MODELLING THE TRANSMISSION DYNAMICS OF AFRICAN ANIMAL TRYPANOSOMIASIS; A CASE STUDY OF SHIMBA HILLS, KWALE COUNTY, KENYA

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DECLARATION

This thesis is my original work and has not been presented in any other University or any other Award

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DEDICATION

I dedicate this work to my immediate family (The Chepkeres) and my parents and siblings for their continued support and encouragement throughout my study.

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ABSTRACT

African Animal Trypanosomiasis (AAT) is caused by parasites of the species *Trypanosoma vivax, Trypanosoma congolense, and Trypanosoma rhodesiense.* Of 48 sub-Saharan African nations, 36 have endemic cases of AAT. The disease is prevalent in savannah and woodland areas. It poses a major threat to livestock production and health in agro-pastoralist communities, many of which are located along the boundaries of wildlife reserves. Most epidemiological studies on AAT around Shimba Hills National Reserve (SHNR) have focused on the vectors (tsetse fly) and the host (cattle). No studies have been done to show how efficiently a trypanosome can be transmitted from tsetse fly to cattle in a certain population. This study used data from previous studies collected from five villages, Kipambane, Msulwa A, Shimba Hills, Pengo, and Mlafyeni, located around SHNR. A conceptual model to represent all the interactions and feedback in the system was developed. It is assumed that transmission occurs between cattle and tsetse flies only. The ordinary differential equations were formulated representing all the interactions and transitions in the model. The parameters and variables of the model were estimated and a compartmental SIR-SI model framework was developed for a period of 120 days, then implemented in RStudio V4.1.1. The basic reproduction number (R_0) was estimated from the next-generation matrix. The model revealed that the susceptible cattle sub-population and tsetse fly sub-population decreased with time, while on the other hand, the infectious cattle and tsetse fly sub-population increased with time. The recovered cattle population also increased over time. The basic reproduction number was obtained as the most dominant eigenvalue of the Next-Generation Matrix (R_0= 2.73) = R_o >1. From the data, the infection rates were high in the tsetse fly population 6.23% (74/1190) compared to the cattle sub-population 5.64% (29/514). From the data, the susceptible, infectious, and removed cattle populations were high in Kipambane village while the susceptible and infectious tsetse fly populations were high in the Shimba Hills region respectively. In conclusion, this study developed a compartmental model to simulate the trypanosome-vector-host transmission dynamics in areas neighboring the SHNR, Kwale County. It also estimated the basic reproduction number and documented the distribution of transmission risk around SHNR. The data indicated that villages close to the National Reserve have high infection rates compared to those far from the park. The estimated basic reproduction number revealed that if the right control measures are not implemented, AAT cannot be easily eliminated in areas around Shimba Hills National Reserve. Information about the distribution of the transmission risk around SHNR can be used to guide farmers on transmission risks given the transmission trend with time and also areas where they can graze and water their livestock. The public health officers and the veterinary officers can also use the same information to manage AAT in villages around SHNR. This study's findings, model predictions, and the estimated R_0, indicated that more efforts and tailored management measures need to be put in place towards successful elimination of AAT in the Shimba Hills region.

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GLOSSARY

Basic Reproduction number	The number of people infected by an infectious person during the average period of illness when everyone is susceptible. When R_0 is less than 1, the disease can be easily eliminated but when its value is above 1 it can cause a pandemic
Compartmental modelling	It is a general modeling technique applied in the modelling of infectious diseases. The model consists of compartments where individuals are placed based on the disease state
Next Generation Matrix	Denoted as K, is a common way for calculating the basic reproduction number (R_0). It consists of a combination of two Jacobian Matrices (J)
Ordinary Differential Equations (ODEs)	It is a differential equation dependent only on one independent variable
Model parameters	Is a configuration variable that is internal to the model and whose value can be estimated from the data
Model variables	There are two sets of variables; dependent and independent. Both variables provide a common reference point for the transfer of default values to a specific product model. Independent indicates that they stand alone and other variables in the model do not influence them while dependent variable (DV) is what you want to use the model to explain

ABBREVIATIONS

AAT	African Animal Trypanosomiasis
HAT	Human African Trypanosomiasis
EANBiT	Eastern Africa Network for Bioinformatics Training
icipe	International Centre of Insect Physiology and Ecology
ITC	Insecticide Treated Cattle
ITT	Insecticides Treated Targets
MDR	Multi Drug-Resistant
NGM	Next Generation Matrix
NR	National Reserve
ODEs	Ordinary Differential Equations
R_o	Basic reproduction number (R-Naught)
SH	Shimba Hills
SHNR	Shimba Hills National Reserve
SI	Susceptible Infectious
SIR	Susceptible Infectious Recovered
SIT	Sterile Insect Technique

CHAPTER ONE

INTRODUCTION

1.1 Background Information

African Animal Trypanosomiasis (AAT) is caused by parasites of the genus *Trypanosoma*. The genus consists of pathogenic species that cause Nagana in cattle: *Trypanosoma congolense, Trypanosoma rhodesiense,* and *Trypanosoma vivax* (Liana et al., 2020). Nagana is the name given to AAT in cattle, goats, and sheep (Pearce, 2022). *Trypanosoma brucei*, *T. vivax, and T. congolense* are the most common trypanosomes that cause havoc in livestock health and agricultural production in Sub-Saharan Africa. Trypanosome parasites mostly affect pastoral communities because many of these parasites are found adjacent to wildlife areas, an example of such a setting is the Shimba Hills region which is adjacent to the SHNR (Ebhodaghe et al., 2021a). Trypanosomes are blood-borne parasites found mainly in the host (cattle) body and tissue fluids. These parasites move using a flagellum. The developmental cycle of trypanosomes ranges from less than a week in *Trypanosoma vivax* to 45 days in *Trypanosoma brucei* complex (Gifford-Gonzalez, 2000). *Trypanosoma vivax, T. brucei,* and *T. congolense* belongs to the sub-genus Duttonella, Trypanozoon, and Nannomonas respectively have been reported to cause Nagana in cattle in areas around Shimba Hills National Reserve, (Ebhodaghe et al., 2021b); Kulohoma et al., 2020).

African Animal Trypanosomiasis is prevalent in 36 of the 48 sub-Saharan African countries (Krafsur & Maudlin, 2018). It is mostly found in woodland and savannah through zones labeled as tsetse fly belts (latitude 10^0N and 20-30^0S) (Maichomo et al., 2021). This has left approximately over 60 million cows reared in Nagana endemic areas at a high risk of infection by AAT (Makhulu et al., 2021).

Shimba Hills in Kwale County is one of the Kenyan locations where AAT is endemic, affecting wildlife and domestic animals (Ebhodaghe et al., 2021b; Kulohoma et al., 2020).

Farmers neighboring Shimba Hills National Reserve (SHNR) practice small-scale cattle farming. Wildlife is a constant reservoir for trypanosome parasites. As a result, high interaction between livestock and wildlife occurs leading to high AAT transmission rates of over ~50.00% in cattle populations in the region (Ebhodaghe et al., 2021b; Gachoki et al., 2021; Kulohoma et al., 2020; Wangwe et al., 2019). Due to the high transmission rates, Kwale County has been labeled a zone with high tsetse infestation (Kulohoma et al., 2020). If not treated, AAT causes irregular fever, anemia, anorexia, adenopathy, petechiae on the mucosa, abortion, bloody diarrhea, and death (Maichomo et al., 2021).

African Animal Trypanosomiasis is a significant barrier to the rearing of livestock rearing and expansion of livestock industries in African countries (Abro et al., 2021; Bukachi et al., 2017; Wilson et al., 1963). Despite several studies done on cattle and tsetse flies, Nagana still poses a threat to livestock health although tsetse control around Shimba Hills National Reserve has been carried out for many years (Gachoki et al., 2021). In Kwale County, farmers use many methods to control and manage Nagana; one of the methods is using curative trypanocides, mostly VeribenB12 complemented by antibiotic is used to manage Nagana in the infected cattle populations. However, trypanosome parasites have been shown to confer resistance to this drug in some regions near Shimba Hills National Reserve (Kulohoma et al., 2020). Some indirect methods are also being implemented towards the control of the tsetse fly vector, targeted towards reducing the tsetse fly population abundance and direct contact with the cattle population.

These include the tsetse repellent collar (TRC) developed by *icipe*; the collar is applied on the livestock to reduce the rate of contact between the tsetse flies and the livestock (Muriithi et al., 2021). Spraying livestock with insecticides and use of Insecticide Treated Traps or targets are also being implemented (Gachoki et al., 2023). African Animal Trypanosomiasis has also caused major economic losses in Africa, in 2010, (Baral, 2010), estimated to be

more than US$1.3 billion annually (Odeniran et al., 2020).

The etiological agent for AAT is trypanosome parasites which belong to the subkingdom Protozoa and genus *Trypanosoma* (Makhulu et al., 2021). These parasites are found worldwide, often transmitted by blood-sucking insects, and cause infection in wild and domestic animals including humans (Truc et al., 2013). The parasites have been present for centuries, but their control and treatment remain elusive (Bett et al., 2008). Tsetse fly feed on a wide range of hosts, but they prefer cattle over other domestic animals (Cherono, 2019). Some of the wild hosts preferred by tsetse flies include warthogs and buffaloes (Aksoy et al., 2014; Ebhodaghe et al., 2021; Gashururu et al., 2021; Wangwe et al., 2019). Tsetse flies get the infection from wildlife reservoirs located at the national reserve, and livestock kept by farmers. *Glossina pallidipes*, *G. austeni*, and *G. brevipalpis* are the tsetse fly species found in Shimba Hills National Reserve, with *G. pallidipes* consisting of the largest population (75%) (Kulohoma et al., 2020; Wamwiri et al., 2013). An understanding of the distribution patterns of tsetse flies requires knowledge of the transmission dynamics of trypanosomiasis. As suggested by Skrip & Townsend, (2019) and Wendelboe et al., (2010) this data is crucial when planning strategic or tailored control measures for both cattle and tsetse flies.

It is critical to understand how efficiently a trypanosome can be transmitted in a certain population from tsetse fly to cattle and vice versa in a particular environment after a bite by an infectious tsetse fly. According to previous research conducted by Wamwenje et al., (2019) the study noted a high prevalence of bovine trypanosomiasis (33.9%) and morbidity rate (29.1%) in Shimba Hills. The findings from this study shows high infection rates on cattle which were attributed to the high trypanosomiasis challenge around the Shimba Hills National Reserve which is subjected to annual re-invasion by Nagana (Mbahin et al., 2013). Kulohoma et al. (2020) discovered a high level of interaction between domestic animals, humans, and wild animals in Shimba Hills, resulting in increased trypanosome transmission rates via tsetse fly bites. Carreton et al., (2021) documented how proximity between human settlements,

wildlife reserves, grazing lands, and Shimba Hills National Reserve (SHNR) led to a high risk of zoonosis. All these studies document the transmission of AAT in Kwale County but none quantifies how efficiently trypanosomes are being transmitted from one host to another in the same area.

Studying trypanosome vector-host transmission dynamics and spatial risk patterns in areas around Shimba Hills National Reserve will guide the identification high risk areas of bovine trypanosomiasis infection. However, these factors have received less attention in villages neighbouring Shimba Hills National Reserve. Faith et al., (2022) discovered that most previous studies conducted in areas neighbouring Shimba Hills National Reserve have analysed trypanosome diversification and the trypanosome infection rates in tsetse flies, with none of those studies examining the infection rates in tsetse flies about vector abundance and bloodmeals.

In previous study, it was found that most epidemiological studies in Africa have majorly concentrated on infection of the tsetse vectors, human and livestock hosts and a few have focused on studying trypanosome infections in wildlife reservoirs (Ebhodaghe et al., 2021b). Most farmers use trypanocides, offered by veterinary officers and extension workers, to treat cattle infected with Nagana (Wangwe et al., 2019). To date, there has been no success due to multidrug resistance and high toxicity rate (Kulohoma et al., 2020; Chitanga et al., 2011; Akazue et al., 2019). Therefore, safeguarding the existing drugs from misuse is important to maintain their effectiveness (Solomon & Workineh, 2018; Baker et al., 2013). Understanding antibiotic resistance has significantly improved because of mathematical modelling (Spicknall et al., 2013).

The Modelling transmission of the AAT has been applied to guide future experiments (Olesen, 2022), public health interventions for disease spread and emerging pathogens (Birkegård et al., 2018), monitoring the spread of drug resistance, grazing seasons and times,

disease hotspots, used to understand the emergence, spread, and development of AAT (Niewiadomska et al., 2019). On the other hand, estimating the basic reproduction number will aid forecast the future trajectory of the disease and guiding control policies as suggested by Knight et al., (2019). Mathematical models have been exploited in epidemiology to describe how diseases are transmitted and develop a better understanding of systems to control or optimize results (Muia et al., 2018a). Thus, infectious disease models are now common place and have helped control the temporal spread of diseases such as Nagana (Wangwe et al., 2019). Tools for reducing tsetse abundance and interrupting disease transmission have been identified. However, their large-scale deployment is hampered by high implementation costs (Gachoki et al., 2021).

Despite the existing efforts towards control Nagana, the disease still poses a constant threat to livestock production in Kwale County. As a result, developing models to help understand the transmission dynamics and measure how efficiently a trypanosome can be transferred from one host to another would assist farmers in making decisions about where to graze their cattle and determining the most effective way to control the spread of Nagana, knowing where the AAT hotspots are in the area. This research, formulated a mathematical model that simulates the trypanosome vector-host transmission dynamics and derives the basic reproduction number (R_0) to measure how efficiently a trypanosome can be transferred from one host to another in Shimba Hills.

1.2 Problem statement

African Animal Trypanosomiasis is a major impediment to sub-Saharan African livestock development (Odeniran et al., 2020; Dagnachew et al., 2015). Many studies have been conducted to suggest better control strategies for AAT. However, the disease still poses a major health threat to livestock production and affects economic development in Africa. Liana and colleagues in 2020 reported that AAT has caused around 500 million farmers in rural African villages to live with food shortages and poverty. African Animal

Trypanosomiasis causes reduced animal work rate, meat, and milk yield, and increases expenses incurred on trypanocides. Economic losses due to AAT can best be approximated through pecuniary losses due to the paucity of large-scale public health records from veterinary practitioners (Wangwe (2018). African Animal Trypanosomiasis is known to cause severe losses estimated to be more than US$1.3 billion annually to the livestock industry (Odeniran et al., 2020).

With various modes of transmission and no vaccine, the control of AAT remains a major challenge (CDC, 2022; Richards et al., 2021). Kulohoma et al., (2020) noted the high interaction of domestic animals and wild animals in Shimba Hills which led to a high transmission rate of AAT in the region due to increased tsetse fly bites. Farmers in the region highly depend on trypanocides for treatment. However, repeated treatment with the same trypanocides and inadequate research for new trypanocides have led to the few available drugs losing effectiveness leading trypanosomes to acquire mutations that confer trypanocidal resistance (Barret & Fairlamb, 1999; Giordani et al., 2016). After the development of trypanocide resistance, and consequently multi-drug resistance (MDR), treatment is less likely to be successful (Richards et al., 2021; Wangwe, 2018). In this case, there is a need to develop alternative solutions to curb Nagana.

There are various management and control practices for African Animal Trypanosomiasis; spraying with insecticides, treating with trypanocidal drugs, rearing trypano-tolerant cattle, using tsetse fly traps, and clearing bushes to alter tsetse fly habitats so that they become unsuitable (Latif et al., 2019; Media, 2022). Because the suggested methods are costly and less effective when applied on a large scale, modelling the transmission dynamics will shed light on the areas that need to be targeted for control as well as less expensive ways to control the spread to other regions (Debroy et al., 2017; Kulohoma et al., 2020; Muhanguzi et al., 2015).

Most epidemiological studies on AAT done in Shimba Hills and the areas around Shimba Hills National Reserve have focused majorly on the vector (tsetse fly) and the host (cattle), and no study has been done to show how efficiently a trypanosome can be transmitted in a certain population from the tsetse fly to cattle and vice versa through estimation of the R_0.

1.3 Justification

Models of vector-borne and neglected tropical diseases have been used to study pathogen transmission dynamics since ancient times (Zhao et al., 2020), study transmission, and viable control of AAT cheaply and directly with no need for comfort and complex experiments (Gervas et al., 2018). The populations most affected by neglected tropical diseases are ordinarily the least resourced. Therefore, modelling the transmission of such diseases can help maximize the utility of restricted assets as suggested by (Luz et al., 2010).

Formulation of mathematical models to describe the natural phenomenon of Nagana and understand its transmission dynamics will help stakeholders in villages around Shimba Hills National Reserve choose better and more effective control and management strategies aimed toward the elimination of the disease in the region and predict future disease outcomes. Likewise documenting the distribution of transmission risk around Shimba Hills National Reserve will shed light on Nagana hotspots and suggest better Nagana management practices. Information on the R_0 will help veterinary and public health officers in the decision-making process and policies toward management and control programs in villages neighboring Shimba Hills National Reserve.

1.4 Objectives

1.4.1 Overall objective

To develop a mathematical model that simulates the trypanosome vector-host transmission dynamics around Shimba Hills National Reserve.

1.4.2 Specific objective

1. To develop a Susceptible-Infectious-Recovered model that simulates the trypanosome vector-host transmission dynamics.
2. To estimate the basic reproduction number (R_0) and document the distribution of transmission risk around Shimba Hills National Reserve.

CHAPTER TWO

LITERATURE REVIEW

2.1 Types and the geographical distribution of tsetse flies

Tsetse flies, both male and female are avid blood-feeding vectors found in Africa (latitude 5°N to 20°S) (Šlapeta, 2022). African trypanosomes are the leading cause of Human African Trypanosomiasis (HAT) in humans and AAT in livestock respectively (Geiger et al., 2005). Although tsetse flies thrive well in fertile regions which are mostly utilized for agropastoral activities, their infestation is limited to their use (Malele, 2011). Tsetse fly vectors transmit trypanosome parasites from one host to another after an infection (Geiger et al., 2018). Tsetse flies in the genus *Glossina* feed on a wide variety of vertebrate hosts which include reptiles, birds, and mammals (Geiger et al., 2018). Both the male and the female species of tsetse flies feed throughout their lifetime (Channumsin et al., 2021). Tsetse flies pick up trypanosome parasites when feeding on infected vertebrate hosts; wildlife, livestock, and human beings (Wamwiri & Changasi, 2016). *Glossina* is classified into three major groups namely:

1. *Palpalis* group comprises *Glossina palpalis gambiensis, G. fuscipes fuscipes, G. palpalis palpalis*. All these are found in estuarine habitats.
2. *Morsitans* group comprises *Glossina austeni, G. swynnertoni, G. morsitans, G. longipalpis* and *G. pallidipes*. They are majorly found in woodland and savannah regions.
3. The *Fusca* group comprises *Glossina brevipalpis, G. longipennis, G. fusca fusca*, and *G. schweitz.* This group is majorly found in the rain forests of West Africa, though *G. longipennis* and *G. brevipalpis* are also found in East Africa.

2.2 The lifecycle of tsetse fly vector

The female tsetse fly mates only once and after seven to nine days it produces one egg which later develops in the uterus as larvae. After about nine days the larvae are buried in the soil and left to develop into a pupa. The production of the larvae continues after every nine days in the female tsetse fly for the rest of its life. After 30 days, the adult tsetse fly emerges from the soil. After emergence, the adult fly matures, and mates and the female flies deposit their first larvae within 12 to 14 days (Liverpool School of Tropical Medicine, 2022). The lifecycle of tsetse fly is represented in Figure 2.1 below;

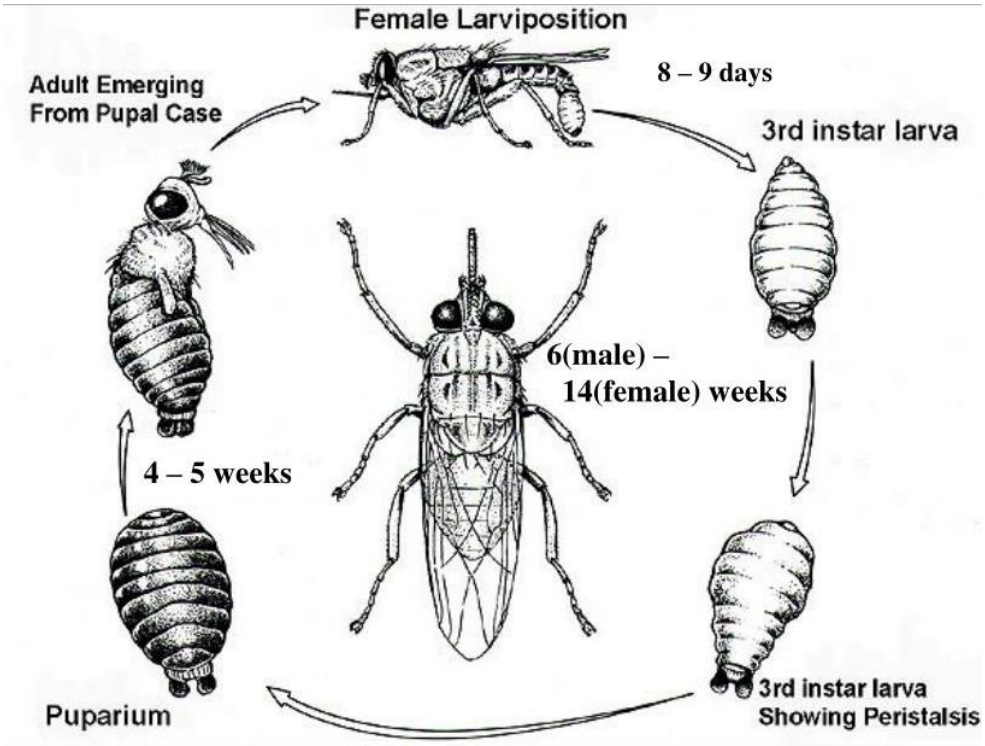

Figure 2.1: Lifecycle of the tsetse fly vector
Source*:* (Liverpool School of Tropical Medicine, 2022)

The presence of a suitable host, competition for resources, shelter, temperature, and moisture are all important factors that determine the dynamics of a tsetse population (Mweempwa et al., 2015).

2.3 Trypanosomiasis and lifecycle of African Trypanosomes

Trypanosomiasis is a zoonosis affecting both domestic animals, wildlife, and humans in both the tropics and sub-tropical countries of the world, thus the name HAT and AAT (Maichomo et al., 2021). The tendency of trypanosomes to survive in vertebrate hosts and transmit to future hosts is critical to their success. Although these goals may be mutually beneficial, they may also contradict because parasite development can harm the host and confine transmission potential (Frank, 1996). A prominent example is the *T. brucei* which is maintained in the mammalian bloodstream by a complex system of antigenic variation system until transmission by the tsetse fly vector (MacGregor et al., 2011). Tsetse flies of the genus *Glossina*, the primary vector of trypanosomes, inhabit about 10 million square kilometers of the continent and affect 37 countries in sub-Saharan Africa (Mbahin et al., 2013b; Media, 2022). Tsetse flies are extensively distributed in Kenya and can be found in 38 of the 47 counties accounting for approximately 138000 square kilometers (23% of the country), putting up to 60 million cattle at risk of contracting an infection each year (Wangwe et al., 2019).

The efficiency with which trypanosomes move between vertebrates and tsetse flies depends on many factors including tsetse-trypanosome interactions. These factors depend on the infecting species (for example; length of developmental cycle), infection prevalence rates, species and age of the fly, vertebrate host-trypanosome interactions. Further these factors are said to be primarily defined by the suitability of the host for trypanosome development and bloodmeal host (defined by abundance and suitability of the host for trypanosome development) (Dalet & Maudlin, 1999; Geiger et al., 2015). The tsetse fly is considered both a host as well as vector for the trypanosome parasite (Okeyo et al., 2018; Wamwiri et al., 2013). There are three groups of the tsetse fly namely *Fusca, palpalis,* and *morsitans* with different biological characteristics belonging to different species or subspecies (Carlson et al., 1993). These vectors transmit trypanosomes to different host species and only 5% of them are reported to cause AAT (Otieno, 2015).

Infected tsetse flies suck blood from their mammalian hosts by injecting the supercyclic trypomastigote into skin tissue. The parasite then enters the lymphatic system and enters the bloodstream (Nagagi et al., 2018). It is then transformed into trypomastigotes in the circulation within the mammalian host, which is transported to other locations throughout the body where it can access other bodily fluids (e.g., lymph, cerebrospinal fluid, and bone marrow), and multiply by division (Tyler et al., 2003). The entire life cycle of African trypanosomes is represented by extracellular stages in both tsetse fly and cattle (Figure 2.2). Through sucking the blood of an infected mammalian host, tsetse flies become infected with trypomastigotes present in the blood. Then, in the midgut of the fly, the parasite transforms into annular trypomastigotes, proliferates by division, and leaves the midgut to transform into epimastigotes (Silvester et al., 2017). Once the epimastigotes reach the fly's salivary glands, they continue to reproduce by binary fission (see Figure 2.2).

The entire life cycle of a tsetse fly takes about three weeks (Figure 2.2).

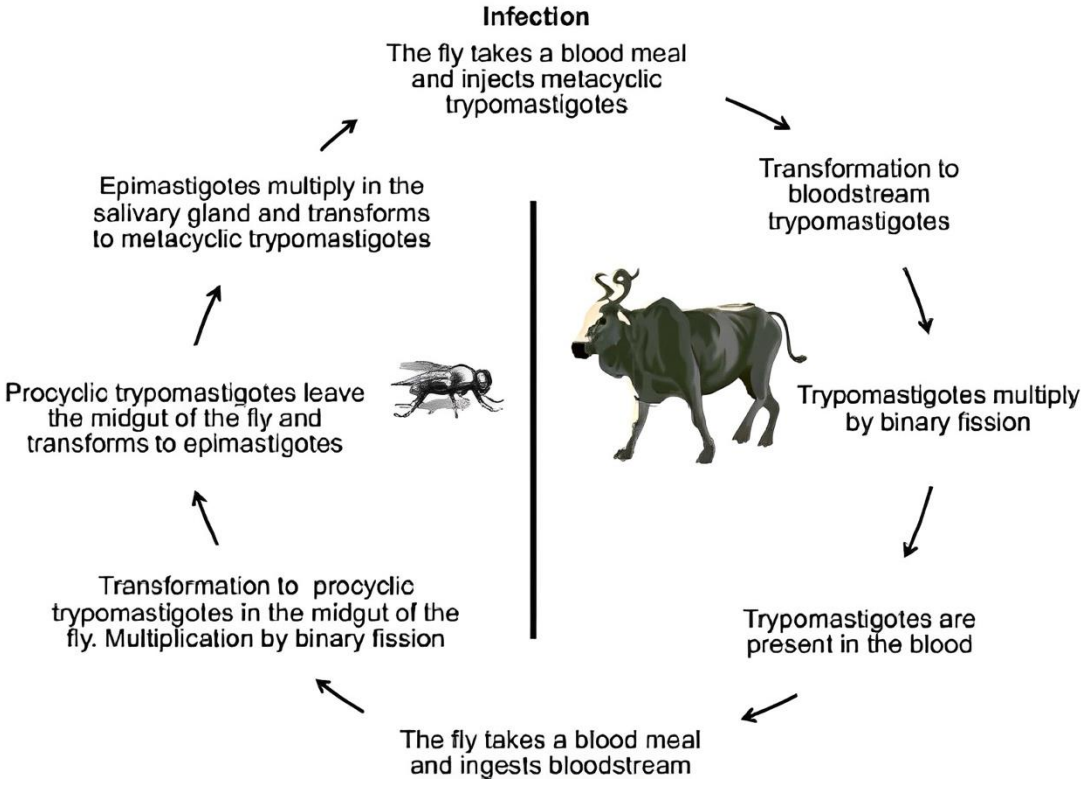

Figure 2.2 : Phases of trypanosome parasite life cycle in tsetse fly and cattle

Source: (Dagnachew & Bezie, 2015)

Once an animal contracts/manifests with Nagana, signs, and symptoms appear within 4 and 24 days. Major clinical signs and symptoms include decreased fertility, anorexia, decreased physical condition and productivity, edema, anemia, intermittent fever, lacrimation, abortion, swollen lymph nodes, premature death in acute form and malnutrition, and ultimately death from the chronic disease often digestive and/or neurological symptoms. However, the most important clinical sign is non-regenerative anemia (Media, 2022).

2.4 The role of wildlife in the spread of African Animal Trypanosomiasis

Currently, it is acknowledged that wildlife is a significant source of emergent animal infections, including parasites (Hodo & Hamer, 2017; Polley, 2005). Wildlife and livestock are at risk of infection by AAT, which carries a high risk of interspecies transmission (Kasozi et al., 2021). Trypanosomes are real multi-host parasites that can infect diverse wildlife species ranging from subfamilies of Pteropodidae, Meliphagidae, Bovinae, Equidae, Paramelidae, Alcephinae, Cercopithecinae, Pantherinae, Sigmodontidae, and Suidae (Anderson et al., 2011; Kasozi et al., 2021). Grazing of livestock near the national reserve, and proximity between human settlements to the national park are among the factors that have been identified to increase the transmission of Nagana to livestock (Latif et al., 2019). Infections between domestic and wild animals are on the rise due to increased human activity and demand for land resources. Makhulu et al., (2021) found out that AAT is actively transmitted in areas near wildlife interfaces and the infection is maintained by multiple hosts. In this regard, communities that live and keep livestock on the periphery of ecosystems with a high concentration of wildlife must implement vector control measures to control the spread of the disease to other areas as suggested by Gunter et al., 2017).

2.5 The social and economic impact of African Animal Trypanosomiasis

African Animal Trypanosomiasis also known as Nagana, derived from the Zulu word meaning ‘useless’, has a major impact on the economic development and cattle production in the African continent. In Sub-Saharan Africa, over 46 million cows are reared in tsetse fly-infested regions (Paling et al., 1991), and approximately 35 million doses annually are used to treat animals (Muhanguzi et al., 2015; Venturelli et al., 2022), costing approximately 35 million dollars (Kristjanson et al., 1999). Spraying with insecticides to control AAT is also costly and needs trained personnel to implement the program, advise on defending the sprayed areas and also provide guidance on preventing re-invasion (Ruiz et al., 2015).

Nagana continues to cause significant damage in Sub-Saharan Africa, estimated at $4.75 billion annually (Shereni et al., 2021). After reviewing several studies done in Africa, South America, and Asia on trypanosomiases and their chemotherapy, Giordani et al., (2016) reported that *T. congolense* is the most pathogenic bovine trypanosome parasite, followed by *T. vivax*. This has led to devastating losses estimated to be from 0-70% ranging from a variety of factors including draft power by 50%, milk, and meat sales by 50%, cattle density up to 70%, mortality rate by 20%, and calving rate by 20% (Holt et al., 2016; Swallow, 1999).

High tsetse-trypanosome infection rates limit the expansion of livestock rearing forcing most farmers in tsetse-infested regions to depend on crop farming (Adungo et al., 2020). In Africa, it is estimated that 80% of the land is cultivated by hand simply because trypanosome infection in cattle reduces the number of draft animals used to till farms and reduces the production of animal waste for manure production, limiting agriculture (Holt et al., 2016; Swallow et al., 1995).

2.6 Control of African Animal Trypanosomiasis and tsetse fly vector

After infection, tsetse fly (vector) and cattle (host) acquire mechanisms for transmission and defense (Barrett et al., 2011; Cnops et al., 2015; Solomon & Workineh, 2018). Some of the

mechanisms include the production of antibodies, immune modulation, producing toxic serum factors, immune destruction from the trypanosome parasite, and antigenic variation (Alves et al., 2008). Trypanosomes evade the host's immune response by changing their surface coverage, making conventional therapeutic vaccine development impossible (Horn, 2014).

The control of AAT involves the use of both direct and indirect control methods (Pandey et al., 2015; Venturelli et al., 2022). The direct control methods involve the use of curative trypanocides. There are few licensed drugs to treat Animal African Trypanosomiasis by the veterinary board which includes Isometamidium chloride (ISM), 40%, and diminazene aceturate (DA), 33% (Kulohoma et al., 2020; Mulandane et al., 2018). Specifically, in Kwale county, farmers use VeribenB12 complemented by antibiotic use. However, trypanosome parasites have been shown to confer resistance to this drug in some regions near Shimba Hills National Reserve (Kulohoma et al., 2020). Trypanocide resistance and the use of poor-quality drugs for treatment often lead to the persistence of the infection in the animal population (MacLennan, 1983).

The indirect control of AAT has focused majorly on tsetse fly vector elimination, the biological vector for AAT (tsetse fly vector), the prompt interventions used by several countries include the Sterile Insect Technique (SIT) which targets reduce the birth rate of the tsetse flies (Hargrove et al., 2012; Venturelli et al., 2022). Spraying insecticides in the environment (Odeniran et al., 2020) has been also used to indirectly control AAT. Aerial spraying and ground spraying target to increase the mortality rate of the tsetse fly vector, hence reducing African Animal Trypanosomiasis's further spread. Recent understanding of the tsetse fly feeding behaviour has also made it possible to introduce the spraying of insecticides directly on the skin surface of the animal which is most preferred by tsetse fly for feeding. This has reduced the cost and effectiveness of insecticides in the elimination of tsetse flies and reducing Nagana infections in areas where tsetse flies persist (Hargrove et al., 2012).

Other insects can mechanically transmit *T. vivax* (Desquesnes & Dia, 2003; Ebhodaghe et al., 2021b). Control of this species, however, requires integrating both trypanosome eradication and other vector control methods compared to other trypanosome species. In Africa, use of insecticide-impregnated targets and traps, and insecticide-treated cattle are used to reduce or kill tsetse flies (Hargrove et al., 2012). Clearing the nearby bushes can also help reduce the tsetse densities, bites, and infections, but this method is not ecologically friendly to the environment. It also reduces the availability of wild and domestic animals who come to hide and graze in the bushes.

The cattle resistance can be increased by rearing trypanotolerant west African breeds of cattle such as Laguna, Somba, Baoule, Muturu, N'Dama, Maasai zebu (East African), and Dahama (West African) can reduce the impact of African Animal Trypanosomiasis. These breeds gain weight easily and have a short oestrus cycle, hence high reproduction capacity with moderate infection (Paling et al., 1999). Trypanotolerant cattle breeds will not only reduce Trypanosomiasis impact but also reduce the cost of treatment and production loss, however, the tsetse fly densities will remain the same.

Farmers also practice various tsetse management practices to mitigate the risk of exposure to Nagana in areas neighboring Shimba Hills National Reserve. This includes the practice of netted zero grazing units to reduce animals from mixing randomly with other animals, reducing the chances for exposure and infection. Smearing the animals with oil ointments and hash is practiced by some farmers in the region as one of the cultural methods of controlling Nagana (Rogers, 1988). Muriithi et al., (2021) and Seyoum et al., (2013) in their studies respectively suggested that farmers should avoid grazing their animals in the late evening and early morning hours, these times of the day are considered high-risk periods when Nagana can be transmitted at higher rates. The farmers are also advised not to graze their livestock near Shimba Hills National Reserve (SHNR) (Ohaga et al., 2007).

2.7 Mathematical models

The application of mathematical models in epidemiology dates back to revisit of Dietz & Heesterbeekli (2002), Kermack- Mc Kendrick model (1927) in disease modelling as described by Brauer, (2017), and Ross, Macdonald (1907) for the dynamics and control of mosquito transmitted pathogens as described by Smith et al., (2012). Developing and the application of compartmental models for vector-borne diseases started with the Ross–Macdonald model when they developed two-dimensional simple malaria model (Smith et al., 2012). The model was improved by Rogers in 1988, to a multi-host model which included domestic, wildlife, and human beings and also included *T. b. gambiense*-transmitted West African trypanosomes (Rogers, 1988).

This model also took into account the time between when an animal becomes infected to the time it becomes infectious, the probability of disease transmission after receiving a bite from a susceptible tsetse fly, a period of temporary immunity for the human host, and the survival rate of the vector during the incubation period (Rogers, 1988). The three-dimensional model analysis that resulted included determining a disease threshold, the equilibrium disease prevalence, and data evaluation for a West African village (Ndondo et al., 2016). Artzrouni and Gouteux (1996) developed a five-variable compartmental model for the dynamics of HAT that included humans and tsetse flies (Artzrouni & Gouteux, 1996). Their model included humans who were susceptible, incubating, asymptomatic, or excluded, and the results were compared to data from the Democratic Republic of the Congo (Artzrouni & Gouteux, 1996).

In a follow-up article, these authors used the model to compare control strategies. This model was extended by Chalvet-Monfray et al. (1998), to model plots and a village. Hargrove et al. (2012) went on to model the control of *T. b. rhodesian*-caused African Trypanosomiasis in various hosts. The model predicted that using pesticides on cattle would be more effective than using trypanocidal drugs on cattle during the HAT treatment process. Kajunguri et al.

(2014) also developed a multi-host model for HAT caused by *T. b. rhodesiense*. They found that applying the pesticide only to the cow's legs and belly (the feeding grounds favoring the trough) provided an effective and affordable method of managing HAT.

Funk et al. (2013) created a multiple-host model for *gambiense* HAT and estimated the basic reproduction number using field data from Bipindi, Cameroon. Rock et al. (2015) provide a thorough survey and a list of mathematical models used in Human African Trypanosomiasis epidemiological modelling. The study also recommended further modelling to find better solutions for the control of HAT and understanding its transmission dynamics (Rock et al. 2015).

Models are widely used in different countries to formulate public health policies because they can predict future outcomes of disease, understand the dynamics of disease transmission, and demonstrate connections between the biological transmission process and the dynamics of infection at the population level (Sterman, 2000). Since 1980s, mathematical modelling has been applied in investigating the impact of interventions, which includes a model developed by Anderson and May (1979), as applied by Bjørnstad et al., (2002) in dynamics of measles epidemics. Examples of high-profile models that have been applied to influence policy and decision-making include; the culling of livestock that brought Foot and Mouth disease under control in 2001 (Keeling, 2005), projections of Ebola cases in Liberia in 2014 (Drake et al., 2015), short-term predictions of deaths related to COVID-19 in the Midlands (Danon et al., 2020) and lockdown exit strategies in the UK during the emergence of the coronavirus pandemic (Keeling et al., 2021). Applying both analytical and arithmetic methods, Banwarth-Kuhn & Sindi, (2020) discovered that mathematical and computational models were already playing an important role in advancing biochemical and biological research. Because they provide statistical and numerical tools, they enable researchers to quantitatively bridge the gap between data collection and method validation.

2.7.1 Designing a mathematical model

Models are developed to solve real-world problems and gain insights into real-world phenomena (Erbas et al., 2014). When creating a mathematical model, the first step is to identify a problem. This includes listing all of the variables and parameters (constants) that will be used in the model, making assumptions, and formulating model objectives (Anhalt & Cortez, 2015). The second step involves coming up with a visual diagram (a conceptual model) which will guide the model formulation step. It is important to note that conceptual models describe all the possible ways in which the variables within a model might interact with one another, as well, and as the key variables within a model. This helps scientists with minimal mathematical backgrounds understand the model and easily develop a similar model (Torres & Santos, 2015). After developing a conceptual model, one should select the most appropriate modelling approach that fits the problem in question before formulating the model. This step is guided by existing literature and experience (Grassly & Fraser, 2008; Ron, 2008).

The third step is formulating the model; all the processes, interactions, and feedback in the model are quantitatively represented in the form of mathematical equations, then implemented in software. The software includes Python and R programming languages (Yilmaz Çağirgan & Cagirgan, 2020). Any further assumptions made at this stage should be noted (Anhalt & Cortez, 2015). The next step is to solve the model and obtain a valid solution. This step should be done carefully to avoid math errors by using appropriate technology, which includes graphics, numerical software, and computer algebraic equations. When the model is solved, the solution is interpreted to determine if it makes sense; if so, then a solution is reported by phrasing it in nontechnical terms so that it is easily understood; If not, the conceptual model is amended until it fits the problem, and the process is repeated over and over until a reasonable solution is obtained (Grassly & Fraser, 2008). This is shown in Figure 2.3 below;

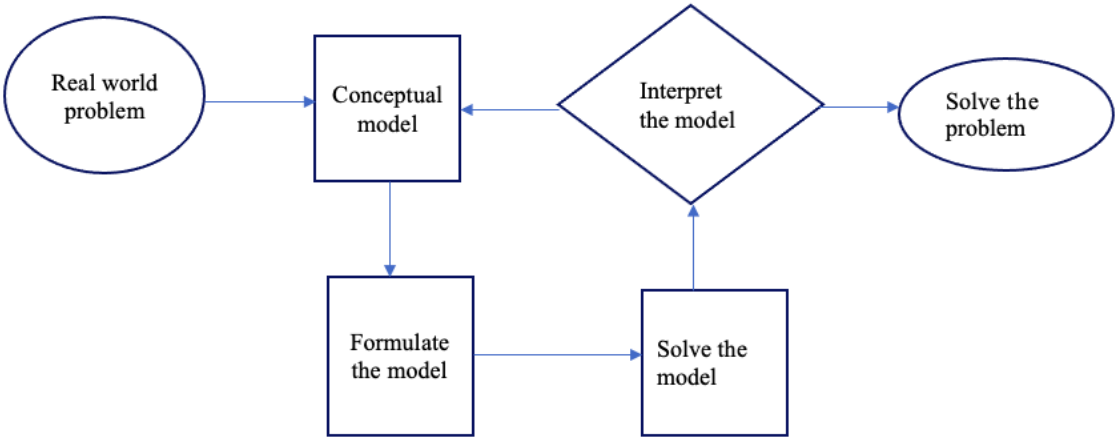

Figure 2.3: Steps for designing a mathematical model

2.7.2 The Susceptible-Infectious-Removed (SIR) model

2.7.2.1 Introduction to SIR compartmental model

Trypanosomiasis, a vector-borne disease, is known to be transmitted from vector to host and from host to vector. The process of disease transmission can be described using the compartment model, a vector-host epidemic model based on differential equations. This is based on previous literature as indicated in the referenced studies (Zhao et al., 2020; Grassly & Fraser, 2008; Hasibeder et al., 1992; Song et al., 2020; Gervas et al., 2018; Gabriel Kuniyoshi & Pio dos Santos, 2017; Liana et al., 2020; Osman et al., 2018).

The Susceptible Infectious Recovered (SIR) model shown in Figure 2.4 predicts the number of susceptible, actively infected, or recovered/removed cattle or tsetse flies at a particular time (Tolles & Luong, 2020).

Figure 2.4: The Susceptible, Infected, Removed, model flowchart

Susceptible- individuals most likely to contact the disease, Infected- those individuals who are infectious and at risk of infecting other individuals, Removed- those individuals who recovered/removed from the model.

The movement of vectors/hosts from one compartment to another based on their disease status is determined by the model parameters and denoted by Ordinary Differential Equations (ODEs). As the outbreak progresses, the number of animals in each compartment fluctuates. Susceptible (S) are cattle and tsetse sub-populations at risk of infection through contact with trypanosome parasites. Infected (I) is a subpopulation of cattle and tsetse flies carrying trypanosome parasites, and recovered cattle (R) is a subpopulation of cattle that have been eliminated (recovered) and are now immune or have died as a result of Nagana infections (Wangwe et al., 2019). In this case, the tsetse fly sub-population is assumed to be infectious throughout its life, hence it does not recover from trypanosome parasite infection.

The model has many dependent variables that are functions of time *(t).* These variables add up the total number of individual vectors or hosts in each compartment. Where *S(t),* denotes the rate of change in the number of vulnerable vectors/hosts, I(t), is the change in the number of infected vectors or hosts, *R(t)* is the change in the number of recovered (eliminated) sub-population of cattle. S(t) is negative because the number of vulnerable hosts and vectors decreases over time.

Another set of dependent variables is the percentage of the total population divided into three compartments. N represents the total number of vectors/hosts when the three compartments are added up together (S, I, and R). S(t)/ N represents a fraction of the susceptible vectors/host, I(t) /N is a fraction of the infected vectors/host, and R(t)/N represents a fraction of the recovered vector/host population. The intensity of infection, or the probability of a

vector or host becoming infected after interaction with an infected vector/host, is denoted by €. Γ is the recovery or removal rate of the cattle population.

1. The susceptible compartment's rate of progression is expressed as;

$$\frac{dS}{dt} = -\frac{€SI}{N}$$

2. The infectious compartment's rate of progression is expressed as;

$$\frac{dI}{dt} = \frac{€SI}{N} - \gamma I$$

3. The recovered compartment's rate of change can be expressed as;

$$\frac{dR}{dt} = \gamma I$$

Two parameters, γ, and € describe the transitions between compartments. γ is also the inverse of ψ, which is the infectious period. The model is based on the assumption of a stable general population N = S + I + R. Thus, the basal reproduction number is thus defined as the ratio of the ratio infection intensity to the recovery rate (R_0 = € /γ) (Prodanov, 2020).

The infection period is the period during which animals infected with trypanosomes can transmit nagana. Time in the deterministic SIR model is always represented in days. γ controls the movement from the infectious to the recovered compartment. € describes how quickly Nagana can move through the population, also known as the "force of infection". It controls the movement of animals from susceptible to an infectious compartment in the model. With this information, it is easy to obtain the basic reproduction number using the Maximum likelihood estimation method (White et al., 2020). The Next Generation Matrix method can also be used to calculate the basic reproduction number as described by Jones, (2007) and Smith et al., (2012) where, he described a simple method of estimating R_0 of the Malaria model, this method was hence adopted in this study.

2.7.2.2 Limitations of the SIR model

Due to the fact that the SIR model is simple, is simple to compute. It does, however, oversimplify complex disease processes (Tolles & Luong, 2020). The model involves the use of few parameters which can cause oversimplification of complex disease processes by not representing some processes like incubation period in the model (Tolles & Luong, 2020).

The SIR model does not take into account the time between the moment when an animal comes into contact with the pathogen and the moment the animal becomes contagious and can infect Nagana among other animals in the population. Demographic data are also excluded from the underlying SIR model.

The SIR compartmental model indicates that all animals in the population are equally likely to come into contact with each other, assuming equal population mixing (Tolles & Luong, 2020). This is not the case for human and wild animal social structures, where the majority of contact takes place within limited networks. In addition, the model assumes a stable population with no demographics (Afzal et al., 2022). The parameters in an original SIR model do not allow the quantification of ambiguity in the model parameters.

2.8 The basic reproduction number

The basic reproduction number (R_0) is among the crucial aspect of mathematical modelling. It refers to the number of people infected by an infectious person during the average period of illness when everyone is susceptible (Song et al., 2020). It is the ratio between € (effective contact rate) and γ (recovery rate) (Tolles & Luong, 2020). The value of R_0 depends on the contagious agent and the characteristics of the population that the agent invades. With this in mind, previously defined values cannot be accepted, or sizes range to a new outbreak unless most complex characteristics, such as population composition and contact structure, are comparable. (Roberts & Heesterbeek 2007). The R_0 is compared to 1 which is the threshold value used to measure the disease severity in a population (Zhao et al., 2020).

Estimated reproductive numbers are used to parameterize models in order to determine effective control and prevention strategies. Fraser, (2007) for example, demonstrated how the reproductive number and amount of pre-symptomatic or asymptomatic transmission can determine the effectiveness of a control strategy. Ferguson et al., (2005) demonstrated a link between the reproductive number and the influenza pandemic containment measures in Southeast Asia.

Similar modelling activities requiring accurate reproductive number estimates exists for many infectious diseases, including Middle East Respiratory Syndrome (MERS), tuberculosis, and malaria (White et al., 2020). These exercises may focus on locating transmission sites, identifying effective control policies, and investigating the impact of vaccines or other pharmaceutical interventions (White et al., 2020). When R_0 is less than 1, the disease will eventually die out, whereas if R_0 is greater than 1, the disease will spread throughout the population, resulting in a pandemic (Zhao et al., 2020). The basic reproductive number(coefficient) reflects the initial transmission of the pathogen. The basic reproduction number can be given by

$$R_0 = \frac{€}{\gamma} = Transmission\ rate \times Infectious\ period$$

Where R_0 – is the basic reproduction number

€ - is the contact rate

γ – is the recovery rate

2.9 The Next Generation Matrix (NGM)

The next generation matrix, denoted as K, is the common way for calculating the basic reproduction number (R_0). It was previously created by Diekmann et al., (1990) used in ecological epidemiology by Roberts & Heesterbeek, (2013) and popularized by Pauline van den Driessche and Watmough (2002) in compartmental model of disease transmission (Van

den Driessche &, 2002). To calculate the basic reproduction number from the Jacobian Matrices (J), the infected subgroup is divided into the sum of two matrices, the transmission (Γ) and transition matrices (Δ) respectively. (Γ) represents the new infections whereas (Δ) represents the movement in and out of the compartments. In the end, these two matrices are combined to derive the basic reproduction number in NGM (Diekmann et al., 2010).

The next-generation matrix is used to estimate the basic reproduction number for Nagana because the transmission routes are different and there is more than one host/vector (Chowell et al., 2007). The constructed matrix contains new infected populations from each type of infected object in the system (Hartemink et al., 2015). The basic reproduction number is expressed as the dominant eigenvalue (spectral radius) of the constructed matrix (Diekmann et al., 1990).

This method is frequently used where the population can be divided into different epidemiological complexities. In the matrix, denote X= {x1, x2, …, xn} represents n-the infected host compartments and denote Y = {y1, y2, …, ym} represents m - other host compartments (Brouwer, 2022), then rearrange the equations (Song, 2016),

$$\frac{d.x_i}{dt} = \mathcal{F}_i(x,y) - \mathcal{V}_i(x,y) \qquad i = 1,\ldots,..,n$$

$$\frac{dy_i}{dt} = \mathcal{G}_j(x,y) \qquad j = 1,\ldots,..,m$$

Where;

m- host compartments

n- vector compartments

X- ratio of the infected host population

Y- ratio of the infectious vector population

$\mathcal{F}_i$ - the rate at which newly infected individuals enter compartment i

$\mathcal{V}_i$- transfer of individuals out of minus into ith compartment

When generating a NGM matrix above, several assumptions are taken in to place which include;

1. There are no new infections if there are no infectious individuals
2. The sum is net outflow
3. We can only have inflow if the compartment is empty

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study site

This study was conducted in the selected villages around Shimba Hills National Reserve, a coastal forest (Malonza et al., 2018) in Kwale County. Several villages with proximity to the Shimba Hills National Reserve, within 5km, were selected: Kipambane, Shimba Hills, Msulwa A, Mlafyeni, and Pengo (Appendix II). The habitats found in the Shimba Hills ecosystem include wetlands (dams, swamps, and dams), woodlands, grasslands, bushlands, and forests (Malonza et al., 2018). The Shimba Hills area experiences an average annual temperature of ~24 °C and rainfall of 1150 mm. Long rains fall from March to May, and short rains fall from October to December in Kwale County, Kenya (Wamwenje et al., 2019). Shimba Hills National Reserve is covered in forest areas, woodlands, and pastures with scattered bushes, providing an ideal habitat for tsetse flies to rest and reproduce. (Gachoki et al., 2021; Schmidt, 1992). The climate is hot and humid, with annual precipitation ranging between 900 and 1500 mm (Luke, 2005). Coconut, cashew nuts, maize, cassava, and mango are commonly cultivated by the communities encircling the Shimba Hills National Reserve (Faith et al., 2022). Goats and cattle are among the livestock kept in the area (Malonza et al., 2018).

This is home to wildlife such as elephants, buffaloes, warthogs, bush hogs, black antelopes, moose, leopards, and monkeys in the area. This creates an advantageous breeding ground for tsetse flies (Mbahin et al., 2013). Ebhodaghe et al. (2021b) indicated that the main economic activities in communities residing at the edge of the reserve are livestock and agricultural production. The all-year green vegetation promotes intensive cropping and discourages seasonal livestock migration (Ebhodaghe et al., 2021b).

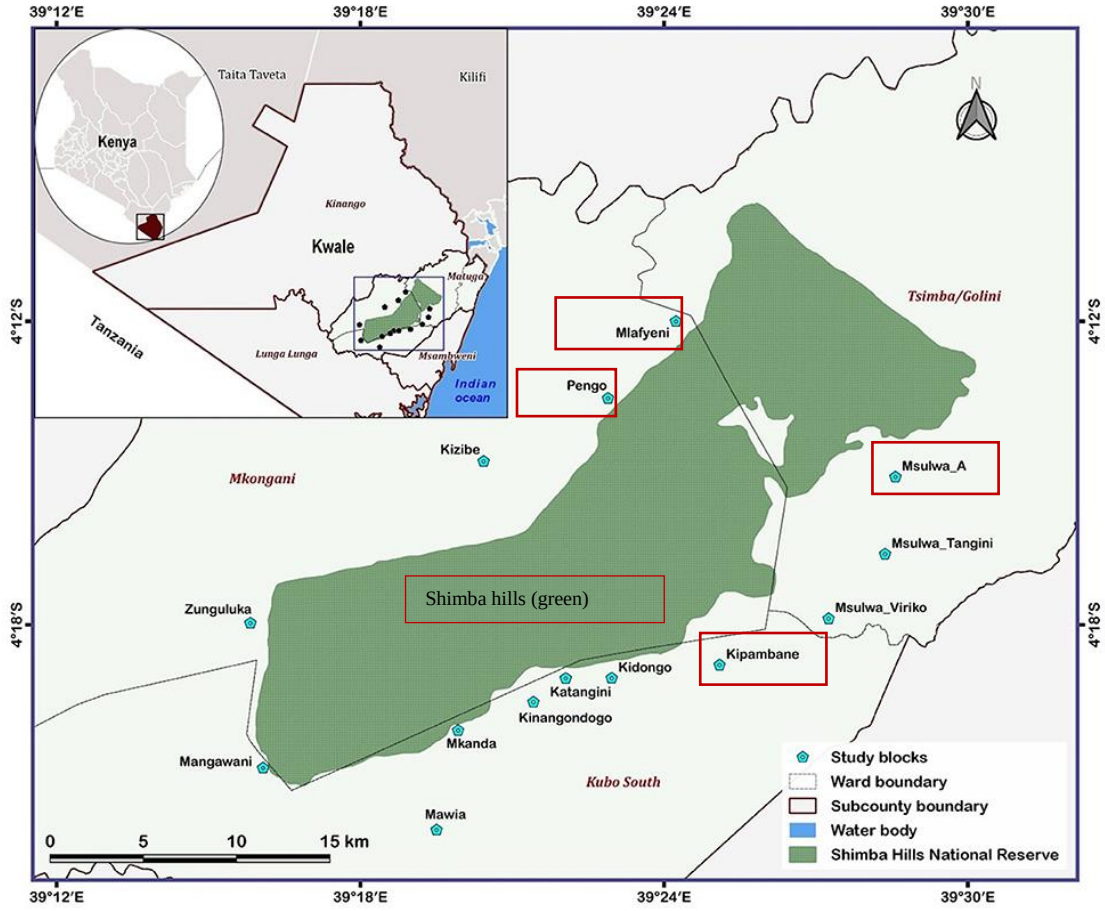

Figure 3.1: Map showing the villages involved in the study and their distance and coordinates to the Shimba Hills National Reserve on the map of Kenya.

Source: (Faith et al., 2022)

Shimba Hills National Reserve is marked as a protected zone (green) in Kwale County and it is indicated as Shimba Hills village in the data. The study sites (marked in red) are within 5km of the national reserve (Figure 3.1) (Faith et al., 2022). The data used in this study was obtained and documented by the Shimba Hills team of International Centre for Insect Physiology and Ecology's Animal Health Theme in April 2021. This was based on past and current research activities in Shimba Hills. The villages mentioned above were selected according to their proximity to the Shimba Hills National Reserve, where the cattle population near the game reserve was at high risk of infection with trypanosome parasites and, therefore highly susceptible. Those cattle that were marked to at high epidemiological risk were selected for this study. The farmers recruited their cattle willingly to participate in the study

where they were given a unique name and id. The cow blood was drawn and taken to the *icipe* lab for further analysis.

The infected cattle population were identified as infected by one or more species of trypanosome parasite; this was indicated in the blood microscopy report that was provided in the data. The population of removed cattle was extracted from the data, where the state of the animal was recorded after a certain period of study (30 days). Where the animals were classified according to the state of the disease which included recovered, out for ploughing, died, did not make to the sample collection site e.tc. only those animals who died were selected to participate in this study. However, there was no consistent data provided indicating whether the cattle who died were treated or not, hence it was not included in the model.

The infected fly population was determined by setting tsetse fly traps in the areas selected to participate in the study. The tsetse traps were given unique ids according to the location they were placed. The sampling was done on different days of the week which included Monday to Friday. After 24 hours the trapped tsetse flies were collected and taken to the *icipe* lab for dissection. All the trapped tsetse flies were considered susceptible and hence included in the study. A total of 1,116 susceptible fly populations were dissected in the lab and the midgut and proboscis were observed for any trypanosome infection, 74 tsetse flies were found to be infected with trypanosome parasites of different species. These data were collected in April 2022.

3.2 Study Design

3.2.1 Steps for developing the study model

The figure 3.2 below summarizes the steps which were involved to develop the study model.

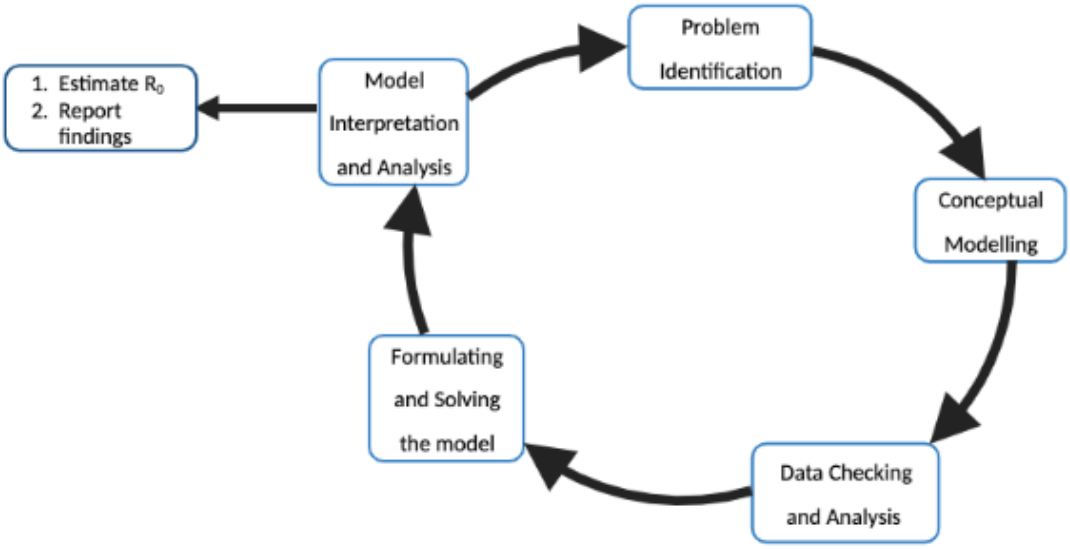

Figure 3.2: The African Animal Trypanosomiasis transmission dynamics model workflow

3.2.2 Problem identification

Areas around Shimba Hills National Reserve have a population mixture of humans, wildlife, and domestic animals. According to a study done by (Channumsin et al., 2021) on *G. pallidipes* which revealed high feeding success in the wild than the domestic hosts in areas near Shimba Hills National Reserve, the blood meal analysis showed that 58% of the sampled tsetse population tested positive for trypanosome infections and fed on multiple hosts, from this, 54% fed on domestic animals and 41% fed on wild animals. Furthermore, 61.5% of the positive cases were recorded from the Zunguluka area (high infection rate), located just a few kilometers from the park. This was supported by a series of previous studies one of which proved a high prevalence of AAT in SHNR, 54.6% of the total cattle sampled population tested positive for trypanosome parasites (Saini et al., 2017) and another done by Mbahin et al., (2013) which found (33.9%) bovine Trypanosomiasis prevalence in Kubo Division, Kwale County all nearing Shimba Hills National Reserve.

Previous studies also reported a bovine Trypanosomiasis morbidity rate of 29.1% (Kulohoma et al., 2020). African Animal Trypanosomiasis continues to be a major obstacle in livestock production and poses a major challenge to large-scale cattle rearing despite many years of control around Shimba Hills National Reserve (Gachoki et al., 2021). Recently, Faith et al., (2022) pointed out that studies that have exploited tsetse-trypanosome interactions, transmission risk patterns, trypanosome epidemiology, and tsetse-host interactions in Shimba Hills are limited. The study further emphasized the need to understand the trypanosome transmission dynamics and spatial risk patterns to help identify potential hotspots for Nagana and identify efficient control and treatment measures.

From these studies previously done in areas around Shimba Hills National Reserve, it was evident that there is a high challenge of AAT in the region therefore there was a need to develop alternative solutions for the control and treatment, and management of AAT. Therefore, our main aim was to develop a mathematical model for trypanosome vector-host transmission dynamics in Shimba Hills, which will help to understand the transmission dynamics of AAT, and estimate the basic reproduction number to help us determine how efficiently is trypanosome transmitted from one host to another region and document the transmission risk patterns in the areas around Shimba Hills National Reserve in the coastal region of Kenya.

3.2.3 Conceptual modelling

A compartmental model developed in this study assumed progression is for a susceptible host to become infected through a bite by an infected tsetse fly. When the animal is infected, it is said to be infectious, the infectious animal then will advance to a non-contagious state or recovery stage (Tolles & Luong, 2020).

This study divided the tsetse and cattle populations into several compartments: susceptible, infected, and recovered/removed. For the cattle population, the contagious animal population becomes infected via an infectious tsetse bite and is removed or dies as a result of infection after or without treatment (Moore et al., 2012). In regard to this, several parameters, variables, and assumptions were made in order to come up with the conceptual model.

The assumptions are described in section 3.2.3.1, while the model variables and parameters are described in table 3.1 and table 3.2 respectively;

Table 3.1: Model variables description and values

Variable	**Description**
N_t	Total tsetse fly population
S_t	Susceptible tsetse fly population
I_t	Infected tsetse fly population
N_c	Total cattle population
R_c	Removed cattle population
I_c	Infected cattle population
S_c	Susceptible cattle population

Table 3.2: Model parameters description and value

Parameter	Description	Value	Source
β	Biting rate of tsetse flies on cattle	0.75	(Wangwe et al., 2019)
α_c	Probability of transmission occurring given a bite by an infectious fly	0.6	(Gervas et al., 2018a; Rogers, 1988)
α_t	Probability of transmission given a bite on infectious cattle	0.4	(Rogers, 1988)
δ	Cattle death rate from nagana	0.7 $(\frac{1}{(\frac{8}{514}*100)})$	Assumed
b_t	Tsetse fly birth rate	0.02 $(\frac{1}{50})$	Assumed
d_t	Tsetse natural death rate	0.03	(Gervas et al., 2018b; Rogers, 1988)

3.2.3.1 Model Assumptions

1. A tsetse fly feeds constantly after every 4 days
2. The infection-to-death time period in cattle is supposed constant and equal to 30 days
3. Tsetse flies are contagious for the rest of their lives; they do not recover from infection.
4. Individuals are only in the population if they can contract the disease

5. Transmission occurs between tsetse flies and cattle only
6. There is a constant biting rate of tsetse flies on cattle
7. African Animal Trypanosomiasis incidence is not affected by environmental factors example, temperature, and rainfall

For the cattle population, a SIR model was developed, and for the tsetse fly population, an SI model was developed as illustrated below in Figure 3.3;

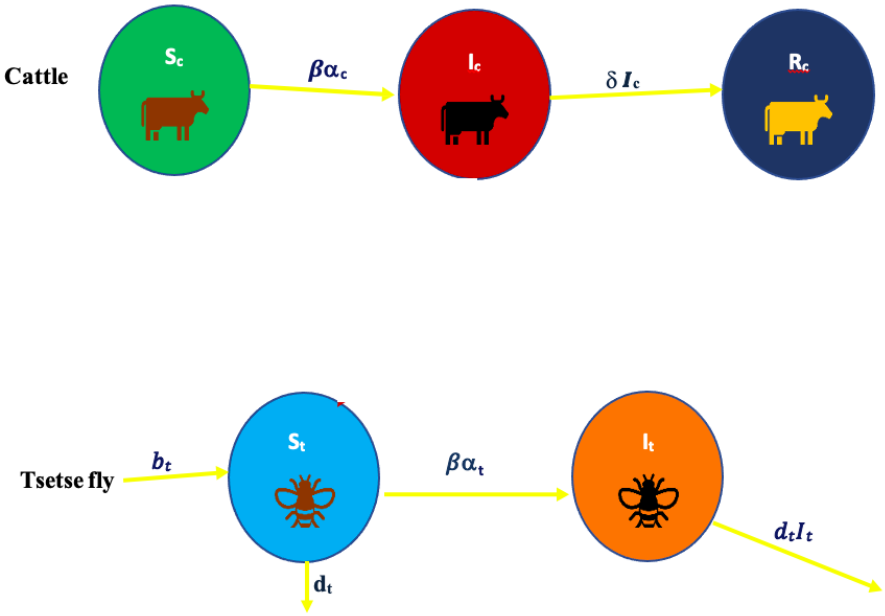

Figure 3.3: African Animal Trypanosomiasis model workflow.

The figure shows how Nagana is transmitted from tsetse fly to cattle and from cattle to tsetse fly respectively.

Compartments in the mathematical model: S_c – Susceptible cattle population (cattle population who are classified to be at a high risk of contracting AAT), I_c- infected cattle (cattle population who are capable/ at risk of contracting AAT), R_c- recovered cattle (cattle population who have died or recovered from AAT after treatment), S_t- susceptible tsetse fly population (tsetse population at risk of being infected with trypanosomes), and I_t- tsetse fly population (tsetse population who are infected with trypanosome parasites).

3.2.4 Data checking and analysis

Data were acquired from experimental work done in Shimba Hills, Kenya, presented as computer spreadsheets, and later analysed using tables, and figures, and applied as variables in simulating the mathematical model. The data was provided by the animal health research theme in the International Centre of Insect Physiology and Ecology, Nairobi, Kenya which is currently involved in conducting tsetse fly and cattle research in Shimba Hills. The Cattle population data was collected in April 2021 on different days of the week (see Appendix III). Several villages around Shimba Hills National Reserve were involved in the study, including Pengo, Kipambane, Mlafyeni, Msulwa A, and Shimba Hills (Appendix III and Appendix IV).

The cattle population data were further classified according to epidemiological risk. Those marked high were at a high risk of contracting AAT, based on the distance to the national reserve where those near the national reserve were marked high, and those far away were marked as low. Only those marked to be at high risk were selected for this study because they were assumed to be highly susceptible. The infected cattle population was selected based on the microscopic analysis that was provided in the data. Those cattle infected with one or more trypanosome species were selected for this study. The removed/ recovered cattle population was selected based on the infectious cattle status recorded after treatment or without treatment. The infectious cattle who were indicated dead were selected for this group.

Tsetse fly population data were collected in April 2022 collected on different days (see appendix IV). The data was obtained from three villages of the Shimba Hills National Reserve region, including Mlafyeni, Msulwa A, and Shimba Hills. The susceptible tsetse fly population was selected from dissected flies in the laboratory suspected of having trypanosome infections. The infected tsetse fly population was dissected and found to have one or more trypanosome species infections.

3.2.5 Formulating and solving the model

This model was created using Wonham and Lewis, (2008) West Nile (WN) virus model. The model concentrated on the West Nile virus, which was first discovered in Africa and then became an emerging epidemic in North America. The WN virus is a vector-borne disease transmitted between the vector (mosquitoes) and the host reservoir (birds). The adopted model focused on the cross-infection between birds and mosquitoes which aided in understanding the transmission dynamics f the virus and provided clear implications for disease management in mammals, humans, and birds. Given that Trypanosomiasis is a vector-borne disease transmitted between host (cattle) and vector (tsetse fly), the purpose of our model was also to examine how cross-infection occurs between tsetse fly and cattle sub-populations respectively in order to help understand the transmission dynamics of Nagana in areas nearing the Shimba Hills National Reserve.

The total cattle population ($N_{c)}$ was divided into susceptible cattle (S_c), infectious cattle (I_c), and recovered cattle population (R_c). The total tsetse population ($N_{t)}$ is divided into susceptible tsetse fly population (S_t), Infected tsetse population (I_t). The positive parameters δ is the cattle death rate from nagana whereas β is the tsetse fly biting rate on the cattle sub-population. b_t denotes the tsetse birth rate, d_t is the tsetse fly death rate.

Taking into account the above-mentioned variables and parameters, the cattle sub-population Ordinary Differential equations according to the model were given by:

The susceptible cattle subpopulation's rate of change is given by;

$$\frac{dS_c}{dt} = -a_c\beta\frac{S_cI_t}{S_c+I_c+R_c} \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

dS_c is a derivative of the susceptible cattle sub-population, with respect to time (d_t). This equation is negative since the number of susceptible cattle decreases with time. The probability of transmission in cattle after being bitten by an infectious tsetse fly is represented by a_c. β is the tsetse fly biting rate on cattle in Kwale County. S_c , I_t represents the susceptible

cattle sub-population and the Infected tsetse fly sub-population respectively. $S_c + I_c + R_c$ = N_c which is the total number of the cattle sub-population in the model.

The infection rate of cattle is given by;

$\frac{dI_c}{dt} = a_c\beta \frac{S_c I_t}{S_c+I_c+R_c} - \delta I_c$ ..... (2)

dI_c is a derivative of the infected cattle sub-population, with respect to time (dt). This equation is positive since the number of cattle infections increases with time. The probability of transmission in cattle after being bitten by an infectious tsetse fly is represented by a_c. S_c , I_t represents the susceptible cattle sub-population and the infected tsetse fly sub-population respectively.

$S_c + I_c + R_c$ = N_c gives the total number of cattle populations in the model. In this equation, we subtract the cattle population who die due to infection by Nagana, therefore δ , I_c represents the cattle death rate from AAT and the infected cattle sub-population respectively.

The recovered cattle sub-population at a particular time is given by;

$\frac{dR_c}{dt} = \delta I_c$ ..... (3)

dR_c is a derivative of the recovered/removed cattle population, with respect to time (dt). This equation is positive since the number of removed/dead cattle increases with time. d_c , I_c represents the cattle death rate from Nagana and the infectious sub-population of cattle respectively. Since the lifecycle of a tsetse fly is much shorter than that of cattle, the demographics are included in the model and that of cattle is ignored (Wonham & Lewis, 2008).

The Ordinary Differential Equations for the tsetse fly sub-population in the model are given by;

The susceptible tsetse sub-population;

$\frac{dS_t}{dt} = b_t(S_t + I_t) - d_t S_t - a_t \beta \frac{S_t I_c}{S_c + I_c + R_c}$ ..... (1)

dS_t is a derivative of the susceptible tsetse sub-population, with respect to time (dt). This equation is negative since the number of susceptible tsetse fly populations decreases with time. b_t is the birth/recruitment rate of tsetse fly, d_t is the tsetse fly natural death rate, a_t is the transmission probability once a tsetse fly bites infectious cattle. S_t, I_c is the susceptible tsetse sub-population and the infectious cattle population respectively. $S_c + I_c + R_c$ = N_c denotes the total cattle population in the model.

Infectious tsetse fly sub-population;

$\frac{dI_t}{dt} = a_t \beta \frac{S_t I_c}{S_c + I_c + R_c} - dtIt$ ..... (2)

dI_t is a derivative of the infected tsetse sub-population, with respect to time (dt). This equation is positive since the number of infected tsetse fly populations increases with time. Given a bite on infectious cattle, a_t is given as the probability of transmission. S_t, I_c is the susceptible tsetse sub-population and the infectious cattle population respectively. $S_c + I_c + R_c$ = N_c denotes the total cattle population in the model. The sub-population of dead tsetse flies is subtracted from the total population, dt, It denotes the tsetse flies natural death rate and the infectious tsetse sub-population respectively. Tables 1 and 2 above show a list of host and vector variables and parameters.

The equations were implemented in the R studio version 4.1.1(RStudio Team, 2020), (See appendix I for the R code). The deSolve package version 1.30 (Soetaert et al., 2010), was used to solve the initial ODEs. This was done by stating the model function, which included specifying the model parameters (β, α_c, d_t, b_t, δ, α_t), timespan (120 days), and initial

conditions (S_c, I_c, R_c, S_t, I_t). lsoda function was then used to solve the model function and the model solution was converted to a data frame which was used to plot the model, all the compartments were plotted on a single plot.

3.2.6 Numerical Simulation

A numerical computer simulation of the model parameters was done using deSolve package in Rstudio V4.1.1 to see how transmission occurs between the tsetse fly vector and the cattle host in areas bordering the Shimba Hills National Reserve, and how individuals are moving between one compartment to another in the model at a particular time. The estimated parameter values (from the literature) in Table 3.1 and assumed parameters (from data) were applied to construct the model in Figure 4.1. These parameters include $\beta = 0.75$, $\alpha_c = 0.6$, $\alpha_t = 0.4$, $\delta = 0.7, b_t = 0.02$, $d_t = 0.03$ (Table 3.2). These parameters are measured per day. The variables used to simulate the model were S_c= 477, I_c = 29, R_c = 8, S_t = 1116, I_t = 74 (Appendix V).

3.2.7 Model interpretation and analysis

Estimating the basic reproduction number is a powerful tool for interpreting and analysing compartmental models (R_0) (Wonham & Lewis, 2008). The basic reproduction number denotes the number of infections resulting caused from a single infectious disease case introduced into a specific population in which all individuals are vulnerable (Padmanabhan & Seshaiyer, 2017). The R_0 functions as an invasion threshold, forecasting disease onset, evaluating existing diseases, and proposing new treatment and control strategies (Zuhairoh et al., 2021). The R_0 is estimated to establish whether a pathogen can establish in a population by integrating all factors that influence the pathogen's establishment and distribution (Hartemink et al., 2008).

When $R_o < 1$ the Decision Feedback Equalizer (DFE) is said to be locally stable. Introducing a small number of infectious individuals will result in no outbreak and the disease will be eventually eradicated from the population (Bello et al., 2019). However, when $R_o > 1$ DFE is locally unpredictable, an outbreak occurs and the disease spread throughout the region causing a pandemic (Padmanabhan & Seshaiyer, 2017; Dietz, 1993).

The basic reproduction number aids in the identification of specific aspects of the disease framework that can be manipulated to reduce the probability of disease outbreaks in a nation or area (Boonpatcharanon et al., 2022). Estimation of the basic reproduction number for this study was done according to previous literature Jones, 2007; Smith et al., 2012b these studies elaborated on estimating the basic reproduction number of a simple compartmental malaria model initially used by Ronald Ross (1911), and George Macdonald (1957). The model was adopted to model many vector-borne diseases because it was amended to incorporate the basic features of African Trypanosomiasis by Rogers (1988), Baker (1988), and Milligan (1988). The estimation of the basic reproduction number was implemented from the simple malaria model method of estimating R_0 (Jones, 2007).

The simple malaria model highlights the cross infection between Mosquitoes and Humans, which also applies to tsetse fly and cattle populations, as they have the same mode of transmission (from vector to the host and from the host to the vector).

$$X^{\cdot} = \mu\beta bY\,(1 - X) - rX \ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$Y^{\cdot} = \beta cX(e^{-gv} - Y) - gY \ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

X is the ratio of the infected cattle sub-population while Y is the ratio of infected tsetse fly sub-population.

African Animal Trypanosomiasis being a vector-borne disease, the same method was used in this study to estimate the basic reproduction number for Nagana transmission in Shimba Hills and the nearby villages. The formula for calculating R_0 was therefore given by;

$$R_0 = \sqrt{\frac{\mu\beta^2 bce^{-gv}}{gr}}$$

Where,

β- tsetse flies biting rate

μ- the ratio of the tsetse fly population to the cattle population

b- the probability that infectious tsetse bite results in cattle infection

c- the probability that tsetse becomes infected following a bite on infected cattle

g- the tsetse death rate

v- the time it takes for a tsetse fly to become infected and infectious

r- cattle removal rate

CHAPTER FOUR

RESULTS

4.1 Sample data

The cattle data was collected in April 2021 and the tsetse fly data in April 2022. Five villages were involved in the study which included Kipambane, Msulwa A, and Pengo villages for the cattle population, and Mlafyeni, Msulwa A, and Shimba Hills villages for the tsetse fly data. All these villages are located around the Shimba Hills National Reserve.

The cattle data was obtained by drawing blood from the identified cattle populations from the mentioned three villages, the cattle were recruited in the study according to the willingness of the farmer. Cattle information such as the sex, color, epidemiological risk, microscopy results, and status after treatment were noted and recorded for a period of 30 days. Other information noted included the epidemiological risk of the cattle, and the infection status. Only the cattle that were marked to be highly susceptible were selected, as they were identified to be at high risk of being infected with one or more trypanosome species.

The tsetse fly data was collected by using the tsetse fly traps that were set in the afore-mentioned three villages. The traps were set every day and the number of the trapped tsetse flies was recorded. The trapped tsetse flies were then taken to the lab and dissection was done on the proboscis of the tsetse fly to confirm the infection status of the flies. The tsetse flies who were found to contain one or more trypanosome species were recorded to be infected. All the tsetse flies trapped were considered to be highly susceptible.

The susceptible, infectious, and recovered cattle populations were high in Kipambane Village, Msulwa A, and Pengo Village respectively as shown in Figure 4.1 below.

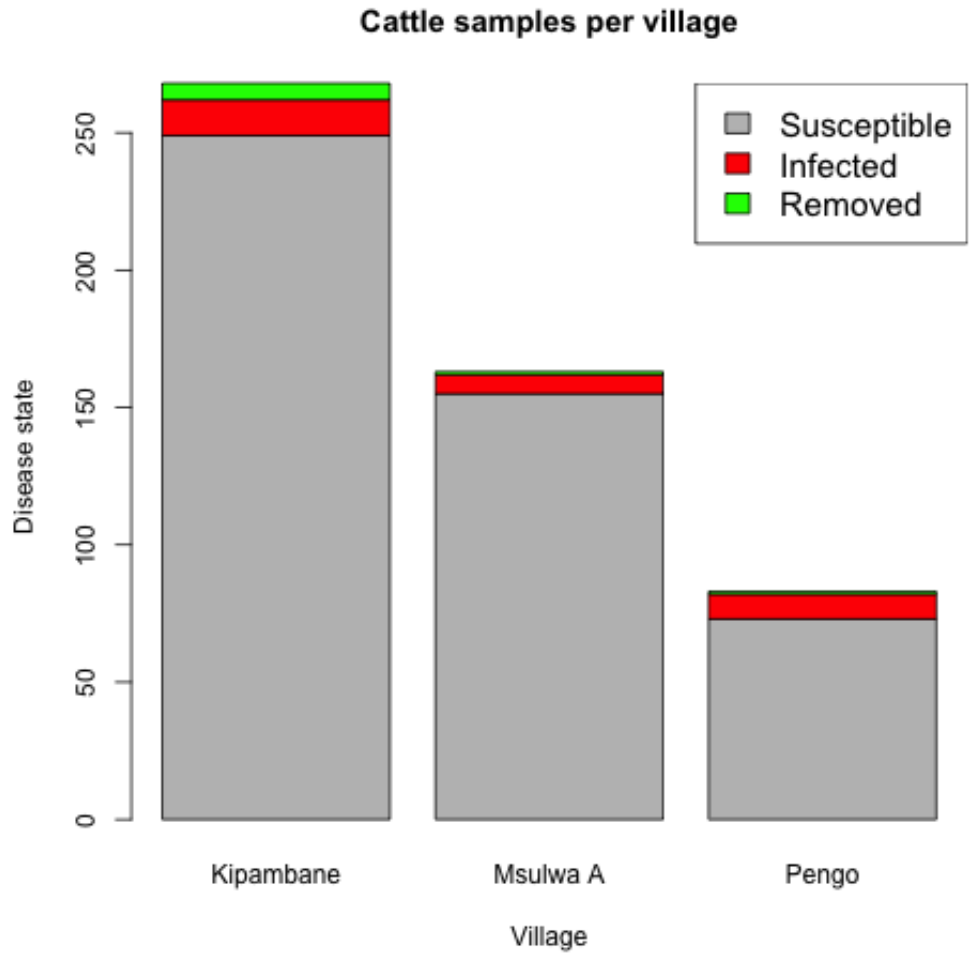

Figure 4.1: The cattle sub-population from different villages that participated in the study.

Kipambane village had a total of 249 susceptible cattle population (S_c = 249), 13 cattle were found to be infected by one or more trypanosome species (I_c = 13), and 6 cattle were recorded dead after infection by Nagana on day 30 of the study (R_c = 6). In Msulwa A, 155 cattle were marked to be susceptible (S_c = 155), only 7 cattle were found to carry trypanosome parasites (I_c = 7), and one cow died as a result of infection (R_c = 1).

Finally, in the Pengo region, 73 cows were sampled as susceptible (S_c = 73), nine cows got infected within the study period (I_c = 9), and one cattle died from Nagana (R_c = 1). From the cattle data, the total infection rate was noted to be 5.64% (29/514) with Kipambane village having the highest sampling rate.

Shimba Hills was noted to have a highly susceptible and infectious tsetse population. Msulwa A had the least number of infectious and susceptible tsetse flies, as shown in Figure 4.2 below.

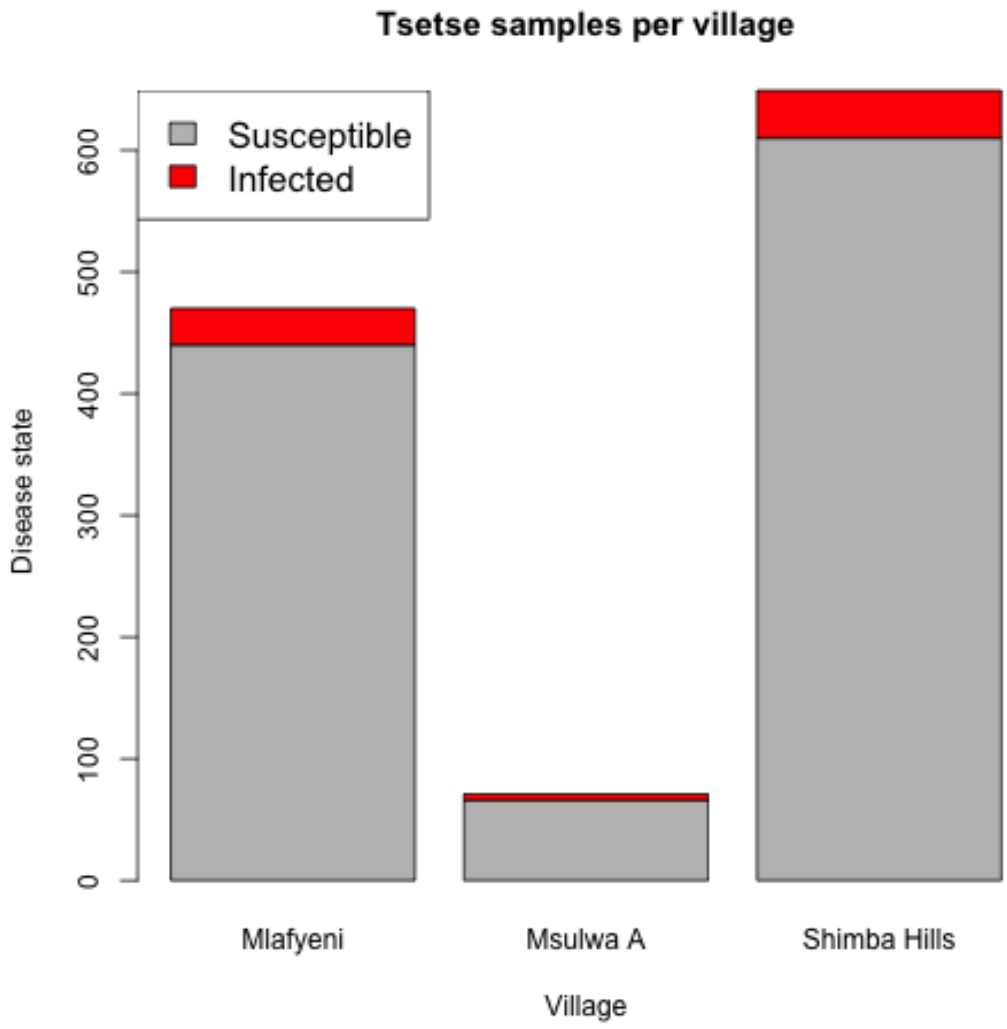

Figure 4.2: The tsetse fly population according to various villages sampled for the study.

Mlafyeni had a total of 440 dissections (St = 440), where a total of 30 tsetse flies were infected with trypanosome species (It = 30). In Msulwa A village, 66 tsetse were taken to the lab for dissection and identified as the susceptible tsetse population (St = 66), out of the susceptible, 5 tsetse flies were found to carry trypanosome species (It = 5). In Shimba Hills, there were 610 total trapped tsetse flies which were later dissected in the lab (St = 610), 39 tsetse flies were infected with the trypanosome parasites (It = 39).

From the total tsetse population data, the total infection rate was noted to be 6.23% (74/1190) with Shimba Hills having the highest sample size and infectious cases compared to other villages.

4.2 The trypanosome vector-host transmission model

An integrated compartmental model was implemented for both tsetse flies and cattle populations, as described by Wonham & Lewis, (2008). The cattle population modeling involved three compartments, Susceptible Infectious Recovered compartments, while the tsetse fly's population modeling comprised two compartments Susceptible Infectious since we assume that the tsetse fly does not recover from infection due to its short lifecycle, therefore the tsetse fly demography was added to the model and the cattle demography data ignored. From the West Nile virus-host model, the removed compartment was added to the cattle sub-population to account for the infectious cattle that died from Nagana infection in Shimba Hills.

The model consists of three dependent variables susceptible (S), infectious (I), and removed (R). These variables are influenced by the parameters β, δ. The tsetse fly and cattle populations vary from t_0- $t_{120,}$ as shown in Figure 4.3. The parameter β is the tsetse biting rate on cattle. This parameter has an impact on the number of the susceptible cattle population; when the biting rate is high, there are more and more cattle getting the infection hence the I*c* curve would be rising steadily while the S_c curve will be seen reducing steadily. We would also have more tsetse flies getting the infection resulting to the It curve rising steadily. The tsetse fly infection rates are also dependent on the number of infected cattle in the area, if the number is high then the probability of more tsetse getting the infection is high. The δ parameter determines the number of the Removed cattle population and hence the shape of the R_c curve. When we have more cattle dying as a result of Nagana or in the case of an epidemic then the R_c curve would rise very fast due to more deaths. The parameter α is categorized into

two, the α_c and α_t they both represent the probability of infection occurring given a bite on infectious cattle/ or by infectious tsetse fly. This determines the infectious curve shape, because if we have a low probability of infection in both tsetse and cattle then the infectious line curve would rise slowly. The stated line curves are presented in Figure 4.3 below;

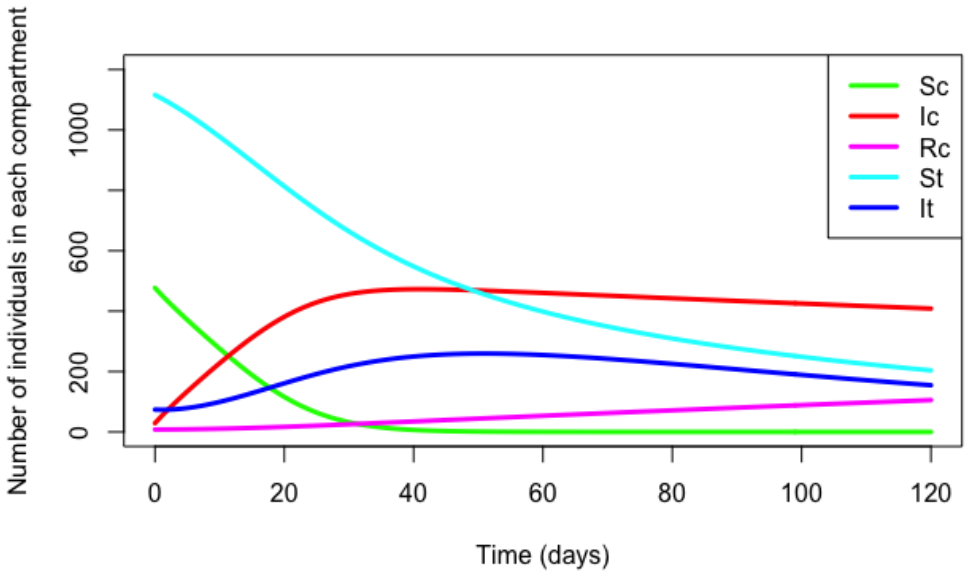

Figure 4.3: The integrated trypanosome vector-host transmission dynamics model.

Figure 4.3 shows the transmission dynamics of Trypanosomiasis between the cattle and tsetse fly populations in Shimba Hill, Kwale County. The susceptible cattle population decreases with time for the first 30 days, then tends to approach zero (Figure 4.3A). As indicated in (Figure 4.3B), the infected cattle population increases with time. The peak of this curve (Figure 4.3B) is attained at 30 days, thereafter the population of cattle starts to decrease. The removed cattle population was increasing slowly (Figure 4.3C).

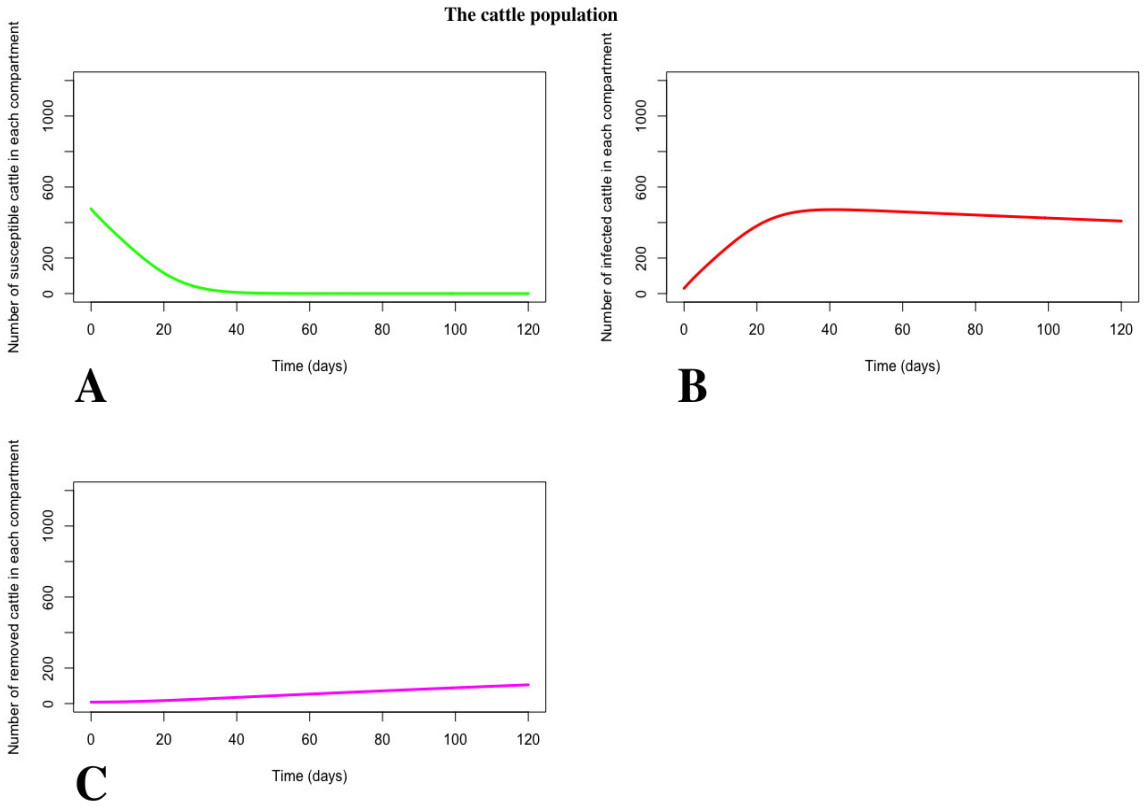

Figure 4.4: Population dynamics of cattle population with time.

(Figure 4.4A) The susceptible cattle population decreases with time until it becomes constant, (Figure 4.4B) the infectious cattle population increases with time from the start of the model as more cattle gets the infection, and (Figure 4.4C) the removed cattle population increases with time as the model progress from day 1- 120. The susceptible tsetse fly population decreases with time as shown in Figure 4.5A. The infectious tsetse population increased with time, its peak was at 50 days, and thereafter it decreased gradually (Figure 4.5B).

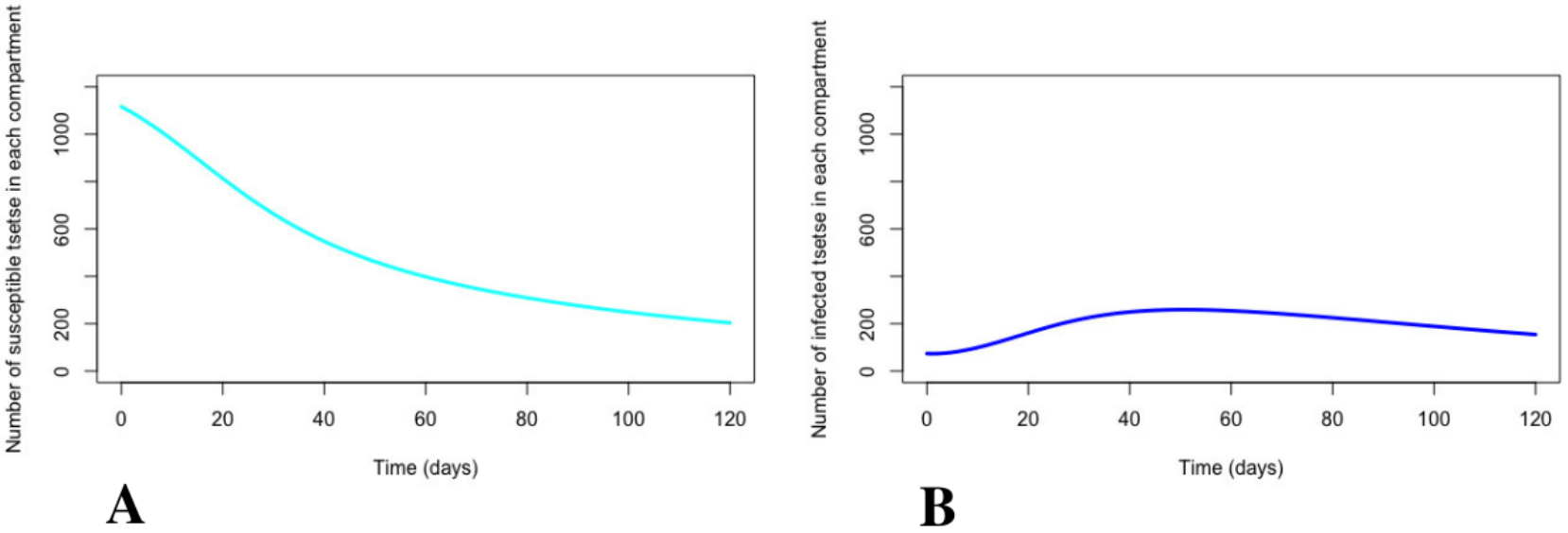

Figure 4.5: The tsetse flies population dynamics.

(Figure 4.5A) the susceptible tsetse population decreases with time, (Figure 4.5B) the infectious tsetse population increases with time and decreases towards the end of the model. The parameter β and α_t influences the shape of curve B (Figure 4.5B) and curve A (Figure 4.5B). When the value of both parameters is high (tsetse biting rate on cattle and the probability of infection when tsetse bites an infected cattle), both curves A and curve B will decrease and increase at a higher rate. The high number of susceptible and infected cattle populations will also cause a rise in curve B (Figure 4.5B).

4.3 The Estimated Basic Reproduction Number (R_0)

The basic reproduction number was obtained from the next-generation matrix below:

$$F = \begin{pmatrix} 0 & \beta b\mu \\ \beta c e^{-gv} & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} -r & 0 \\ 0 & g \end{pmatrix}$$

These result into

$$FV^{-1} = \begin{pmatrix} 0 & \frac{-\beta b\mu}{g} \\ \frac{\beta c e^{-gv}}{r} & 0 \end{pmatrix}$$

The dominant eigen value of FV^{-1} is

$$R_0 = \sqrt{\frac{\mu\beta^2\, bce^{-gv}}{gr}}$$

The basic reproduction number was estimated to be: ($R_0 \approx 2.73$) = $R_0 > 1$.

CHAPTER FIVE

DISCUSSION

5.0 Discussion

This study developed a mathematical model to depict and understand the transmission of AAT over a period of 120 days (four months) in the five villages bordering the Shimba Hills National Reserve, including the Shimba Hills, Mlafyeni, Pengo, Kipambane, and Msulwa A. the findings from this study however is subject to some major limitations. There was limited access to data which caused the inconsistency observed in the data. This made most of the collected data be scrapped and only a few data for a short period of time be used to carry out the study. Most data did not contain the metadata necessary to include in the study hence it was a challenge to put it all together. There was insufficient sample data available after filtering out to only obtain the consistent data samples. This resulted in using only data for short periods and few areas to be included in the study which caused underestimation and overestimation of some model variables and parameters. The cattle sample collection procedure and data were missing hence it was difficult to figure out the cattle breeds who participated in the study and also if the sick animals were treated and recovered or died.

Despite the various limitations, the model revealed that the susceptible cattle population decreased with time. This is because more susceptible animals come into contact with the infectious tsetse fly population. Due to the high biting rates of tsetse flies on cattle, they get infected and move to the infectious stage. These findings are consistent with those made by Abdelatif, (2015) and Otieno & Akinyi, (2015), who developed a mathematical model for optimal livestock management and found that the number of vulnerable populations is steadily declining.

These results were also in line with studies done on HAT (Rachah & Torres, 2015), Ebola in West Africa (Rachah & Torres, 2015), and dengue fever in Singapore (Chowell et al., 2007).

An increase in the infectious population of cattle is influenced by the cattle infection rate and death rate. At this stage, more cattle get AAT infection at the start of the model, as they progress, the infectious animals decrease because the cattle recover or die from nagana. The model clearly indicates that more cattle are getting nagana as we move from day 1-120. This indicates that AAT transmission is high and more animals and tsetse get infected as the model progresses. This finding is consistent with studies by Abdelatif, (2015); Gabriel Kuniyoshi & Pio dos Santos, (2017); Luz et al., (2010); Osman et al., (2020); Otieno, (2015) who found that the number of infectious cattle sharply increased with time thereafter gains a steady state which describes a disease-free equilibrium or endemicity of African Trypanosomiasis.

The death rate of the cattle (δ) determines the removed cattle population. The removed cattle population increased because more cows were infected at the start of the model. As time progresses, the infectious animals decrease because the cattle recovered/ died from nagana. The resulting curve implies that as the model progresses, more infected cattle succumb due to the severity of the disease. However, no information/data was provided indicating whether the cattle who died from nagana were treated or not. The increase in the number of cattle in this compartment is inverse to the susceptible cattle population as they are moved to the infected compartment. The tsetse fly population did not recover from trypanosome parasite infection due to their short lifecycle. Therefore, they remain infectious throughout their lifetime until death.

The increasing recovered cattle sub-population greatly supports similar previous studies (AlQadi & Bani-Yaghoub, 2022; Luz et al., 2010; Muia et al., 2018; Rachah & Torres, 2015)

The susceptible tsetse fly population decreases with time because more susceptible flies come into contact with the infectious cattle population, and spraying with insecticides reduces vulnerable vector abundance. This implies that the tsetse population gets more infections as the model progresses. In case of an infection, the infected tsetse population is moved to the

infectious compartment which is dependent on the infection rate of the tsetse fly ($\beta, \boldsymbol{\alpha_t}$) on cattle. Odeniran et al., (2020) obtained similar results in west Africa upon modelling the transmission of AAT using interactive agents such as wildlife, and other biting flies (tabanids, stomoxyines).

The basic reproduction number estimation (2.723) was obtained from all five villages involved in the study. This documents how efficiently trypanosome parasites are transmitted from cattle to tsetse flies in areas around Shimba Hills National Reserve. The R_0 value $(R_0 = 2.73)$ signifies that Nagana disease has a very high infectivity rate in the study areas. More cattle and tsetse flies are also susceptible to AAT infection. Therefore, AAT cannot be easily eliminated, unless the right control measures are put in place. This is due to the fact that the levels of AAT make it difficult to implement control and surveillance methods in areas around Shimba Hills National Reserve. The R_0 value suggests that there are more infections and cattle deaths from nagana are expected in the future and the disease can cause an epidemic in Shimba Hills if not controlled.

The findings corroborated with previous findings by Kajunguri, (2013), with R_o value of 2.59 $(R_o > 1)$, the value was obtained in the absence of veterinary treatment. The obtained value is similar to the one obtained in this model since it does not include any treatment parameters. Zhao et al., (2019) obtained an R_0 value greater than one (1.675) after analyzing the impact of seasonal variations in the transmission of African Trypanosomiasis in Kinshasa, Democratic Republic of Congo. The significance of the basic reproduction number was also described by various authors in their previous studies (Gervas et al., 2018; Jones, 2007; Muia et al., 2018b; Osman et al., 2020; Otieno, 2015; van den Driessche & Watmough, 2002).

This study showed that the susceptible, infectious, and removed cattle populations are high in Kipambane Village. Kipambane village is located less than 2km from the Shimba Hills National Reserve (Ebhodaghe et al., 2021a). It is therefore perceived that grazing animals near

the National reserve, sharing water points, and sharing grazing lands with wildlife predispose cattle to Nagana infections in these villages. These results are consistent studies by Latif et al., (2019) and Mwaseba & Kigoda, (2017), suggesting that grazing near national park, sharing pastures, and watering holes with wild animals are the major cause of livestock Trypanosomiasis in communities bordering Tanzania's Serengeti National Park and high virulence of trypanosomes in cattle near South Africa's Kwazulu-natal Game Reserve, respectively. Kimaro et al., (2018) supported this finding by conducting a survey to determine "the occurrence of trypanosome infections in cattle by season, livestock movement, and management practices of Maasai pastoralists in northern Tanzania". It was found that 100% (130 over 130) of Maasai herders reported the presence of wild animals at the grazing lands and water points when trying to access these amenities (Kimaro et al., 2018).

The herders also reported the presence of wild animals in different villages and cattle interacting with giraffes (Kimaro et al., 2018). Otieno & Akinyi, (2015) suggested that wildlife significantly impacts disease dynamics in cattle populations in a study of developing a mathematical model for managing bovine Trypanosomiasis.

There is a high trypanosome tsetse fly infection rate of 6.23% (74/1190) compared to the cattle infection rate of 5.64% (29/514). These findings suggest that despite the high biting rates and tsetse abundance in villages nearing Shimba Hills National Reserve, the trypanosome tsetse fly infection rates are below 10%. The tsetse fly infection rates (5.64%) are similar to those found by Kulohoma et al., (2020) (3.7%) on trypanosome-infected tsetse flies in rates in Shimba Hills, Kenya, in October 2015. Studies done on the neighboring counties have also shown low tsetse prevalence. It includes a study done on trypanosome-infected *G. pallidipes* tsetse species in Mtito Andei, Makueini county by Nthiwa et al., (2015), (5.77%), in April to May 2012. Similar results were also obtained in Burkina Faso by Bouyer et al., (2013), of infection rate of (10%). They conducted an epidemiological study on the dynamics of tsetse natural infection levels with respect to environmental factors in the

Mouhoun river. Aksoy, (2003) indicated that many studies on field-caught tsetse have shown trypanosome infections in tsetse flies to be equal to or below 10%. Odeniran et al., (2020), confirmed the low prevalence of trypanosome tsetse fly infection rate Nigeria, which documenting a decline in AAT prevalence over the past 60 years.

It was expected the trypanosome infection rates in cattle to be higher in this study. Contrary to the expectation, the trypanosome infection rates in cattle were at 5.64% (29/514). This was due to underestimation because of inconsistent data. The research used data that was collected for only four months, compared to previous studies which used data collected for about one year or more. A recent study conducted by Faith et al., (2022) showed a trypanosome cattle infection rate of 13.06%, in areas around Shimba Hills National Reserve in November 2018 and September 2019 Shimba Hills. Kulohoma et al., (2020) also found bovine Trypanosomiasis prevalence to be at 33.9%, whereas in Kubo division, Kwale County, the cattle infection rate was at 33.9% (Mbahin et al., 2013). The trypanosome infection rates in cattle could have been low compared to those done in previous studies due to the tsetse control programs that are currently being implemented in Shimba Hills. However, there is a need for further research on the effects of tsetse control measures and management practices on cattle infection rates in Shimba Hills.

Generally, the results of the study indicate low trypanosome infection rates in cattle, a decrease in the infectious tsetse fly population after 30 days, and a decrease in the susceptible population. This may be due to spraying of cattle with insecticides, death of infected cattle populations, infectious cattle recoveries, or development of herd immunity by the cattle which led to less infection in the cows and the susceptible tsetse fly population (Odeniran et al., 2020). This is supported by several studies which were done before, to model AAT in West Africa (Muia et al., 2018b; Odeniran et al., 2020; Otieno & Akinyi, 2015).

The findings from this study also confirm that susceptible and infectious tsetse fly populations are high in Shimba Hills. This is because Shimba Hills village is located at the wildlife reserve interface, adjacent to the Shimba Hills National Reserve. There is a high biting rate due to high tsetse density, and wild animals act as reservoirs for trypanosome parasites hence high infection rates. This study's findings corroborate with previous studies by Kulohoma et al., (2020) and Faith et al., (2022) in the same area. It was also similar to results from studies conducted in nearby regions and other East African Countries, Maasai Steppe, Nothern Tanzania (Kimaro et al., 2018; Salekwa et al., 2014; Simwango et al., 2017), Mtito Andei, and Makueni County (Nthiwa et al., 2015), Serengeti National Park (Auty et al., 2016; Muturi et al., 2011). These findings contrasted with those obtained in Malawi's Nkhotakota Game Reserve (NGR) (Gondwe et al., 2009). The study documented that the distribution of tsetse fly populations was generally low at the Nkhotakota Game Reserve interface. This was attributed to the lack of a fence separating the game reserve intended to prevent poaching. The villages situated along the interface, and the presence of human settlements, cause an increase in human activities, making it unfavourable for tsetse flies to breed. It is noted that Shimba Hills National Reserve has a fence separating villages surrounding the park; hence, this might be the major reason for the contrasting results.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

In summary, modelling transmission dynamics of AAT help predict the spread of nagana and estimate how effectively the disease can be transmitted from one host to another in areas near Shimba Hills National Reserve, Kwale County. This study developed a SIR and SI compartmental model for both the cattle host and the tsetse fly vector. These models were integrated to depict how Trypanosomiasis is transmitted in Shimba Hills over time between the vector and host.

The study will give small-scale cattle farmers knowledge on transmission risks given the transmission trend with time and also areas where they can graze and water their livestock. Knowing the distribution patterns of the susceptible, infectious, and recovered cattle and tsetse fly population will give insights on when to start the control measures and also know the peak of the infection. This information can be used to develop control measures that are effective and appropriate. The integrated model also sheds light on the future projection of how Nagana would affect the study population in the coming months or years. This helps the farmers; game rangers and public health officers prepare for any outcome in case an epidemic occurs.

This study has proved that proximity to the national reserve leads to high AAT transmission and high biting rates because wild animals are reservoirs for trypanosome parasites and high tsetse densities respectively. Villages located far from the Shimba Hills National Reserve were found to have fewer cases of infectious tsetse flies compared to those far from the National Reserve.

Overall, the findings suggest that, despite the high tsetse abundance and biting rates in areas near Shimba Hills National Reserve, infection rates on cattle are minimal and trypanosome parasites do not infect the whole cattle population even after an infinite amount of time. When the infectious cattle population is depleted, not the susceptible cattle population, AAT will be depleted in the population. The peak of infection in both cattle and tsetse fly populations is significant because it determines the maximum strains and effects of the disease in the villages involved in the study.

The model developed in this study will further help mathematicians and epidemiologists develop more complex and suitable models to represent different disease scenarios to help researchers and public health officers better understand the modeling strategies and implement better control measures for African Animal Trypanosomiasis. Mathematicians and epidemiologists will use the developed model as a starting point in developing more complex models that incorporate more parameters and more data since this model is the first one to be developed for AAT transmission dynamics in Shimba Hills. The significance of the R_0 values is applied by the public health officers in providing guidance to farmers, for example, in this study, the R_0 value is ~2.7. This is a high value indicating that AAT can cause an epidemic to cattle in Shimba Hills, hence the public health officers can advise farmers to do tailored control measures and introduce quarantine practices to contain the spread to other regions.

The study's findings, including mathematical model predictions and the basic reproduction number, will assist farmers, authorities, and decision-makers in areas near the Shimba Hills National Reserve in making decisions about AAT management, control, and treatment. The farmers will benefit in knowing the distribution patterns of nagana hence imposing measures that will reduce the spread. The projections of the future disease spread helps the authorities and decision makers plan for future instances of disease and device effective control measures for the same.

This research work proved that tsetse distribution has a great impact on the control and management of Nagana in Shimba Hills. There were high infection rates in areas where the tsetse population was high compared to those where tsetse density was low. More efforts should therefore be applied to control the tsetse fly vector near the National Reserve to avoid further spread.

6.2 Recommendations

This study was carried out using data for four months only. This was due to a lack of consistent data and metadata. For better results, consistent data presented with respective metadata for up to 2 years from several villages can be used to observe the behaviour of the model.

African Animal Trypanosomiasis transmission and control have been shown to be affected by Environmental (temperature, rainfall, humidity, wind speed), vegetational (degradation, deforestation, overcrowding) factors, application of insecticides and other biting flies (tabanids and stomoxyines). A more complex model can be developed that incorporates these factors and conditions to determine the stability of the model. More parameters can be incorporated into the model. The model incorporated only a few parameters, due to a lack of consistent data, future work can consider incorporating more parameters for better results.

In this research study, the data were collected from five villages. In this case, it is not easy to relate AAT incidence when the study covers a small area of study. Assessment can be done for a larger area, covering many villages, for better results. Future work should consider determining the effects of control strategies that reduce infections in the flies and cattle.

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APPENDICES

Appendix I: R code for Trypanosome vector-host transmission dynamics compartmental model solution

Github Link: (https://github.com/glado718/Developing-a-model-for-the-transmission-of-African-Trypanosomiasis-in-Shimba-Hills-Kenya./blob/main/Model_trypanosomiasis_dynamics .R)

```
# Loading the required packages for the model
library(deSolve)
#Write a function that computes the system of ODEs and returns a list containing the derivatives

SIRSImodel <- function(t, x, parms) {
  with(as.list(c(parms, x)), {
    dScdt= - alphac * beta * (Sc * It/(Sc +Ic + Rc))
    dIcdt = alphac * beta * (Sc * It/(Sc + Ic + Rc)) - delta * Ic
    dRcdt = delta * Ic
    dStdt= bt* (St + It) - dt * St - alphat * beta * (St * Ic /(Sc + Ic+ Rc))
    dItdt = alphat * beta * (St* Ic/ (Sc + Ic + Rc))- dt * It
    res <- c(dScdt,dIcdt , dRcdt, dStdt, dItdt )
    list(res)
  })
}
##Define the initial conditions, parameters and times

pars  <- c(beta = 0.75, alphac = 0.46 , alphat = 0.025, delta = 0.002,
           dt = 0.03, bt = 0.02)
## The time of the model
times  <- seq(0, 120, by = 1)
```

```
## Start values for steady state
y = xstart <- c(Sc= 477, Ic = 29, Rc = 8, St = 1116, It = 74)

## Solving
out <-  lsoda(y = xstart, time = times, func = SIRSImodel, parms = pars,)
out = as.data.frame(out)
head(out)

#Plot the solution for all model compartments on a single plot
plot(out$time, out$Sc,
    type = 'l', col = 'green', ylab = "Number of individuals in each compartment",
    xlab = "Time (days)", lwd = 3, ylim = c(0,1200))

lines(out$time, out$Ic, col = 'red', lwd = 3)

lines(out$time, out$Rc, col = 'magenta', lwd = 3)

lines(out$time, out$St, col = 'cyan', lwd = 3)

lines(out$time, out$It, col = 'blue', lwd = 3)

legend("topright", legend = c("Sc","Ic", "Rc", "St", "It"), col = c("green","red",
"magenta","cyan","blue"), lwd = 3)
```

Appendix II: Cattle and tsetse fly population sampling per village R code

```
#Cattle population dynamics
#Cattle population sampling per village
# Creating the input vectors.
colors = c("grey","red","green")
months <- c("Kipambane","Msulwa A","Pengo")
regions <- c("Susceptible","Infected","Removed")

# Creating the matrix of the initial conditions
Values <- matrix(c(249,155,73,13,7,9,6,1,1), nrow = 3, ncol = 3, byrow = TRUE)
Values
# Giving the chart file a name
png(file = "barchart_stacked_cattle_distribution.png")

# Creating the bar chart
barplot(Values, main = "Cattle samples per village", names.arg = months, xlab = "Village",
ylab = "Disease state", col = colors)

# Adding legend to the chart
legend("topright", regions, cex = 1.3, fill = colors)
# Saving the created file
dev.off()
# Tsetse sub-population sampling per village
# creating the input the vectors
colors = c("grey","red")
months <- c("Mlafyeni","Msulwa A","Shimba Hills")
regions <- c("Susceptible","Infected")
```

```
# Creating a matrix of the variables
Values <- matrix(c(440,66,610,30,5,39), nrow = 2, ncol = 3, byrow = TRUE)
Values
# Giving the chart file a name
png(file = "barchart_stacked_tsetse_distribution.png")

# Creating the bar chart
barplot(Values, main = "Tsetse samples per village", names.arg = months, xlab = "Village",
ylab = "Disease state", col = colors)

# Adding legend to the bar chart
legend("topleft", regions, cex = 1.3, fill = colors)

# Saving the created file
dev.off()
```

Appendix III: Cattle population involved in the study

Cattle population			
	Susceptible	Infectious	Removed
Kipambane	249	13	6
Msulwa A	155	7	1
Pengo	73	9	1

Appendix IV: Tsetse fly population involved in the study

Tsetse fly population		
	Susceptible	Infectious
Mlafyeni	440	30
Msulwa A	66	5
Shimba Hills	610	39

Appendix V: A table indicating the model variable values

Variable	**Value**
S_c	477
I_c	29
R_c	8
S_t	1,116
I_t	74