions could be subjected to prolonged exposure.

The types of tsetse control insecticides (Aerial Spraying) techniques are:

(a) **Residual Techniques**

In carrying out these techniques, vehicle-mounted spraying machines are used, for instance, on all terrain vehicles such as Mercedes Unimog in Botswana and Zambia [46]. Helicopters were used in Nigeria and Cameroon where high insecticide dosages, such as ultra-low volume (ulv) formulations of endosulfan at 1kg/ha, were needed to provide a residual effect [46]. Similar operations were carried out in a number of West African countries with lower dosages of endosulfan and with synthetic pyrethroids, but the indiscriminate nature of these methods caused environmental contamination and the technique has been largely discouraged and discontinued. Residual spraying has had some severe impacts on areas applied. This spraying of organochlorine from helicopters and trucks was monitored in West Africa and showed mortality among the same groups as were affected by indiscriminate ground spraying, and amphibia, monkeys and fruit bats were also killed [37]. As the result of this, there was a disappearance of some bird and anthropod species from the treatment area for up to a year. However, this does suggest that, even with the very high dosages used to give a long term persistence, the effects on non-targeted populations are not irreversible.

(b) **Non-Residual Techniques**

In order to overcome those problems posed by pupal development, while simultaneously reducing the dependence upon residual insecticides, sequential aerial spraying technique (SAT) was designed to deliver a series of low dosage, non-residual insecticides aerosols, which would drift through the target area to kill all the adult tsetse flies. This process needs to be sustained or repeated because juveniles continue to emerge from underground for the duration of the pupal period. In reducing its environmental impact and cost, the inter-spray period must be timed to ensure that newly emerged females do not mate and deposit new larvae before the next application, as it would prolong the underground development and thus the num-

ber of treatments. Most successful SAT operations have employed five treatments at intervals of 15-20 days. Aerial spraying for tsetse control developed from crop-spraying techniques. This method was improved, notably at the Tropical Pesticides Research Institute in Tanzania, until large-scale trials were carried out in Zambia, and with very encouraging success in Botswana [36].

2.4.5 Ground Spraying

Ground spraying is mostly carried out using pressurized knapsack sprayers with a capacity of about 12 litres pre-set to dispense the insecticide at a constant pressure of about 30 p.s.i. The greater the pressure, the finer the spray, and residual deposits require a coarse spray with droplet diameters in range of 500-2000 μm [46]. Ground-spraying techniques did not always achieve the required level of tsetse reduction in a single season and retreatment was common. To reduce the effects of reinvasion between seasonal campaigns, each operation had to penetrate deep into the tsetse infestation and this was well illustrated in Zimbabwe where ground-spraying barriers were used for many years to protect agricultural activities south of the fly belt [46]. These barriers were extended, and some areas were sprayed up to 13 times over a period of 20 years [40].

In 1980, this method resulted in the eradication of the entire tsetse population up to the barrier provided by Lake Kariba [46]. Ground spraying almost certainly removed tsetse flies from a greater area of Africa than any other single technique, with some 400,000 km^2 treated from the 1950s to 1980s [46]. However, as environmental safety became a major concern, the use of residual insecticides and financial constraints curtailed the use of logistically demanding, labour-intensive, public-sector activities, and ground spraying was almost universally discontinued.

2.4.5.1 Impacts of SAT and Ground Spraying:

The sensitivity of tsetse to insecticides such as ensulfan or deltamethrin, and the carefully calculated sequence of applications timed to match the fly's almost unique life cycle, confer a degree of specificity on this technique [46]. Almost immediately after spraying, a few hours at most, the insecticide is not detectable in the terrestrial environment, though it can last for several days in still water. At the population level, non-target species are consequently less seriously affected than with the residual techniques. Endosulfan has been rigorously monitored for non-target effects in Botswana [16, 19, 53]. These studies revealed a temporary depression of non-target aquatic and terrestrial invertebrate populations but fish were the main concern, because of their particular susceptibility to this insecticide.

While the impacts of ground spraying are as follows:

- (a) Ground-spraying indiscriminately has caused severe non-target acute outcomes on other animals, such as: birds, insects, fish, reptiles and small mammals [46]. A pilot study conducted on this means of intervention in Zimbabwe concluded that dichlorodiphenyltrichloroethane (DDT) residues were accumulating in some wildlife species and appeared to substantiate claims by local environmentalists that DDT was causing eggshell thinning in fish, eagles and other raptors [45].
- (b) Ground spraying, often in remote wilderness or hilly areas, is arduous and can lead to potentially dangerous contact with wild animals in the sprayed areas. There is also a high risk of operators being exposed to the spray which might cause some health problems [46]. Other control operations using alternative insecticides such as deltamethrin have been successful, but at a high cost [35].

2.4.6 Sterile Insect Technique and Area Wide Integrated Pest Management of Tsetse Control

Usually applied as part of an integrated pest management system approach, is the sterile insect technique (SIT). In order to fully appreciate SIT, one needs to clearly understand the fundamental principle of Area Wide Integrated Pest Management of Tsetse (AW-IPM).

2.4.6.1 Fundamental Concepts of Area Wide Integrated Pest Management Control

Pest management practices are meant for suppression, eradication or prevention of unwanted organisms that are causing environmental and agricultural problems. Pest suppression and control measures are generally used to shrink the population levels of pests. This method does not make the population of insect extinct but rather reduces the population to a more tolerable level [11]. Unlike pest suppression, pest eradication means total removal of pest from a chosen area [27]. The method of eradication is quite expensive over very large areas, and there has been a little success in this approach.

A long term, preventive and limited toxicity measure of pest control, which is the Integrated Pest Management (IPM), was first developed for the agricultural industry and other institutions because its principles became very relevant to the protection of farmers' holdings [42]. Clearly, the particular requirements of an IPM plan must be tailored to the specific cultural institution. Before making a decision on the implementation of an IPM program, one needs to consider some of the key advantages and disadvantages of an IPM program over traditional pest control measures. Traditional pest control measure in this context, is considered as the repeated application of chemical, without an in-depth understanding of the species or number of pests present.

Integrated pest management focuses on optimizing benefits and minimizing undesired environmental impact and other risks. It involves combining arrays of different techniques and approaches, including biological, cultural, physical, mechanical, educational and chemical methods in site-specific combinations into a sustainable systems approach

for pest management. IPM approaches are normally designed for farmers' application at the field-by-field level [42]. A major challenge for efficient IPM is the management of pests in areas where beneficiaries independently decide whether or not to participate in the intervention campaign. When the concept of area-wide pest management was developed, it was first regarded as an approach for managing a single pest or a small group of pests over a large region, whereas IPM was considered to incorporate all pests within an agro-ecosystem into a management programme that is primarily conducted on a farm-to-farm basis. A firm basis for merging both approaches has since emerged and area-wide programmes not only monitor and attempt to manage a key pest but also to address secondary pests and non-targets, including beneficial arthropods [11]. Therefore, the term 'area-wide IPM' provides a more accurate description for this pest and agro-ecosystems management approach.

There are several advantages that result from an area-wide IPM approach, listed in [11] as follows:

- (i) More effective and more efficient pest management than pest control on an individual farm-by-farm basis;
- (ii) Long-term solutions to key pest problems in larger agro-ecosystems as opposed to quick-fix solutions on a few hectares;
- (iii) Integration of the best and most environmentally benign management techniques;
- (iv) Bio-rational management strategies for secondary and other key pests; and
- (v) Prevention of major pest outbreaks and provision of more sustainable pest management procedures.

Any control or elimination efforts against tsetse and trypanosomiasis disease should take advantage of the associated benefits that come with implementing the principles of Area wide Integrated Pest Management. The African Trypanosomiasis is a trans-boundary disease problem that can effectively be sustained even by low-density tsetse

populations. This problem constitutes a primary blockage for enhancing sustainable agriculture and rural development . The principles for area-wide integrated pest management should serve as a road-map in the planning and implementation process of tsetse and trypanosomiasis control measures, and thus avoid some of the typical shortcomings of some conventional field-by-field IPM approaches [21].

2.4.6.2 Advantages of IPM

The advantages of using Integrated Pest Management System are as follows:

- (i) It reduces the use of chemical application which in turn reduces the risks posed to health workers or staff.
- (ii) It reduces the use of chemical application, which might result in a financial saving.
- (iii) It is also environmentally friendly mainly in the area where it is implemented.
- (iv) It also provides the only possible alternative in the long-run for controlling pests in areas where the application of chemical has not been suitable.
- (v) It enables pest control authorities to have knowledge of pest activity within their facility.
- (vi) More importantly, it is the pest control measure of choice by farmers.

2.4.6.3 Disadvantages of IPM

The disadvantages of using IPM are as follows:

- (i) It requires a larger number of man-hours than traditional pest management.
- (ii) To work suitably, it will need a coordinated effort from all staff members.
- (iii) It might be more expensive from the outset than traditional pest management.

2.5 Fundamental Principles of Sterile Insect Technique (SIT) and its Impacts

SIT involves the production and systematic release of reproductively sterile insects among the indigenous population, sustained over several generations of the pest population [46]. When this is done, sterile male insects mate and inseminate female insects, thus making them become effectively barren for the rest of their lifetime. The sterile and released insects are spread in particular rearing facilities. Males insects are mostly sterilized by radiation at the appropriate development stage of their life and they are taken to the identified target areas and released. In contrast to the applications of insecticide, which might cost the same amount irrespective of the population density of insects, which is much more cost-effective when the target population is high, SIT is mostly cost-effective when the population density is low [46]. SIT can be used for suppression, localized eradication or prevention of insect or pests. It has been observed that SIT used for either eradication of mediterranean fruit fly is economically competitive with conventional intervention methods that are based on monitoring and the application of insecticides [18].

In 1966, at Lake Kariba, Zimbabwe, *G. m. morsitans* adults were collected, sterilized and released, which subsequently reduced the targeted tsetse population below detectable levels within 26 months [13]. Following two aerial applications at Tanga, Tanzania in 1976, SIT component was used to reduce the targeted tsetse population by 81% [83].

2.6 Overview of the Chapter

The review of related literature (chapter two) contains five sections, which summarized the following: tsetse population dynamics, birth rate, transmission probability and its feeding preference, the life circle of the disease in tsetse and human host, the burden of the disease in humans and livestock, tsetse control and intervention techniques, and lastly the fundamental principles of sterile insect technique (SIT) and its impacts.

Chapter 3

Economic Assessment Framework of Livestock Disease Control, Previous Benefit-Cost Studies of Tsetse Control, Methodology and Material Used

The major content of this chapter is the methodology of our work, which is introduced by economics literature on insecticide importance in pests control within the context of crop production, which has been adapted to our trypanosomiasis control context. This is achieved by discussing different theoretical concepts and approaches on the economic assessment, and a framework of livestock disease control, and the methodology and material used. These theoretical or intangible frameworks and their methods used in analyzing the economics of cattle trypanosomiasis control interventions and the productivity assessment of insecticide and trypanocide treated cattle are fully discussed.

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3.1 The Economic Problems of Livestock Diseases

Livestock production is a commercial activity that involves a change processes in which livestock raw materials are used to produce livestock products for both consumers and farmers benefit [15]. These change processes can be impaired by livestock diseases [44, 58]. This means "in economic terms, a livestock disease is a specific class of undesirable influences in the value creating processes based on using livestock as economic resources" [47]. Undesirable effects of diseases on animal production are variable; and the loss in output from animal production due to diseases recognized within the cattle production farming system can be divided into the following groups: weight loss, death, lactation effects , and reproductive loss [51, 52, 69].

Trypanosomiasis can modify many different physiological processes related to the disease effects, leading to the weakening of production in affected animals [69]. These functional disorders and negative impacts lead to output, which is translated into measurable economic effects, affecting the productivity of inputs used in the production process.

3.2 Economic Costs and Losses Concepts

In health economics, the Disability Adjusted Life Year (DALY) is a quantitative indicator of the burden of human disease that reflects the total amount of healthy life lost [5]. In order to quantify the exact losses due to human, plant, or animal diseases, one needs to know the actual incidence and prevalence rates of the disease, and the nature and magnitude of the losses in hosts infected (human, animal or plant) [58]. Applying the concept for plant diseases in [41] to our trypanosomiasis intervention context, where different definitions of production loss corresponding to different levels of livestock output, can be illustrated below as:

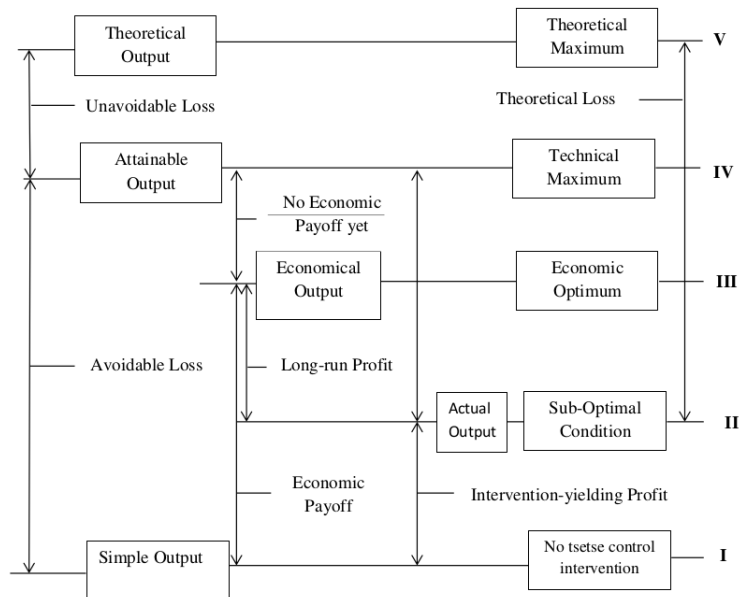


Figure 3.1: **Cattle Production Output Levels and Losses.** See text (below) for explanation. Source: Adapted and modified from [41].

In Figure 3.1 above, the theoretical output (V) is hypothetical, which is assumed to occur under ideal conditions where cattle experience full production potential. This theoretical output is not of interest because analysis is focused on cattle production in a real world setting. Therefore, assuming that attainable output (IV) is an output that a farmer can acquire under real farming conditions in the absence of the disease. If cattle are bitten by infectious flies and become infected, the attainable output level (IV) reduces to a minimum level (I) or a simple output level, provided no intervention measure is implemented. The Economic output (III) suggests that any intervention measure against the disease has an associated cost that is an economic option if the output value to be saved offsets the cost of intervention. There may be an economic loss between (III-IV) that a farmer might incur, and should be accepted without intervention because an attempt to intervene might be more costly than incurring the loss. Long run profit is acquired between (II-III) as a result of disease intervention efforts that reduced output loss. The difference between (II-I) is the intervention yielding profits deriving from disease control measures, starting from a simple output (I)—where there is no control measure.

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Lower than the economic output (III) is the actual output (II) or sub-optimal condition. A higher sub-optimal condition induces investment in disease control measures, thus enabling the actual out (II) to surpass economic output (III), thereby resulting in economic losses.

3.3 Production Functions and Valuation of Cattle Output

The application of the production function framework in animal production has been less frequent compared to crop production. The effect of animal diseases in a given production system is to reduce the efficiency with which inputs are converted into outputs [60, 69]; these animal diseases can be treated within the production function framework, for which economic principles, a well developed set of concepts, and analytical procedures do exist [47].

3.3.1 Prices and Values of Cattle Production

In formalizing the output of cattle production system, it is important to distinguish between recurrent and embodied productions [50]. The former products are as follows: draught power, manure, and milk; and the latter products are the change in body weight and the changes in the number of cattle per herd [50]. Embodied production is measured by subtracting the embodied production at time t from embodied production at end of the time $t+1$. The value of a recurrent production ($V_{(i,t)}^R$) for a particular monitored period t is given as:

$$V_{(i,t)}^R = \sum_{i=1}^n \sum_{j=1}^k q_{(j,i)} p_{(j,i)} \quad (3.3.1)$$

where $q_{(j,i)}$ is the exact quantity of the recurrent production j in period t produced by cattle i and $p_{(j,i)}$ is the monetary value of recurrent output j obtained in per unit q , k is the number of recurrent products and the total number of cattle in the herd is denoted by n .

The worth of embodied production ($V_{(i,t)}^E$) for a monitored period t is found by adding

25 3.4. Disease Damage Control Model and Framework in Cattle and Plant Production

the embodied production of individual cattle (i) in the herd. Individual cattle embodied production is found by deducting the selling price of the cattle (i) at the end of the period $P_{i(t+1)}$ from the selling price $P_{i(t)}$ at the start of the period. For clarity, we define embodied production as:

$$V_{(i,t)}^E = \sum_{i=1}^n (P_{i(t+1)} - P_{i(t)}) \quad (3.3.2)$$

3.4 Disease Damage Control Model and Framework in Cattle and Plant Production

In the production of cattle and crops, production levels has been categorized into three types: potential, attainable and actual level [78]. These levels do correspond directly to similar growth conditions, defined by three main groups of growth factors, namely: growth defining, growth limiting and growth reducing factors. Growth potential and production levels are determine by the growth defining factor; these include: genetic characteristics of cattle or plant and climate driven factors that are outside the farmer's control. We define potential in our context, as potential growth or output as the highest production level that is achievable within a given physical environment and genetic characteristics of both cattle and plants, assuming that there are no growth limiting or growth reducing factors. Growth limiting factors are the scarcity of water and other nutrients, and output becomes attainable when these factors occur. Farmers can control the level of water and nutrients by irrigation, fertilizing and supplementing feed to cattle to attain a certain output level. Achievable output level assumes no growth reducing factors, such as weeds, pests, and cattle diseases. For growth reducing factors, the production level reduces further to actual output level, and when nothing is done to control the growth reducing factors, the output is reduced to simple output [78].

The impact of control interventions on cattle output loss is presented graphically in Figure 3.2 below, where Q_{max} is the total output of the cattle herd obtained assuming that trypanosomiasis is under complete control or does not occur (potential output or optimum growth condition). At output level **O**, there is a total output loss due to maximum

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damage from trypanosomiasis; this might be an exception because in most instances, the actual minimum output that a cattle owner may obtain from his herd is always greater than zero except for extreme situations. The output level Q_{min} represents output obtained when no direct control or interventions inputs are used, which is determined by factors like the natural immune system of cattle or the presence of trypano-tolerant cattle within the herd. The potential output loss is the difference between Q_{max} and Q_{min} , which corresponds to the measure of productivity limit of trypanosomiasis control inputs due to the use of trypanocide-treated cattle and insecticide-treated cattle. The actual output Q_{min} may tend towards zero, thus increasing loss in potential output, if the immune resistance of cattle is low and there exist a limited number of trypano-tolerant cattle within the herd [78].

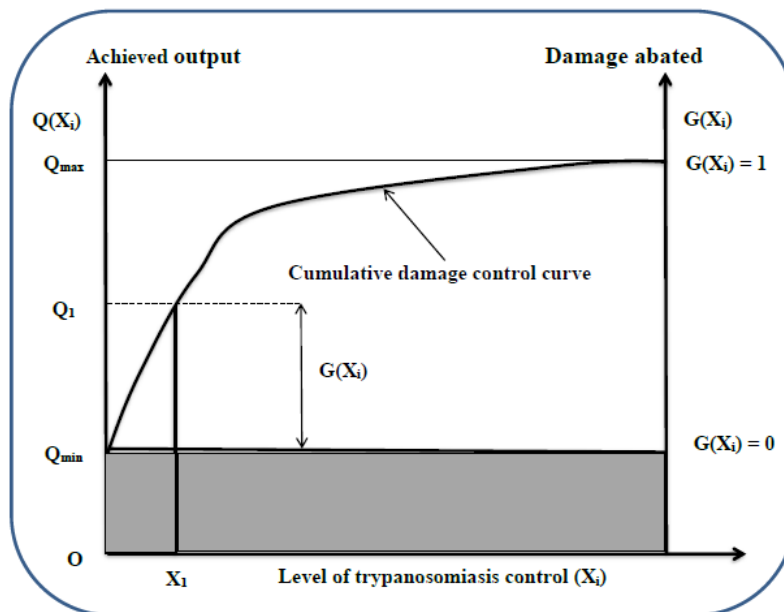


Figure 3.2: Impact of Disease Control on Potential Output Loss: Damage Control. Source: Adapted and modified [1]

The above modeling approach discussed has virtue in treating cattle diseases in a damage control framework. The primary reason for using such models is to explain any

possible overestimation of inputs [9]. However, there may be limitations, and results might be different depending on model[1, 56].

3.5 Economic Relationship Between Costs of Control Interventions and Output Loss Within a Cattle Herd

The suggested view of neoclassical economists is that productivity of production factors in a production process can be analyzed based on the principle of marginal productivity—that an input is used until its marginal cost is equal to its marginal output. In our context of trypanosomiasis control, the optimal level of intervention inputs is attained when the cost of an additional unit of the inputs (insecticide or trypanocide) recover additional value of output (cattle or human) saved. The relationship between the cost of trypanosomiasis intervention inputs and the potential output loss saved is described in the Figure 3.3 below. We observed that without control interventions, potential output losses would amount to L_1 , and also as the cost of control intervention increases, potential output losses will eventually decrease but at a diminishing rate due to the diminishing marginal returns to the control intervention efforts. The efficiency frontier line L_1L_2 shows the lowest potential output losses obtained for any cost to control intervention. The Line MN is the production isocost line, which indicates potential output loss and control interventions cost combinations that amount to the same cost of control intervention. Management control strategy indicated by the point of tangency (P), is the lowest intervention cost that is achieved, incurring an intervention cost of C_p that corresponds to a potential output loss of L_p . The principle of marginality is fulfilled at this point of tangency (P) and the optimum disease control can be reached.

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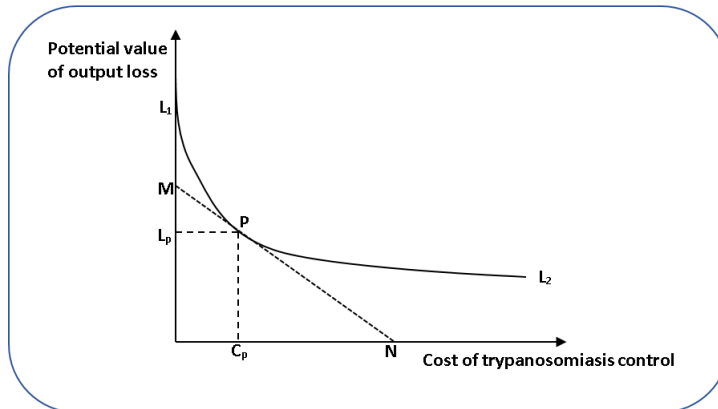


Figure 3.3: Schematic Diagram of the Relationship Between Potential Output Loss of Cattle and Cost of Trypanosomiasis Intervention Inputs. Source: Adapted and modified from [47].

3.6 Productivity of Insecticide and Trypanocide Usage in a Trypanosomiasis Regime

In a trypanosomiasis control setting, control intervention inputs (ITC and TTC) tend to subject farmers to some problems that do arise in connection with a direct increase in their inputs [9]. The problem of growing trypanocide resistance to its inputs in a control process has important economic consequences that are crucial for the interpretation of damage abatement inputs productivity, and the use of ITC through restricted application has now answered question about cattle endemic stability within a herd [1, 9]. The impact of the effectiveness of insecticide and trypanocide within a cattle herd in the presence of trypanosomiasis is illustrated graphically in Figure 3.4 below, where Q_{min} represents simple output when no intervention measure is applied, and $G_1(X_1)$ and $G_2(X_1)$ represent the intervention of insecticide and trypanocide, respectively. When trypanosomes develop drug resistance, trypanocide becomes less effective, and as a result the cumulative damage control curve for trypanocide becomes lower than the cumulative damage control curve for ITC. The actual output Q_1 in a ITC control situation will be higher compared to the actual output Q_2 in a TTC control situation. Within the same cattle herd and a trypanosomiasis setting, more damage will be abated with the

use of insecticide then that of trypanocide, thus making $G_1(X_1) > G_2(X_2)$ as indicated in Figure 3.4 below, the values $G_1(X_1)$ and $G_2(X_1)$ are defined on the scale $[0, 1]$, which reduces output by $[1 - G_1(X_1)]$ and $[1 - G_2(X_1)]$, respectively. In the same control environment, $[1 - G_2(X_1)]$ will represent the uncontrolled damage due a to drug resistance situation as the result of trypanocide usage, which will be higher than $[1 - G_1(X_1)]$ —the uncontrolled damage for ITC situation. As a result, the cost of the disease, which is the sum of the value of output loss and the costs of control interventions will be greater for TTC than ITC situation.

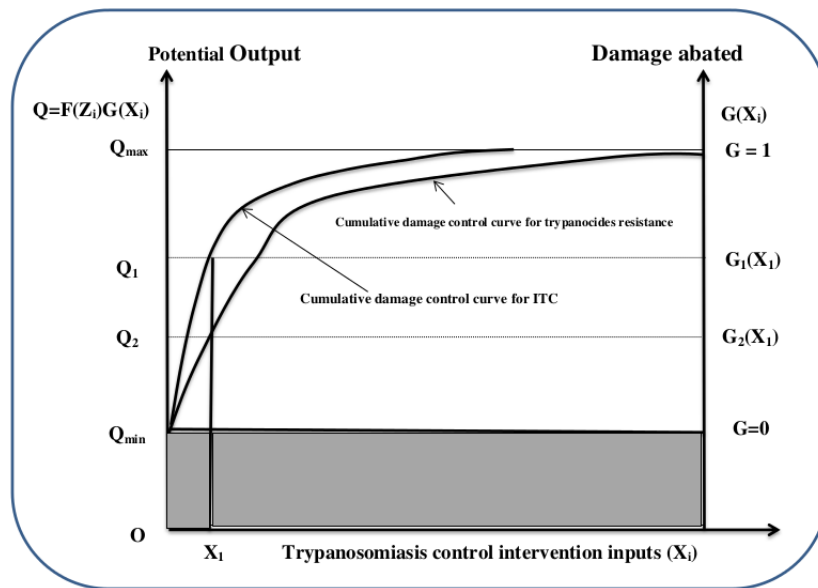


Figure 3.4: ITC and TTC Impact on Cattle Productivity within a Trypanosomiasis Regime. Source: Adapted and modified from [1].

3.7 Previous Benefit-Cost Analysis Studies of Trypanosomiasis Control

A benefit-cost analysis of trypanosomiasis control should be a major tool for policy makers in tsetse-infected areas in order to allow them make rational allocations of their scarce resources. Overall socio-economic development requirements should be seen in

Chapter 3. Economic Assessment Framework of Livestock Disease Control, Previous Benefit-Cost Studies of Tsetse Control, Methodology and Material Used 30

conjunction with control measures in determining the level of effectiveness of the control intervention. In economics and management, the application of benefit-cost analysis for evaluating projects and planning is of great importance, but such analysis has not been widely used for assessing animal health interventions that could lead to increased productivity. The reasons for benefit-cost analysis are: firstly, where total gains exceed total losses and, secondly, the rate of return per unit of expenditure in terms of present values [49]. Studies have measured the costs of control of African Animal Trypanosomiasis, its benefits and the potential returns it brings into research [38], and have mapped, in East Africa, the economic benefits that livestock keepers acquire from intervention against bovine trypanosomiasis [61]. Estimated costs of tsetse control interventions were explored in Uganda, and economic benefits that farmers obtain from village cattle production system estimated for a high tsetse infestation area within the Southwest region of Ethiopia [31, 64]. Costs of tsetse control have been estimated for a user friendly, cheap and safe method of tsetse control [6, 76].

3.8 Methodology and Materials Used

In order to conduct an economic analysis of the control or elimination of trypanosomiasis, one needs to model the human and animal form of the disease. We adapted earlier ITC and TTC models [33, 34] for *T. vivax* infection, which mainly infects cattle [57], thereby making it possible to compute benefits and costs before and after intervention. Detailed descriptions of these models are given in Figure 4.1 for both ITC and TTC interventions. In performing the benefit-cost analysis, we first surveyed the disease state of both models in order to compare both models' performance with findings from established literature and then performed a sensitivity analysis to examine the contribution of all parameters in both models toward the control or elimination of the disease. Thereafter, we conducted a benefit-cost analysis for both models, using costs and benefits estimates from [31, 61]. The cost parameters or estimates include: administrative costs or basic production costs and cost of trypanocide and insecticide, while the benefit parameters include: quantity of milk produced, days of work performed by oxen,

sale of work oxen and sale of meat. All of the benefit parameters were converted to monetary value, which then enables us to compute the benefit-cost ratio for all cattle benefit parameters in order to identify the best yield benefit parameters in both models. We then extended the adapted models, which incorporate the biology of the *T. b. rhodesiense* trypanosome, which is infectious for humans [57]; this enabled us to conduct a cost-effectiveness analysis and calculate cost-effectiveness ratio (number of cases prevented per dollar spend) indicator. Benefit-cost analyses were inappropriate in this case, because of the impossibility of assigning the benefit of saving a human life a monetary value [57]. In both *T. vivax* and *T. b. rhodesiense* infections intervention regimes, the cattle, human to tsetse ratio used is similar to that used in [59], that is, 50 cattle, 300 humans to 5000 tsetse.

3.9 Overview of the Chapter

This chapter fully discussed the theoretical framework, methodology and materials used for livestock disease control in seven sections, namely: the economic problems of livestock diseases, economic costs and losses concepts, production functions and valuation of cattle output, disease damage control model and framework in cattle and plant production, economic relationship between costs of control interventions and output loss within a cattle herd and productivity of insecticide and trypanocide usage under a trypanosomiasis regime, previous benefit-cost studies of tsetse control, methodology and material used.

Chapter 4

Mathematical Models and Analysis

This chapter (chapter 4) summarises recent papers, which served as one of our motivations for this work, but it also incorporate one of our contributions, that is, the benefit-cost analysis for intervention against *T. vivax* infection through ITC and TTC applications. Using a dynamical model to explore the benefit-cost analysis of trypanosomiasis control gives this work a unique characteristic to that of previous works, that is, by fully exploring the impact of both insecticide and trypanocide interventions against *T. vivax* infection by carrying out mathematical and computational analyses. The succeeding chapter, chapter 5, which is an extension of the ITC and TTC Models in chapter 4, reflects the biology of *T. b. rhodesiense* infection–human form of the disease, enabling us to preformed a cost-effectiveness analysis due to the difficulty in quantifying the benefit of saving a human life against the disease. The endemic equilibrium was not explicitly calculate because this has been done in [33, 34], which extensively dealt with the mathematics.

4.1 ITC Mathematical Model against *T. vivax* Infection

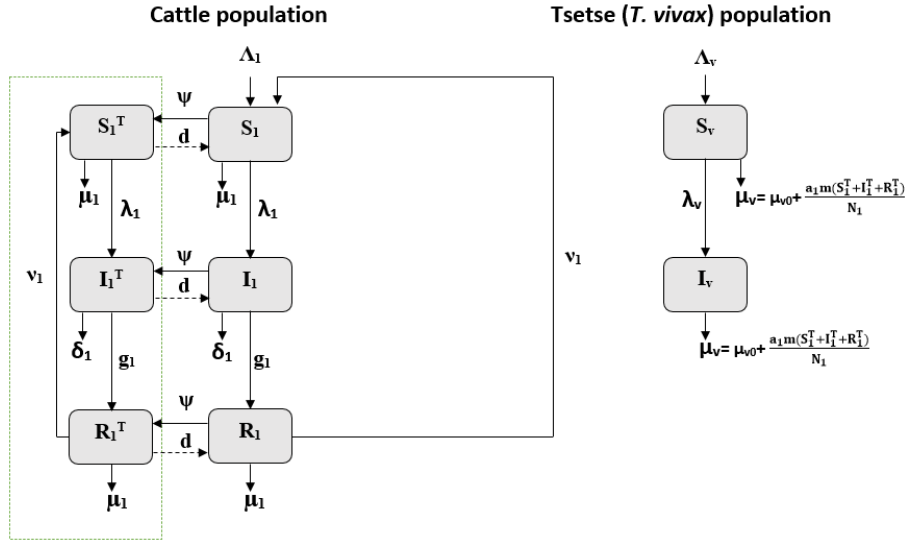


Figure 4.1: **Compartmental ITC Model for *T. vivax* infection**, using ITC as an intervention indicated in the green dashed rectangle. Source: Adapted from [34]. The forces of infection of the cattle and vector populations are λ_1 and λ_v , respectively.

Definition of ITC and TTC Models parameters	
Parameters	Definitions
B_j	Birth rate for host j
B_v	Recruitment rate for tsetse
μ_{v0}	Tsetse natural mortality
μ_j	Natural mortality of host j
m_v	ITC induce mortality in tsetse
a_j	Tsetse-host biting rate
β_j	Probability of an infectious fly bite producing an infection in host j
α_j	Probability of the first infected blood meal from host j that gives an infection in flies
σ_j	Mortality rate of an infected host j
g_j	Recovery rate of an infected host j
ν_j	Loss of immunity rate in recovered host j
T_v	Incubation period for tsetse flies
T_j	Incubation period for host j
ψ	Proportion of cattle treated with insecticide/trypanocide per day
d	Rate of loss for insecticidal and trypanocide killing effect
ϵ	Efficacy of trypanocide

Table 4.1: Definition of models parameters for both ITC and TTC Models

4.1.1 ITC *T. vivax* Infection Model Description

From Figure 4.1 above, all host populations are separated into the following classes: Susceptible (S_1), Infectious (I_1) and Recovered (R_1), the vector population is also separated into three classes: Susceptible vectors (S_v), Infectious vectors (I_v). Due to the presence of treatment (ITC), which enables the treatment of cattle at a rate ψ and then move into the treated classes, S_1^T, I_1^T and R_1^T representing susceptible, infectious and recovered treated cattle respectively. The effect of insecticide decreases with time, lasting for $1/d$ days. Due to insecticidal effect decrease, each cattle in the treated compartment return to S_1, I_1 and R_1 at a rate d . The feeding of tsetse flies is at a rate a per day, therefore on average a fly takes a blood meal of $1/a$ days. It is assumed that flies feed on n host but with a fixed preference of feeding f_j of its blood meal from a host, where $\sum_{j=1}^n f_j$ and $j = 1, 2, \dots, n$, where $j = 1$ for cattle population; therefore, flies take a meal from a host at rate $a_j = af_j$ per day, with $a = \sum_{j=1}^n a_j$ and $j = 1, 2, \dots, n$. The incubation period of the disease in host species is denoted as T_1 and T_v for cattle and tsetse respectively. B_v is the flies' constant birth rate. Susceptible teneral flies become infected after taking their first blood meal from an already infectious host with a likelihood of α_j and transfer to the infectious class I_v . Tsetse flies die at a natural mortality rate μ_{v0} plus an insecticidal imposed death rate. Each vertebrate host has a constant recruitment rate, B_j , including both immigration and birth. Due to the bite of an infectious tsetse, susceptible hosts becomes infected with a probability of β_j and a recovery rate of g_j as the result of treatment. Recovered hosts lose immunity at a rate ν_j , thus becoming susceptible again. Treated and untreated cattle become infected when an infectious fly meal is taken from a cattle with a probability β_1 and the same recovery rate g_1 when treated.

The additional mortality due to insecticidal effect, is obtained when flies feed on treated cattle, which is given in [34] as:

$$\mu_v = \mu_{v0} + \frac{a_1 m_v (S_1^T + I_1^T + R_1^T)}{N_1} \quad (4.1.1)$$

where μ_{v0} is the natural mortality rate of tsetse, a_1 is the biting rate of tsetse on cattle, m is tsetse average knock down mortality, which is assumed to be dependent on the area of the cattle body cover by insecticide and $\frac{(S_1^T + I_1^T + R_1^T)}{N_1}$ is the proportion of cattle kept on insecticide.

ITC *T. vivax* Model Equations

$$\left. \begin{aligned} \dot{S}_1 &= B_1 + \nu_1 R_1 + dS_1^T - (\psi + \mu_1)S_1 - \lambda_1(t - T_1)S_1(t - T_1), \\ \dot{I}_1 &= \lambda_1(t - T_1)S_1(t - T_1) + dI_1^T - (\psi + g_1 + \delta_1)I_1, \\ \dot{R}_1 &= g_1 I_1 + dR_1^T - (\psi + \mu_1 + \nu_1)R_1, \\ \dot{S}_1^T &= \psi S_1 + \nu_1 R_1^T - (\mu_1 + d)S_1^T - \lambda_1(t - T_1)S_1^T(t - T_1), \\ \dot{I}_1^T &= \psi I_1 - \lambda_1(t - T_1)S_1^T(t - T_1) - (d + g_1 + \delta_1)I_1^T, \\ \dot{R}_1^T &= \psi R_1 + g_1 I_1^T - (d + \mu_1 + \nu_1)R_1^T, \\ \dot{S}_v &= B_v - e^{-\mu_v T_v} \lambda_v(t - T_v)S_v(t - T_v) - \mu_v S_v, \\ \dot{I}_v &= e^{-\mu_v T_v} \lambda_v(t - T_v)S_v(t - T_v) - \mu_v I_v, \end{aligned} \right\} \quad (4.1.2)$$

where

$$\lambda_1(t) = \frac{a_1 \beta_1 I_v(t)}{N_1(t)}, \quad (4.1.3)$$

and

$$\lambda_v(t) = \frac{\alpha_1 a_1 (I_1(t) + I_1^T(t))}{N_1(t)} \quad (4.1.4)$$

The total population size for cattle (N_1) and for vectors (N_v) are as follows:

$N_1 = S_1 + I_1 + R_1 + S_1^T + I_1^T + R_1^T$ and $N_v = S_v + I_v$, respectively. The subscript 1 assigned to cattle population may not be needed here since there is only one host, but however, it is convenient to use it here, for cattle only, in order to make it explicit the

way this model forms a part of the model in Figure 5.2.

In the presence of treatment, the reproduction number (R_0) was calculated in [34] using the next generation matrix method and given as:

$$R_0^{ITC} = \sqrt{\frac{e^{-\mu_v T_v} B_v}{\mu_v^2} \left(\frac{\alpha_i a_1^2 \mu_1 \beta_1}{B_1 (g_1 + \delta_1)} \right)}$$

where B_v is the flies birth rate and μ_v is given in Equation 4.1.1. R_0^{ITC} is the cattle-vector reproduction number in the presence of treatment, which is the secondary cases of infection fashioned in a susceptible host population by an infectious fly in the presence of ITC.

4.2 TTC Mathematical Model against *T. vivax* Infection

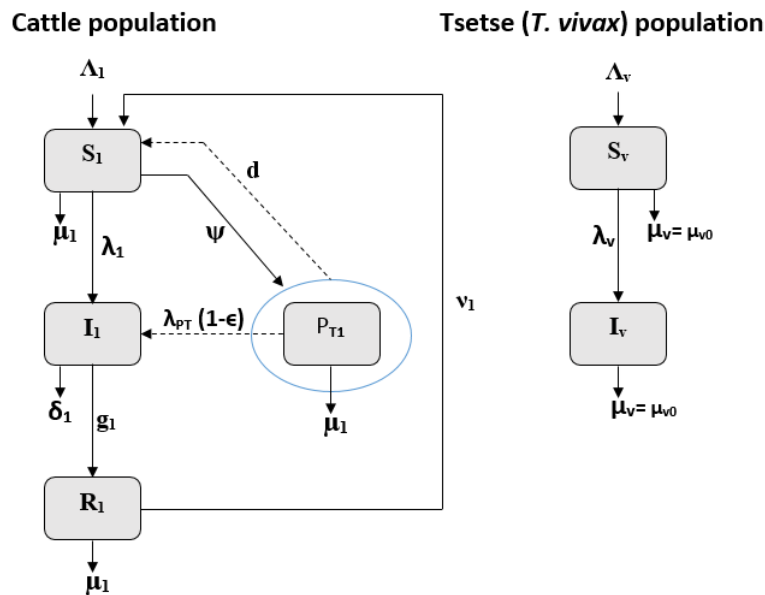


Figure 4.2: **Compartmental TTC Model for *T. vivax* infection**, using TTC as an intervention indicated in the blue circle. Source: Adapted from [33]. The forces of infection of the cattle and vector populations are λ_1 and λ_v , respectively.

4.2.1 TTC *T. vivax* Infection Model Description

The model description of the adapted TTC Model in Figure 4.2 above, where the populations of host species are separated into the following classes, namely: susceptible (S_1), infectious (I_1) and recovered (R_1), while the tsetse population is separated into two classes: Susceptible vectors (S_v) and Infectious vectors (I_v). The presence of trypanocide, which allows the treatment of cattle at a rate ψ , and then move to trypanocide treated cattle class (P_{T1}). Due to the loss of trypanocidal effect, cattle within the trypanocide-treated compartment return to the susceptible class at a rate d -the loss of trypanocide killing effect lasting on average $1/d$ days. The feeding of flies is done at a rate a per day, which means on average a tsetse fly takes a blood meal of $1/a$ days. It is assumed that flies feed on n host but with a fixed preference of feeding f_j of its blood meal from a host, where $\sum_{j=1}^n f_j$ and $j = 1, 2, \dots, n$; therefore, flies feed on a host at a rate $a_j = a f_j$ per day, where $a = \sum_j^n a_j$. The incubation period of the disease in host species is denoted as T_1 and T_v for cattle and tsetse respectively. B_v is the flies' constant birth rate. Susceptible teneral flies become infected after taking their first blood meal from an already infectious host species with a likelihood of α_j and transfer to the infectious class I_v . Each vertebrate host has a constant birth rate, B_j . Due to the bite of an infectious fly, a susceptible host becomes infected with a probability of β_j and a recovery rate of g_j as the result of treatment. Recovered hosts lose immunity at a rate ν_j , thus becoming susceptible again. Treated and untreated cattle become infected when an infectious fly meal is taken from a cattle with a probability β_1 and the same recovery rate g_1 when treated. Since the application of trypanocide does not induce additional tsetse mortality, therefore $\mu_v = \mu_{v0}$.

TTC *T. vivax* Model Equations

$$\left. \begin{aligned}
\dot{S}_1 &= B_1 + dP_{T_1} + v_1R_1 - (\psi + \mu_1)S_1 - \lambda_1(t - T_1)S_1(t - T_1), \\
\dot{I}_1 &= \lambda_1(t - T_1)S_1(t - T_1) - (g_1 + \delta_1)I_1 + \lambda_{PT}(t - T_1)P_{T_1}(t - T_1), \\
\dot{R}_1 &= g_1I_1 - (\mu_1 + v_1)R_1, \\
\dot{P}_{T_1} &= \psi S_1 - (d + \mu_1)P_{T_1} - \lambda_{PT}(t - T_1)P_{T_1}(t - T_1), \\
\dot{S}_v &= B_v - e^{-\mu_v T_v} \lambda_v(t - T_v)S_v(t - T_v) - \mu_v S_v, \\
\dot{I}_v &= e^{-\mu_v T_v} \lambda_v(t - T_v)S_v(t - T_v) - \mu_v I_v,
\end{aligned} \right\} \quad (4.2.1)$$

where

$$\lambda_1(t) = \frac{a_1 \beta_1 I_v(t)}{N_1(t)}, \lambda_v(t) = \frac{\alpha_1 a_1 I_1(t)}{N_1(t)},$$

and

$$\lambda_{PT} = \frac{a_1(1 - \epsilon \pi_{PT_1}) \beta_1 I_v(t)}{N_1(t)}$$

N_1 and N_v are the total population of cattle and tsetse respectively, which are also expressed as follows: $N_1 = S_1 + I_1 + R_1 + P_{T_1}$ and $N_v = S_v + I_v$.

The reproduction number in the presence of TTC was computed in [33] using the next generation method and found to be:

$$R_0^{PT_1} = \sqrt{e^{-\mu_v T_v} \left(\frac{B_v \alpha_1 a_1^2 \mu_1 \beta_1 (1 - \epsilon(\pi_{PT_1}))}{\mu_v^2 B_1 (g_1 + \delta_1)} \right)}$$

where $\pi_{PT_1} = \frac{\psi}{(\psi + d + \mu_1)}$, $(1 - \epsilon(\pi_{PT_1})) > 0$. $R_0^{PT_1}$ reflects secondary infections fashioned within a susceptible host population by an infectious fly bite in the presence of trypanocide, which is also the cattle-vector reproduction number in the presence of treatment, and if $R_0^{PT_1} > 1$ implies that the disease will remain persistent at least within a host population and the disease goes extinct when $R_0^{PT_1} < 1$.

4.2.1.1 Simulation Results on the Prevalence and Incidence Rates for Both ITC and TTC Models involving *T. vivax* Infection

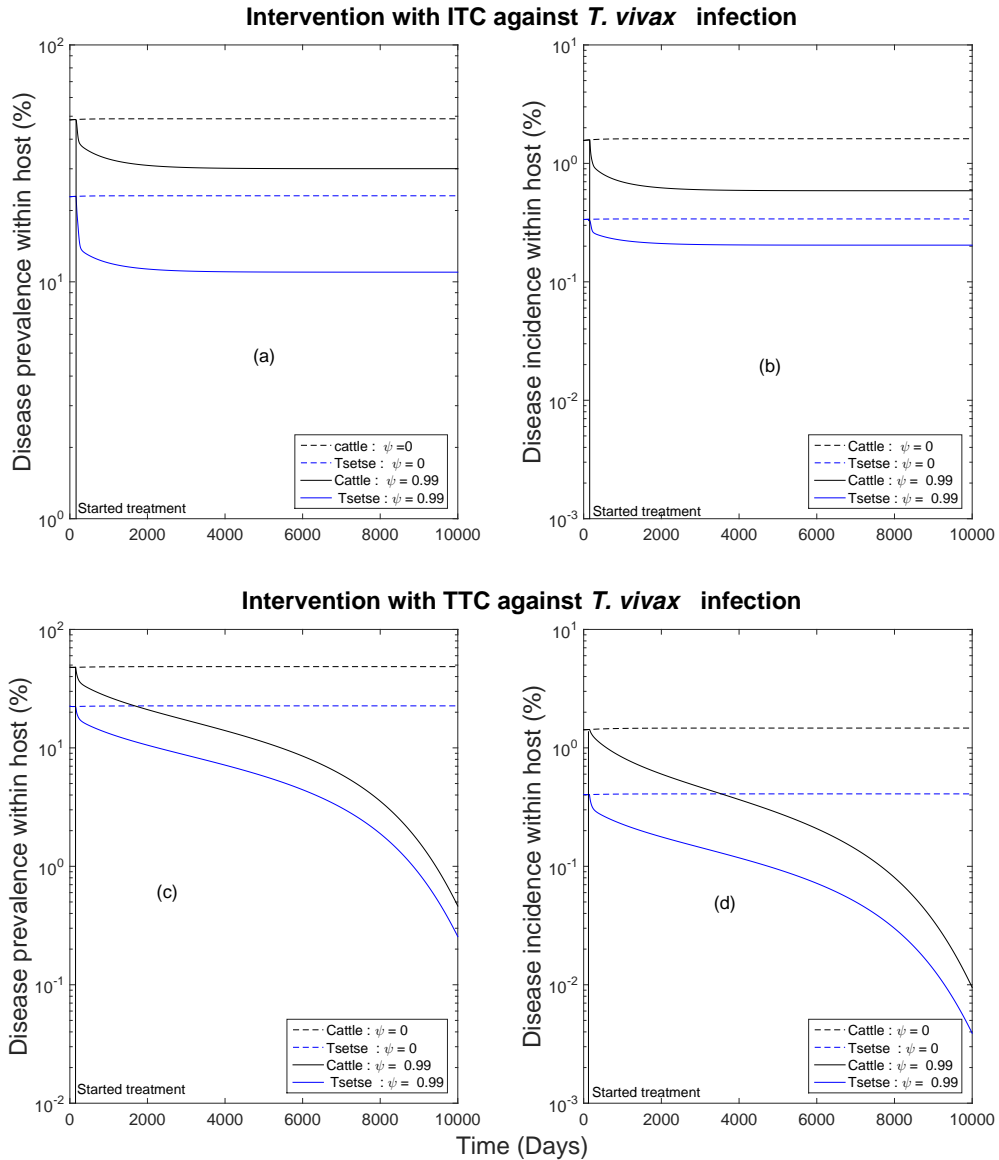


Figure 4.3: **Disease State within Hosts for ITC & TTC *T. vivax* Infection Model.** (a) Prevalence rates within host populations ITC Model, (b) Incidence rates within host populations for the ITC Model, (c) Prevalence rates within host populations TTC Model, and (d) Incidence rates within host populations for the TTC Model.

In Figures 4.3(a-d) above, we explored the disease state of the adapted ITC and TTC

models of [34] and [33], respectively, for *T. vivax* infections. In Figure 4.3(a) above is the equilibrium prevalence rate of the disease, which was found to be at 47% and 24% within the cattle and vector population indicated by the black and blue dashed lines, respectively, in the absence of intervention with ITC and is similar to previous findings [59]. After ITC was initiated, that is, treating 99% of the cattle population, there was a considerable decline in the prevalence within both host species before levelling off as indicated by the black and blue solid lines for cattle and tsetse populations, respectively, as found earlier [28] for *T. vivax* infection in an open population subject to constant tsetse invasion. Also in Figure 4.3(b), where the disease incidence rate of the ITC Model with *T. vivax* infection is given, it is observed that the disease equilibrium incidence rate without intervention was at 1.4% in cattle and 0.33% in tsetse as indicated in the black and blue dashed lines, respectively. After ITC intervention the incidence rate of the disease also declined, before levelling off in both host populations.

Figures 4.3(c-d) show the prevalence and incidence rates of the disease obtained from the TTC Model for *T. vivax* infection, respectively. Its equilibrium prevalence and incidence rates are observed to be same as the ITC for Model *T. vivax* infection indicated in Figure 4.3(a) and Figure 4.3(b) for both cattle and tsetse hosts. It was found that the control of the disease was possible by applying continuous trypanocide treatment to 99% of the cattle population.

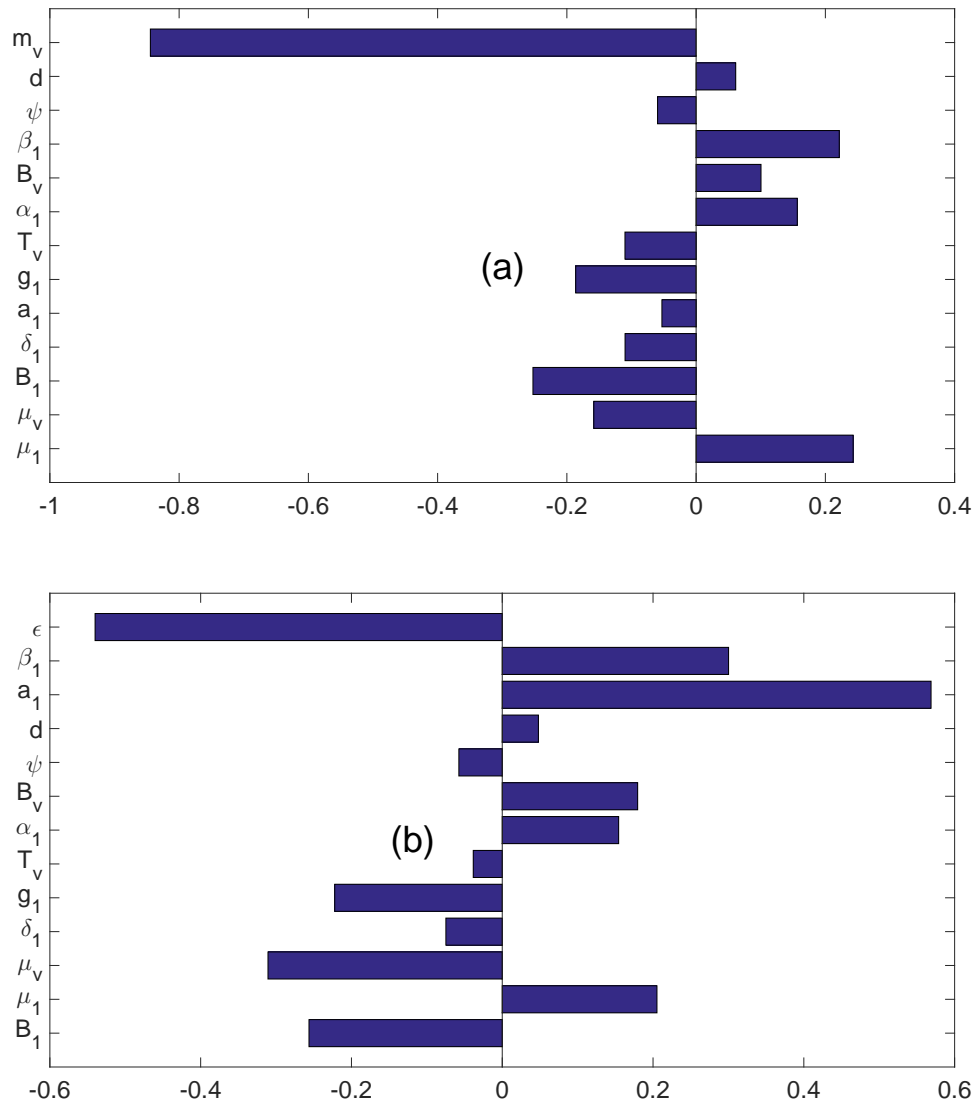
4.2.1.2 Sensitivity Analysis for Both ITC and TTC Models with *T. vivax* Infection

Figure 4.4: **Sensitivity Analysis of ITC & TTC *T. vivax* Infection Model.** (a) Sensitivity analysis of ITC *T. vivax* Model, and (b) Sensitivity analysis of TTC *T. vivax* Model.

The sensitivity analysis for both the adapted ITC and TTC Models are presented in Figure 4.4(a) and Figure 4.4(b), respectively. In the sensitivity analysis in Figure 4.4(a) for ITC, *T. vivax* model, it is observed that increased tsetse mortality due to the presence of

insecticide (μ_v) contributes to the decline of the disease. In Figure 4.4(b) the sensitivity analysis of the TTC model shows that increased use of trypanocide efficacy (ϵ) leads to increased control of the disease. Figure 4.4(b) also suggests that tsetse biting rate on cattle (a_1) contributes to an increase in the disease reproduction number. The reason for this is that trypanocides only kill trypanosomes: they do not kill tsetse, which still feed on them.

4.3 Overview of the Chapter

In chapter 4, we presented the adapted models of [34] and [33] for ITC and TTC Models, respectively, with *T. vivax* as the vector trypanosome species. The models were analyzed and simulation results support results from established literature and sensitivity analysis was also conducted to know the contribution of both models' parameters of their respective reproduction numbers.

Chapter 5

Models Extension and Analysis

5.1 Mathematical Model for *T. b. rhodesiense* Infection with ITC Intervention

In this chapter, we extended the ITC and TTC Models with *T. vivax* infection for the human form of the disease cause by *T. b. rhodesiense* trypanosomes.

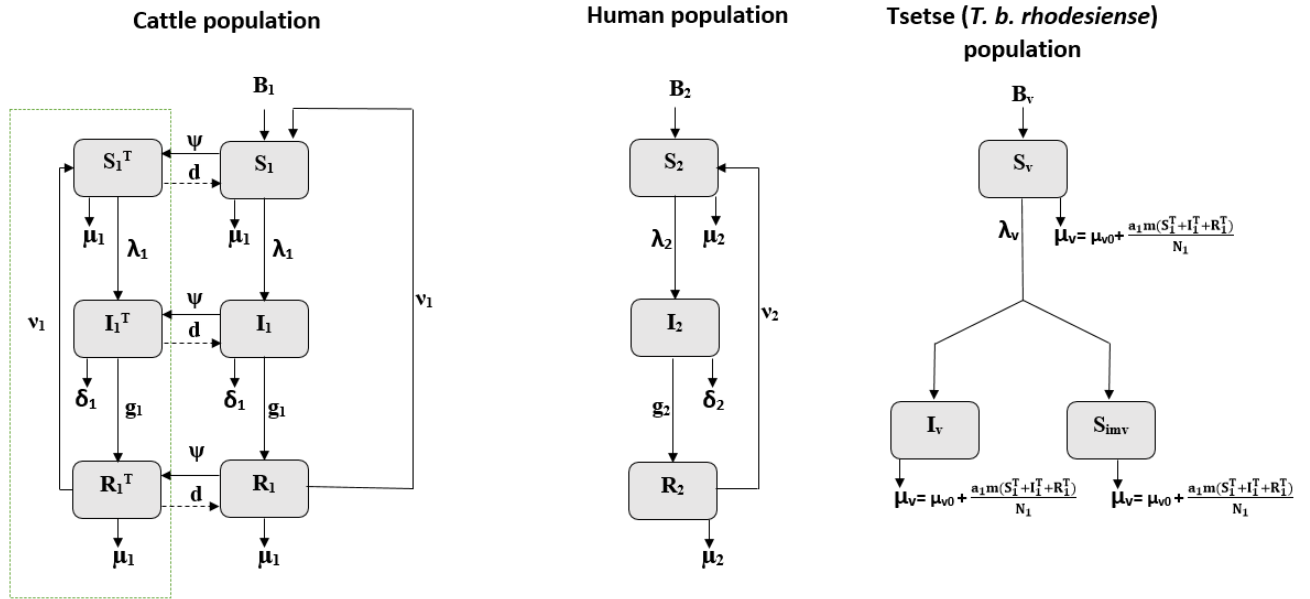


Figure 5.1: **Extension of the ITC *T. vivax* Infection Model in Figure 4.1.** This is a compartmental model of *T. b. rhodesiense* infection within a multi-host situation using ITC as interventions as indicated in the green dotted rectangle. The forces of infection of the cattle, human and vector populations are λ_1 , λ_2 and λ_v respectively. Source: Adapted and Extended from: [34]

5.1.1 ITC *T. b. rhodesiense* Infection Model Description

The model description of the extended ITC Model in Figure 5.1 above, is the same as in Section 4.1.1, except that we have added another host (human) to the model and an immune class of vectors (S_{imv}). This extra class has been added because of the observation that tsetse appear to be refractory to *T. b. rhodesiense* infections after they have taken their first blood-meal [59]. All host populations are divided into the following classes, namely: Susceptible class (S_1, S_2) for susceptible cattle and humans, respectively, Infectious class (I_1, I_2) for infectious cattle and humans, respectively, and Recovered class (R_1, R_2) for recovered cattle and humans, respectively, the vector population is also divided into three classes: Susceptible vectors (S_v), Infectious vectors (I_v) and Immune vectors (S_{imv}). (S_{imv}), which is a sub-class of the model equations for intervention against the disease, is the immune vector population that do not get infected after

their first blood-meal. The use of insecticide as treatment enables cattle to be treated at a rate ψ and then moved into the treated classes, S_1^T , I_1^T and R_1^T , representing susceptible, infectious and recovered treated cattle, respectively. The loss of insecticide effect on cattle ($1/d$), tsetse natural death rate (μ_{v0}), flies feeding rate (a) and the incubation period for the disease in cattle and tsetse and other model parameters are denoted as the same as in Section 4.1.1. The incubation period of the disease in a human host is denoted as T_2 .

ITC *T. b. rhodesiense* Infection Model Equations

$$\begin{aligned}
 \dot{S}_1 &= B_1 + \nu_1 R_1 + dS_1^T - (\psi + \mu_1)S_1 - \lambda_1(t - T_1)S_1(t - T_1), \\
 \dot{I}_1 &= \lambda_1(t - T_1)S_1(t - T_1) + dI_1^T - (\psi + g_1 + \delta_1)I_1, \\
 \dot{R}_1 &= g_1 I_1 + dR_1^T - (\psi + \mu_1 + \nu_1)R_1, \\
 \dot{S}_1^T &= \psi S_1 + \nu_1 R_1^T - (\mu_1 + d)S_1^T - \lambda_1(t - T_1)S_1^T(t - T_1), \\
 \dot{I}_1^T &= \psi I_1 + \lambda_1(t - T_1)S_1^T(t - T_1) - (d + g_1 + \delta_1)I_1^T, \\
 \dot{R}_1^T &= \psi R_1 + g_1 I_1^T - (d + \mu_1 + \nu_1)R_1^T, \\
 \dot{S}_2 &= B_2 + \nu_2 R_2 - \mu_2 S_2 - \lambda_2(t - T_2)S_2(t - T_2), \\
 \dot{I}_2 &= \lambda_2(t - T_2)S_2(t - T_2) - (g_2 + \delta_2)I_2, \\
 \dot{R}_2 &= g_2 I_2 - (\mu_2 + \nu_2)R_2, \\
 \dot{S}_v &= B_v - a_1 S_v - (a_2 + \mu_v)S_v, \\
 \dot{I}_v &= \lambda_v(t - T_v)S_v(t - T_v) - \mu_v I_v, \\
 \dot{S}_{imv} &= a_1 S_v \left(\frac{S_1 + S_1^T + I_1(1 - \alpha_1) + (1 - \alpha_1)I_1^T + R_1 + R_1^T}{N_1} \right) + \\
 &\quad a_2 S_v \left(\frac{S_2 + (1 - \alpha_2)I_2 + R_2}{N_2} - \mu_v S_{imv} \right)
 \end{aligned} \tag{5.1.1}$$

where

$$\lambda_1(t) = \frac{a_1 \beta_1 I_v(t)}{N_1(t)}, \lambda_2(t) = \frac{a_2 \beta_2 I_v(t)}{N_2(t)}$$

and

$$\lambda_v(t) = \frac{a_1\alpha_1(I_1(t) + I_1^T(t))}{N_1(t)} + \frac{a_2\alpha_2 I_2(t)}{N_2(t)}$$

The total population size for cattle (N_1), human host (N_2) and for vectors (N_v) are as follows: $N_1 = S_1 + I_1 + R_1 + S_1^T + I_1^T + R_1^T$, $N_2 = S_2 + I_2 + R_2$ and $N_v = S_v + I_v + S_{imv}$ respectively.

The treatment reproduction number within a multi-host population found in [34], which is mentioned in Equation 4.1.5 when extended to account for two host species becomes:

$$R_0^{ITC} = \sqrt{R_1^{ITC} + R_2^{ITC}} = \sqrt{\frac{e^{-\mu_v T_v} B_v}{\mu_v^2} \left(\frac{\alpha_1 a_1^2 \mu_1 \beta_1}{B_1 (g_1 + \delta_1)} + \frac{\alpha_2 a_2^2 \mu_2 \beta_2}{B_2 (g_2 + \delta_2)} \right)}$$

where R_0^{ITC} is the total secondary cases of infection produced in a susceptible population of cattle and humans by an infectious fly in the presence of ITC and μ_v is given in Equation 4.1.1. R_1^{ITC} and R_2^{ITC} are the cattle-vector and human-vector reproduction numbers, respectively, in the presence on insecticide.

5.2 Mathematical Model for *T. b. rhodesiense* Infection with TTC Intervention

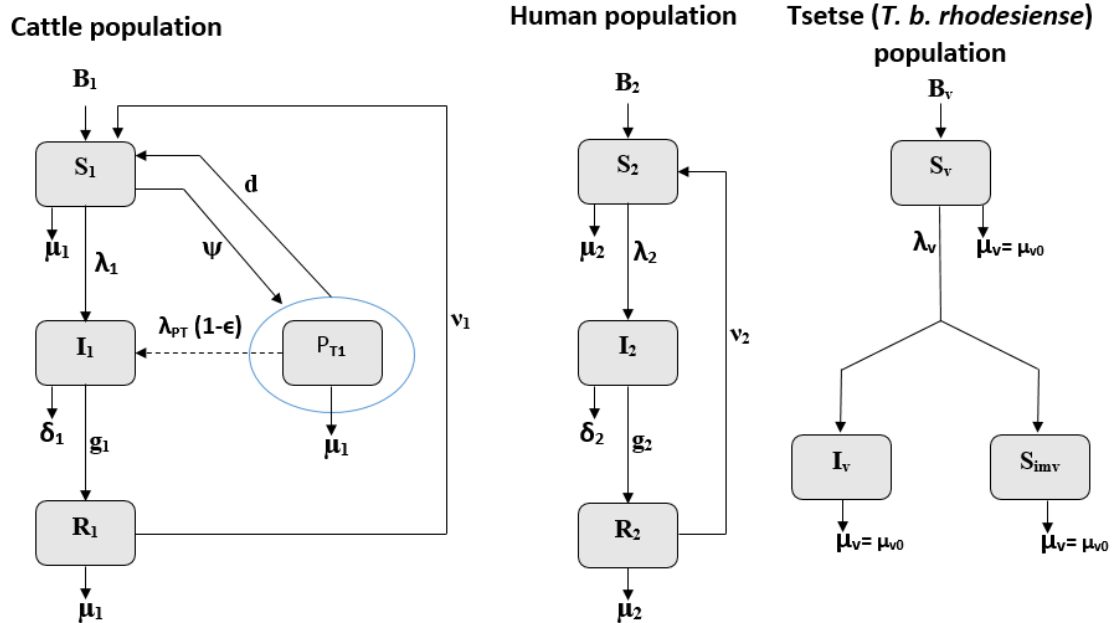


Figure 5.2: **Extension of the TTC *T. vivax* Infection Model in Figure 4.2.** This is a compartmental model of *T. b. rhodesiense* infection within a multi-host situation using TTC as interventions as indicated in the blue circle. The forces of infection of the cattle, human and vector populations are λ_1, λ_2 and λ_v respectively. Source: Adapted and Extended from: [33]

5.2.1 TTC *T. b. rhodesiense* Infection Model Description

The model description of Figure 5.2 above, is an extended version of the TTC Model description in Section 4.2.1, which now integrates a class of human and an immune class of the vector. The host populations are separated into three classes, namely: Susceptible hosts (S_1, S_2), Infectious hosts (I_1, I_2) and Recovered hosts (R_1, R_2), and the vector population is separated into three classes: Susceptible vectors (S_v), Infectious vectors (I_v) and Immune vectors (S_{imv}). (S_{imv}), which is a sub-class of the model equations for intervention against the disease, is the immune vector population that do not get infected after

their first blood-meal. Cattle are treated at a rate ψ due to the presence of trypanocide, and then move to trypanocide treated cattle class (P_{T1}). The loss of trypanocidal effect ($1/d$), the feeding rate of flies (a) and the proportion of blood meal taken from host and other model parameters remain denoted the same as in Section 4.2.1. The incubation period for human host is denoted as T_2 . Since the application of trypanocide does not induce additional tsetse mortality, therefore $\mu_v = \mu_{v0}$.

TTC *T. b. rhodesiense* Model Equations

$$\left. \begin{aligned}
 \dot{S}_1 &= B_1 + dP_{T1} + \nu_1 R_1 - (\psi + \mu_1)S_1 - \lambda_1(t - T_1)S_1(t - T_1), \\
 \dot{I}_1 &= \lambda_1(t - T_1)S_1(t - T_1) - (g_1 + \delta_1)I_1 + \lambda_{PT}(t - T_1)P_{T1}(t - T_1), \\
 \dot{R}_1 &= g_1 I_1 - (\mu_1 + \nu_1)R_1, \\
 \dot{P}_{T1} &= \psi S_1 - (d + \mu_1)P_{T1} - \lambda_{PT}(t - T_1)P_{T1}(t - T_1), \\
 \dot{S}_2 &= B_2 + \nu_2 R_2 - \mu_2 S_2 - \lambda_2(t - T_2)S_2(t - T_2), \\
 \dot{I}_2 &= \lambda_2(t - T_2)S_2(t - T_2) - (g_2 + \delta_2)I_2, \\
 \dot{R}_2 &= g_2 I_2 - (\mu_2 + \nu_2)R_2, \\
 \dot{S}_v &= B_v - a_1 S_v - (a_2 + \mu_v)S_v, \\
 \dot{I}_v &= \lambda_v(t - T_v)S_v(t - T_v) - \mu_v I_v, \\
 \dot{S}_{imv} &= a_1 S_v \left(\frac{S_1 + I_1(1 - \alpha_1) + (1 - \alpha_1)P_{T1} + R_1}{N_1} \right) + \\
 &\quad a_2 S_v \left(\frac{S_2 + (1 - \alpha_2)I_2 + R_2}{N_2} - \mu_v S_{imv} \right)
 \end{aligned} \right\} \quad (5.2.1)$$

where

$$\lambda_1(t) = \frac{a_1 \beta_1 I_v(t)}{N_1(t)}, \lambda_2(t) = \frac{a_2 \beta_2 I_v(t)}{N_2(t)}$$

$$\lambda_{PT}(t) = \frac{a_1(1 - \epsilon \pi_{PT1}) \beta_1 I_v(t)}{N_1(t)}$$

and

$$\lambda_v(t) = \frac{a_1 \alpha_1 I_1(t)}{N_1(t)} + \frac{a_2 \alpha_2 I_2(t)}{N_2(t)}$$

49 5.2. Mathematical Model for *T. b. rhodesiense* Infection with TTC Intervention

The total population size for cattle (N_1), human host (N_2) and for vectors (N_v) are as follows: $N_1 = S_1 + I_1 + R_1 + S_1^T + I_1^T + R_1^T$, $N_2 = S_2 + I_2 + R_2$ and $N_v = S_v + I_v + S_{imv}$ respectively.

The reproduction number in the presence of TTC within multi-host populations (cattle and humans) found in [33] which is mentioned in Equation 4.2.2 when extended to account for two host species, which then becomes:

$$R_0^{PT_1} = \sqrt{R_1^{PT_1} + R_2^{PT_1}}$$

$$R_0^{PT_1} = \sqrt{e^{-\mu_v T_v} \left(\frac{B_v \alpha_1 a_1^2 \mu_1 \beta_1 (1 - \epsilon(\pi_{PT_1}))}{\mu_v^2 B_1 (g_1 + \delta_1)} \right) + e^{-\mu_v T_v} \left(\frac{B_v \alpha_2 a_2^2 \mu_2 \beta_2}{\mu_v^2 B_2 (g_2 + \delta_2)} \right)}$$

where $R_0^{PT_1}$ reflects the number of secondary infections fashioned in a susceptible host population involving two host species by an infectious fly bite in the presence of trypanocide, and if $R_0^{PT_1} > 1$ implies that the disease will persist at least within a host population and the disease goes extinct when $R_0^{PT_1} < 1$. $R_1^{PT_1}$ and $R_2^{PT_1}$ are the cattle-vector and human-vector reproduction numbers, respectively, in the presence of trypanocide, while $\pi_{PT_1} = \frac{\psi}{(\psi + d + \mu_1)}$ and $(1 - \epsilon(\pi_{PT_1})) > 0$.

5.2.2 Simulation Results on the Prevalence and Incidence Rates for Both the Extended ITC and TTC Models involving *T. b. rhodesiense* Infection

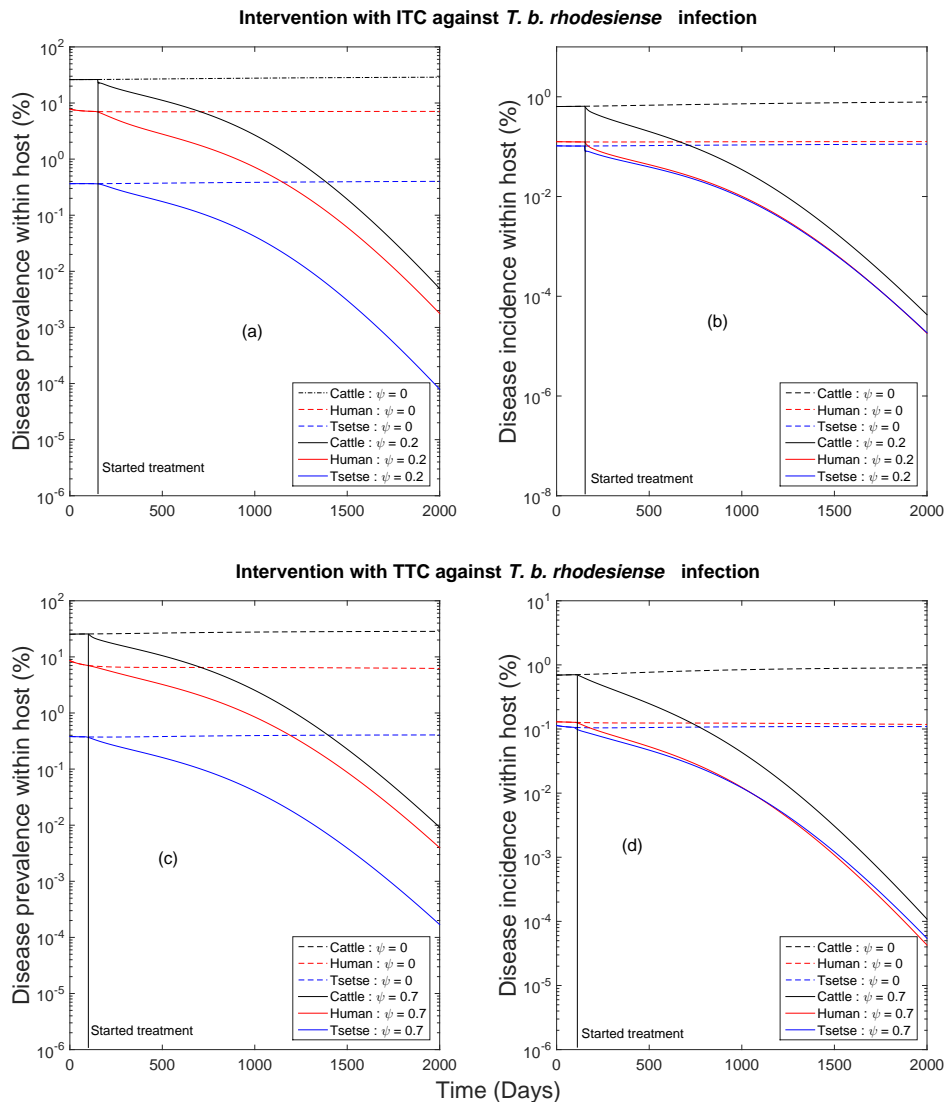


Figure 5.3: **Disease State within Hosts for ITC & TTC *T. b. rhodesiense* Infection Model.** (a) Prevalence rates within host populations ITC Model, (b) Incidence rates within host populations for the ITC Model, (c) Prevalence rates within host populations TTC Model, and (d) Incidence rates within host populations for the TTC Model.

The disease state of the extended ITC and TTC Models for *T. b. rhodesiense* infections

was explored as indicated in Figure 5.3(a-d) above. The results show equilibrium prevalence rates of the disease in the absence of ITC intervention within hosts at: 27%, 7% and 0.38% for cattle, humans and tsetse indicated by the black, red and blue dashed lines, respectively, (Figure 5.3 a) and an equilibrium incidence rates of: 0.73%, 0.12% and 0.10% indicated by black, red and blue dashed lines for cattle, humans and tsetse hosts, respectively, (Figure 5.3 b). Application of insecticide to 20% of the cattle population was enough to eliminate *T. b. rhodesiense* infection from host populations.

Like the extended ITC Model, the disease state of the extended TTC Model was also explored. Its equilibrium prevalence and incidence rates without TTC intervention in Figure 5.3(c) and Figure 5.3(d), respectively, turned out to be the same as the extended ITC Model. It was observed that applying trypanocide to 70% of the cattle population the elimination of *T. b. rhodesiense* infection could be achieved.

5.2.3 Sensitivity Analysis for Both Extended ITC and TTC Models with *T. b. rhodesiense* Infection

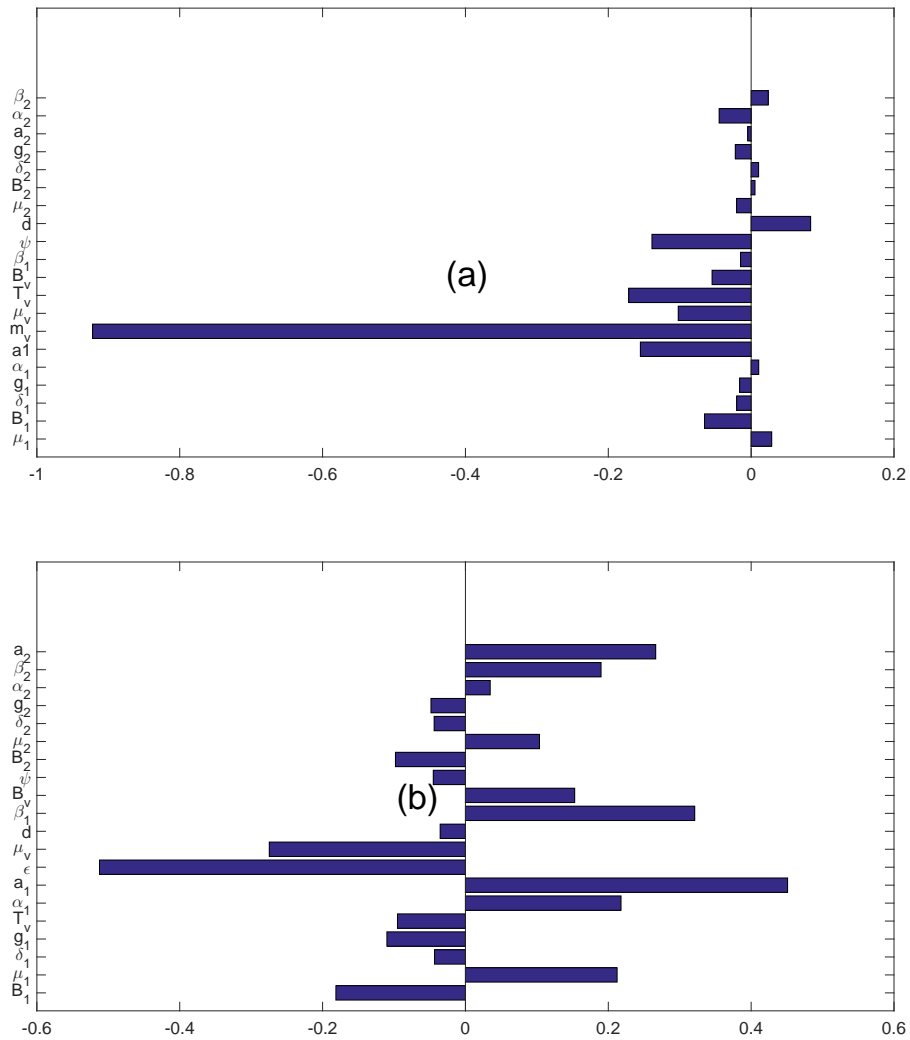


Figure 5.4: **Sensitivity Analysis of ITC & TTC *T. b. rhodesiense* Infection Model.** (a) Sensitivity analysis of ITC *T. vivax* Model, and (b) Sensitivity analysis of TTC *T. vivax* Model.

Sensitivity analysis of the extended models was also conducted. The results were similar to those for the adapted models, in that, in the extended ITC model, increased tsetse

mortality due to insecticide application (μ_v) led to the elimination of the disease (Figure 5.4 a). Also, the sensitivity analysis of the extended TTC Model in Figure 5.4(b) gave similar results to that of the adapted TTC Model, that is, trypanocide efficacy (ϵ) accounting more for the elimination of *T. b. rhodesiense* disease form.

5.3 Economics Analysis Performed, its Simulations and Results

Essential for any decision-making with regards to tsetse control are data on costs and benefits of interventions, in order to handle the economic aspects of the disease and its control [64]. Accordingly, we used the benefit-cost ratio (BCR) to identify which mode of intervention for the models with *T. vivax* infection yielded a higher cattle production output. The computational formula use for the BCR is as follow:

$$\mathbf{BCR} = \frac{\text{Change in total benefit}}{\text{Change in total cost}} \quad (5.3.1)$$

5.3.1 Economics of the Extended Models with *T. b. rhodesiense* Infection

We presented and discussed in this segment the economics of the extended models taking into consideration the epidemiology of *T. b. rhodesiense* by performing a cost-effectiveness analysis. Within this analysis, the cost effectiveness ratio (CER) was computed, that is, the number of cases prevented per dollar spent, in order to identify which mode of intervention yielded the highest CER. The CER was computed from:

$$\mathbf{CER} = \frac{\text{Units of effectiveness}}{\text{Total cost incurred}} \quad (5.3.2)$$

5.3.2 Benefits and costs estimates used

The acquire benefits and costs estimates in Table 5.1 below were used to compute cattle productivity parameters by the following equations:

$$\text{Milk Production} = (S_1 + (1 - r) * I_1 + R_1 + S_1^T + (1 - r) * I_1^T + R_1^T) * pbf * dmp * pcmpl$$

$$\text{Work Ox Days} = (S_1 + I_1 * (1 - oxwdr) + R_1 + S_1^T + (1 - oxwdr) * I_1^T + R_1^T) * woawds * powox * woxdc$$

$$\text{Work Ox Sale} = (S_1 + R_1 + I_1 + S_1^T + I_1^T + R_1^T) * powox * pcwox$$

$$\text{Sale of Meat} = (S_1 + (1 - rcaw) * I_1 + R_1 + S_1^T + (1 - rcaw) * I_1^T + R_1^T) * caw * pcm$$

Where,

- r = reduction in cattle milk production due to the disease,
- dmp = lactation offtake per day,
- pbf = proportion of breeding female cattle in the herd,
- $pcmpl$ = price of milk per litre,
- $oxwdr$ = the reduction in Ox work days due to the disease,
- $woawds$ = Work Ox average working days per year,
- $powox$ = proportion of Work Ox in the herd,
- $woxdc$ = fees of Work Ox average day work,
- $powox$ = proportion of Work Ox,
- $pcwox$ = price of Work Ox live-weight,
- $rcaw$ = is reduction in cattle average weight due to the disease,

- caw = average weight of cattle in kg,
- pcm = price of cattle meat per kg.

Note that r , pbf , $oxwdr$, $woxdc$, $pwox$, $rcaw$, and caw values were adapted from [30, 31, 38]

5.3.2.1 Acquired Benefits and Costs from Intervention within a Cattle Production System

Benefit acquire within a cattle production system		
Key cattle benefit parameters	Benefit acquired within cattle production system	References
Lactation offtake (liters per annum)	285 ⁺ / 306 ⁻	[61]
Liter of milk(US\$)	0.33	[61]
Work ox days's work per annum	100 ⁺ / 108 ⁻	[61]
Fees of ox average day's work (US\$)	2.1	[61]
Price of working ox live-weight	300	[61]
Price of meat per kg	5.25	[43]
Production costs against the disease within a cattle production system		
Cost parameters	Costs incur(US\$)	References
Basic production costs per animal per annum	22	[61]
Cost of trypanocide per dose	2.35 ^a	[61]
Cost of insecticide per animal per annum	6	[64]

Table 5.1: **Benefits acquired and costs incurred within a cattle production system.** Note: ^a The cost of a dose of trypanocide per animal within a agro-pastoral farming system and four doses costing ($\$2.35 * 4 = \9.40) are administered per animal per annum [61]. Note: without trypanosomiasis(-) and with trypanomiasis(+).

5.3.3 Benefit-Cost Analysis Simulation Results for the ITC and TTC Models involving *T. vivax* Infection

In the figure below, we present the economics analysis of key cattle production parameters for the adapted (ITC and TTC) models with *T. vivax* infection.

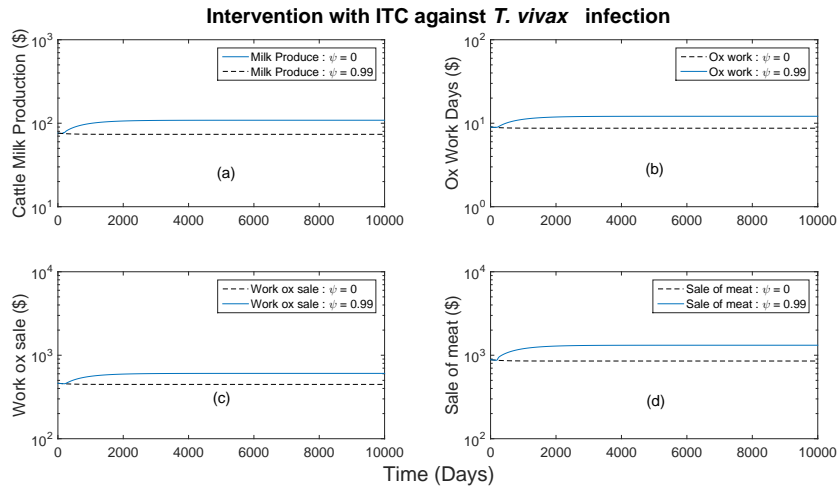
5.3.3.1 Benefit-Cost Analysis for Both ITC and TTC Models with *T. vivax* Infection

Figure 5.5: **Benefit-cost Analysis of the ITC *T. vivax* Infection Model.** (a) Cattle Milk Production, (b) Ox Days Work, (c) Sale of Meat and (d) Sale of Work ox.

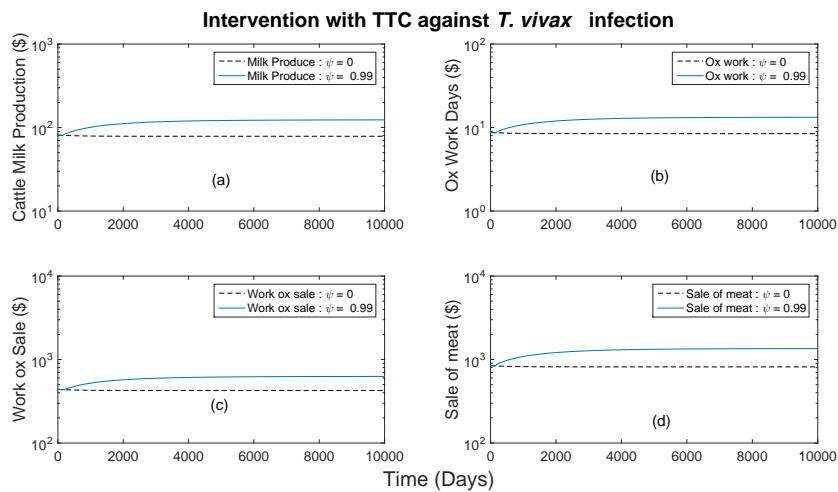
5.3.3.2 Benefit-Cost Analysis for TTC Model with *T. vivax* Infection

Figure 5.6: **Benefit-cost Analysis of TTC *T. vivax* Infection Model.** (a) Cattle Milk Production, (b) Ox Days Work, (c) Sale of Meat and (d) Sale of Work ox.

We present the benefit-cost analysis of key cattle production output parameters for both ITC and TTC Models with *T. vivax* infections using Equation 5.3.1 to compute the equilibrium benefits from production output parameters before and after interventions as indicated in Figures 5.5(a-d) and Figures 5.6(a-d) above for both ITC and TTC Model, respectively. Summaries of the benefit-cost analysis from the ITC and TTC Models are given in Table A.1 and Table A.2 of the Appendix, respectively. The results in both summary tables suggest that, although cattle production output parameters of the TTC Model yield slightly more benefit after intervention than that of the ITC Model, all of the ITC Model cattle production output parameters yield a higher benefit-cost ratio than that of the TTC Model.

5.3.4 Cost-Effectiveness Analysis (CEA) for Both ITC and TTC Models involving *T. b. rhodesiense* Infection

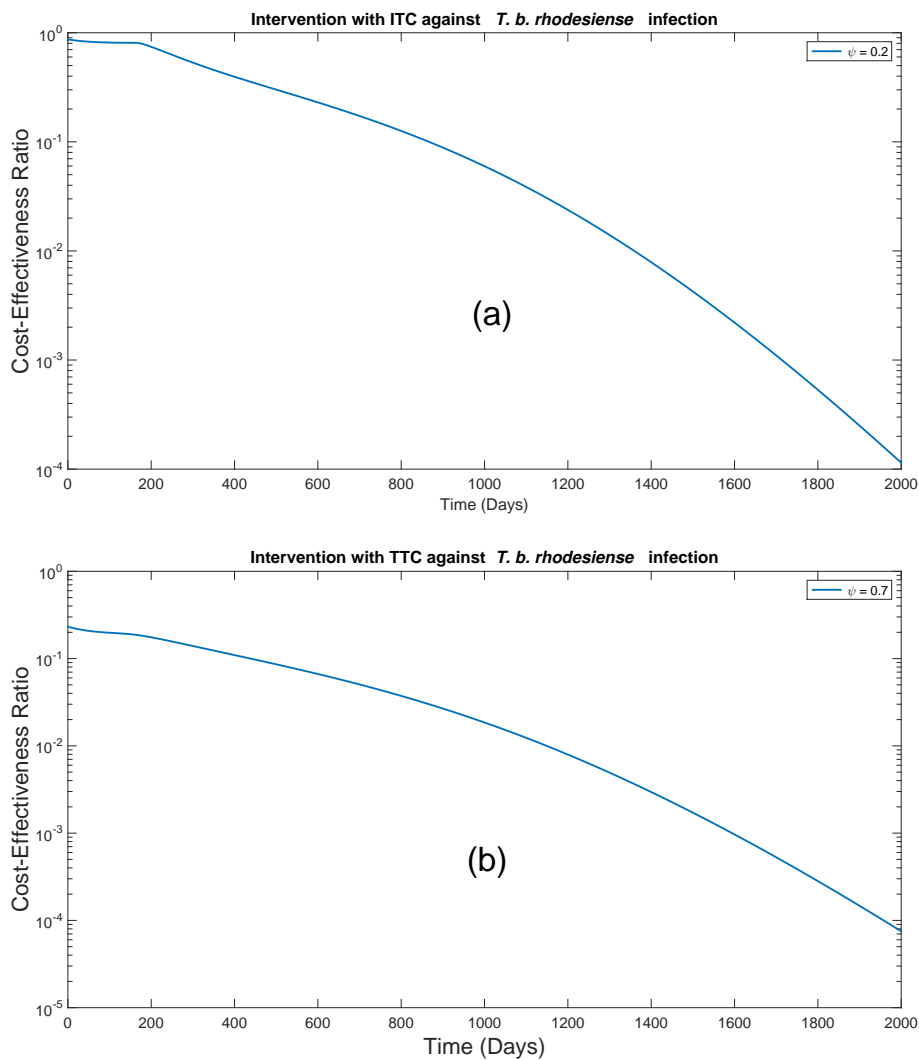


Figure 5.7: CEA of the Extended ITC and TTC *T. b. rhodesiense* Infection Models. (a) CEA of the extended ITC Model, and (b) CEA of the extended TTC Model. Source: Model simulation

The cost-effectiveness analysis of the extended ITC and TTC Models for *T. b. rhodesiense* infections are presented in Figure 5.7(a) and Figure 5.7(b), respectively. Cost effectiveness ratios (CERs or number of cases prevented per dollar spend) on both interventions

are computed from Equation 5.3.2. The results from both models clearly suggest that more cases were prevented per dollar spent using ITC than TTC (Figure 5.7). The CERs were not quantified because of the lack of reasonable benefit estimates that one can acquire due to treatment.

5.4 Overview of the Chapter

In this chapter, we extended the ITC and TTC Models, which made the extended models to capture most of the biological characteristics of *T. b. rhodesiense* infection. The models were also analyzed with regard to their disease states (prevalence and incidence rates) along with the sensitivity of the parameters. Thereafter, the economics analysis was conducted, namely: the benefit-cost analysis for the ITC and TTC Models with *T. vivax* infection in Chapter 3, and the cost-effectiveness analysis for the extended ITC and TTC Models.

Chapter 6

Discussion and Conclusion

This work supports earlier findings regarding the importance of insecticide treatment of cattle [6, 28, 76]. It also explored the competitive advantage that the use of ITC provides farmers, not only in the control or elimination of disease in animals but also its cost effectiveness in controlling the human form of the disease.

Simulation results in Figure 4.3(a-b) confirm published results that, for a population subject to vector invasion, disease control is impossible – even with 99% coverage of cattle with insecticide disease control [28]. Modelling also shows that disease control is only possible if at least 99% of the cattle are kept on continuous and effective trypanocidal treatment as indicated in Figure 4.3(c-d), which also confirm findings in [28]. Simulation results in Figure 5.3(a-d) of the extended ITC and TTC Models for *T. b. rhodesiense* infections also confirm published results that the control or elimination of *T. b. rhodesiense* infection is only possible with insecticide or trypanocide coverage of at least 20% and 70% of the cattle population, respectively [28]. It is important to note that results in Figure 4.3(a-d) and Figure 5.3(a-d), regarding the equilibrium prevalence rates of both *T. vivax* and *T. b. rhodesiense* infections in the absence of treatment, are similar to findings in [59]. Sensitivity analysis was also conducted in order to demonstrate the relationship between the model's reproduction number and its parameters.

In the benefit-cost analysis involving the ITC and TTC Models against *T. vivax* infection in Figure 5.5 and Figure 5.6, respectively, which show the equilibrium benefits that a farmer can obtain from all cattle production parameters before and after intervention as indicated by the black dash and solid blue lines, respectively. The results also suggest that cattle production output parameters of the TTC Model in Figure 5.6 yield a slightly higher benefit than that of the ITC Model shown in Figure 5.5, while the benefit-cost ratio analysis shows that all of the cattle production output parameters of the ITC Model gave a higher benefit-cost ratio than the TTC Models as given in Table A.1 and Table A.2, respectively, in the Appendix. Also, in the cost effectiveness analysis of the extended models, results in Figure 5.7(a) and Figure 5.7(b) from the extended ITC and TTC Models, respectively, suggest the better performance of the extended ITC Model, which yield a higher cost-effective ratio (number of cases prevented per dollar spent) compared to the extended TTC Model.

The results suggest that ITC can provide a cost-effective means of controlling human trypanosomiasis. Under certain circumstances it may also be used for the elimination of cattle disease, enabling farmers to maximize cattle production output at a limited cost. This will only be possible when there is an appropriate density of cattle in the tsetse infested area.

We are aware of the limitations or constraints regarding the modelling process, in that, there are other relevant effects (e.g. seasonality, age structure amongst others) that are not modelled, which could be included in future work. Another constraint is that the scarcity of data on the economics the disease control, which makes it difficult in validating the performance of model to real world situation or data.

Appendix A

Appendix

A.0.0.1 Summary of Cost Benefit Ratio for ITC Model with *T. vivax* Infection

Benefit-Cost Ratios(CBRs) Summary of the ITC Model (<i>T. vivax</i>)				
Cattle Production Output Parameters	Intervention Status	ITC Total Cost (US \$)	Total Benefit (US \$)	Benefit-Cost Ratios (BCRs)
Milk Production	Without Intervention	3.013 ^b	75	48.66
	With Intervention	3.835 ^c	115	
Ox Work Days	Without Intervention	3.013 ^b	9	4.86
	With Intervention	3.835	13	
Ox Work Sale	Without Intervention	3.013 ^b	448	184.90
	With Intervention	3.835 ^c	600	
Cattle Meat Sale	Without Intervention	3.013 ^b	855	541
	With Intervention	3.835 ^c	1,300	

Table A.1: **Summary of the adapted ITC Model with (*T. vivax*) benefit-cost ratios.** Note: ^b The total basic cost of production per day for treating 50 cattle ($\$22 * 50/365 = \3.013), which is without intervention cost. ^c The total insecticide plus basic production costs per day for treating 50 cattle ($\$6 * 50/365 + \$22 * 50/365 = \$3.835$) or the total cost of intervention.

A.0.0.2 Summary of Cost Benefit Ratio for TTC Model with *T. vivax* Infection

Benefit-Cost Ratios(BCRs) Summary of the TTC Model (<i>T. vivax</i>)				
Cattle Production Output Parameters	Intervention Status	Administering TTC Total Cost (US \$)/Day	Total Benefit (US \$)/Day	Benefit-Cost Ratios (BCRs)
Milk Production	Without Intervention	3.013 ^b	75	41.18
	With Intervention	4.30 ^d	128	
Ox Work Days	Without Intervention	3.013 ^b	9	4.66
	With Intervention	4.30 ^d	15	
Ox Work Sale	Without Intervention	3.013 ^b	448	156.95
	With Intervention	4.30 ^d	650	
Cattle Meat Sale	Without Intervention	3.013 ^b	855	462.32
	With Intervention	4.30 ^d	1,450	

Table A.2: **Summary of the adapted TTC Model with (*T. vivax*) benefit-cost ratios.**
 Note: ^dThe total cost four doses of trypanocide plus basic production costs per day for treating 50 cattle ($\$2.35 * 4 * 50/365 + \$22 * 50/365 = \$4.30$) or the total cost of intervention.

Models Parameters Values					
Parameters	Definitions	Tsetse	Cattle($f=1$)	Human($f=2$)	References
Hosts parameters					
B_j	Birth rate for host j	-	$\mu_1 * N_1; N_1 = 50$	$\mu_2 * N_1; N_2 = 300$	[59]
μ_j	Natural mortality of host j	-	0.00055	0.000055	[82]
f_j	proportion of tsetse blood meal from host j	-	0.7	0.3	[59]
a_j	Tsetse-host biting rate	-	$a f_1$	$a f_2$	-
β_j	Probability of an infectious fly bite producing an infection in host j	-	$T. vivax: 0.29$ $T. b.r.: 0.62$	$T. vivax: -$ $T. b.r.: 0.62$	[59]
α_j	Probability of that infectious blood meal from host j that gives an infection in flies	-	$T. b.r.: 0.065$ $T. vivax: 0.177$	$T. b.r.: 0.065$ $T. vivax: 0.177$	[59]
δ_j	Mortality rate of an infected host j	-	0.006	0.004	[14]
T_j	Incubation period for host j	-	12	12	[59]
δ_j	Recovery rate of an infected host j	-	0.014	0.012	[14]
$1/v_j$	Loss of immunity rate in recovered host j	-	1.00	1.00	[12]
Vector parameters					
$1/a$	Tsetse feeding circle	4	-	-	[12]
μ_{v0}	Tsetse natural mortality	0.03	-	-	[59]
B_v	Tsetse birth rate	$N_v X \mu_v; N_v = 5,000$	-	-	[14]
T_v	Incubation period for tsetse flies	$T. vivax: 10$ $T. b. rhoetziense: 25$	-	-	[59]
ITC and TTC parameters					
ψ	Proportion of cattle treated with trypanocide and insecticide per day	-	vary	-	-
$1/d$	Average duration of insecticidal and trypanocidal efficacy	-	4 weeks(ITC) 16 weeks(TTC)	-	[70]
m_v	Tsetse additional mortality due to insecticide	-	0.57	-	[70]
ϵ	Efficacy of trypanocide	-	vary	-	-

Table A.3: Numerical values for all models parameters. Note: N_1, N_2 and N_v represent the total population of cattle, humans and tsetse, respectively

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