



Faculty of Computer Science and Information Technology

**Individual-based Modelling on Vector Heterogeneity of Leptospirosis
Transmission in Sarawak**

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Individual-based Modelling on Vector Heterogeneity of Leptospirosis
Transmission in Sarawak

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DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.



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ABSTRACT

Leptospirosis is a zoonotic disease prevalent in various places, particularly the tropical and subtropical regions. The infectious disease is endemic across Malaysia, especially in Sarawak. In recent years, the threats of leptospirosis continue to grow as the number of confirmed cases in Sarawak has risen since 2010. Compartmental models are popular in disease modelling. However, the models are not suitable if heterogeneity in the population is taken into account. For zoonotic or vector-borne diseases, the heterogeneity of the hosts or vectors can significantly influence disease transmission. Hence, this research proposes an individual-based model or IBM to model the leptospirosis spread as it has the ability to capture the heterogeneity of the population, such as vectors' active period and movement range. From the sensitivity analyses, the higher vector birth rate and higher transmission rate from susceptible to infected vectors generate more infected humans and vectors. The results also show that the active period durations of vectors do not influence leptospirosis transmission. However, a wider movement range of vectors causes more people and vectors to be infected. In the model validation with the actual prevalence data of leptospirosis in 2017, the coefficient of determination of more than 90% and normally distributed residuals for all three outbreaks indicate that IBM can model the leptospirosis spread in Sarawak. The actual prevalence data show three leptospirosis outbreaks occur within a year. By finding the correlation matrices, Pearson's correlations deduce that temperature rise and precipitation influence disease transmission. Additionally, other factors such as misdiagnosis of leptospirosis as well as occupational and recreational exposures affect the infection.

Keywords: Individual-based Model, leptospirosis, vector behaviour, active period, movement range

***Pemodelan Berasaskan Individu pada Kepelbagaian Vektor bagi Penularan
Leptospirosis di Sarawak***

ABSTRAK

Leptospirosis merupakan suatu penyakit zoonosis yang berleluasa khususnya di kawasan beriklim tropika dan sutropika. Penyakit berjangkit ini adalah endemik di Malaysia, terutamanya di Sarawak. Pada kebelakangan ini, ancaman leptospirosis didapati semakin meningkat dengan lonjakan kes di Sarawak sejak tahun 2010. Model kompartemen digunakan ramai dalam pemodelan penyakit. Tetapi, model kompartemen adalah tidak sesuai jika kepelbagaian populasi diambil kira. Bagi penyakit zoonotik atau penyakit bawaan vektor, kepelbagaian hos atau vektor dapat mempengaruhi wabak penyakit dengan ketara. Justeru, kajian ini menawarkan sebuah model berasaskan individu bagi penularan leptospirosis oleh sebab ia mempunyai kemampuan untuk mengambil kira kepelbagaian populasi seperti tempoh aktif vektor dan jarak pergerakan vektor. Melalui analisis sensitiviti, kadar kelahiran vektor dan kadar penularan daripada vektor yang mudah terdedah ke vektor yang berjangkit yang tinggi mengakibatkan lebih ramai orang dan banyak vektor dijangkiti leptospirosis. Dari segi sifat vektor, tempoh masa aktif vektor tidak mempengaruhi penyebaran leptospirosis. Walau bagaimanapun, jarak pergerakan vektor yang luas akan menyebabkan ramai individu dan banyak vektor dijangkiti penyakit. Dalam proses pengesahan model dengan perbandingan data pada tahun 2017, pekali penentu yang lebih 90% dan sisa yang bertaburan normal bagi ketiga-tiga wabak menunjukkan model berasaskan individu dapat meramalkan penularan wabak leptospirosis di Sarawak. Data tersebut juga menunjukkan terdapat tiga gelombang leptospirosis dalam tempoh setahun. Melalui matriks korelasi berserta kolerasi Pearson, peningkatan suhu dan taburan hujan merupakan antara faktor yang mempengaruhi penularan penyakit tersebut. Tambahan pula,

faktor lain seperti kesalahan diagnosis dan pendedahan dari segi pekerjaan serta aktiviti rekreasi juga menjejaskan penularan wabak.

Kata kunci: *Model berasaskan individu, leptospirosis, sifat vektor, tempoh aktif, jarak pergerakan*

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LIST OF ABBREVIATIONS

ABM	Agent-based Model
COVID-19	Coronavirus Disease 2019
CSV	Comma Separated Values
DOSM	Department of Statistics of Malaysia
IBM	Individual-based Model
MAE	Mean Absolute Error
MAPE	Mean Absolute Percentage Error
MCO	Movement Control Order
MOH	Ministry of Health
MLE	Maximum Likelihood Estimate
MSE	Mean Squared Error
MSEIR	Maternally Derived Immunity - Susceptible - Exposed - Infected – Recovered
MSEIRS	Maternally Derived Immunity - Susceptible - Exposed - Infected - Recovered – Susceptible
OLS	Ordinary Least Squares
RMSE	Root Mean Squared Error
SEI	Susceptible - Exposed - Infected
SEIR	Susceptible - Exposed - Infected - Recovered
SEIRS	Susceptible - Exposed - Infected - Recovered - Susceptible
SEIS	Susceptible - Exposed - Infected - Susceptible
SI	Susceptible - Infected
SIR	Susceptible - Infected - Recovered

SIRS	Susceptible - Infected - Recovered - Susceptible
SIRS-SI	Susceptible - Infected - Recovered - Susceptible - Susceptible - Infected
SIS	Susceptible - Infected - Susceptible
SMAPE	Symmetric Mean Absolute Percentage Error
UI	User Interface
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 Research Background

Malaysia is a country blessed with amusing diversity of natures and cultures. In East Malaysia, Sarawak or the ‘land of hornbill’, is a place steeped in rich natures and indigenous cultures. Although the tropical climate contributes to biodiversity in Sarawak, the weather conditions also cause some negative consequences simultaneously. For instance, the spreading of infectious disease by pathogenic microorganisms or pathogens. From a medical perspective, there are many ways for diseases spreading such as contact transmission (direct contact or indirect contact), droplet transmission (via coughing or sneezing), and airborne transmission (via inhalation of the air) (Stilianakis & Drossinos, 2010). As Sarawak is large in geographical area, it requires extra caution when monitoring the conditions of diseases spreading in the region.

Infectious diseases bring numerous devastating impacts to public health and economic growth across various countries. In 2013, China experienced an outbreak of H7N9 avian influenza that caused more than 680 confirmed cases including 275 deaths (Qiu et al., 2018). At the same time, the poultry industry of China underwent more than RMB 40 million in economic loss (Qiu et al., 2018). In the context of Malaysia, from September 1998 to July 1999, the Nipah virus outbreak occurred throughout the country. The disease had caused acute encephalitis with more than 260 notified cases and nearly 110 deaths (Looi & Chua, 2007). The infection brought deep impacts on the hog-raising industry and resulted in more than RM 500 million in economic loss to Malaysia (Hosono et al., 2006).

Apart from the Nipah virus outbreak, Malaysia also suffered from Coronavirus Disease 2019 or COVID-19. Compared to the Nipah virus, the impacts of COVID-19 were destructive to the economy and societies of the country. Malaysia lost RM2.4 billion a day during the Movement Control Order (MCO) period (Hashim et al., 2021). MCO was an enforced strategy of the government to control the COVID-19 outbreaks in the country and close most of the economic sectors same time (Hashim et al., 2021). Besides impacting the economy, COVID-19 caused many issues in societies. For example, the increase of negative emotions such as stress and anxiety among people, and job or domestic violence including suicide (Yong & Sia, 2021).

Disease control and prevention are essential as infectious diseases bring devastating and chaotic impacts to societies. One of the measures is through modelling as it is a technique of transforming a situation into a model for problem-solving and future prediction. The implementation of modelling in infectious disease studies allows the researchers to understand the epidemiology of the infections. Furthermore, the obtained results can predict the possible outcomes of disease transmission. As a result, modelling possesses a significant role in public health and epidemiology as model formulation covers the planning and implementation of the public health response to overcome the crisis brought by infectious disease (Lessler & Cummings, 2016).

In Sarawak, the local authorities and the public are aware of the disease outbreaks in recent years such as leptospirosis outbreaks. Leptospirosis is a widespread zoonosis caused by the pathogenic *Leptospira* (Levett, 2001). This infectious disease is endemic in tropics such as East Sub-Saharan Africa, Southeast Asia, the Caribbean and Oceania (Rajapakse, 2022). Leptospirosis is curable; however, it is also an underreported and underdiagnosed

disease (Sembiring, 2018). The disease is hard to diagnose as the infected people will show symptoms identical to other diseases such as dengue fever and influenza (Biscornet et al., 2020). Therefore, leptospirosis is hard to be detected unless the individual has gone through clinical laboratory examinations. The following Chapter 2 will discuss the historical aspect, transmission route, clinical features and threats of leptospirosis in Sarawak in more detail.

1.2 Research Motivation

Leptospirosis endangers people throughout Malaysia. The most critical situation was 1,976 cases in 2011 skyrocketed to 8,291 cases in 2015 (Malaysia Ministry of Health [MOH], 2018). A similar occasion also occurred in Sarawak where 157 cases were reported in 2011 and increased to 844 cases in 2016 (Malaysia MOH, 2018). In the preliminary work of Chong et al. (2022), the Susceptible-Infected-Recovered-Susceptible-Infected (SIRS-SI) model is not suitable to model the spread of the disease in Sarawak as the result of the second wave of the outbreak does not fit well with the real prevalence data. The details will be further explained in Section 2.9. Therefore, the considerations of the other models such as the individual-based model (IBM) and other factors that might affect the disease transmission to increase the validity between the simulated results and real prevalence data become another motivation for this research.

1.3 Problem Statement

The compartmental models such as SIR, SIRS, SI and SIRS-SI (Chong et al., 2022) assume homogeneity exists in a population whereby each individual shares the same characteristics and behaviours. However, the compartmental models are not adequate for the system or model that considers the individuals who possess significant differences (Black & McKane, 2012). Each individual possesses unique attributes that change with time such as

psychological traits and social behaviours which lead to the existence of heterogeneity in the population (Willem et al., 2017). These individuals can represent animals or plants in a habitat, transportation in traffic, people in a group or autonomous characters in games and animation (Hwang et al., 2009). For zoonotic or vector-borne diseases, the heterogeneity of the hosts or vectors can significantly influence the transmission of the disease (Kilpatrick et al., 2006). For instance, the highly significant heterogeneity in mosquito feeding on the American robins indicated that the American robins are the super spreader of the West Nile virus transmission if compared to other types of birds (Kilpatrick et al., 2006). Therefore, IBM would be more suitable to model the disease as it can capture the heterogeneity of the population. Although there are many studies for leptospirosis transmission by using a compartmental model, the research on studying the spread of leptospirosis in the form of IBM is limited. Therefore, the research aims are to propose an IBM for the spread of leptospirosis and to identify the behaviour of the rats that affects the leptospirosis transmission.

1.4 Research Objectives

The objectives of the research are to:

- i. propose an individual-based model of leptospirosis transmission in Sarawak
- ii. analyse the proposed model to identify the behaviour of the rats affects leptospirosis transmission

1.5 Scope of the Research

The study is focusing on leptospirosis outbreaks in the Sarawak region for the year 2017. There are a few transmission routes for the spread of the disease. However, this research will only focus on the direct contact between the vectors or rats and humans. In the model simulation, the transmission of leptospirosis occurs when humans have direct contact with the infected vectors. Yet, it does not mean humans are immediately infected when they directly touch the infected vectors. Currently, there is no available data and information to indicate the rate of transmission from the excretion such as urine of the infected vectors to the human through direct contact. Therefore, the spread of leptospirosis via direct contact between humans and infected vectors is then assumed as the humans' direct contact with the urine of the infected vectors in the model simulation. For the model verification of IBM, a comparison between IBM and SIR model is made to ensure that IBM is correctly implemented. In this research, the Mean Absolute Percentage Error (MAPE) is calculated for the model verification. However, the MAPE is not validated as most of the comparisons between IBM and SIR are in terms of the patterns of the population behaviours. Therefore, there is no available data to reflect whether the obtained MAPE is good or bad.

1.6 Research Outline

Chapter 2 contains a review of the past outbreak that occurred in Sarawak. The chapter also discusses other significant aspects of the leptospirosis disease such as background, disease transmission, and clinical characteristics, including the reviews on the modelling of leptospirosis spread and reviews on the IBM.

Chapter 3 is the methodology and formulation of IBM. The chapter will describe the methodology, rules, parameters and flowcharts for the interactions and behaviours of the

human and vector agents. The following Chapter 4 will focus on the implementation of IBM by utilising the NetLogo software, including the pseudocode and the user interface for the IBM simulation.

The analysis of the IBM results including the model verification and validation will be presented in Chapter 5. This chapter contains the details for finding the number of runs required, simulation results, validation results and sensitivity analyses.

The final Chapter 6 is the conclusion that discusses the summarisation of the project, the limitations of the project and suggestions for future works.

CHAPTER 2

LITERATURE REVIEW

2.1 Outline

The focus of this chapter is to review the background and epidemiology of leptospirosis followed by the chronology and situations of the disease in Sarawak to provide a clearer view of the situations of leptospirosis locally. This chapter also reviews some of the works on the compartmental models of leptospirosis transmission and individual-based models (IBM).

2.2 Historical Aspect of Leptospirosis

Leptospirosis is an ancient disease. Previous ancient records or texts have proven the disease has been existing for a few centuries like other contagions. For instance, rabies and malaria. In ancient China, leptospirosis was an occupational hazard as most of the people during that time were involved in agriculture, especially rice harvesting on paddy farms. As a result, the ancient Chinese texts indicated this typical disease as “rice field jaundice” (Adler, 2015). Alternatively, leptospirosis had other appellations in Japanese communities like “*akiyami*” or “autumn fever” (Levett, 2001) and “*nanukayami*” or “seven-day fever” (Gupta & Bala, 2016). Leptospirosis also had other forms of address such as “swine-herd’s disease” or “cane-cutter’s disease” in Europe and other countries (Adler, 2015).

The interpretations of leptospirosis prove the disease appears ancients before the official reports and descriptions regarding it by a Professor of Medicine, Adolf Weil in Heidelberg. In 1886, Weil reported the clinical syndrome of the infection with descriptions like splenomegaly, jaundice, and nephritis (Koizumi & Watanabe, 2009). Splenomegaly is

the enlargement of the spleen in terms of size and weight. Jaundice typically refers to the condition whereby the skin, mucous membrane and sclera turn yellow. Lastly, nephritis is the inflammation of the kidneys. With the historical documentation of the findings of Weil, the severe state of leptospirosis is synonymous with Weil's Disease. However, the possible source of the disease remained unknown until the year 1907.

In the year 1907, the “yellow fever” of a patient brought the discovery of the organism that was the source of infection. Stimson (1907) disclosed the bacterium and named it *Spirochaeta icterohaemorrhagiae*. A few years later, in 1915 Inada et al. (1916) identified the occurrence of the disease. They succeeded in the bacteria transmission by using the blood of infected animals and transfusing it to the guinea pigs. In the year 1918, Noguchi (1928) conducted comprehensive microscopic observations. He named the bacteria “*Leptospira*” which meant thin and spiral. The valuable discoveries of the source of infection, *Leptospira*, become the interests of further explorations like the methods of transmission and clinical features of the disease.

2.3 Transmission of Leptospirosis

Leptospirosis is a zoonotic disease, which means the infections ordinarily occur from the infected animals to the humans. These infected animals or reservoir hosts could be wild or domestic and they spread the disease to the environment and humans (Yadeta et al., 2016). Figure 2.1 illustrates the specific mechanism of leptospirosis transmission.

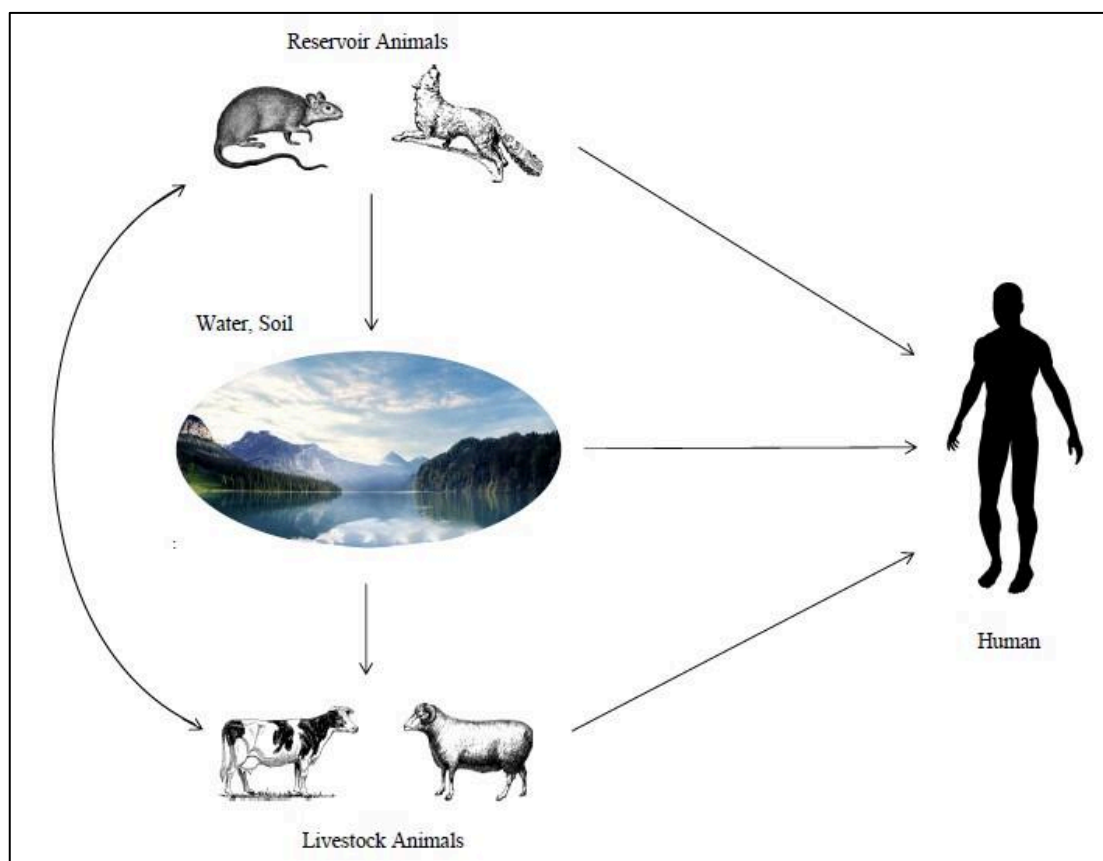


Figure 2.1: Leptospirosis Transmission Cycle

Based on Figure 2.1, the infected animals transmit the disease directly or indirectly to the hosts. The excretion of these creatures contaminates the soil and water (Picardeau, 2017). When humans or animals with wounds or scars are in direct contact with the polluted mediums or the creatures drink contaminated water, they will end up being infected by the disease. The infected livestock can transmit the infection to other beings like rodents and become the new reservoir hosts.

Although leptospirosis is zoonotic, there are some possibilities whereby the transmission of the disease occurs between humans. However, this extraordinary circumstance happens rarely. The disease can spread between humans through sexual

intercourse (World Health Organisation [WHO], 2003). In addition, infants or children tend to become the victims of the disease during pregnancy or drink breast milk from the infected mother (WHO, 2003). The urine of the infected patient should be considered infectious (WHO, 2003). Alternatively, the blood of the infected patient is contagious as the leptospire can transmit through blood transfusion (WHO, 2003).

Leptospirosis is endemic in tropical and sub-tropical regions. To confront the issue, the determination of the severity of the disease becomes a significant aspect. However, it is difficult to obtain the real figures for the global incidence. The recent estimation for the impacts of the disease is more than one million notified cases, nearly 59,000 deaths and roughly 10,000 hospitalisations of severe cases annually worldwide (Costa et al., 2015; Tique et al., 2018).

Leptospirosis is a hazardous occupational disease. Particularly the individuals who work as miners, sewer and sewage workers, livestock farmers, veterinarians and army personnel are the high-risk groups for exposure to leptospirosis (Bharti et al., 2003). Urban service workmen are also at risk of the disease as their jobs include water treatment, sewage and drainage cleaning, road sweeping and garbage collection (Sulong et al., 2011). Agriculture workers endanger against leptospirosis as their manual work practices expose them to the water and soil. The excretion of infected animals may contaminate the plantation environments (Ridzuan et al., 2016). In general, the occupations whose job descriptions involve direct contact with water and soil possess a more significant probabilities to be infected by leptospirosis.

2.4 Leptospirosis Reservoir Host, Rats

Rodents commonly are dominant animals that composing of about 43% of mammalian species and are widely distributed across the world (Wilson & Reeder, 1993, as cited in Lacey & Solomon, 2003). Rodents typically belong to the order of *Rodentia*, and they are gnawing mammals that are herbivorous (feed on plants) and omnivorous (feed on plants and animal origins). In Malaysia, they typically consist of four families in Peninsular Malaysia such as *Muridae* or rats and mice, *Rhizomidae* or bamboo rats, *Sciuridae* or ground and tree squirrels and *Hystricidae* or porcupines (Lim, 2015), and three families in Malaysian Borneo: *Muridae*, *Sciuridae* and *Hystricidae* (Hamdan et al., 2017). Among four families of *Rodentia*, *Muridae* or rats are frequently found in Malaysia and there are 20 species and 200 sub-species of them (Paramasvaran et al., 2012).

Rats have limited life expectancy. The average lifespan of a rat is believed to be 2.5 to 3.5 years (Fallon, 1996, as cited in O'Malley, 2005). The rat has a gestation period of 21 to 23 days and gives birth to 6 to 12 pups (O'Malley, 2005; Mail, 2015). In terms of thermoregulation, rats naturally have few sweat glands. This means they acquire bad heat tolerance, and deaths ordinarily occur when the temperature exceeds 37°C. Inversely, they possess good cold tolerance which allows them to adapt to the cold climate and environment (O'Malley, 2005). In various places in the cities and towns in Malaysia, the *Rattus norvegicus* (*R. Norvegicus*) or Norway rats and *Rattus rattus* (*R. Rattus*) or house rats are the two most common rats.

The origin habitats of *R. Rattus* are from India and the Malaysian Peninsula. The rats spread across the world with the opening of trade routes from the East during the Middle Ages (O'Malley, 2005). In Malaysia, the rats are usually brown in appearance. *R. Rattus* in

common are nocturnal animals and travel from house to house through cable and power lines by utilising their skilful climbing technique. Meanwhile, *R. Rattus* are extremely social animals as they travel and sleep in groups (Grimzek, 2003). The typical habitats of these rats are varying, such as ships, fruit plantations, palm trees, bushes, wooden buildings, sewage, cellar and even trees can be their places to live (Grimzek, 2003).

R. Norvegicus originated from Asia, and they immigrated to England through Norway aboard ships during the 18th century (Modlinska & Pisula, 2020). *R. Norvegicus* tend to live everywhere with their strong adaptability to the environments, yet they fare well to stay in the hotter climate areas (Grimzek, 2003). These rats are associative living with human places, whereby most of them live in urban, suburban, and agricultural areas, particularly sites with rubbish and food sources (Trani et al., 2007). *R. Norvegicus* is less capable of climbing, but they can swim across middle-distance islands (Foster et al., 2011; Russell & Clout, 2004). Additionally, *R. Norvegicus* are nocturnal, social animals as they live and hunt in the form of a group (Grimzek, 2003).

R. Rattus and *R. Norvegicus* eventually are pests as they act as the reservoir hosts of the pathogenic microorganisms and develop health crises in various countries. The study typically indicated the microorganisms carried by the rats like resistant *E. coli* and pathogenic *Leptospira spp.* (Strand & Lundkvist, 2019). *R. Rattus* and *R. Norvegicus* undoubtedly bring threads to the mortality and morbidity of humans in the cities. They are believed as the sources of pathogens, for example, zoonotic *Leptospira interrogans* and Seoul hantavirus (Himsworth et al., 2013). As a result, the effective control of numbers of *R. Rattus* and *R. Norvegicus* is necessary for rat-borne disease handling and prevention. However,

urban rats are complex to properly manage as they live associated with humans (Byers et al., 2019).

2.5 Clinical Features of Leptospirosis

The incubation phase of leptospirosis in humans is different for most individuals. In addition, the duration from the likely disclosure of the disease to the onset of the symptoms is 2 to 26 days with an average of 10 days (Day et al., 2019). However, some individuals typically undergo a duration as short as 3 days or as long as a month (Al-orry et al., 2016). With the proper medical care, infected people can recover from the disease, but the treatment for leptospirosis consumes an extensive period. The recovery phase of leptospirosis requires 6 to 12 weeks for an individual to heal after the initial exposure to the infection. Nevertheless, some individuals ordinarily require years of experience to be completely recovered from the disease (Izurieta et al., 2008).

Ultimately, there are four boards of classifications for the symptoms of leptospirosis (Gupta & Bala, 2016), which are mild, influenza-like illness or acute febrile illness; Weil's syndromes like jaundice (yellow of skin) and bleeding or haemorrhage; respiratory failure in associate with pulmonary haemorrhage; and meningitis (brain and spinal cord with the inflammation of membrane). Apart from the classifications, the individuals who are affected by leptospirosis will typically experience high fever, muscle ache, headache, diarrhoea, abdominal pain, vomiting and red eyes. Although the mild symptoms of the infection are notifiable, the misdiagnosis or underdiagnosis of the disease occurs frequently. The initial exposures to leptospirosis contain similarities with the syndromes of other diseases. For specific instances, dengue, the flu, and influenza. Meanwhile, the severe state of

leptospirosis causes death and symptoms like jaundice, renal failure, and bleeding (Umei & Ichiba, 2017).

2.6 The Situation of Leptospirosis in Sarawak

In Sarawak, the first appearance of leptospirosis was regarding the reported case at the Mulu Caves in Gunung Mulu National Park. The infected individuals were the people who participated in cave exploring. In the subsequent years, there were many cases of leptospirosis reported in media or research. The spotted infection places transferred from the caves to the rural and urban areas. Table 2.1 summarises the precise locations of some of the incidences of leptospirosis in Sarawak as reported in research or newspapers.

Table 2.1: Locations of Documented and Reported Leptospirosis Incidences in Sarawak

Year	Location of Leptospirosis Incidence	Reference
1984	Mulu Caves, Miri	Waitkins (1986), as cited in Benacer et al. (2016)
1994	Gunung Buda, Miri	Roger and Mortimer (2005)
2010	Permai Road recreational pond, Sibü and Pond in Junako Park National Service Training Camp, Sibü	“Virus Leptospirosis Dikesan” (2010)
2011	RSAT Army Camp at Penrissen Road Batu 8, Kuching	Thayaparan et al. (2013)
2011	Blok 10, Kem Semenggok, Kuching	Thayaparan et al. (2013)
2012	Tiong Hua Road, Sibü	Thayaparan et al. (2013)
2016	Kapit	“Teenager hospitalised” (2016)

Table 2.1 continued

2016	Sibu	Sman (2016)
2018	Lily pond at Jalan Penghulu Nyanggau and Jalan Mamora, Kapit	“Leptospira detected” (2018)
2018	Kapit	“Nanzi changwei bushi” (2018)
2019	Sibujaya, Sibu	“Fagaoshao butui” (2019)
2020	Daro, Mukah	“Yisi shuniaobing” (2020)
2020	Kapit	“Huan shuniaobing” (2020)

The first recorded incidence was in 1984. From the exploration of Mulu Caves in Gunung Mulu National Park, 16 people were ill and five of them had fever and hepatomegaly. They were confirmed to have leptospirosis infections by undergoing serological tests (Benacer et al., 2016). In 1994, a 37-year-old man was sickened by leptospirosis after returning to the United States from his reconnaissance work at Gunung Buda, Sarawak. The symptoms developed approximately 10 days after his last cave trip with chills, headache, myalgias and a temperature of 40°C (Roger & Mortimer, 2005). When entering the 2000s, leptospirosis begins to be notified by the government and the public. In 2010, two places located in Sibu detected the appearance of *Leptospira*. These two places were Permai Road recreational pond and the pond in the Junako Park National Service Training Camp (“Virus Leptospirosis Dikesan,” 2010). The following year in 2011, 5 army recruits from RSAT Army camp at Penrissen Batu 8, Kuching confirmed having leptospirosis after they underwent the serological test. The infection source of the disease

was the small river near the army camp. Additionally, 2 military recruits from the Blok G10, Kem Semenggok, Kuching showed serologically positive for leptospirosis as well in the same year (Thayaparan et al., 2013). In 2012, the health authority of Sarawak notified the appearance of a leptospirosis outbreak that occurred in the drains along the Tiong Hua Road in Sibu (Thayaparan et al., 2013).

In 2016, a 16-year-old boy from Kapit had suspected to have a leptospirosis infection and the boy was in a coma condition when dispatched to Sibu Hospital (“Teenager hospitalised,” 2016). In Sibu District, many reported incidences occurred around the logging camp because of the hygiene problem. The people threw food leftovers that attracted rats to gather around the places (Sman, 2016). In 2018, the local authorities detected *Leptospira* in the water of a lily pond at Jalan Penghulu Nyanggau and Jalan Mamora. With the presence of the bacteria, the local authorities declared the place to be hazardous and warned the public to stay away from fishing, swimming and bathing (“Leptospira detected,” 2018). In 2018, a 42-year-old man from Kapit felt indigestion and fever. He was confirmed to be infected by leptospirosis and dispatched to Sibu Hospital in severe condition (“Nanzi changwei bushi,” 2018). In 2019, a man who lived in Sibu Jaya, Sibu confirmed that he had an infection after underwent through a serological test (“Fagaoshao butui,” 2019). In 2020, a 45-year-old Indonesian man who worked in an oil palm estate in Daro district had suspected to be infected by leptospirosis. He was sent to the hospital in Sibu with a severe condition (“Yisi shuniaobing,” 2020). In a similar year, a 45-year-old man from Kapit who worked in an oil palm estate suffered from vomiting and diarrhoea. He was urgently sent to the Sibu Hospital and diagnosed for having leptospirosis including malaria (“Huan shuniaobing,” 2020).

Apart from the newspapers and research, there were many reported cases in which the official documentation of leptospirosis started in the year 2004. The data highlight a stable trend for the disease outbreak from 2004 to 2011 with the numbers does not exceed more than 100 cases. However, starting in 2011 the data shows an increasing trend and in 2016 the number reaches 844 which realistically is the highest state (Thayaparan et al., 2013; Malaysia MOH, 2018). This typical situation indicates that leptospirosis undoubtedly becomes serious starting in 2011 and the existence of the disease is alarming the public. Although the reported cases decreased to 636 in 2017 (Malaysia MOH, 2018), the local records in 2018 showed an increased number of cases. According to the Sarawak health director, 692 cases of leptospirosis were reported from 1 January to 27 October 2018. The numbers are increasing compared with the corresponding period of the year 2017 in Sarawak (Boon, 2018). Figure 2.2 illustrates the number of confirmed cases from the year 2004 to 27 October 2018.

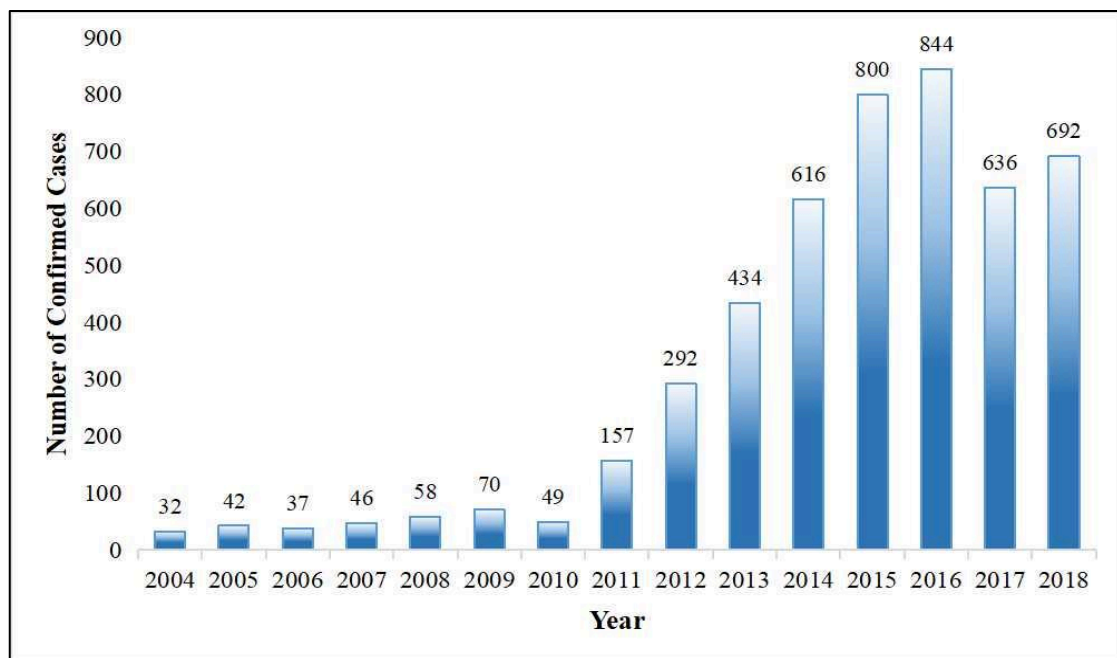


Figure 2.2: Number of Leptospirosis Cases in Sarawak from 2004 to 27 October 2018

2.7 Related Works on Compartmental Models for Leptospirosis Transmission

As leptospirosis becomes alarming in various countries, research to study the epidemiology of the disease is getting more significant. The Susceptible-Infected-Recovered (SIR) model is one of the frequently used frameworks to study the disease interactions between populations (Weissman, et al., 2020). The model has popularity as it is simpler for the modeller to apply a small number of parameters for estimating disease behaviour (Tolles & Luong, 2020). SIR is a compartmental model, and it categorises the population into three groups: susceptible, infected, and recovered groups. The susceptible group refers to the individuals who are at risk of the disease infection. Alternatively, the infected group is the people who suffered from infection. Meanwhile, the recovered group refers to the individuals who recovered from the disease.

Apart from SIR, there are other specific types of developed compartmental models like SI, SEI, SEIR, MSEIR, SIS, SIRS, SEIS, SEIRS and MSEIRS (Hethcote, 2000). There are certain situations whereby individuals are exposed to the disease and remain uninfected. These individuals are under the class of the Exposed (E) group. In addition, when a mother is infected, the antibodies will produce and passes to the infant. As a result, the infant naturally acquires temporary passive immunity and is classified as the M class (Hethcote, 2000). Although some individuals recovered from the infection, yet likely have possibilities exist as they will be infected by the disease again. Therefore, the compartmental models, for example, SIRS, SEIRS and MSEIRS were developed to represent this situation. Table 2.2 is the tabulation of the related research on compartmental models for leptospirosis transmission.

Table 2.2: Related Research on Compartmental Models for Leptospirosis Transmission

Year	Author	Title	Model Applied	Study Area
2012	Pongsumpun	Mathematical Model for the Transmission of Leptospirosis in Juvenile and Adults Humans	SIR-SI	Thailand
2013	Pimpuchat et al.	Mathematical Model of Leptospirosis: Linearized Solutions and Stability Analysis	SIR-SI	-
2017	Ismail et al.	Approximate Analytical Modeling of Leptospirosis Infection	SEIR-SEI	-
2018	Babylon et al.	Modelling leptospirosis in livestock	SI	New Zealand
2019	Bhalraj and Azmi	Mathematical modelling of the spread of Leptospirosis	SIRS-SI	-
2019	Ideris et al.	A stochastic model for relative risk estimation of leptospirosis in Malaysia	SIR-SI	Malaysia
2019	Rafiq et al.	Numerical Modeling for Transmission dynamics of Leptospirosis Disease in Juvenile and Adult Humans	SIR-SI	-

Table 2.2 continued

2020	Alemneh	A co-infection model of dengue and leptospirosis diseases	SIR-SI	-
2021	Paisanwarakiat and Thamchai	Optimal Control of a Leptospirosis Epidemic Model	SEIR-SEI	-
2021	Chadsuthi et al.	The effects of flooding and weather conditions on leptospirosis transmission in Thailand	SIR-SIR-L	Thailand
2022	Chong et al.	Mathematical Modelling of Leptospirosis Spread in Malaysia	SIRS-SI	Malaysia

Referring to Table 2.2, a SIR model was applied to study the spread of leptospirosis in juvenile and adult humans in Thailand (Pongsumpun, 2012). The study indicated that the basic reproductive number, R_0 , can influence the transmission rate and disease outbreak. Other researchers investigated the transmission rate of leptospirosis by forming a SIR model based on two factors (Pimpuchat et al., 2013). The two factors are the transmission rate from infected vectors to susceptible humans and the transmission rate from infected to susceptible vectors. In addition, the two factors are dependent on rainfall throughout the research. Ismail et al. (2017) investigated the relationship between the fractional derivative order and the subgroups of the human and vector populations by formulating the SEIR model. The number of susceptible and recovered individuals increases slowly when fractional derivative order approaches one. On the other hand, the number of exposed and infected groups for humans

and vectors at first slightly declines, then increases slowly to an endemic state when the fractional derivative order is close to one. Babylon et al. (2018) modelled the leptospirosis transmission with the SI model to study the spread of disease among livestock and humans in New Zealand. They showed that the increasing death rate of leptospires resulted in the decline of infections in livestock and humans.

Bhalraj and Azmi (2019) formulated the SIRS model to estimate basic reproduction numbers as the outbreak of disease depended on the basic reproduction number. Additionally, juvenile humans are likely to be infected by the disease when compared with adult humans as juvenile humans do not possess immunological defences. Ideris et al. (2019) estimated the relative risk of leptospirosis in Malaysia by formulating a SIR model. The research deduced that Malaysia was at risk of leptospirosis. Kelantan and Terengganu were the two states in Malaysia that vulnerable to the disease as leptospirosis outbreaks occurred in places with heavy rainfall and flooding. Rafiq et al. (2019) formulated a SIR model to study leptospirosis transmission in juvenile and adult humans in Pakistan. The study indicates that the existing scheme such as the Euler method or Runge-Kutta order 4 (RK-4) method was not dependable to solve a continuous model. Although the two methods had limitations, they were conditionally convergent and workable for the small size of the time step. A study regarding leptospirosis transmission in Malaysia by forming the SIRS-SI model had been conducted (Chong et al., 2022). The study indicated the transmission rate from susceptible to infected vectors was a parameter that possessed significant influence in the disease outbreaks as compared to other parameters.

On the other hand, some studies applied the advanced form of the SIR model. Alemneh (2020) conducted a special study on co-infection between leptospirosis and dengue

with the formulation of the SIR-SI model. The research indicated the increase in recovery rate reduced the leptospirosis and dengue transmissions including the co-infections of the two diseases among the individuals. The decreasing contact rate of dengue or leptospirosis influenced the co-infection between two diseases within the population. Paisanwarakiat and Thamchai (2021) formulated an SEIR-SEI model to study leptospirosis transmission by introducing optimal control variables in their model. From the simulation results, the control strategies were effective as the susceptible groups for both human and vector populations were maximised. Another SIR model was formed by considering the transmission routes from the *Leptospira*-contaminated environment (L) (Chadsuthi et al., 2021). They concluded that flooding boosted the leptospirosis spreading in Thailand communities. Additionally, they suggested the people who worked in the *Leptospira*-contaminated environment be provided public education.

From all the studies, the SIR model allows the modellers to have insights into the changes in population behaviours for the transmission of diseases such as leptospirosis. The compartmental model can provide information regarding the basic reproduction number or R_0 that can influence the disease outbreak after solving the model. The modellers also improve understanding of the epidemiology including the transmission mechanisms of leptospirosis through the compartmental model. The compartmental model has the advantage as it is simple and easy to compute. Furthermore, the modellers apply the compartmental models to optimise the control measures for controlling the spread of the disease. However, the modellers assume populations are homogeneously mixing for the compartmental models whereby the infective individual has an equal probability to contact with any one of the susceptible individuals in the population and this assumption is unrealistic (Sattenspiel & Simon, 1988).

2.8 Individual-Based Modelling and Related Research

In reality, heterogeneities exist within a population whereby the individuals in the population have unique attributes that change with time such as spatial location, psychological traits and social behaviours (Willem et al., 2017). From the perspective of zoonotic or vector-borne diseases, the heterogeneity of the hosts or vectors can significantly affect the disease spreading (Kilpatrick et al., 2006; Burr & Chowell, 2008). The compartmental models are not suitable to deal with the problem that considers the individuals present significant differences (Black & McKane, 2012). In such a view, the frameworks that consider the individual as a unique entity are the most prominent such as Individual-based models (IBM) or agent-based models (ABM) (Nepomuceno et al., 2016).

IBM is a modelling approach to simulating populations which consist of discrete agents that represent individual organisms with sets of traits that are different within agents (DeAngelis & Mooij, Individual-Based Modeling of Ecological and Evolutionary Processes, 2005). IBM is also referred to as ABM and many authors apply the terms interchangeably (DeAngelis & Grimm, 2014; Parrott, 2008). The application of IBM or ABM covers many fields of study. For example, in terms of ecology, the IBM or ABM is used to study population dynamics, and species relationships, as well as to understand how animals adapt to the environment (DeAngelis & Mooij, 2005). The ABM is also used to simulate the team working in an engineering environment and to investigate the factors that affect the team performance (Crowder et al., 2012). In general, the IBM or ABM is used to model the dynamics of the population and interactions of agents in an environment with the presence of heterogeneity (DeAngelis & Mooij, 2005; Hamil & Gilbert, 2016).

IBM showed superiority if compared to compartmental models for the accuracy of prediction with the research performed by Eisinger and Thulke (2008). The simulation results indicated that the eradication of rabies among the fox population in Germany can be achieved with a 60% of immunisation level by using IBM instead of 70% with the application of compartmental models and the results were in complete agreement with the real-time data (Eisinger & Thulke, 2008). IBM is the same as the compartmental model at some points where both models concern the interactions between two entities for forecasting the transmission of the disease throughout the time (Van Dyke Parunak et al., 1998). However, IBM can capture the heterogeneity in the populations including the dynamic factors of the disease spreading which the compartmental model is unable to do so. This feature becomes an advantage of IBM and makes it becomes useful in the epidemiology of infectious diseases. Therefore, the trend of using IBM in the modelling of disease transmission is increasing and Table 2.3 shows some of the related research.

Table 2.3: Individual-based Modelling Related Research

Year	Title	Remark	Reference
2017	Agent-Based Modelling and Simulation of Mosquito-Borne Disease Transmission	Study of mosquito-borne disease transmission	Jindal and Rao
2017	Lessons from a decade of individual-based models for infectious disease transmission: a systematic review (2006 – 2015)	Survey of IBM implementation	Willem et al.

Table 2.3 continued

2018	A Survey of the Individual-Based Model applied in Biomedical and Epidemiology Research	Survey of IBM implementation	Nepomuceno et al.
2018	Agent-based models of malaria transmission: a systematic review	Study of malaria transmission	Smith et al.
2020	An Agent-Based Simulation of the Spread of Dengue Fever	Study of dengue transmission	Mahmood et al.
2020	A Spatial Agent-Based Model to Assess the Spread of Malaria in Relation to Anti-Malaria Interventions in Southeast Iran	Study of malaria transmission	Gharakhanlou et al.
2020	A Simulation Study of Coronavirus as an Epidemic Disease Using Agent-Based Modeling	Study of coronavirus transmission	Alzu'bi et al.
2021	3D Agent-Based Model of Pedestrian Movements for Simulating COVID-19 Transmission in University Students.	Study of coronavirus transmission	Alvarez Castro and Ford

Referring to Table 2.3, Jindal and Rao (2017) researched mosquito-borne diseases by using ABM and deduced that ABM overcame the limitations of the compartmental models in determining the factors of interactions between hosts and vectors that drive the disease transmission. These factors include mobility and distributions of the host and the

vector populations and geographical including weather conditions. ABM allows the estimation of the parameters, which are hard to determine such as the mosquito's sensing distance. Willem et al. (2017) reviewed the IBM applications in infectious disease transmission. The IBMs have been widely used to explore the spread of infectious diseases that can be influenced by the heterogeneous between-host interactions instead of using the compartmental models. Nepomuceno et al. (2018) surveyed IBM applications in biomedical and epidemiological research. IBM allows the consideration of the specific characteristics of individuals and recognised them as heterogeneous. This is a feature of IBM as the compartmental models assume the distributions of the population to be temporally and spatially homogeneous. The homogeneous assumptions of the compartmental models eventually lead to the fragility of the models.

Smith et al. (2018) did a systematic review on the applications of ABM in the modelling of malaria transmission. The study emphasized stochasticity in the low transmission setting, high resolution of spatial simulation, and heterogeneities in drug and vaccine efficiencies were essential for the ABM formulation. Mahmood et al. (2020) formulated an ABM for investigating the dengue fever transmission among people in Pakistan. The model concerned the behaviour of mosquitoes such as biting rate and environmental factors including temperature, the permeable water surfaces in the region, rainfall, and humidity for the spread of dengue fever. The results indicated the disease transmission was dependent on the temperature. The temperature rise increased the biting rate of mosquitoes and caused the dengue cases to multiply. Meanwhile, Gharakhanlou et al. (2020) proposed an ABM for studying malaria transmission. They proposed and implemented two interventions in the households with a percentage of coverage rate. The first approach was adding insecticides to the ceiling and internal walls of houses.

Subsequently, the second technique was the installation of insecticidal nets on the window and door. From the simulation results, the combined implementation of dual interventions with a high coverage rate, 40% of households effectively reduced more than 91% average number of infected human agents.

Alzu'bi et al. (2020) formed an ABM for simulating the coronavirus transmission in an urban area. They investigated several measures for reducing infections and deaths among individuals. Based on the findings, isolation policies and controlling procedures on the movement of the communities could influence the effects of disease transmission. Alvarez Castro and Ford (2021) studied the spread of coronavirus among university students by implementing the ABM. The model focused on the relationships between locations including activities of the students and the influences on transmission of the disease. The results indicated the implementation of preventive measures such as wearing face masks, early lockdown, and a self-isolation approach could greatly reduce coronavirus transmission and ensure the safety of the students.

2.9 Justification of Modelling Leptospirosis Spreading with Individual-Based Model

In the previous section, some of the related work on compartmental models for leptospirosis disease have been reviewed. Chong et al. (2022) formulated a SIRS-SI model for the leptospirosis spread in Malaysia.

$$\frac{dS_h}{dt} = \mu_h N_h - \lambda_h S_h - \theta_h I_v S_h + \delta_h R_h \quad \text{Equation 2.1}$$

$$\frac{dI_h}{dt} = \theta_h I_v S_h - \lambda_h I_h - \gamma_h I_h \quad \text{Equation 2.2}$$

$$\frac{dR_h}{dt} = \gamma_h I_h - \lambda_h R_h - \delta_h R_h \quad \text{Equation 2.3}$$

$$\frac{dS_v}{dt} = \mu_v N_v - \lambda_v S_v - \theta_v I_v S_v \quad \text{Equation 2.4}$$

$$\frac{dI_v}{dt} = \theta_v I_v S_v - \lambda_v I_v \quad \text{Equation 2.5}$$

Based on the SIRS-SI model, S_h , I_h and R_h are the susceptible, infected and recovered groups of the human population. As for the S_v and I_v , both constants represent the susceptible and infected groups of the vectors. There are a few parameters that manipulate the changes in population dynamics. The μ_h and μ_v refer to the birth rates of humans and vectors whereas λ_h and λ_v are the death rates for both populations. Meanwhile, a few parameters also influence the changes in disease dynamics. The γ_h represents the recovery rate from infection and δ_h indicates the rate of immunities loss in the human body against the disease. For θ_h and θ_v , both parameters are the disease transmission rates among both populations. Although the preliminary work focused on transmission in Malaysia, the same model can be incorporated with the Sarawak data. Figure 2.3 to Figure 2.5 are the comparisons between the real data in the year 2017 and the obtained results from the simulations.

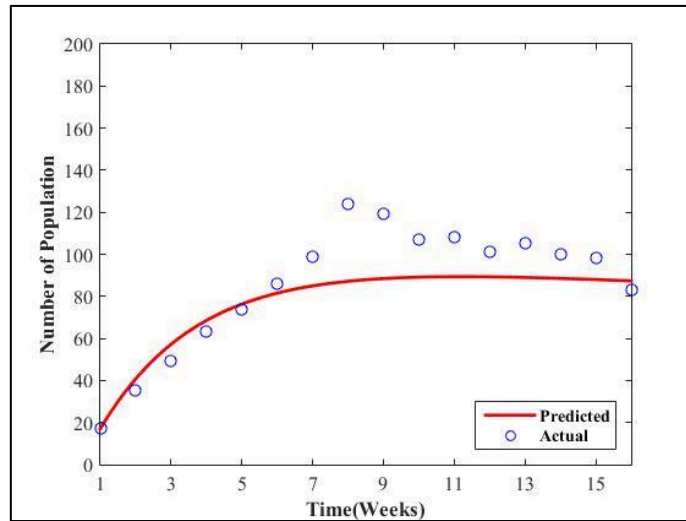


Figure 2.3: The Comparison from Epid Week 1 to Epid Week 16 for Sarawak Leptospirosis Cases in the Year 2017

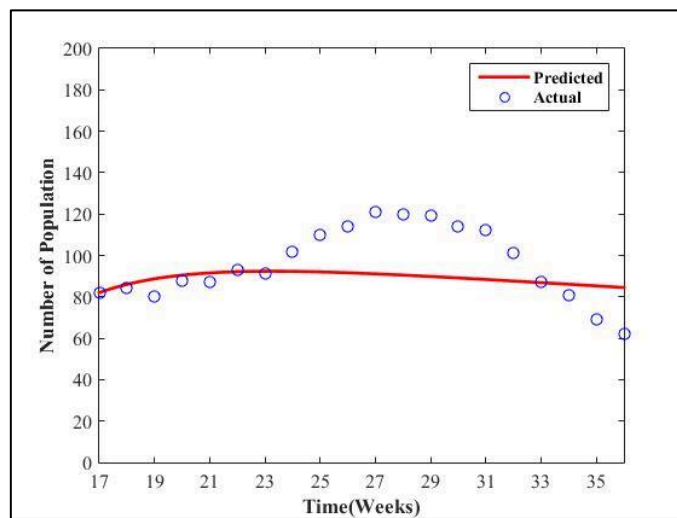


Figure 2.4: The Comparison from Epid Week 17 to Epid Week 36 for Sarawak Leptospirosis Cases in the Year 2017

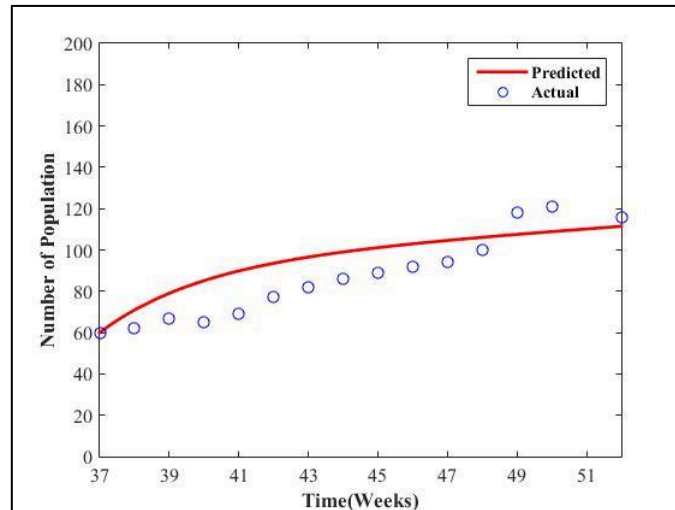


Figure 2.5: The Comparison from Epid Week 37 to Epid Week 52 for Sarawak Leptospirosis Cases in the Year 2017

To determine whether the simulated results are a good fit for the real data or not, a trend analysis is performed. Trend analysis is a statistical measure that examines the patterns in the data over time to show the trend in the data (Chao et al., 2018). Trend analysis has the advantage to predict the future development of the trends based on the current or historical trend (Haralayya, 2021). It also helps to investigate the uncertainties or variability in various time points of data in association with the factors (Chao et al., 2018). Trend analysis is used in public health and epidemics. For example, Wild et al. (2004) implemented trend analysis for the estimation of the prevalence of diabetes including the number of people with diabetes for all ages for the year 2000 and projection for the year 2030. Xie et al. (2021) applied trend analysis to fit the estimation and forecast of daily incidence of hand, foot, and mouth disease in Hubei, China by using the Prophet model.

There are different trends of data such as linear, nonlinear, or absent (Xu et al., 2020). On the other hand, the techniques to find the trends of the data are the ones from the regression analysis or others (Chandler & Scott, 2011). As the tools of the trend analysis are

the same as the regression analysis, widespread use of the performance metric which is the coefficient of determination or r^2 can be a choice for the analysis (Chicco et al., 2021). Compared to other metrics such as mean squared error (MSE), root mean squared error (RMSE), mean absolute error (MAE), mean absolute percentage error (MAPE) and symmetric mean absolute percentage error (SMAPE), the r^2 is a more suitable metric to evaluate the regression for any scientific area (Chicco et al., 2021). Although MSE, RMSE, MAE and MAPE are useful, however, these rates have interpretability limitations which the values of the rates do not describe much about the performance of the regression as the values range from between zero and positive infinity (Chicco et al., 2021). Furthermore, as compared to SMAPE, the rate of r^2 is more informative and truthful as it is the only metric that considers the distribution of values and it projects a high score only if the regression correctly estimates most of the values (Chicco et al., 2021).

r^2 is a numeric measure of goodness of fit for the regression and the range of r^2 is usually between 0.00 or 0% to 1.00 or 100% (Frost, 2020). r^2 more approaches to 1.00 indicate a nearly perfect prediction and model closely fits the data whereas r^2 more approaches to 0.00 reflect a poor prediction and bad fits of a model (Chicco et al., 2021). Meanwhile, the values of 0.75, 0.50, and 0.25 are described as substantial, moderate, and weak respectively for the r^2 (Hair et al., 2011). The r^2 for the three waves of leptospirosis outbreak was 87.40%, 36.09% and 76.06% respectively. Although the r^2 of 87.40% and 76.06% for the first and third waves imply good predictions and the model fits with the data, the r^2 for the second wave refers to a moderate prediction and only 36.09% of the simulated results fit the real data. In summary, the r^2 reflects the compartmental model is not appropriate to simulate the leptospirosis transmission in Sarawak as the model cannot predict well for all three outbreaks consistently.

From Section 2.8, a lot of research had applied IBM for studying various contagious diseases. However, to the best of our knowledge, there is no research regarding the modelling of leptospirosis transmission by using IBM. IBM allows the researchers to know the interactions between the hosts and humans as it captures the heterogeneities of the interactions. This has become the advantage of the model. This special property indicates the behaviours of the individuals such as humans or hosts are considered during the formulation of the IBM. Based on the reviews, most of the modelling research on leptospirosis transmission does not see the actions or life habits of the vectors as one of the considerations. Hence, it is necessary to investigate the relationship between the spread of disease and the behaviours of vectors as the vectors' behaviours can affect the disease transmission based on the reviews from the literature.

2.10 Summary

This chapter reviewed some of the historical aspects of leptospirosis, the host or vector that spread the disease and some of the clinical features of the infection. The current situation of the disease in Sarawak was also presented where the number of confirmed cases is on the increasing trend. Some of the related work on compartmental models for leptospirosis was presented followed by the related work on IBM for other diseases. Finally, the justification for modelling the leptospirosis spread using IBM was presented at the end of the chapter.

CHAPTER 3

INDIVIDUAL-BASED MODEL FORMULATION

3.1 Outline

This chapter covers the formulation of the individual-based model (IBM) for leptospirosis transmission. The methodology comprises six phases of IBM formulation. Before proceeding to the formulation stage, it requires the set-up of model assumptions for the agents. There are two types of agents which are human and rat agents. Following the declaration of rules, the subsequent step of parameter identification determines the constants that will be used for the model.

3.2 Methodology

Figure 3.1 shows six main phases for the model formulation. Each phase consists of its activities and tasks to perform.

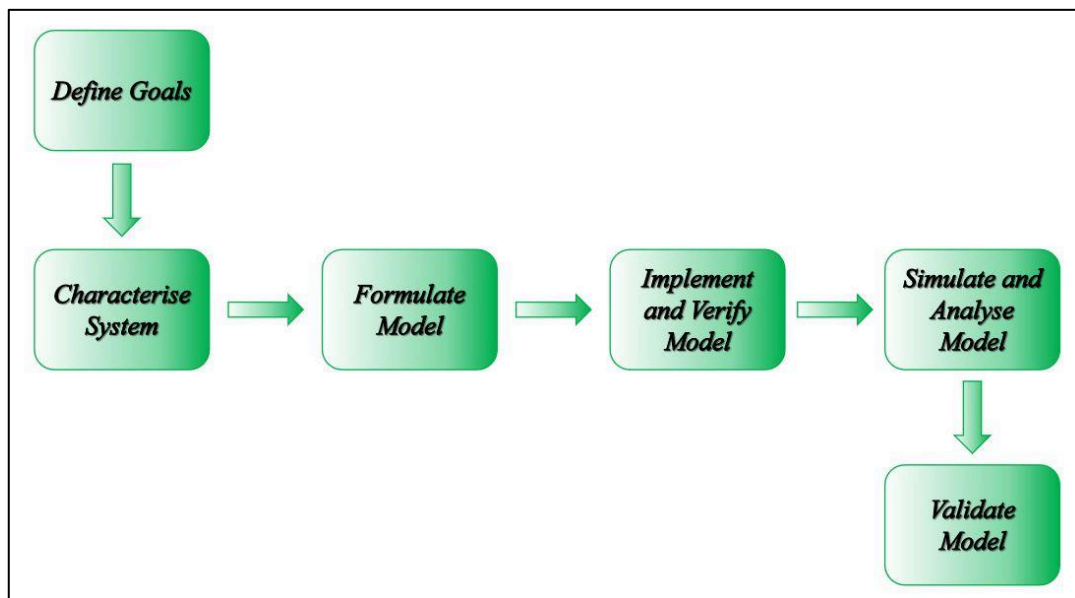


Figure 3.1: Individual-based Modelling Phases

In the stage of defining goals, the determination of the goals or objectives is significant, and the most focused objective of this research is to construct an IBM of leptospirosis transmission. The subsequent phase is the characterisation of the system. The IBM concerns two populations, humans, and vectors in the transmission of the disease. For the human population, there are three categorised groups which are susceptible, infected, and recovered. Meanwhile, the vector population consists of two groups: susceptible and infected. The recovered group is not of concern for the vector as they will die naturally or due to disease after being infected by the disease. Next is the model formulation phase. This phase requires the set-up of model assumptions and determination of parameters before formulating the IBM. The formulated IBM allows individuals to possess their own set of attributes or variables and behaviours.

The next stage is model implementation and verification. This stage discusses the utilisation of software tools such as NetLogo including the designation of pseudocode and the user interface of the model. This stage also covers the comparison of the results between SIR and IBM for model verification. Furthermore, the number of runs for each simulation will be determined as IBM is stochastic whereby each simulation will produce distinctive results. Next is the model simulation and analysis phase. In this phase, the process uses the averaged results from the simulations for analysis purposes. The final phase is the model validation. This stage discusses the trend analysis for the simulated and actual prevalence data from the institutions or agencies such as the Department of Statistics of Malaysia (DOSM), and the Ministry of Health (MOH) Malaysia. In addition, the trend analysis will determine the coefficient of determination or r^2 and the normality of the residuals that can be observed from the normal probability plot. The final phase also includes the sensitivity

analysis through OLS and explores the effects of the parameters on the infected humans and vectors.

3.3 Rules of the Agents

The model assumptions are essential for the model formulation. If the assumptions are not set up appropriately, the distortion of the nature of the problem occurs and the problem becomes more complex (Seino, 2005). As a result, the rules must be clear and specific for the human and vector agents.

3.3.1 Human Agents

The assumption for the human population includes the perspectives of agents' movements and the situations in leptospirosis transmission. Furthermore, the determination of several states of disease dynamics allows the agents to have more human-like health status in the transmission of leptospirosis. The assumptions for the human population are:

- i. The humans are stationary in their housing area.
- ii. There are principally three states of human health conditions: Susceptible, Infected and Recovered.
- iii. The incubation period of the leptospirosis is assumed negligible.
- iv. The death of infected humans due to disease is not considered.
- v. The spreading of leptospirosis typically involves humans and vectors only.
- vi. Leptospirosis is transmitted directly when humans have direct contact with the infected vectors as there is no information to address the rate of transition of bacteria from the infected vectors' urine to humans when humans have direct contact with the urine of the infected vectors.

- vii. The indirect transmission of leptospirosis from the bacteria-contaminated environment is not in consideration.
- viii. Humans are considered immune once they are recovered from the infection.

3.3.2 Vector Agents

The assumptions for the vectors are relatively identical to the human population as well. However, some specific elements are different if compared to the assumptions of human agents. The assumptions for the vector agents are:

- i. The vectors are referring to the rodents.
- ii. The vectors are active at certain periods. Other than the active period, the rodents will stay at their nests.
- iii. The vectors are wandering around outside their nests and approaching the humans' housing areas during the active period.
- iv. There are two states of vector health conditions: Susceptible and Infected
- v. The transmission of leptospirosis occurs when the vectors are active and moving around for 12 hours of the dark cycle.
- vi. The susceptible vector is infected directly when its direct contact with the infected vector as the information regarding the rate of transition of bacteria from the contaminated environment or the urine of the infected vector to the body of the susceptible vector is not available.
- vii. The death of vectors due to leptospirosis infection is not considered.
- viii. The typical lifespan of a vector is naturally between 26 - 40 months.

3.4 Parameters of the Model Formulation

After the declaration of the model assumptions for the human and vector agents, the next step is the identification of the applied parameters in the model formulation. Table 3.1 shows the parameters of IBM.

Table 3.1: The Parameters of the IBM to Address the Population Dynamics and State Transition of Leptospirosis in Humans and Vectors

Parameter	Descriptions
μ_1	The natural birth rate of the human population
μ_2	The natural birth rate of the vector population
ϑ_1	The transmission rate of disease from susceptible human to infected human
ϑ_2	The transmission rate of disease from susceptible vector to infected vector
λ_1	The natural death rate of the human population
λ_2	The natural death rate of the vector population
γ	The recovery rate of the infected human from disease infection
δ	The immunity loss rate against the disease

Table 3.2: The Parameters of the IBM to Incorporate the Heterogeneities in the Behaviour of the Vector Population

Parameter	Descriptions
α_s	The active period start time of the vector
α_e	The active period end time of the vector

Table 3.2 continued

α_d	The active period duration of the vector
η	The movement range of the vector

3.5 Formulation of Individual-based Model

All individuals are unique. IBM can capture the heterogeneities of the vectors' behaviours which are the active period durations and the movement range of the vectors. Following the declarations of assumptions for the agents and the respective parameters, Figure 3.2 shows the interactions of the two populations within IBM.

By referring to Figure 3.2, the interactions of two populations, humans and vectors are formed according to the established rules earlier. The introduced natural birth rates, μ_1 and μ_2 , allow the agents to enter both humans and vectors. The determination of the natural death rates, λ_1 and λ_2 , ensure the populations are not being overpopulated by managing the numbers within both parties. This scenario fulfils the flow whereas the individuals undoubtedly must leave when they experience death. Otherwise, they would remain in the population.

The introduction of diverse states provides more realistic disease dynamic processes to the human and vector groups. The human population covers three subgroups which are susceptible, infected, and recovered. Alternatively, two states for the vectors: susceptible and infected. Susceptible typically refers to individuals who are at risk of the disease infection. As for the infected, the individuals are being affected by the disease and the recovery, and they are in the stage of recovery from the infection.

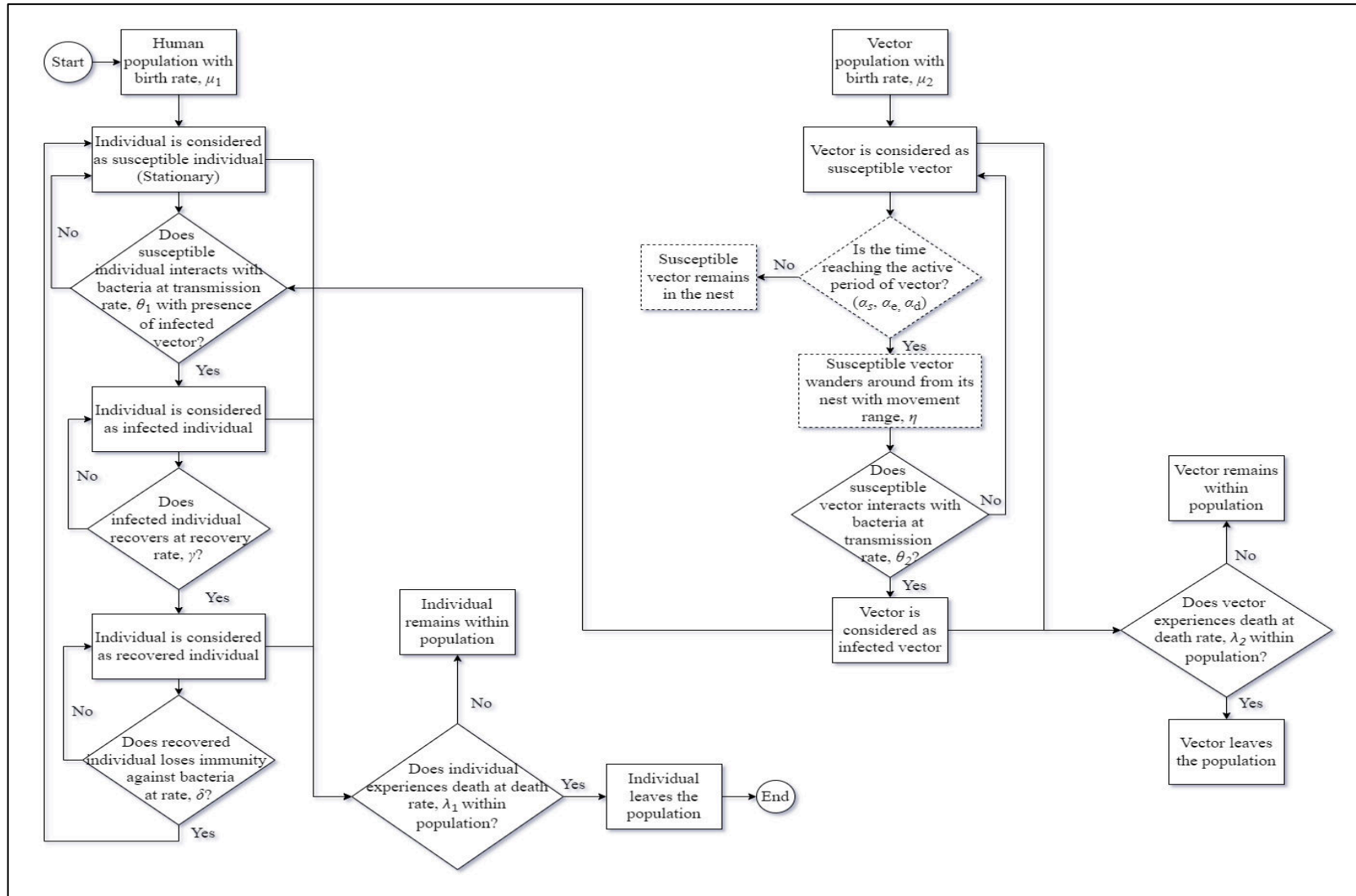


Figure 3.2: Flowchart of IBM for Leptospirosis Transmission

Figure 3.3, Figure 3.4 and Figure 3.5 explain the process of changing one to another state. The key reason whereby the vector population exclusively experiences two altered states is the medicine or vaccine is unavailable for the vectors or the rats. In terms of movement of the individuals, they are wandering around the places. However, the disease does not spread across cities or towns as this aspect is initially unconcerned. The active period (α_s to α_e) is a period that the vectors or rats are active and α_d is the active period durations. The rats are wandering around from their original locations with a movement range, η . However, the vectors remain in their places when they are inactive. The rats spread the bacteria or pathogenic *Leptospira* when they are active. The disease will be further transmitted to humans when the infected rats interact with humans.

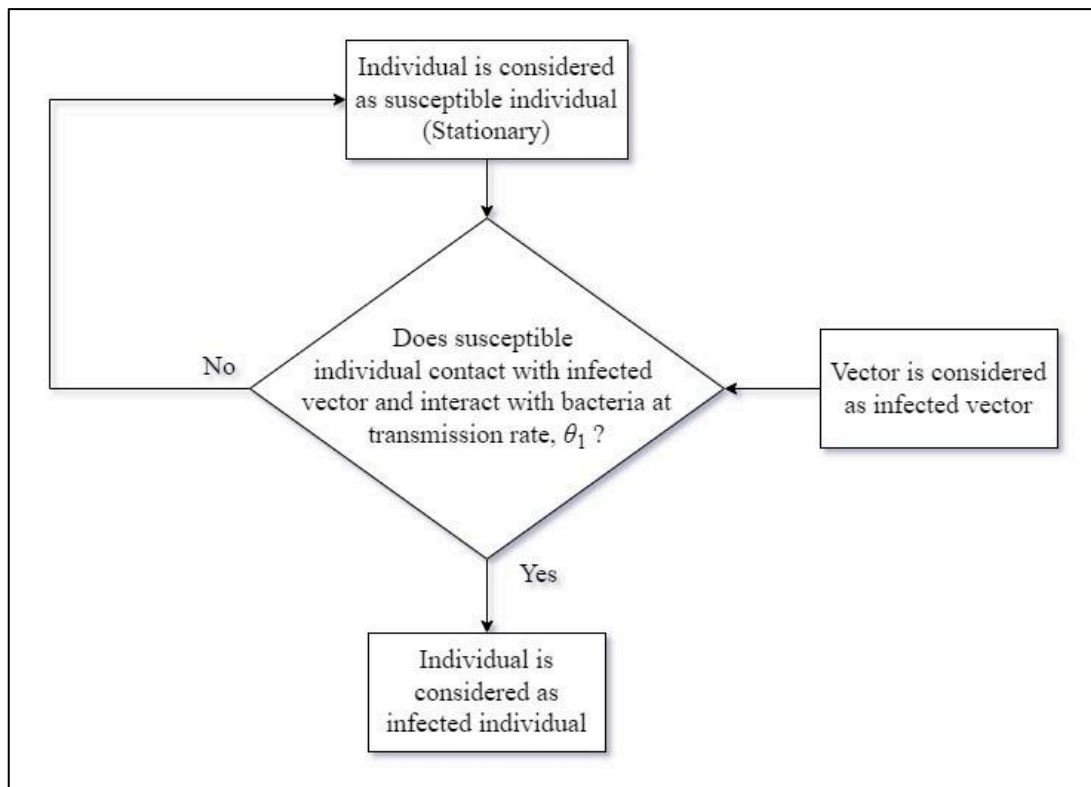


Figure 3.3: The Process of Disease State Transition from Susceptible Individual to Infected Individual with the Presence of Infected Vector at Transmission Rate, θ_1

Figure 3.3 introduces the gradual transition from susceptible to infected status. Initially, humans are considered susceptible. Once these people contact the infected vectors, they typically interact with the bacteria at a transmission rate of θ_1 . As the susceptible individual interacts with the bacteria, they are considered infected. If the people are not in contact with the infected vectors or the bacteria, then the individuals remain susceptible status.

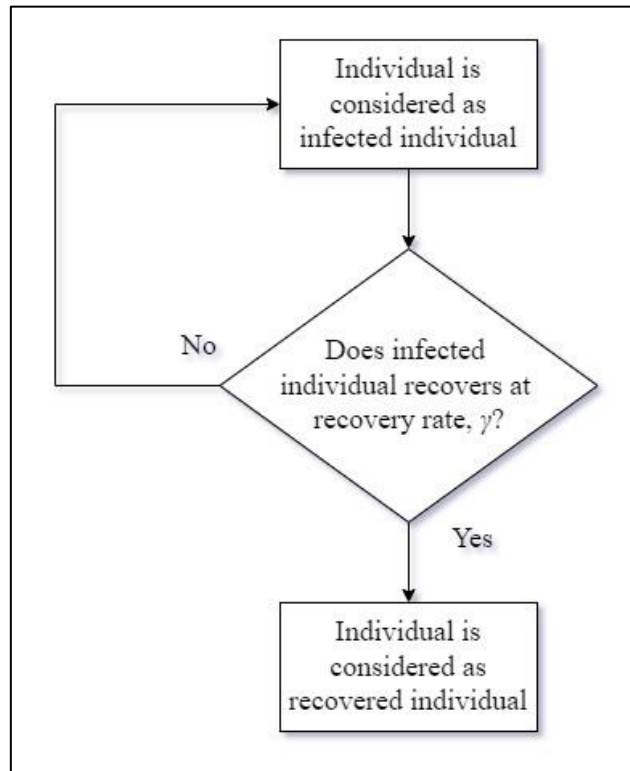


Figure 3.4: The Process of Disease State Transition from Infected Individual to Recovered Individual with the Recovery Rate, γ

Figure 3.4 shows the process of transition from the infected to the recovered status. Leptospirosis is a curable disease. The infected humans can typically recover from the disease infection if they undergo proper treatment and receive medicine. As a result, the infected people transit to become the recovered individual at a recovery rate of γ . However,

if the individuals do not reveal any signs of recovery from disease infection, then they remain in infectious stage.

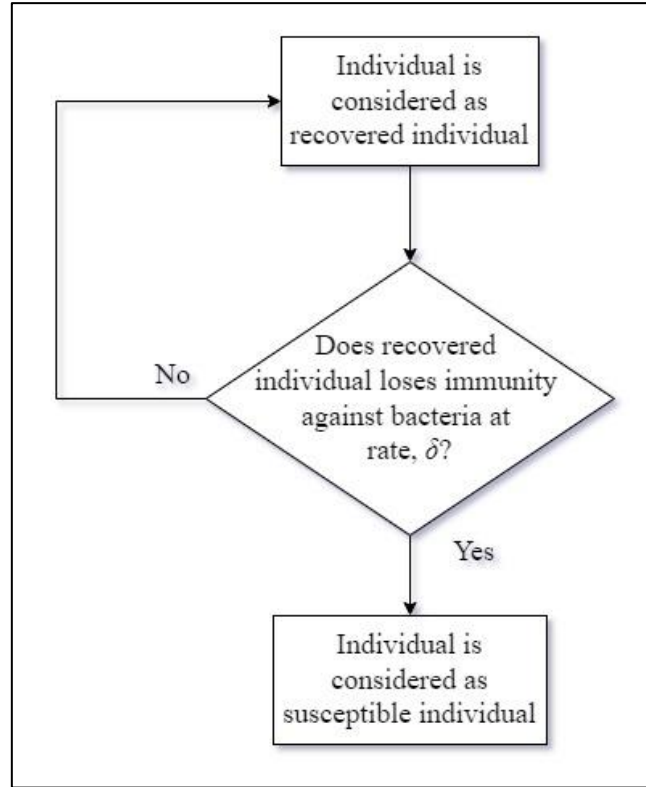


Figure 3.5: The Process of Disease State Transition from Recovered Individual to Susceptible Individual with the Immunity Loss Rate, δ

Figure 3.5 illustrates the process of transforming recovered individuals into susceptible individuals. In recent medical research and studies, there is no evidence to prove once an individual is infected with leptospirosis, the immunity to the disease is not lasting forever in the human body (Sembiring, 2018; Rees et al., 2022). Therefore, the recovered individual may become a susceptible individual again with an immunity loss rate of δ .

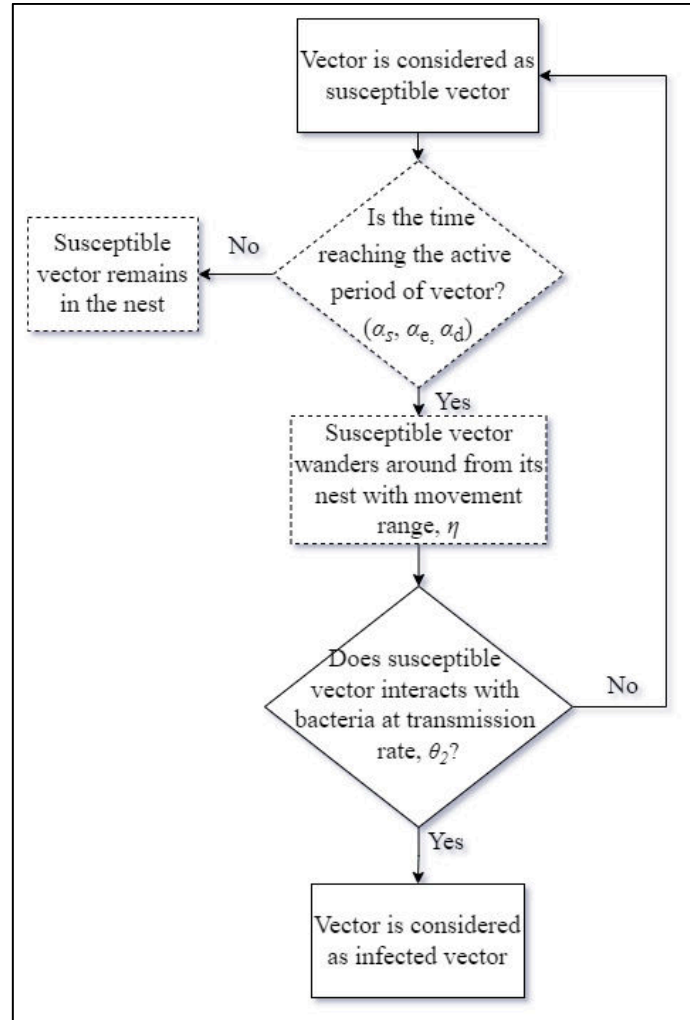


Figure 3.6: The Process of Disease State Transition from Susceptible Vector to Infected Vector with the Transmission Rate, θ_2

Figure 3.6 presents the transition from susceptible to infected status among the vector population. The presence of the active period naturally results in the susceptible vectors wandering around with a movement range of η during the moment. The rats are typically interacting with the bacteria or pathogenic *Leptospira* and become infectious when they are active at a transmission rate, θ_2 . However, if the susceptible vectors do not encounter such situations, then they remain in a similar status.

3.6 Summary

This chapter described the methodology and the formulation of the IBM for leptospirosis transmission. Before formulating the model, the humans and vector agents required assumptions to exhibit behaviours and act accordingly to the situation. Apart from the assumptions, the introduction of parameters showed the factors and conditions that affected the transmission of leptospirosis. Meanwhile, the proposal of the basic disease dynamic states enabled the agents to express more realistic situations in leptospirosis transmission. The subsequent chapter will describe the implementation of IBM in detail.

CHAPTER 4

MODEL IMPLEMENTATION

4.1 Outline

This chapter contains a few parts for applying the individual-based model (IBM). Section 4.2 describes the hardware configuration and utilised software for IBM implementation. The subsequent Section 4.3 describes the pseudocode and the user interface (UI) for the IBM simulation.

4.2 Software Utilised and Hardware Configuration

NetLogo (Wilensky, 1999) is open-source software that is applicable on many platforms such as Windows, Mac Operating System (OS), Linux, and UNIX. The program is favourable in 2D or 3D simulation for academic or research purposes. NetLogo accompanies many essential functions and libraries. Ultimately, it is simple to adequately understand (Abar et al., 2017). This project applies the NetLogo version 6.2.0 as it contains the extension “Time”, and this extension is only executable for versions 6.1 and above. Additionally, the IBM implementation accompanies a few components such as Windows 10, Intel® Core™ i3-8100 processor, 64-bit OS and 4GB of Random Access Memory (RAM).

4.3 NetLogo Application for IBM Implementation

The IBM implementation includes the disease transition states for humans as well as the vectors and the regulations that represent the assumptions based on Chapter 3. A file which is `Leptospirosis_transmission_simulation.nlogo` compromises all the regulations and parameters for IBM. These sets of regulations enable the agents to behave according to the assumptions of the model. For plotting the outcomes by using Microsoft Excel, the extraction

of the Comma Separated Values (CSV) files from NetLogo is important as these files contain the data of the IBM simulation.

4.3.1 Pseudocode of NetLogo Algorithm

The procedures of defining the regulations for the agents are important for IBM implementation. The descriptions of the procedures are in the form of pseudocode to highlight the required functions in the simulation. The pseudocode is given as follows with the figures that show the settings in `Leptospirosis_transmission_simulation.nlogo`:

Pseudocode for `Leptospirosis_transmission_simulation.nlogo`

1. Start
2. Define the initial conditions and behaviours for both populations
3. Define active period start time and active period end time of vector

```
create-humans initial-susceptible
[
  set color blue
  set shape "person"
  set size 1.5
  set infected? false
  set stationary? false
  set recovered? false
  setxy random-pxcor random-pycor
]

ask n-of initial-infected humans
[
  set color red
  set infected? true
  set stationary? false
]

ask n-of initial-recovered humans
[
  set color green
  set recovered? true
  set stationary? false
]
```

Figure 4.1: Settings of Initial Conditions and Assigning Behaviour to Human Agents

```

create-vectors initial-susceptible-rats
[
  set color orange
  set shape "rat"
  set size 0.5
  set infected? false
  set stationary? false
  set recovered? false
  set active? false
  setxy random-pxcor random-pycor
]

ask n-of initial-infected-rats vectors
[
  set color violet
  set infected? true
  set stationary? false
  set active? false
]

```

Figure 4.2: Settings of Initial Conditions and Assigning Behaviour to Human Agents

```

to setup-activeStart
  set time time:create activeStart
end

to setup-activeEnd
  set time time:create activeEnd
end

```

Figure 4.3: Settings of Active Period Durations of Vector Start Time and End Time

4. Define the regulations for the natural birth of the human population
5. Define the regulations for the natural death of susceptible, infected, and recovered humans
6. IF vectors are within an active period THEN
7. Define the regulations for the infection of susceptible humans with infected vectors are nearby
8. ENDIF
9. Define the regulations for the recovery of infected human
10. Define the regulations for the recovered human to become susceptible

```

to human-birth
  ask humans
  [
    .
    .
    .
  ]
end

```

Figure 4.4: Function of Setting Natural Birth for Human Population

```

to susceptible-human-death
  ask humans with [not infected? and not recovered?]
  [
    .
    .
    .
  ]
end

```

Figure 4.5: Function of Setting Natural Death for Susceptible Human

```

to infected-human-death
  ask humans with [infected?]
  [
    .
    .
    .
  ]
end

```

Figure 4.6: Function of Setting Natural Death for Infected Human

```

to recovered-human-death
  ask humans with [recovered?]
  [
    .
    .
    .
  ]
end

```

Figure 4.7: Function of Setting Natural Death for Recovered Human

```

to infect-human
  ask vectors with [infected?]
  [
    .
    .
    .
    ask humans in-radius vector_mov_range with [infected? = false]
    [
      .
      .
      .
    ]
  ]
end

```

Figure 4.8: Settings of Disease State Transition from Susceptible to Infected for Human Population

```

to recover
  ask humans with [infected?]
  [
    .
    .
    .
  ]
end

```

Figure 4.9: Settings of Disease State Transition from Infected to Recovered for Human Population

```

to re-susceptible
  ask humans with [recovered?]
  [
    .
    .
    .
  ]
end

```

Figure 4.10: Settings of Disease Transition State from Recovered to Susceptible for Human Population

11. Define the regulations for the natural birth of the vector population
12. Define the regulations for the natural death of susceptible and infected vectors
13. IF vectors are within an active period THEN
14. Define the regulations for the vector agents to wander
15. Define the regulations for the infection of the susceptible vector
16. ELSE
17. Define the regulations for the vector agents to be stationary at a place
18. ENDIF
19. Define the calculation of the active period durations
20. Stop

```
to vector-birth
  ask vectors
  [
    .
    .
    .
  ]
end
```

Figure 4.11: Function of Setting Natural Birth for Vector Population

```
to susceptible-vector-death
  ask vectors with [not infected?]
  [
    .
    .
    .
  ]
end
```

Figure 4.12: Function of Setting Natural Death for Susceptible Vector

```

to infected-vector-death
  ask vectors with [infected?]
  [
    .
    .
    .
  ]
end

```

Figure 4.13: Function of Setting Natural Death for Infected Vector

```

to vector-wander
  ask vectors
  [
    .
    .
    .
  ]
end

```

Figure 4.14: Function of Setting Vector Population to Wander During Active Period Durations

```

to infect-vector
  ask vectors
  [
    .
    .
    .
  ]
end

```

Figure 4.15: Function of Settings of Disease State Transition from Susceptible to Infected for Vector Population

```

to count-active-duration
  .
  .
  .
end

```

Figure 4.16: Function of Calculating the Active Period Durations of Vector

Figure 4.1 and Figure 4.2 shows the settings of initial conditions as well as assigning behaviours for the human and vectors to act according to the model assumptions. Next, Figure 4.3 is the settings of active period durations of the vectors with start time and end time. As for the natural birth and natural death of humans, the procedures are represented in Figure 4.4 to Figure 4.7. On the other hand, Figure 4.8 to Figure 4.10 are the transitions of susceptible, infected, and recovered states that show the infectious disease dynamics among the human population. From Figure 4.11 to Figure 4.13, the figures consist of the settings of natural birth and natural death for the vectors. From the model assumptions in Chapter 3, the transmission of leptospirosis occurs when the vectors are active and wandering from their nests during the active period. The functions that represent the movement of vectors and the transition from susceptible to the infected state of the vectors are shown in Figure 4.14 and Figure 4.15. Lastly, Figure 4.16 is the function to calculate the active period durations of the vectors.

4.3.2 NetLogo UI Design of the IBM Simulation

NetLogo offers a model environment that is user-friendly that can allow the user to perform a model simulation with the desired UI. By setting up the UI, the user can manipulate the initial conditions for the human and vector populations and the parameter values that are linked to the designed functions in the nlogo file. The changing of initial conditions and the values of the parameters allows the user to explore various kinds of situations and produce varying outputs. In addition, the user can setup the plots to illustrate the changes in population behaviours of the humans and vectors throughout the simulation. Figure 4.17 to Figure 4.22 show the UI design for IBM by using NetLogo.

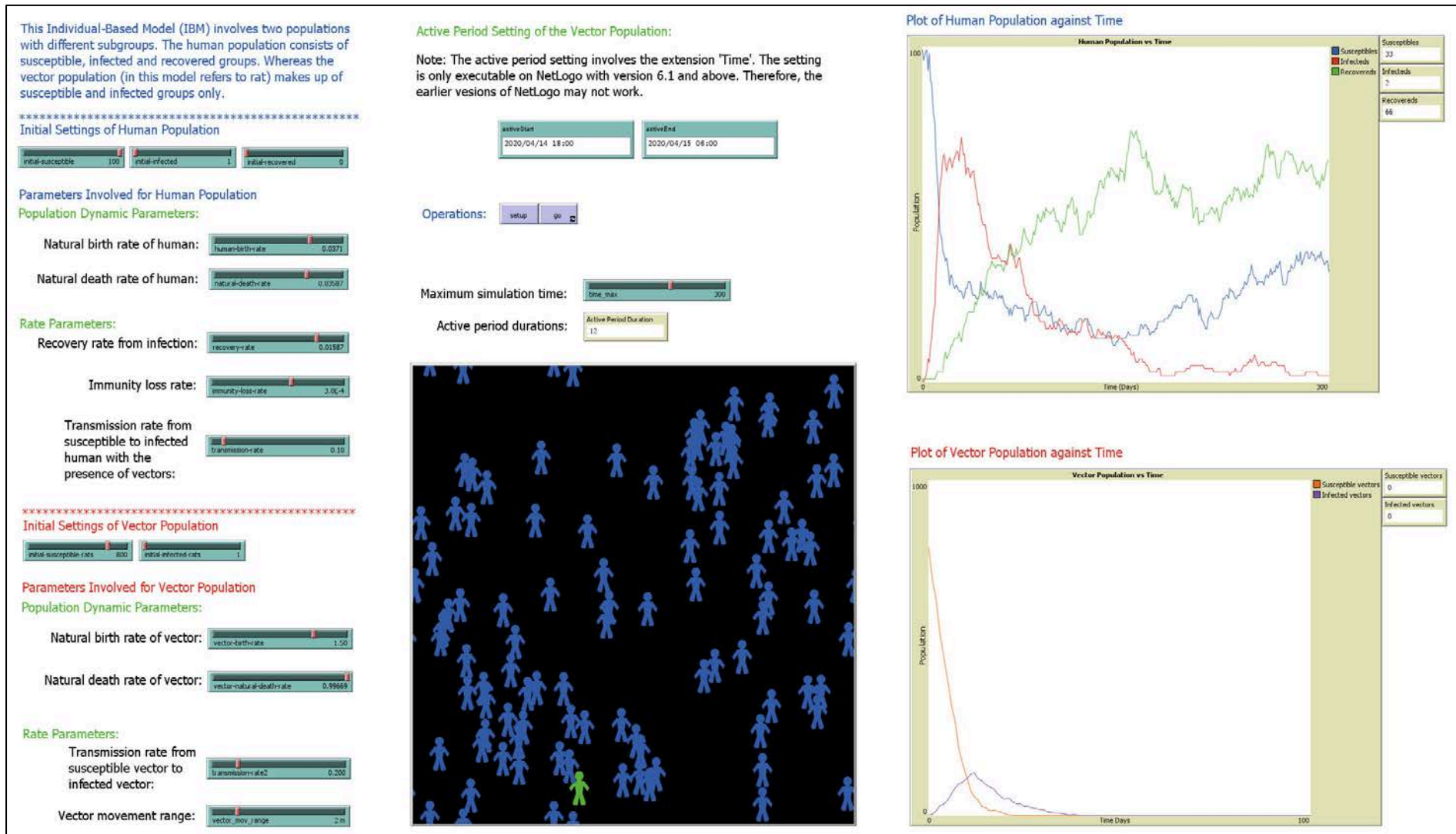


Figure 4.17: UI Design of the IBM by NetLogo

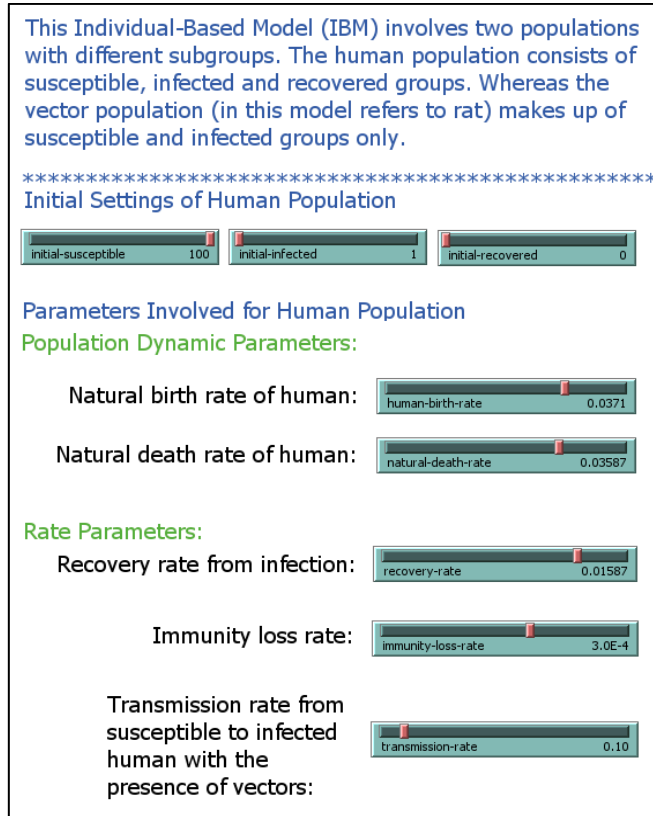


Figure 4.18: Model Descriptions, Initial Settings and Parameters of Human Population

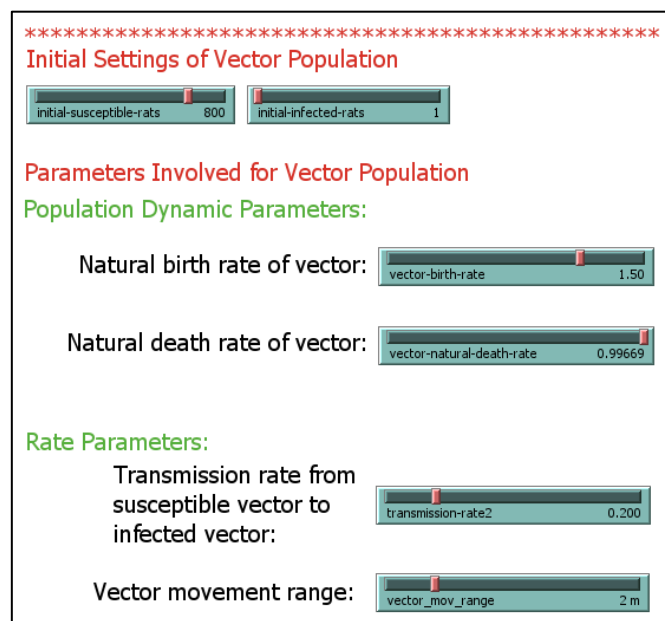


Figure 4.19: Initial Settings and Parameters of Vector Population

Active Period Setting of the Vector Population:

Note: The active period setting involves the extension 'Time'. The setting is only executable on NetLogo with version 6.1 and above. Therefore, the earlier vesions of NetLogo may not work.

activeStart
 2020/04/14 18:00

activeEnd
 2020/04/15 06:00

Operations: setup go

Maximum simulation time: time_max 300

Active period durations: Active Period Duration 12

Figure 4.20: Active Period Settings for Vector Population, Model Operations, Maximum Simulation Time and Monitor to Show Active Period Durations of the Vector

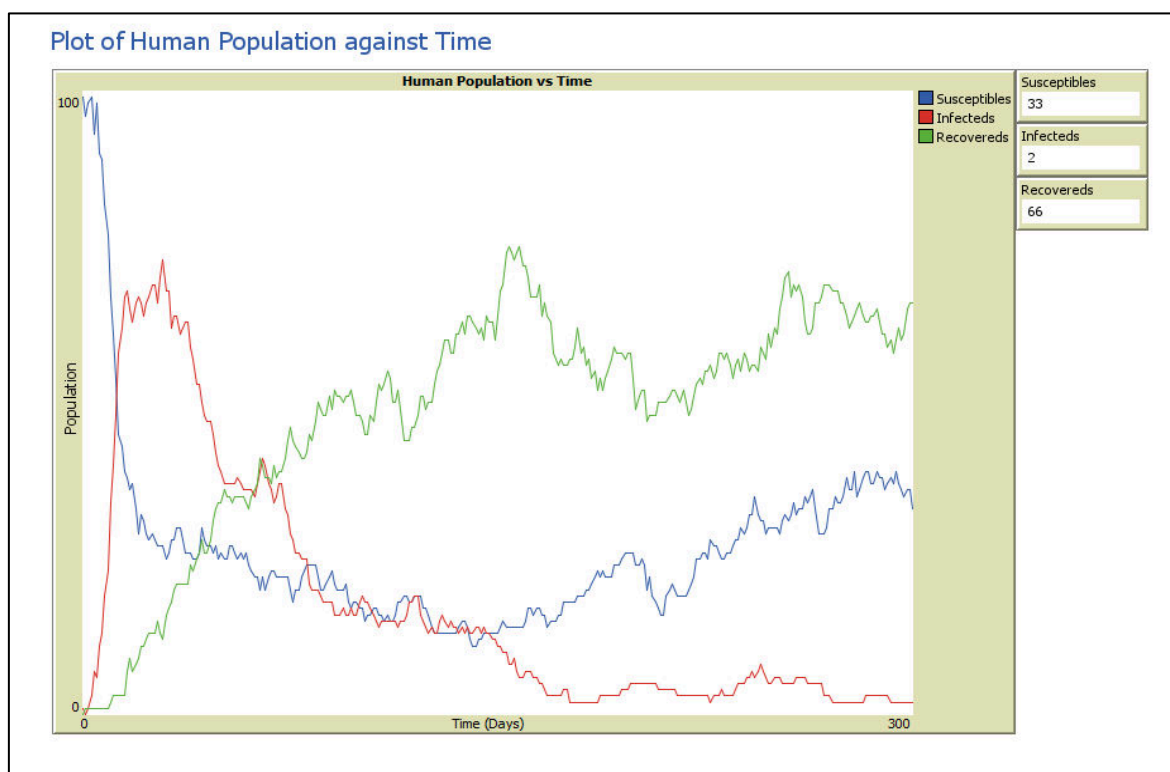


Figure 4.21: Human Population Plots

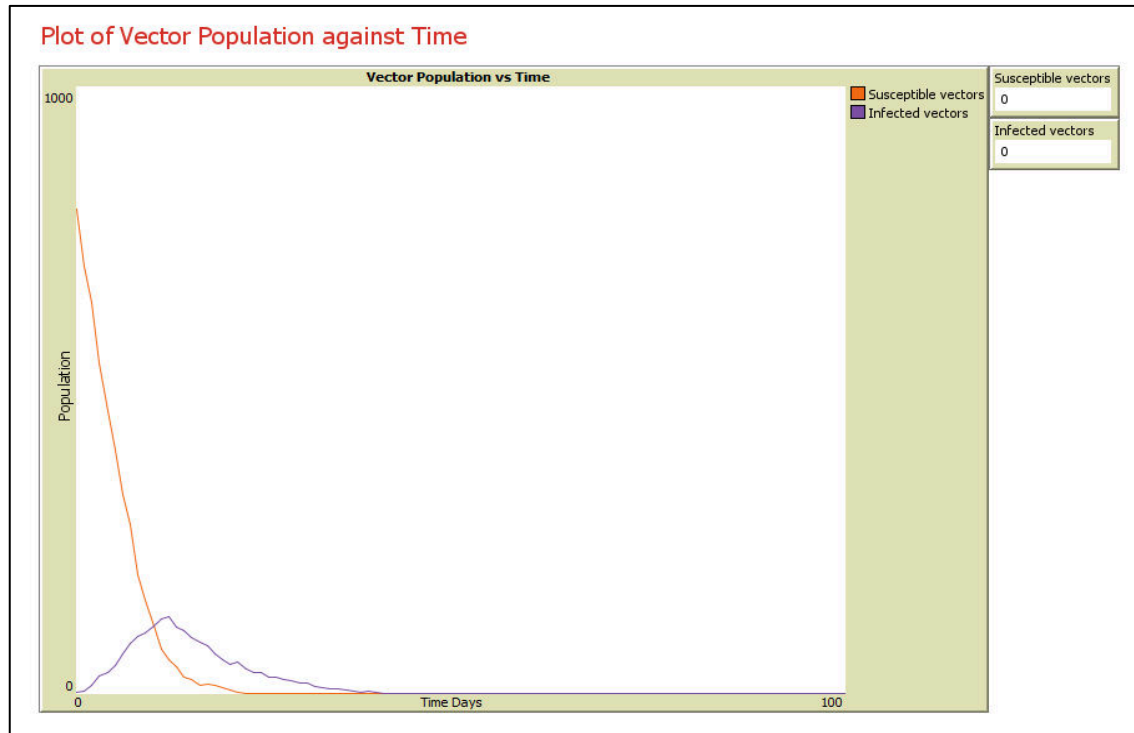


Figure 4.22: Vector Population Plots

Figure 4.17 shows the UI of the implementation of IBM, and it consists of several essential parts. The components are model description shown in Figure 4.18, initial values and parameters settings in Figure 4.18 and Figure 4.19 and set up of active period durations and simulation time including calculation of the length of durations in Figure 4.20. Additionally, the interface includes model operations, model environment, and plots. There are two plots; one plot is for the humans which is Figure 4.21 and another one is for the vector population of Figure 4.22. Before running the IBM simulation, the model requires the set-up of initial values and parameter values of the respective groups. In addition, the active period duration including the maximum simulation time of the model allows the agent to act within a period for the simulation process. After the completion of settings, the pressing of the “setup” button establishes the model environment. Figure 4.23 and Figure 4.24 shows all the outcomes after running the NetLogo.

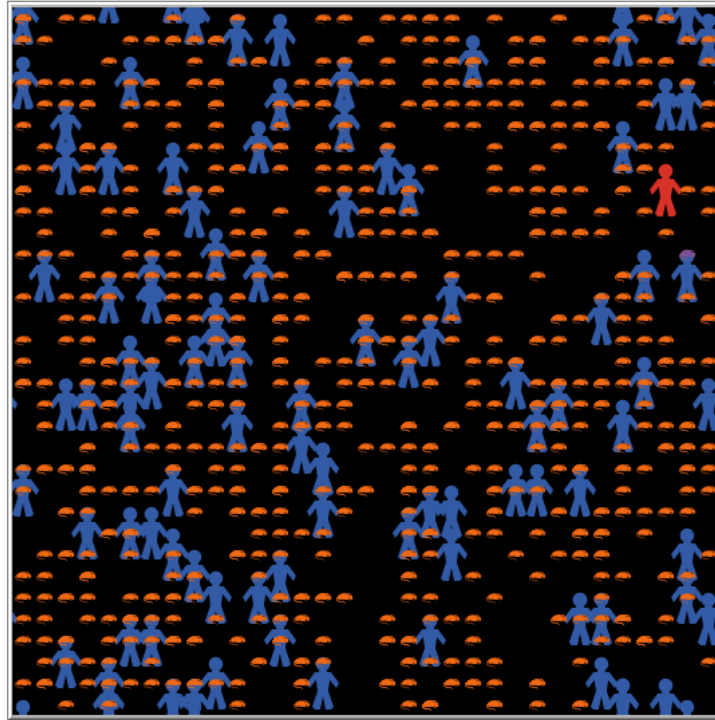


Figure 4.23: The NetLogo Environment when Setup the Model

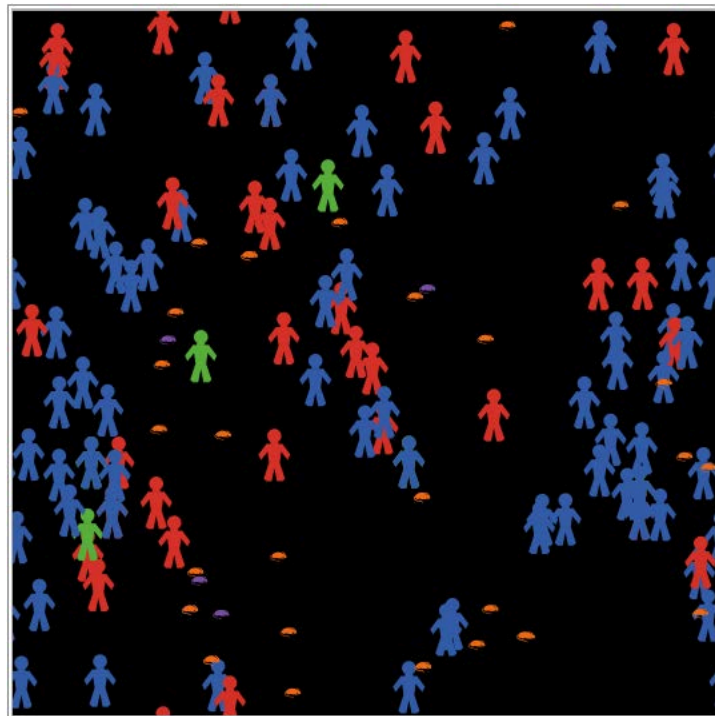


Figure 4.24: The NetLogo Environment when Running the Model Simulation

Figure 4.23 is the model environment that shows the setup agents when pressing the button “setup”. By pressing the button “go”, the simulation starts and the modeller can witness the interactions of the agents within the model environment which is shown in Figure 4.24. For discontinuation of the simulation, there are two ways. First is re-clicking the button “go” and the process will stop. The second way is by waiting for the model simulate until the maximum time that is being set at the UI. From both figures, the blue, red and green-coloured human-like agents represent the susceptible, infected, and recovered humans respectively. Whereas the orange and purple coloured rat-like agents are susceptible and infected vectors.

When performing model simulation, the changing colour of the agents indicates the disease state transition of the population. When the blue-coloured agent changes to red, it means that the susceptible human is infected with the presence of a purple rat-like agent which is the infected vector. For the agent that changes colour from red to green, it refers that the infected human is recovered. However, some green agents become blue implying that the recovered individual losses immunity and transits to a susceptible state. As for the orange agent that changes to purple, it means that the susceptible vector is infected. After running the model simulation, the results are shown in the plots which can be seen in Figure 4.21 and Figure 4.22. To further analyse the data, the process requires the exportation of the CSV files from the plots and uses Microsoft Excel to present all the data.

4.4 Summary

This chapter described the implementation of IBM by applying the NetLogo application in detail. NetLogo was an open-source software and accompanied lots of specific functions and libraries. Ultimately, this software was a wise choice for the IBM simulation as it was more comprehensible when it came to the implementation process. Like other programs, the creation of the pseudocode adequately served as the practical guidelines in the model development. In addition, the designed UI allowed the user to perform the simulation. The interface consisted of several specific sections such as model description including initial and parameter values settings. Apart from the values, the setting of active periods enabled the vectors to act within a duration. Lastly, the next chapter will describe the analysis and discussions of the simulation outcomes.

CHAPTER 5

RESULTS AND ANALYSIS

5.1 Outline

This chapter contains discussions of the individual-based model (IBM) simulation. Section 5.2 describes the model verification by comparing the results of IBM with the Susceptible-Infected-Recovered (SIR) model. Section 5.3 contains the descriptions and the calculation of the parameters. Meanwhile, Section 5.4 and Section 5.5 discusses the outcomes of the model simulation and the results of comparing with actual prevalence data. The subsequent Section 5.6 covers the effects of the parameters on the infected humans and vectors.

5.2 Verification of the Individual-based Model (IBM)

IBM is a stochastic model whereby the results are different for each execution. Due to the stochastic properties of IBM, the generated results lack clarity of continuous models and the simulation of IBM may turn into rambling easily (Ferrer et al., 2008). This situation will lead the simulated results to become difficult to be analysed and understand by the modeller (Ferrer et al., 2008). Therefore, the determination of the number of runs is important to overcome the stochasticity of the model. The coefficient of variation (C_v) is one of the methods that can determine the required number of simulations (Lorscheid et al., 2012). The formula for the coefficient of variation is the ratio of standard deviation to the mean (Hendricks & Robey, 1936) and is given by:

$$C_v = \frac{s}{\mu} \quad \text{Equation 5.1}$$

Based on Equation 5.1, s is the standard deviation and μ is the arithmetic mean. Table 5.1 shows the C_v for susceptible, infected, and recovered groups. The stopping criteria is the error tolerance, $\varepsilon = 0.01$. When the error tolerance, $\varepsilon < 0.01$, the iteration stops earlier.

Table 5.1: The Coefficient of Variation (C_v) for Each Group

n	C_v (Susceptible)	C_v (Infected)	C_v (Recovered)
5	1.16	0.68	0.94
10	1.05	0.56	1.04
15	1.01	0.56	0.93
20	0.96	0.55	0.88
25	0.96	0.55	0.88
30	0.96	0.55	0.88

Based on Table 5.1, the coefficient of variation for all three groups is identical with $n \geq 20$. As the coefficient of variation reaches equilibrium when $n \geq 20$, the following model simulations are performed with 20 runs decided. After deciding the number of simulations, the comparison between the population behaviours of the IBM and SIR is performed for verification purposes. Figure 5.1 displays the SIR results based on Witten and Poulter's (2007) work and the simulated IBM.

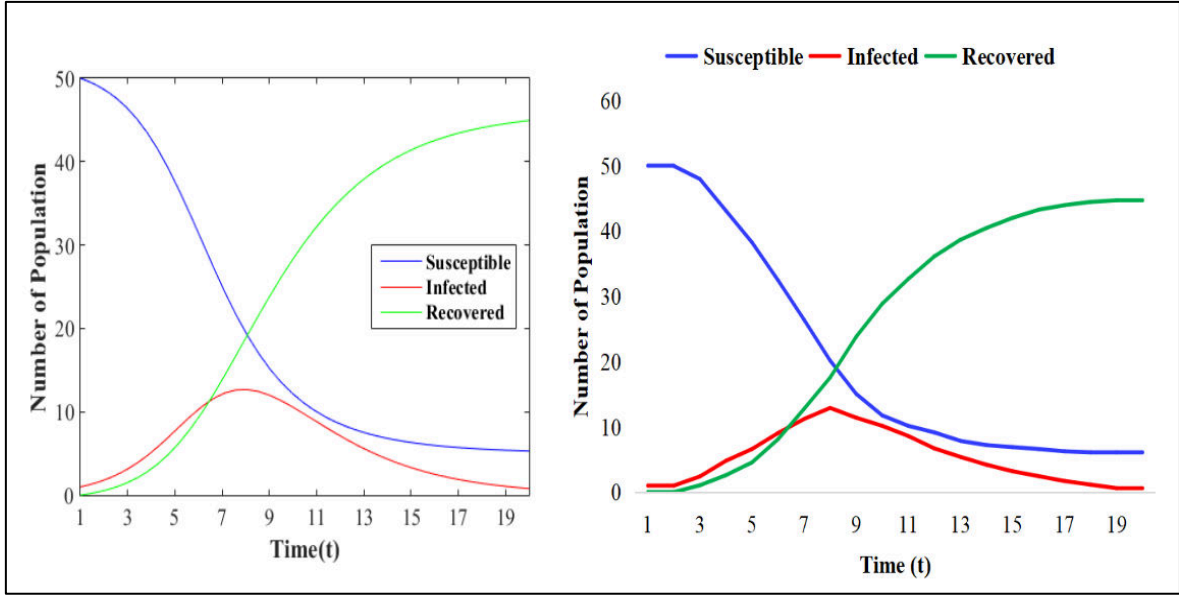


Figure 5.1: Generated SIR Model (Witten & Poulter, 2007) and IBM with Averaged 20 Simulations

For the model verification, the comparison between the IBM and SIR model is performed by using the initial conditions and the parameter values from Witten and Poulter (2007). The initial conditions for the respective groups in Figure 5.1 are $S_0 = 50$, $I_0 = 1$ and $R_0 = 0$. The values of the parameters for the model such as disease transmission rate, β is 0.02 and the recovery rate, γ is 0.4. Furthermore, the model simulation starts from $t = 1$ until $t = 20$. For both models, the susceptible group starts to decline from $t = 2$ and reaches to stable state at $t = 15$ with a number less than 10. As for the infected group, the number increases up to a peak at $t = 8$ and decreases until stable at $t = 17$. In addition, the recovered group rises and reaches equilibrium at $t = 18$. To summarise, the population behaviours for IBM show similar patterns for the three subgroups if compared with the SIR model. Apart from the patterns of population behaviours, the accuracy of IBM is checked by calculating the Mean Absolute Percentage Error (MAPE). Figure 5.2 is the comparison between SIR and IBM for finding MAPE.

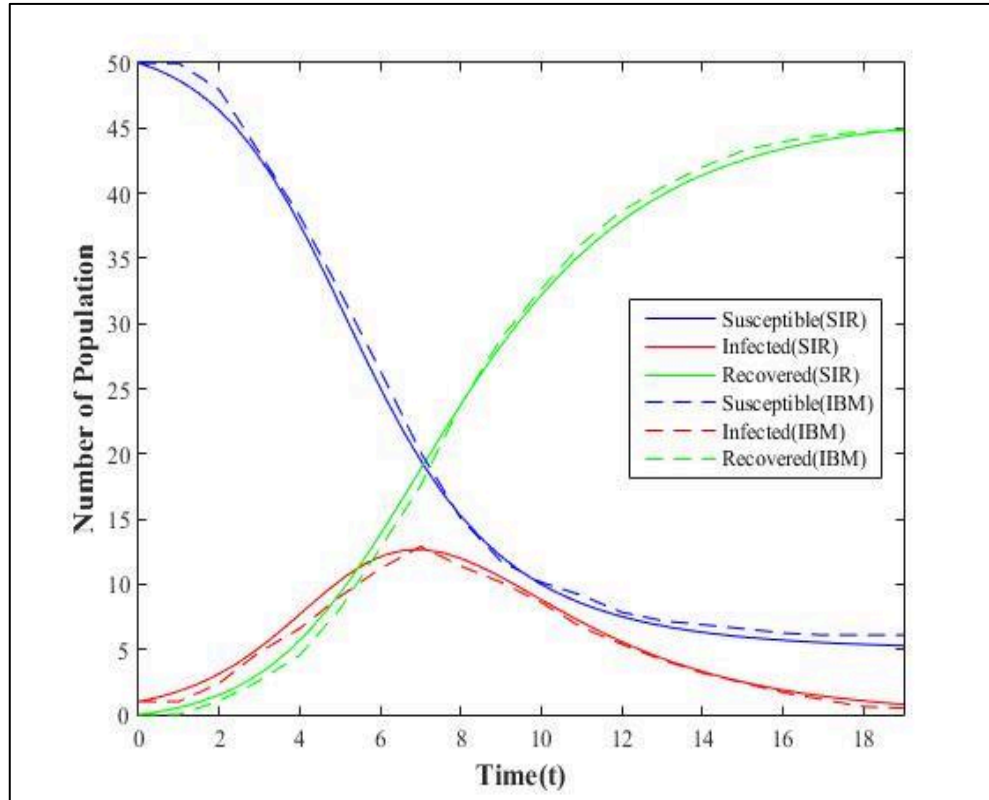


Figure 5.2: The Generated Behaviours of the Groups for SIR and IBM with An Average of 20 Simulations

From Figure 5.2, the overall MAPE of the comparison is 7.63%. Unfortunately, when it comes to MAPE for IBM verification, there is insufficient information to indicate whether 7.63% of MAPE is a good or bad result. More importantly, many researchers do not specifically describe the model verification process in their research such as Mahmood et al. (2020) and Alvarez Castro and Ford (2021). If there are researchers who describe the model verification in their studies, taking Alzu'bi et al. (2020) as an example, they only compare their IBM or ABM with the compartmental model in terms of the pattern of population behaviour instead of calculating errors for the comparison. In summary, the implementation of IBM can produce similar patterns of population behaviours to the SIR model by referring to Figure 5.1 with a MAPE of 7.63%.

5.3 Parameter Values

Before proceeding to simulations, it is significant to decide the values for each of the parameters in the model. This section covers some of the necessary calculations for the values and references for typically obtaining the related information.

5.3.1 Parameters for the Human Population

- i. The birth rate of the human population in days, μ_1

The per capita birth rate of the Sarawak population in 2017 is 13.6 (Department of Statistics Malaysia [DOSM], 2021). Therefore, the human birth rate in days is

$$\mu_1 = 13.6 \times \frac{1}{365} = 0.03726027397 \quad \text{Equation 5.2}$$

- ii. The mortality rate of the human population in days, λ_1

The life expectancy of the Sarawak population is 76.5 years (DOSM, 2019). So, the human mortality rate on daily basis is

$$\lambda_1 = \frac{1}{(365 \times 76.5)} \times 1000 = 0.03581341212 \quad \text{Equation 5.3}$$

- iii. The transmission rate from susceptible human to infected human, θ_1

A small transmission rate, θ_1 is unable to influence the disease outbreak in IBM simulation. Therefore, the parameter value for θ_1 is 0.10 based on past research (Bhalraj & Azmi, 2019).

- iv. The recovery rate from leptospirosis infection, γ

The time required for an infected individual to recover from leptospirosis takes 6 - 12 weeks (Izurieta et al., 2008). Therefore, the recovery rate is

$$\gamma = \frac{1}{\left(\frac{42 + 84}{2}\right)} = 0.01587301587 \quad \text{Equation 5.4}$$

- v. The immunity loss against leptospirosis, δ

The immunity against leptospirosis lasts not more than ten years in the human body (Leptospirosis Information Center, n.d.). The rate of immunity loss by taking nine years into the consideration is

$$\delta = \frac{1}{365 \times 9} = 0.000304414 \quad \text{Equation 5.5}$$

5.3.2 Parameters for the Vector Population

- i. The natural death rate of the vector population, λ_2

The lifespan of the rat is about 26 - 40 months (Frohlich, 2020). So, the natural death rate of the vector population is

$$\lambda_2 = \frac{1}{\left(365 \times \left(\frac{2.2 + 3.3}{2}\right)\right)} \times 1000 = 0.99626401 \quad \text{Equation 5.6}$$

- ii. Active periods start time, α_s and active period end time, α_e of the vector population

The rats are highly active at night as they are nocturnal animals (Hawkins & Golledge, 2017). Therefore, considering twelve hours dark cycle factor, the active period starting time of the rats, α_s is 18:00. Alternatively, the rats will become inactive when reaching the active period end time, $\alpha_e = 06:00$. Meanwhile, the active period duration, α_d of the vector population is the difference between α_s and α_e .

iii. Movement range η of the vector population

The necessary information regarding the movement range of the rats is significantly limited. However, there are specific studies indicating that Norway rats travelled with a movement range from 10 to 20 m (Tanaka & Kawashima, 1951). However, this species of vectors is not in consideration in this research. Therefore, the movement range η goes with 20 m under the implementation of using the in-radius function in NetLogo of scaling one represents 10 m.

5.3.3 Parameters List for Both Populations

Table 5.2 consists of the parameter values and descriptions. From the table, three parameters require value estimation as the information for these values is limited. These parameters are the vector birth rate, transmission rate from susceptible to infected vectors and the movement range of the vector. For estimating the parameter, the trial and error approach is a technique that can be applied to find the values. Although this approach is highly subjective, the approach is still widely favoured in industries including academics and research (Sin & Gernaey, 2016). Meanwhile, the trial and error approach is often used in practical with time constraint circumstances (Sin & Gernaey, 2016). More importantly, the usage of the trial and error approach has the advantage to allow the person to learn the background of the problem and find alternative options for the problem. This is supported by the literature whereby (Tönnsen, 2021) has concluded that the trial and error approach is not an insufficient technique. On the contrary, the approach can encourage the person to explore the problem by modifying the variables. In this way, the person can gain experiences and knowledge relating to the problem as well as be aware of feasible options that can affect the outcomes of the problem (Tönnsen, 2021).

Table 5.2: The Respective Parameter Values for Simulation of IBM

Notation	Value	Description	Remark
μ_1	0.03726	the birth rate of the Sarawak human population in days corresponds to 13.6 per capita birth	DOSM (2021)
λ_1	0.03581	the natural mortality rate of the Sarawak human population in days corresponds to 76.5 years of life expectancy for Sarawakian	DOSM (2019)
ϑ_1	0.10	transmission rate from susceptible human to infected human with the presence of infected vector	Bhalraj and Azmi (2019)
γ	0.01587	recovery rate in days corresponds to 6 - 12 weeks for recovering from leptospirosis infection	Izurieta et al. (2008)
δ	0.00030	the rate of immunity loss against leptospirosis in days for 9 years (immunity lasts not more than 10 years)	Leptospirosis Information Center (n.d.)
μ_2	1.10	per capita birth rate of vector population in days	Assumed
λ_2	0.99626	the natural death rate of the vector population in days corresponds to 26 - 40 months of the lifespan of the vectors	Frohlich (2020)
ϑ_2	0.20	transmission rate from susceptible vector to infected vector	Assumed

Table 5.2 continued

α_s	18:00	active periods start time of vector population	Hawkins and Golledge (2017)
α_e	06:00	active periods end time of vector population	Hawkins and Golledge (2017)
α_d	12	active periods duration of the vector population	Difference between α_s and α_e
η	20	the movement range of the vector population	Assumed

5.4 Simulation of IBM

After considering the values for the parameters, the subsequent task is to decide the initial conditions for each subgroup of the population.

5.4.1 Simulation Results for Human Population

The total population of Sarawak in 2017 is 2770000 (DOSM, 2021). However, NetLogo cannot afford to conduct the model simulation with a significantly massive scale of numbers of agents. The leptospirosis cases reported during 2017 did not exceed 50 cases throughout the 52 epidemiological weeks. Therefore, the initial number for the susceptible human is 100. As for the infected and recovered individuals, the initial values are set as one and zero respectively. Figure 5.3 to Figure 5.8 illustrate the population behaviour of each group of the human population.

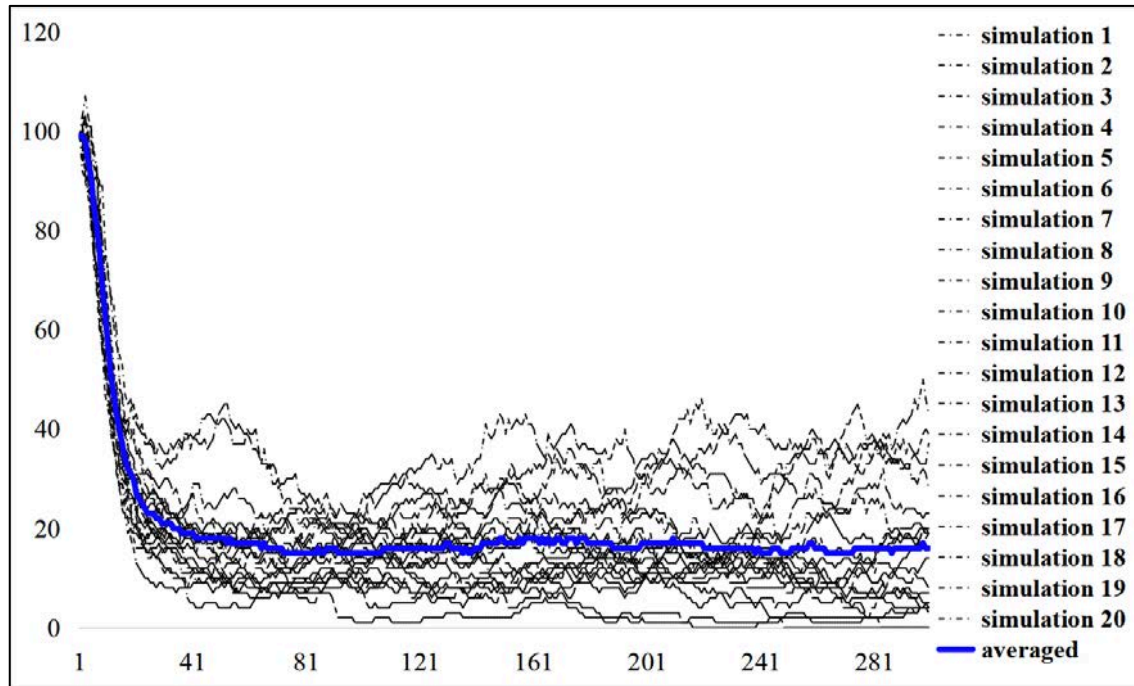


Figure 5.3: Simulation Results of Susceptible Human for 300 Days

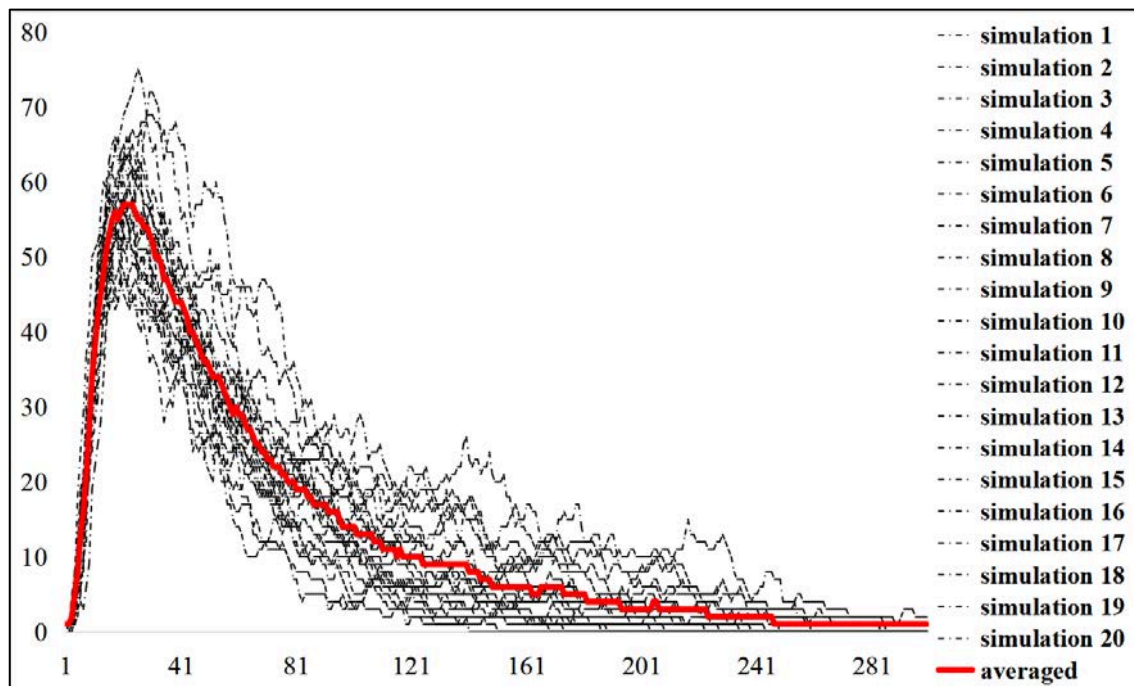


Figure 5.4: Simulation Results of Infected Human for 300 Days

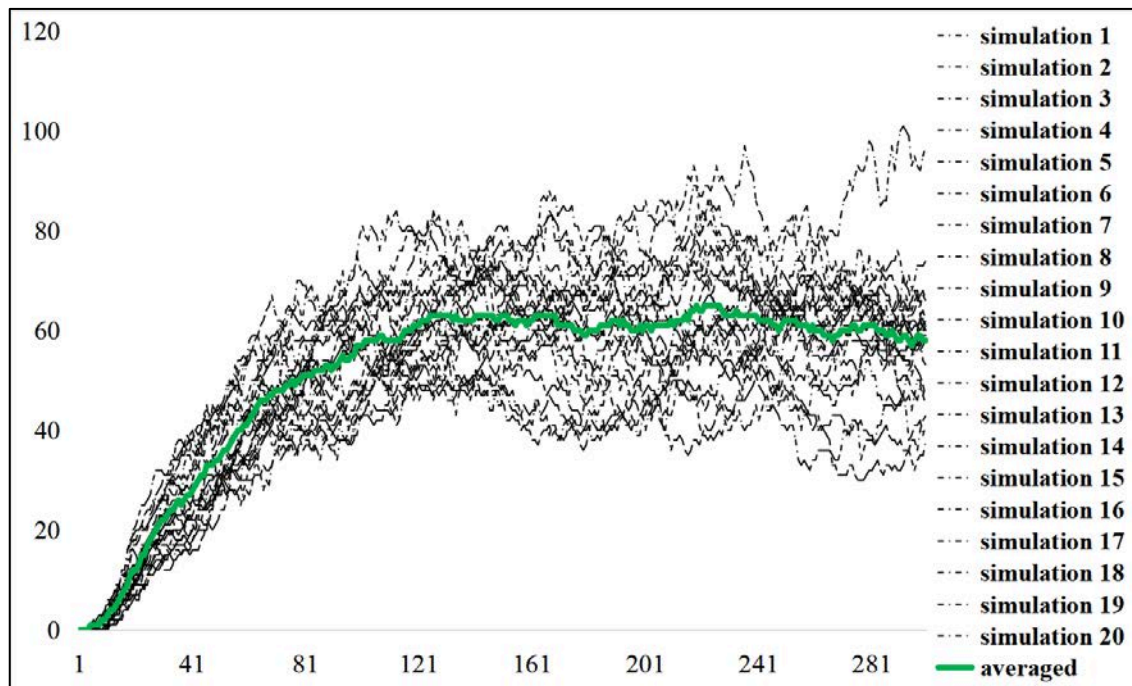


Figure 5.5: Simulation Results of Recovered Human for 300 Days

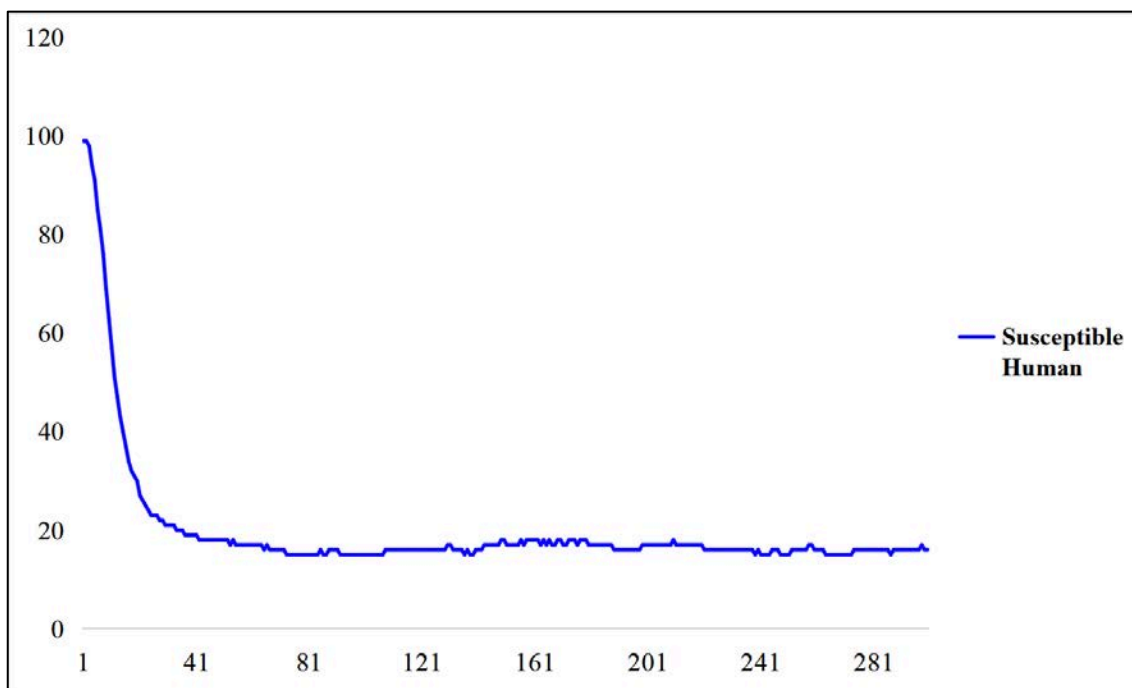


Figure 5.6: The Averaged Population Behaviours of Susceptible Human for 300 Days

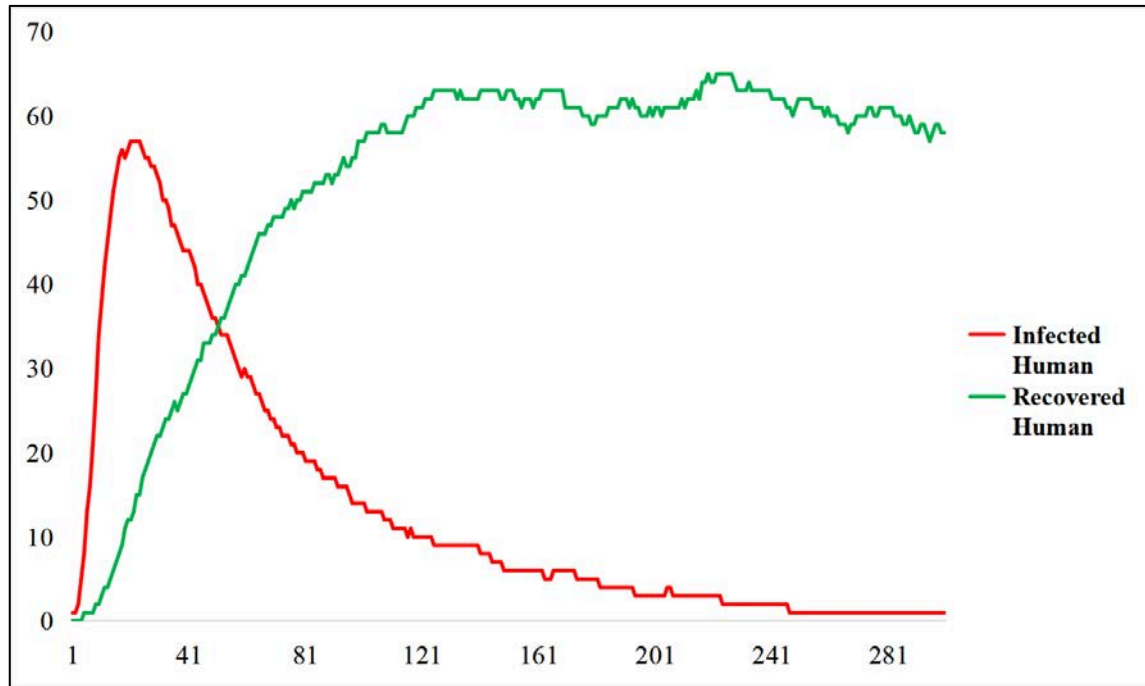


Figure 5.7: The Averaged Population Behaviours of Infected and Recovered Humans for 300 Days

Figures 5.3 to Figure 5.5 show the simulation results for susceptible, infected, and recovered humans for 300 days. These practical results exhibit the changes in the numbers of each subgroup by acquiring the 20 times simulations. As for Figures 5.6 and 5.7, the plots represent the population behaviours for all three human subgroups with averaged simulations of 20 runs. From all the figures, the results indicate the susceptible humans decrease initially and are followed by an equilibrium stage. As for the infected individuals, the numbers escalate from the beginning and reach a steady state after a gradual decline. For the recovered humans, the population trend is different from the other two subgroups as the numbers increase to a peak and remain stable as time increases.

5.4.2 Simulation Results for Vector Population

There are no specific data to accurately represent the numbers of actual vector populations locally. Therefore, the setting of the initial condition for the susceptible vector group includes the consideration of one person living associatively with eight rats (Garba et al., 2017). If the susceptible human typically consists of 100 individuals, then there will be a total of 800 for the susceptible vector. As for the infected subgroup, there is one rat to be naturally infected at first. Figure 5.8 to Figure 5.11 show the respective changes in population behaviours of the vectors.

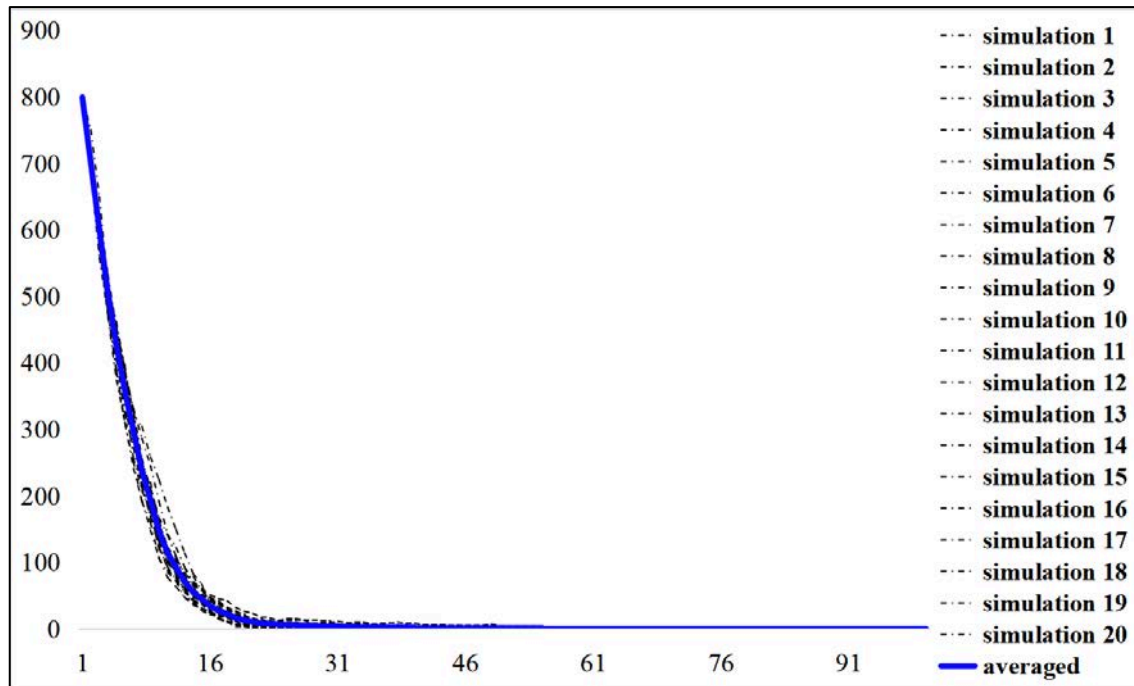


Figure 5.8: Simulation Results of Susceptible Vector for 100 Days

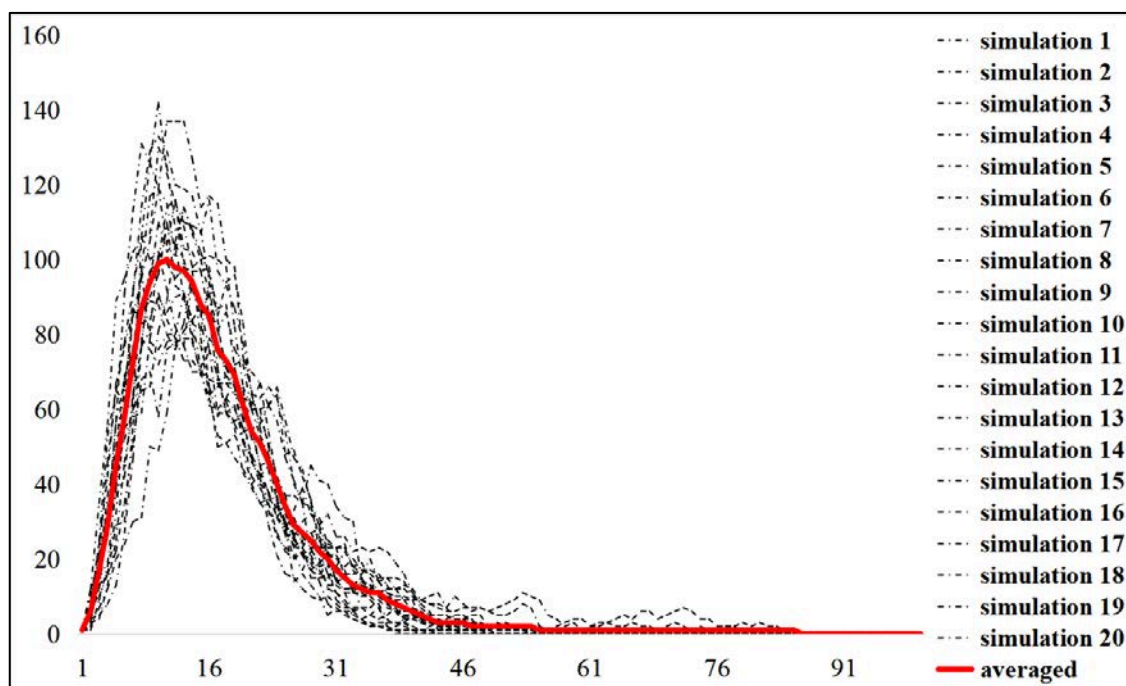


Figure 5.9: Simulation Results of Infected Vector for 100 Days

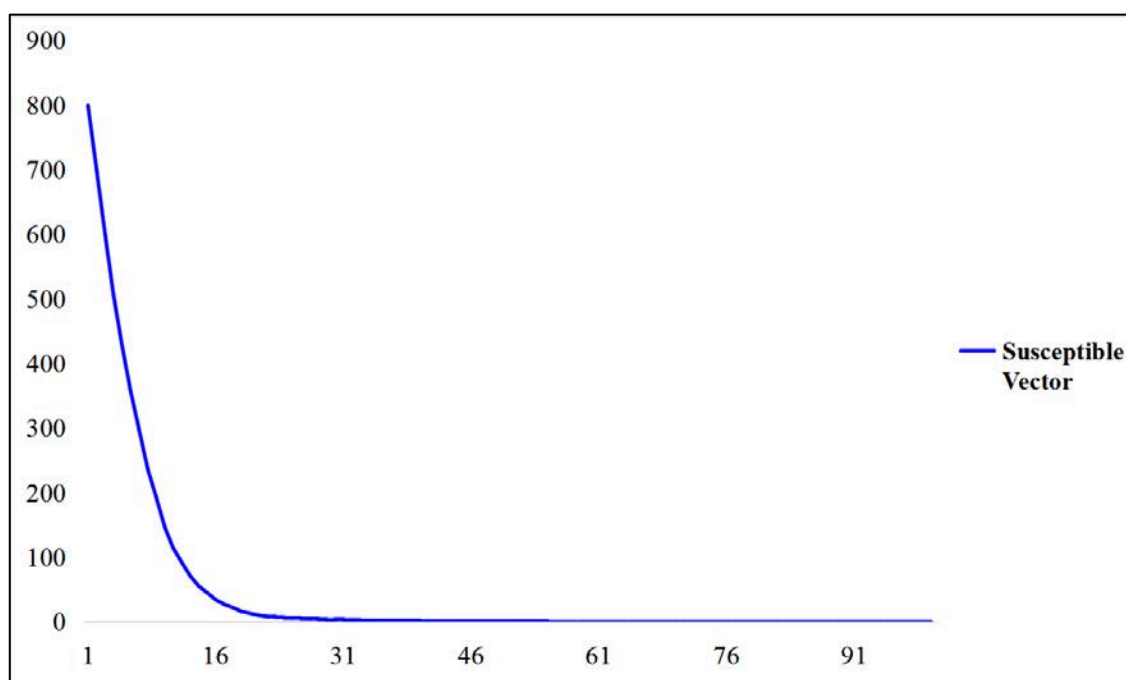


Figure 5.10: The Averaged Population Behaviours of Susceptible Vector for 100 Days

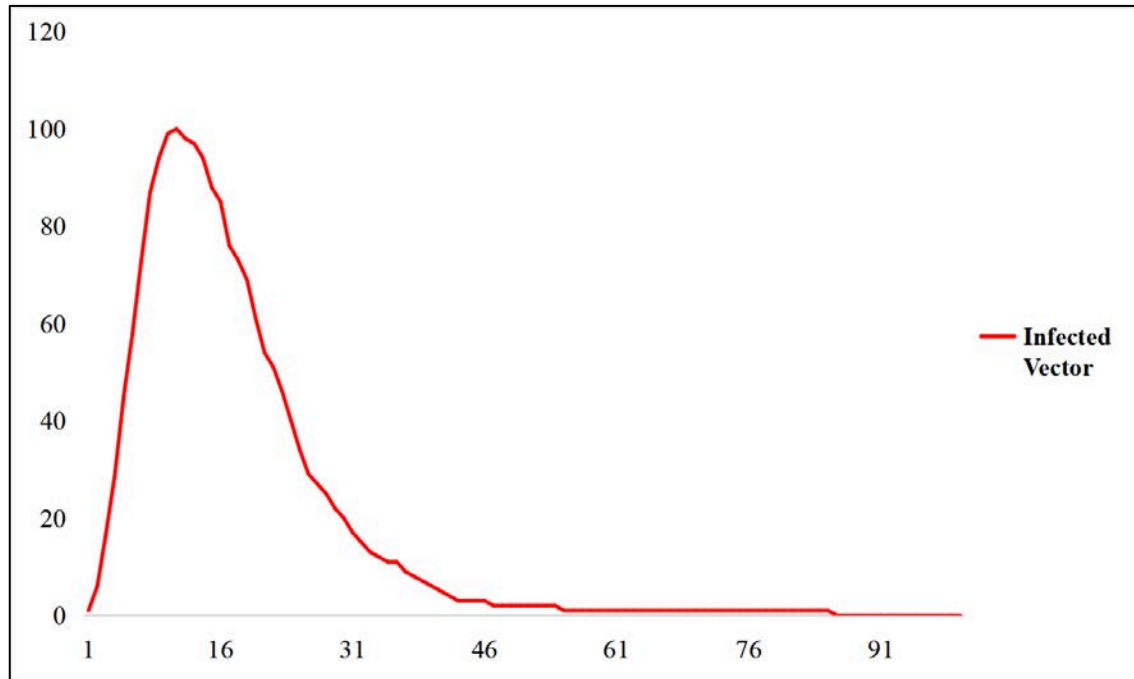


Figure 5.11: The Averaged Population Behaviours of Infected Vector for 100 Days

Figure 5.8 and Figure 5.9 display the changes in the number of susceptible and infected vectors respectively for one hundred days. Figure 5.10 and Figure 5.11 represent the trends for both subgroups in the rat population with the averaged results. The number of susceptible vectors decreases throughout the model simulation. Meanwhile, the infected vector group increases initially and decreases after reaching the peak. As the rats die naturally, therefore both groups end up at zero or closely to zero.

5.5 IBM Validation with the Actual Prevalence Data

The validation phase is significant as the process is to compare the simulated results with the actual prevalence data. The raw data from MOH contains only the number of cases for each epidemiological week. Therefore, it is necessary to process the information by transforming the raw data into actual prevalence data. Figure 5.12 represents the leptospirosis raw data obtained from MOH whereas Figure 5.13 shows the processed actual

prevalence data of the leptospirosis confirmed cases. For the transformation of the prevalence data, the required formulae the transformation are as follows:

- i. For epidemiological week two to week eight:

$$Prevalence = Confirmed\ Cases_i + Confirmed\ Cases_j \quad \text{Equation 5.7}$$

- ii. By considering the nine-week recovery period, from week nine and onwards:

$$Prevalence = Confirmed\ Cases_i + Confirmed\ Cases_j - Recovered\ Cases \quad \text{Equation 5.8}$$

i refers to the number of confirmed cases for the current week and j is the number of confirmed cases for the previous week. Meanwhile, the number of recovered cases starts to be included from epidemiological week one when transforming the prevalence data from week nine and onwards.

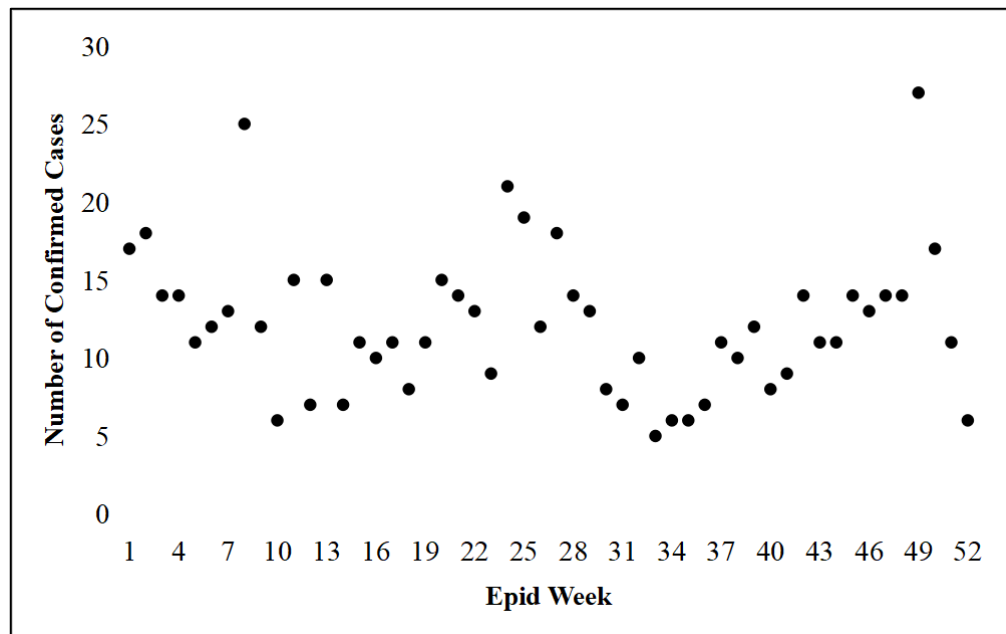


Figure 5.12: The Raw Data of Leptospirosis Confirmed Cases (MOH, 2018)

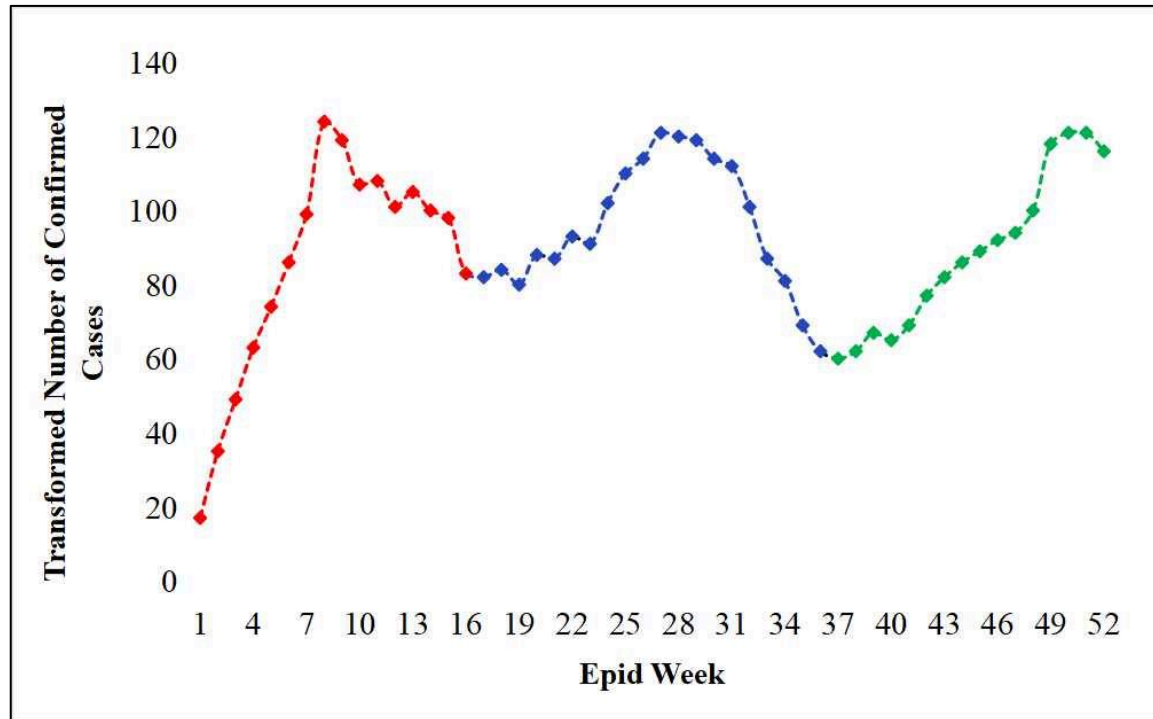


Figure 5.13: The Actual Prevalence Data of Leptospirosis Confirmed Cases

As mentioned in the previous section, the NetLogo is better in running simulations with a minor scale of population. By referring to the prevalence data, the number of leptospirosis cases throughout the 52 weeks is not exceeding 200 for every epidemiological week. Therefore, the initial condition for the susceptible human is set as 200. Figure 5.13 visualises there are three waves of leptospirosis outbreaks. The first wave starts from week one to week sixteen, the second outbreak is from week seventeen to week thirty-six whereas the third wave begins at week thirty-seven and continues to week fifty-two. For the IBM simulations, the initial values of the infected humans for the three outbreaks are 17, 82 and 60 respectively. For the recovered subgroup, the initial condition is zero. Apart from the initial conditions, the parameter values require changes to be calculated on weekly basis.

For the validation phase, the trend analysis can examine the patterns of data over time to show the trend in the data (Chao et al., 2018). To analyse the trend of the data, the evaluation metric of coefficient of determination or r^2 can be a choice for the trend analysis (Chicco et al., 2021) as the tools for analysing the trend of data for trend analysis are the same as regression analysis (Chandler & Scott, 2011). Furthermore, r^2 is the most suitable technique to evaluate regression in any scientific area if compared to other performance metrics (Chicco et al., 2021). Therefore, for the IBM validation, the trend analysis is performed to examine the trends of the simulated data and the actual prevalence data. Meanwhile, r^2 is chosen to analyse the trends of both data.

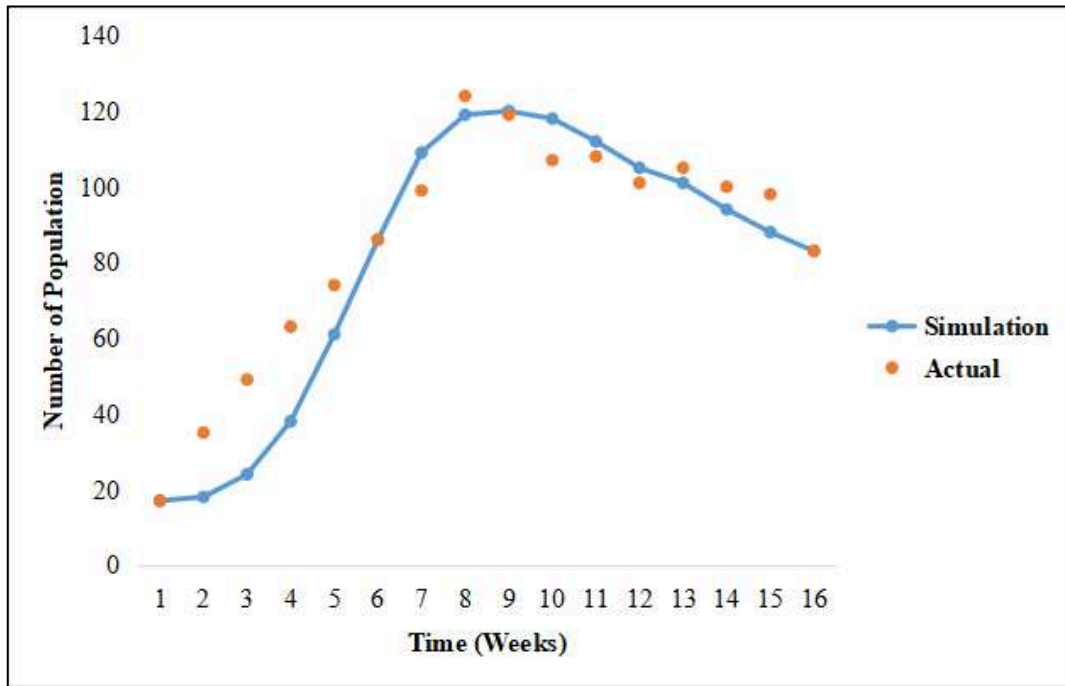


Figure 5.14: The Comparison from Epid Week 1 to Epid Week 16 with $\mu_v = 7.15$, $\theta_v = 0.35$, $\alpha_d = 12$ hours, $\eta = 22$ m

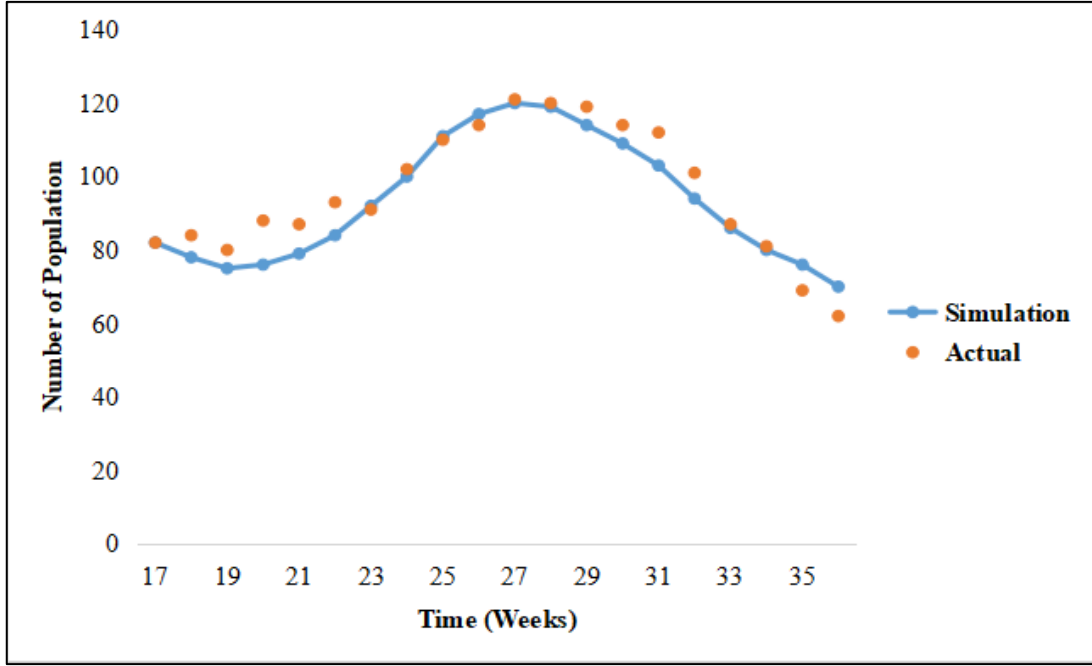


Figure 5.15: The Comparison from Epid Week 17 to Epid Week 36 with $\mu_v = 7.15$, $\theta_v = 0.35$, $\alpha_d = 12$ hours, $\eta = 19$ m

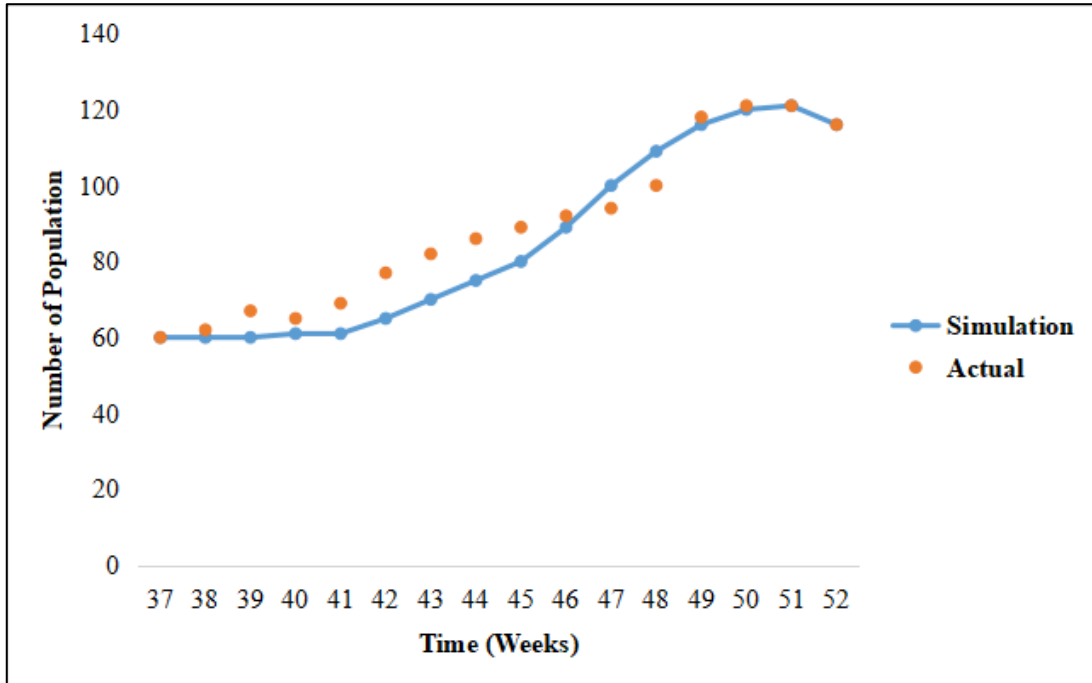


Figure 5.16: The Comparison from Epid Week 37 to Epid Week 52 with $\mu_v = 7.15$, $\theta_v = 0.35$, $\alpha_d = 12$ hours, $\eta = 16$ m

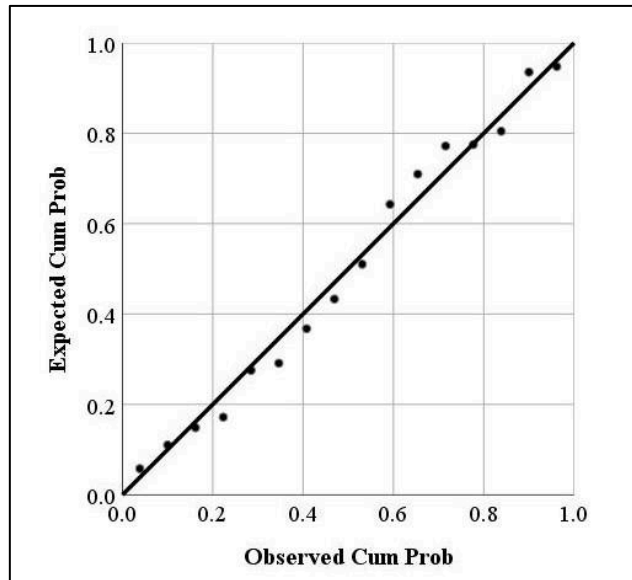


Figure 5.17: Normal Probability Plot of the Data Comparison from Epid Week 1 to Epid Week 16

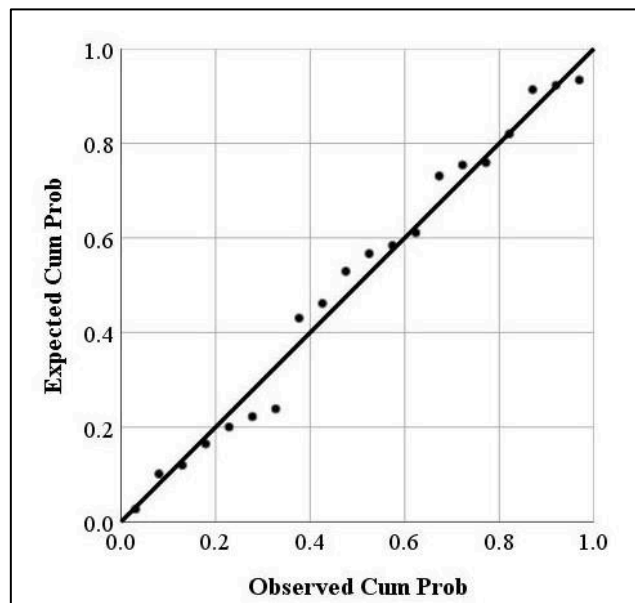


Figure 5.18: Normal Probability Plot of the Data Comparison from Epid Week 17 to Epid Week 36

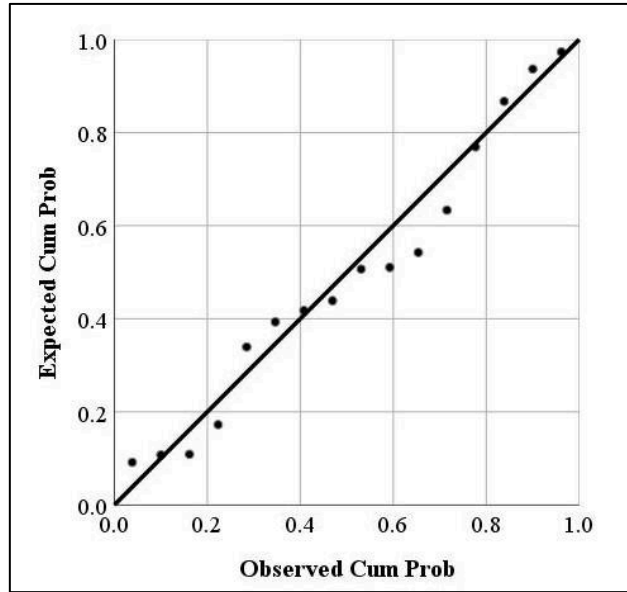


Figure 5.19: Normal Probability Plot of the Data Comparison from Epid Week 37 to Epid Week 52

Figure 5.14, Figure 5.15, and Figure 5.16 represent the comparison between the simulation results using IBM with the actual prevalence data of each outbreak in Sarawak for the year 2017. The r -squares (r^2) or the correlations of determination for the three outbreaks are 96.08%, 91.01% and 94.68% respectively. Fundamentally, if the r^2 approaches 100%, it indicates the simulated results closely fit the actual data and the model has a nearly perfect prediction (Chicco et al., 2021). Apart from r^2 , the residuals have to follow a normal distribution to produce unbiased estimations and indicate the model is fitted well with the data (Frost, 2020). To check the normality of the residuals, the easiest way is to assess a normal probability plot (Frost, 2020). For a normal probability plot that indicates the results show a normal distribution, the residuals follow a straight line (Frost, 2020). Furthermore, the residuals in the lower and upper quartiles are not deviated significantly from the straight line to show that there are no significant outliers and imply the residuals are relative to a normal distribution (Frost, 2020).

Figure 5.17, Figure 5.18, and Figure 5.19 are normal probability plots to show the normality of the residuals. Through observations from the three figures, the plots indicate the residuals follow the straight line and there are no significant outliers in the lower and upper quartiles. Therefore, the three probability plots imply the residuals are normally distributed. Ultimately, the combination of results showing high r^2 with more than 90% and residuals with normal distribution for the three respective outbreaks deduce that the IBM is adequate to model the leptospirosis transmission in Sarawak. In addition, the r^2 found by using IBM is better than the r^2 by the compartmental model. As compared to the r^2 obtained by Chong et al. (2022) which are 87.40%, 36.09% and 76.06% through the compartmental model, the r^2 found by IBM is more than 90% for the three outbreaks after concerning the behaviour of the vectors in the simulations. Meanwhile, from our validation which is shown in Figure 5.14 to Figure 5.19, the vector movement range in Sarawak is between 16m to 22m as these values produce the best results in trend analysis. This is important as it can be a suggestion for public health officers to monitor and prevent leptospirosis transmission through vector control.

Figure 5.13 shows there are three leptospirosis outbreaks. Currently, there is no available novelty or fact sheets to describe that there are three leptospirosis outbreaks within a year in Sarawak. However, there is literature or research to show that the causes of leptospirosis outbreaks are due to climate (Chadsuthi et al., 2021) or monsoon seasons (Kira et al., 2021). Chadsuthi et al. (2021) have mentioned that the regions that are frequently accompanied by flooding result in a higher number of individuals suffering from leptospirosis. In addition, Kira et al. (2021) have described that increasing annual rainfall or precipitation and water vapour pressure during the monsoon season contribute to more leptospirosis cases occurring in Sarawak. To investigate the relationship between the

occurrence of three leptospirosis outbreaks with monsoon seasons in Sarawak, the Pearson correlation analysis is a suitable technique to apply as it can measure the relationship between the two constructs (Coakes, 2005).

Sarawak has two monsoon seasons, the northeast monsoon, and the southwest monsoon. The northeast monsoon starts from November to March whereas the southwest monsoon begins from May until September (Sa'adi et al., 2017). As precipitation is a climate factor during monsoon seasons, the information on the precipitation in Sarawak, which can assist in finding the correlation can be obtained from the Weather and Climate website (Weather and Climate, n.d.). Figure 5.20, Figure 5.21 and Figure 5.22 are the plotted graphs for the number of weekly leptospirosis cases and weekly precipitation based on the three waves of outbreaks in Sarawak. Meanwhile, Table 5.3, Table 5.4 and Table 5.5 are the correlation matrices for the leptospirosis cases and precipitation in Sarawak.

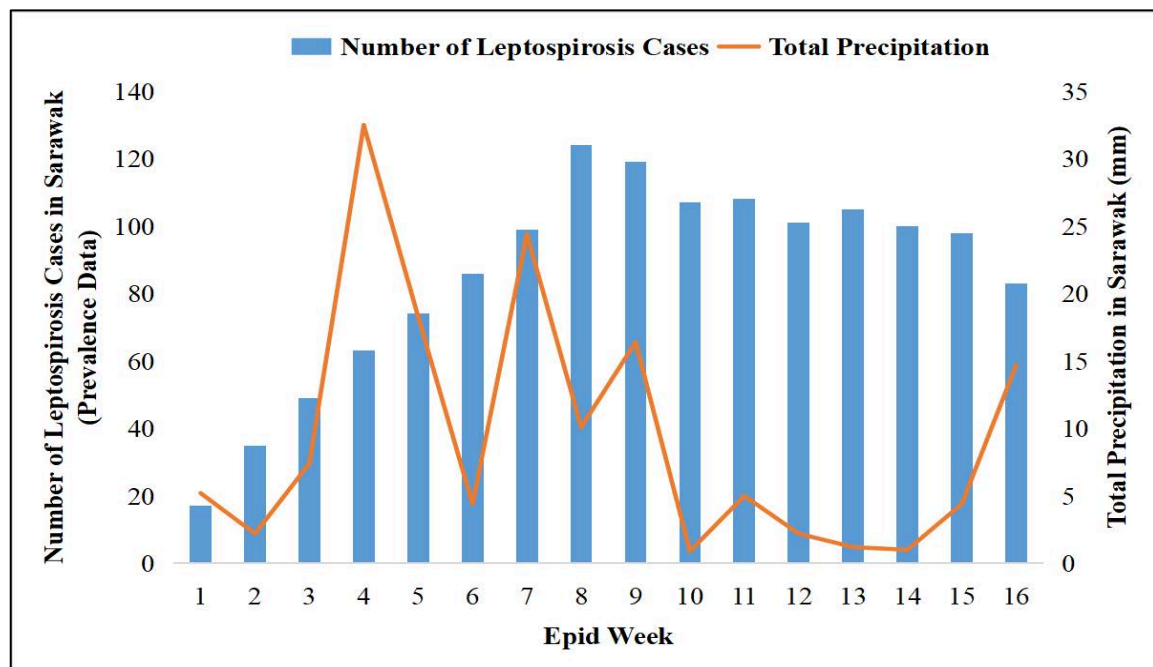


Figure 5.20: Weekly Leptospirosis Cases and Weekly Precipitation in Millimeter (mm) in Sarawak (Week 1 to Week 16)

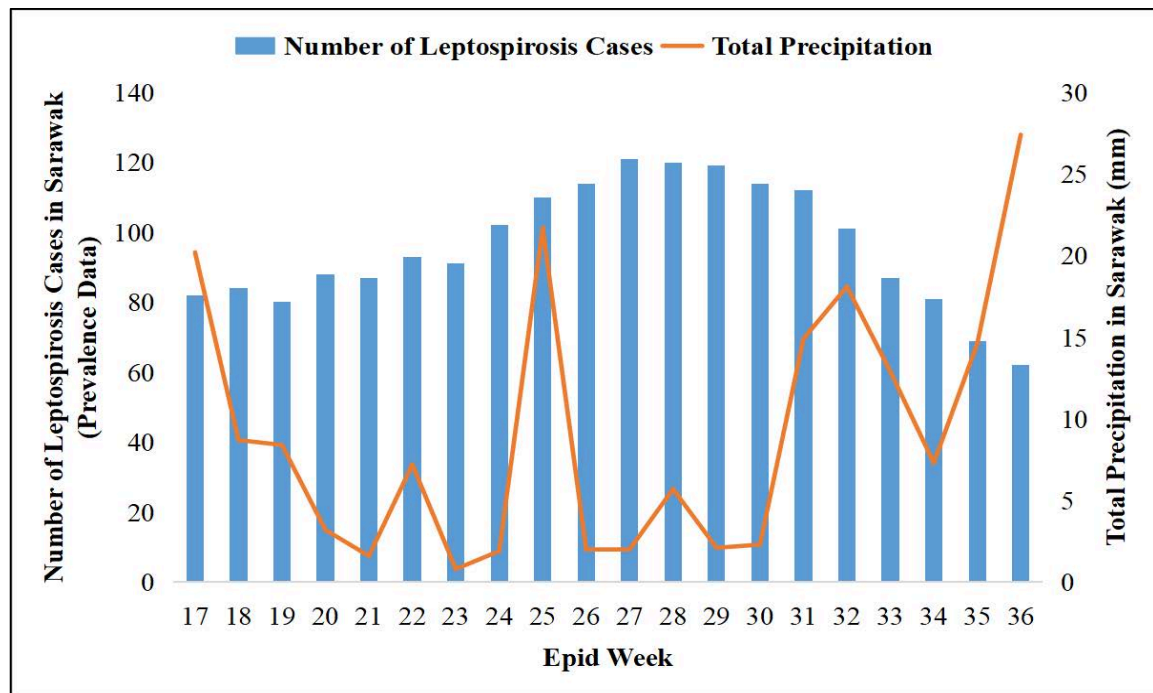


Figure 5.21: Weekly Leptospirosis Cases and Weekly Precipitation in Millimeter (mm) in Sarawak (Week 17 to Week 36)

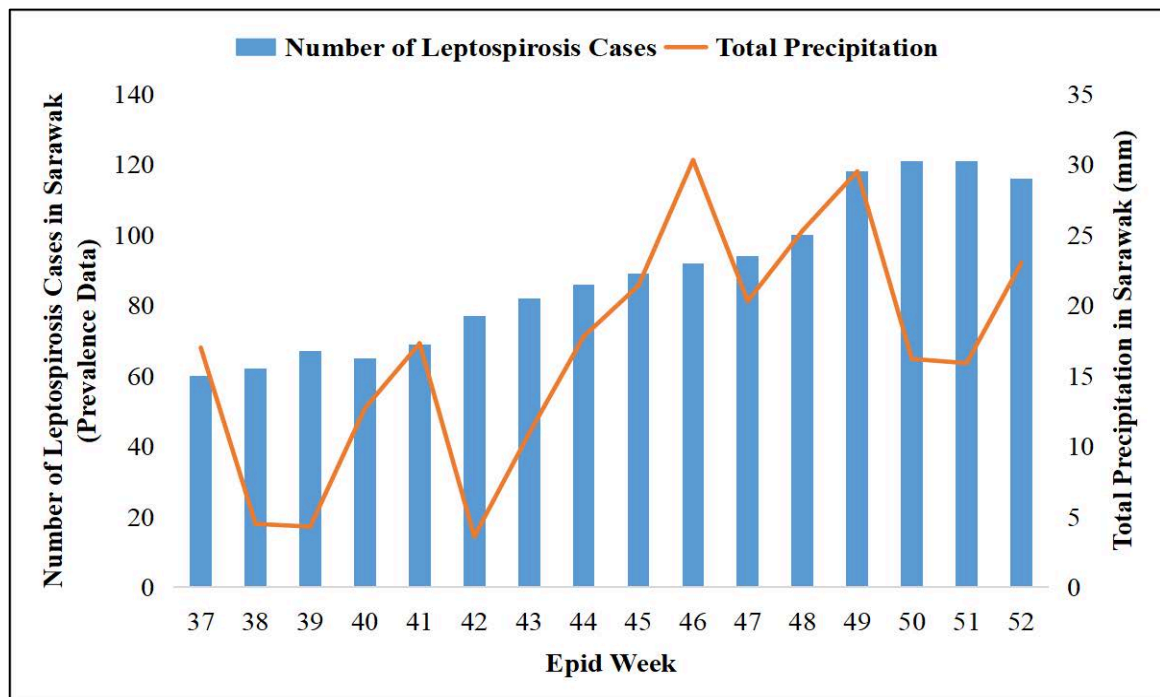


Figure 5.22: Weekly Leptospirosis Cases and Weekly Precipitation in Millimeter (mm) in Sarawak (Week 37 to Week 52)

Table 5.3: Correlation Matrix for the Weekly Leptospirosis Cases and Weekly Precipitation in Millimeter (mm) in Sarawak (Week 1 to Week 16)

		Weekly Leptospirosis Cases	Weekly Precipitation in mm
Weekly Leptospirosis Cases	Pearson Correlation	1	-0.044
	Sig. (2-tailed)		0.873
	N	16	16
Weekly Precipitation in mm	Pearson Correlation	-0.044	1
	Sig. (2-tailed)	0.873	
	N	16	16

Table 5.4: Correlation Matrix for the Weekly Leptospirosis Cases and Weekly Precipitation in Millimeter (mm) in Sarawak (Week 17 to Week 36)

		Weekly Leptospirosis Cases	Weekly Precipitation in mm
Weekly Leptospirosis Cases	Pearson Correlation	1	-0.435
	Sig. (2-tailed)		0.055
	N	20	20
Weekly Precipitation in mm	Pearson Correlation	-0.435	1
	Sig. (2-tailed)	0.055	
	N	20	20

Table 5.5: Correlation Matrix for the Weekly Leptospirosis Cases and Weekly Precipitation in Millimeter (mm) in Sarawak (Week 37 to Week 52)

		Weekly Leptospirosis Cases	Weekly Precipitation in mm
Weekly Leptospirosis Cases	Pearson Correlation	1	0.570*
	Sig. (2-tailed)		0.021
	N	16	16
Weekly Precipitation in mm	Pearson Correlation	0.570*	1
	Sig. (2-tailed)	0.021	
	N	16	16
*. Correlation is significant at the 0.05 level (2-tailed).			

For the Pearson correlation, there are a few stratifications to interpret the correlation coefficient (Schober et al., 2018). A coefficient less than 0.1, indicates a negligible whereas a coefficient more than 0.9 refers to an extraordinarily strong correlation (Schober et al., 2018). When a value is between 0.1 and 0.39 for Pearson's correlation, it deduces a weak relationship (Schober et al., 2018). Conversely, a strong relationship refers to the coefficient in which the value is between 0.7 and 0.89 (Schober et al., 2018). For a moderate correlation, Pearson's coefficient will be between 0.4 and 0.69 (Schober et al., 2018). By referring to the first correlation matrix which is Table 5.3, Pearson's correlation of -0.044 indicates a negligible relationship. For the second correlation matrix which is shown in Table 5.4, Pearson's correlation of -0.435 refers to a negative moderate relationship. As for Table 5.5

which shows the third correlation matrix, Pearson's correlation of 0.570 implies a positive moderate relationship.

The coefficient for the third correlation matrix reflects the leptospirosis cases increase in association with higher precipitation during the northeast monsoon. This result is in agreement with the research of Kira et al. (2021) whereby more leptospirosis cases occur when the precipitation increases during the monsoon season. Pearson's correlation of the second matrix reflects a reverse situation if compared to the third matrix as it implies that lower precipitation causes a higher number of cases. This situation can be explained by the higher temperature during the southwest monsoon season led to increased exposure to the bacteria (Lau et al., 2010). The decrement of precipitation during the southwest monsoon season results in the rise of temperature. The increased temperature encourages more water-based activities and simultaneous exposure to the *Leptospira*-contaminated environment for both humans and animals (Lau et al., 2010).

For the first matrix, Pearson's correlation reflects an insignificant relationship between the number of leptospirosis cases and the precipitation in Sarawak. Supposedly, the coefficient should have a nearly similar value to the third matrix as the data for the Pearson correlation analysis are based on the northeast monsoon season. However, the results do not show such a situation and it means that the climatic condition is may not the only factor to cause the first wave of disease outbreaks. A few researchers explain some factors that could affect the leptospirosis outbreak besides climates such as misdiagnosis of the disease (Alia et al., 2018) and occupational exposures (Garba et al., 2018). In Malaysia, leptospirosis is frequently misdiagnosed as tropical fevers since the clinical manifestation of the disease is similar to other illnesses (Alia et al., 2018) such as influenza and flu with the symptoms like

fever, chill, and others. On the other hand, some people like plantation workers, rubbish collectors and town cleaners are at high risk of the disease infection (Garba et al., 2018). The reason these people are hazardous groups is due to the often contact with contaminated water and soil by the rats' urine which causes an elevated risk of leptospirosis infection when protective clothing is not worn (Garba et al., 2018).

5.6 Effects of Parameters on the Leptospirosis Transmission

In this research, one of the objectives is to identify the vectors' behaviours that affect leptospirosis transmission. There are two parameters involved in the analysis, the active period duration of the vectors, α_d and the movement range of the vectors, η as these two parameters are representing the behaviours of the vectors. Furthermore, the analysis involves the natural birth rate of vector, μ_2 and the transmission rate from susceptible to infected vectors, θ_2 as well due to the changes in the values that would influence the scale of leptospirosis transmission (Chong et al., 2022).

To investigate the effects of these parameters, sensitivity analysis is a suitable approach to find the effects of the parameters. Ordinary least squares (OLS) estimate is one of the methods that is favoured for sensitivity analysis as it is simpler compared to other methods such as maximum likelihood estimate or MLE (Luo, 2016). By performing OLS, a regression equation to show the linear relationship will be obtained and it is given as:

$$\hat{Y}_i = \beta_0 + \beta_1 X_i \quad \text{Equation 5.9}$$

Based on Equation 5.9, $\hat{Y}_i$ is the estimated number of cases whereas X_i is the actual prevalence number of cases. β_0 is the intercept and β_1 is the slope of the regression equation. Meanwhile, i is the increment of 1, 2 and until n . When performing OLS, the IBM is evaluated by tuning the value of one parameter through a trial and error approach whereas

the values of the other parameters are kept constant. For the evaluation metrics after obtaining the regression equation, the classic measures that can be applied are intuitive and easy to understand including MSE, RMSE and MAE (Mayilvahanan, 2016). As the purpose to perform OLS is for sensitivity analysis instead of finding or comparing the trends of data, the MSE would be a better choice as it can indicate the value that gives the best results for the parameters (Jindal & Rao, 2017). The formula of MSE is given by:

$$\text{MSE} = \frac{1}{n} \sum_{i=1}^n (Y_i - \hat{Y}_i)^2 \quad \text{Equation 5.10}$$

From Equation 5.10, n is the total number of the epidemiological week for a particular wave of outbreak, Y_i is the simulated prevalence number of confirmed cases, $\hat{Y}_i$ is the estimated number of cases and i is the increment of 1, 2 and until n . After finding the MSE, the results are shown in Figure 5.23 to Figure 5.34. Firstly, Figure 5.23 to Figure 5.25 show the MSE of the natural birth rate of vector, μ_2 for respective outbreaks. Secondly, the MSE of the transmission rate from susceptible to infected vectors, θ_2 of the outbreaks is represented in Figure 5.26 to Figure 5.28. In addition, Figure 5.29 to Figure 5.31 indicate the MSE of vector movement range, η whereas Figure 5.32 to Figure 5.34 is the MSE of the active period durations of the vector, α_d of the three outbreaks.

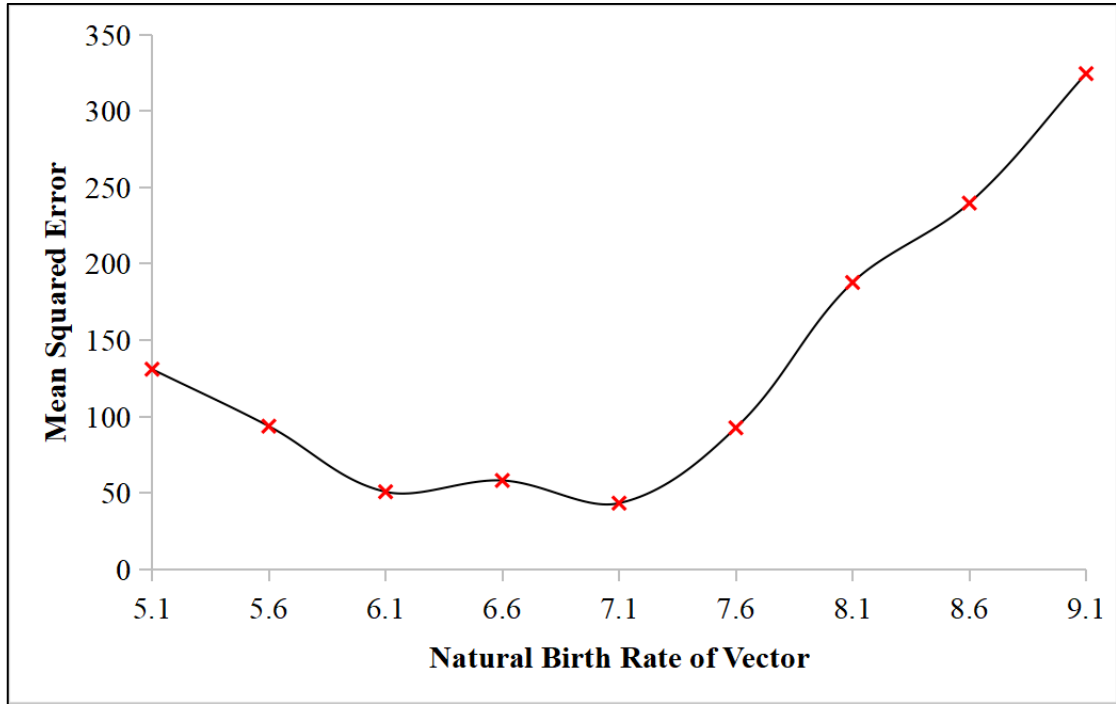


Figure 5.23: MSE of Natural Birth Rate of Vector, μ_2 for Epid Week 1 to Week 16

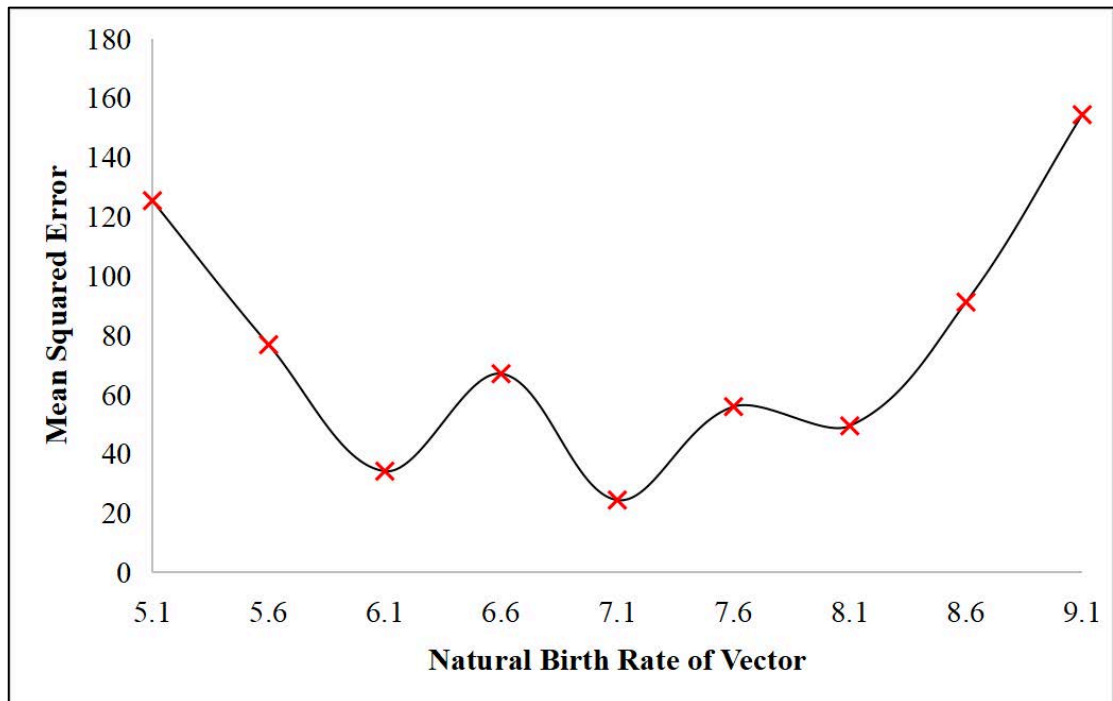


Figure 5.24: MSE of Natural Birth Rate of Vector, μ_2 for Week 17 to Week 36

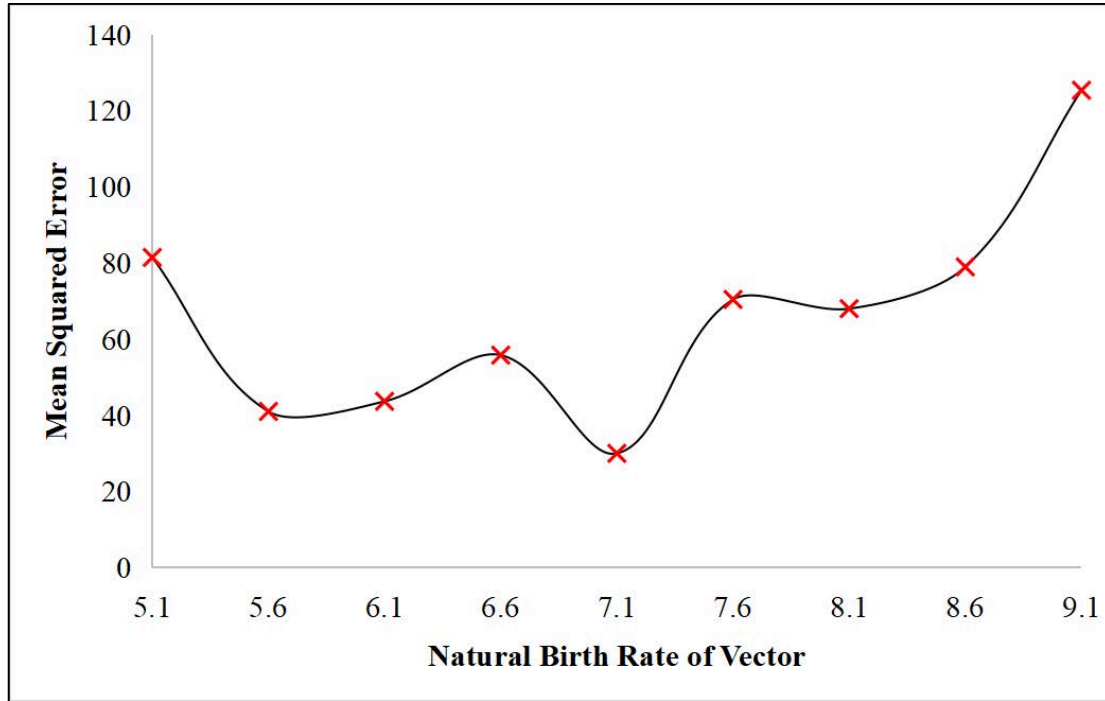


Figure 5.25: MSE of Natural Birth Rate of Vector, μ_2 for Week 37 to Week 52

In general, the smaller MSE which is nearer to zero indicates the estimated value is nearly fitted for the parameter (Chicco et al., 2021). Based on Figure 5.23 to Figure 5.25, the error decreases and reaches the lowest point when the natural birth rate of vector, μ_2 increases from 5.1 to 7.1. However, starting from value 7.1, the MSE increases as the vector birth rate, μ_2 gets higher. The changes in the errors by performing the sensitivity analysis indicate that the vector birth rate, μ_2 is a sensitive parameter. Meanwhile, the value of 7.1 is the best result for the parameter as the MSE of value 7.1 are 43.27, 24.37 and 30.02, which are the lowest compared to other values for the respective three outbreaks.

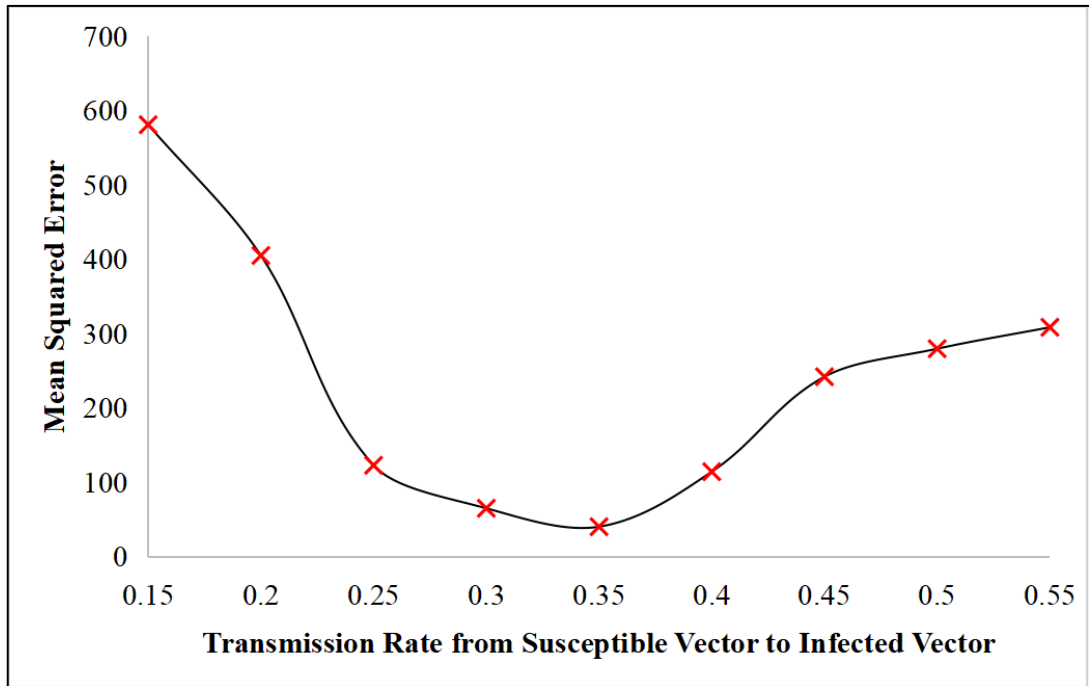


Figure 5.26: MSE of Transmission Rate from Susceptible to Infected Vectors, θ_2 for Week 1 to Week 16

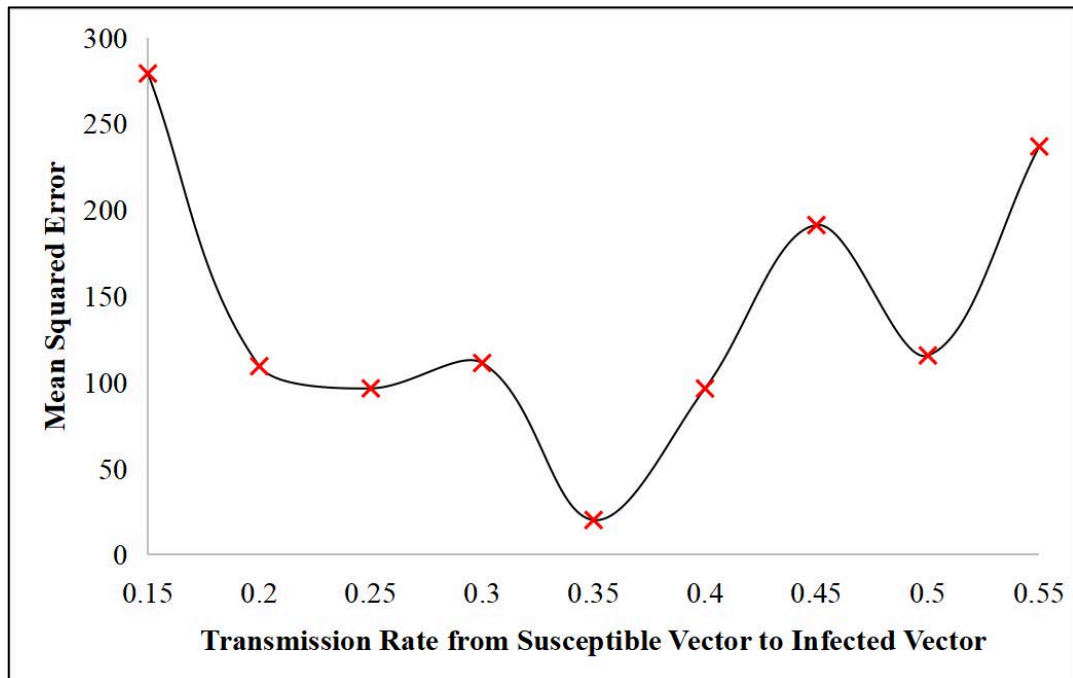


Figure 5.27: MSE of Transmission Rate from Susceptible to Infected Vectors, θ_2 for Week 17 to Week 36

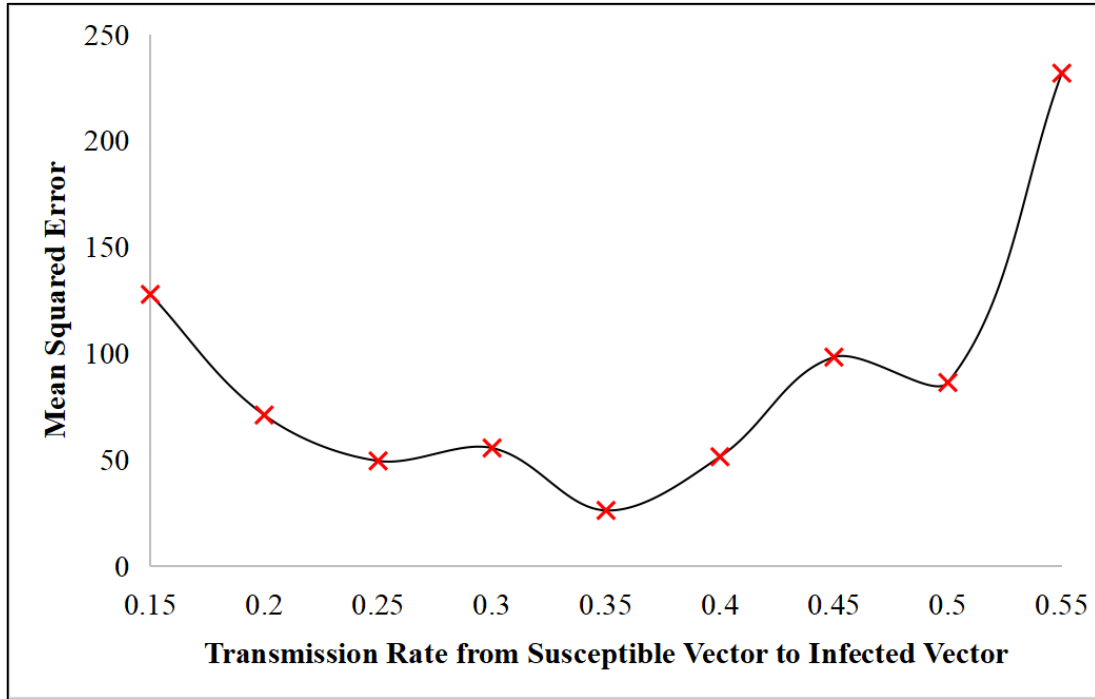


Figure 5.28: MSE of Transmission Rate from Susceptible to Infected Vectors, θ_2 for Week 37 to Week 52

Figure 5.26 to Figure 5.28 show that the MSE for the transmission rate from susceptible to infected vectors, θ_2 declines until the minimum point when the parameter value rises from 0.15 to 0.35. Conversely, the error gets bigger with the increasing transmission rate from 0.35 and onwards. The changes of MSE imply that the transmission rate from susceptible to infected vectors, θ_2 is another sensitive parameter. The lowest MSE of 40.08, 20.17 and 26.12 for the three waves of outbreaks respectively refers that the value of 0.35 being the best result for the parameter.

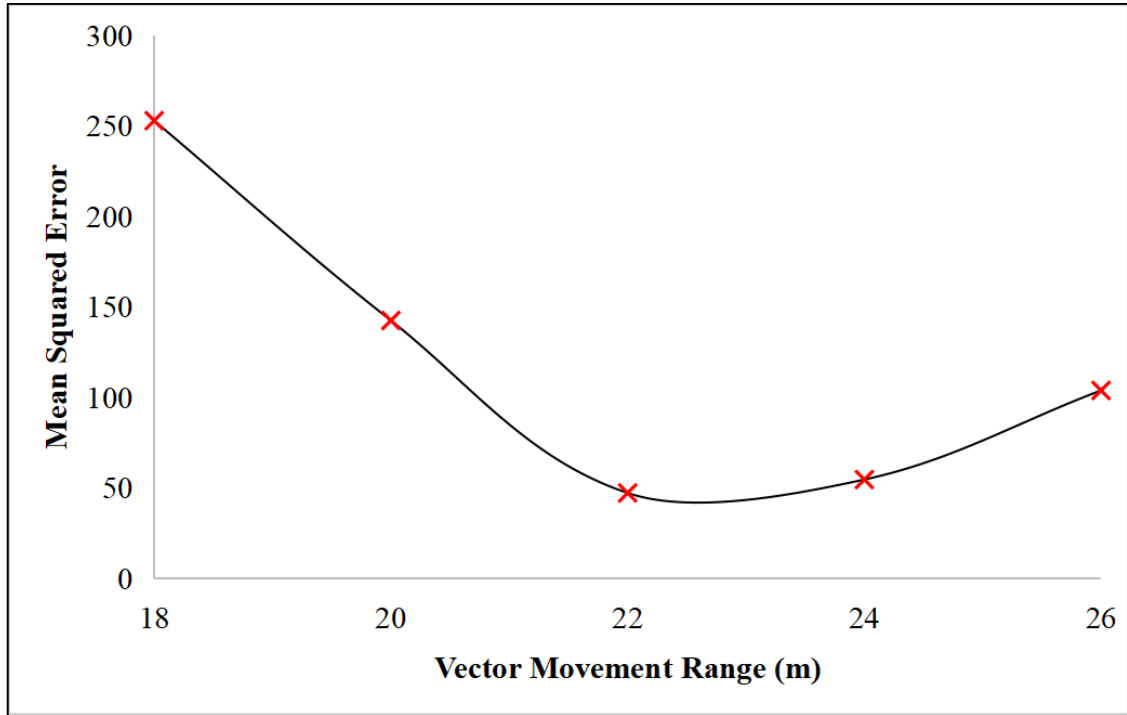


Figure 5.29: MSE of Movement Range of the Vector, η for Week 1 to Week 16

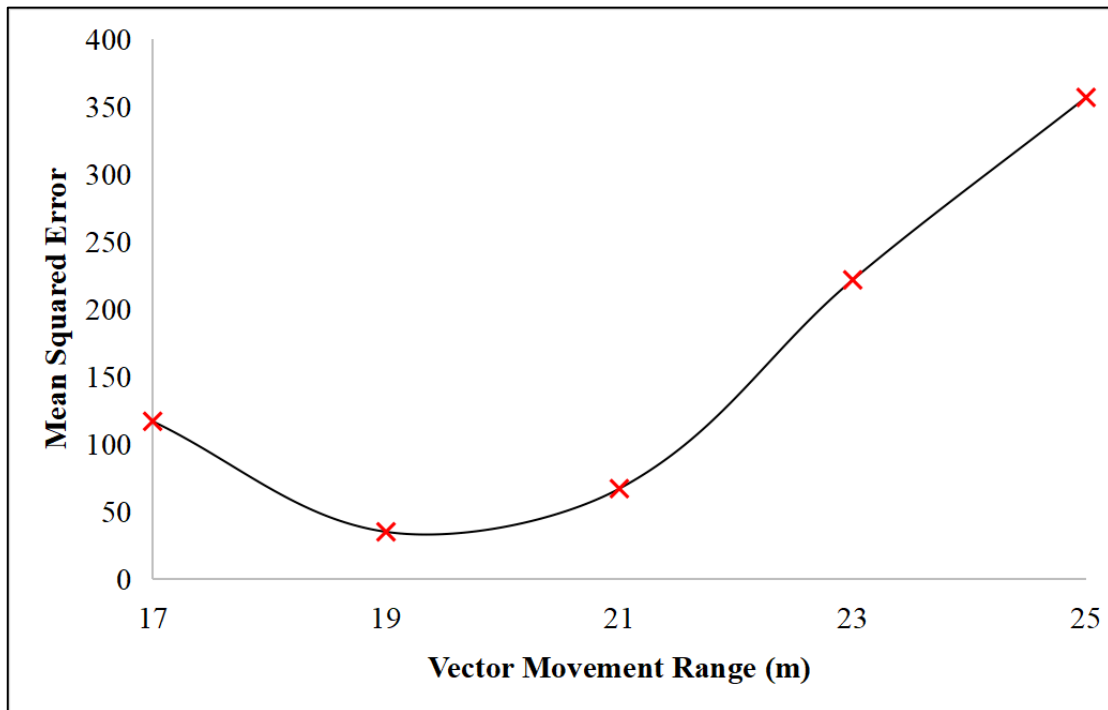


Figure 5.30: MSE of Movement Range of the Vector, η for Week 17 to Week 36

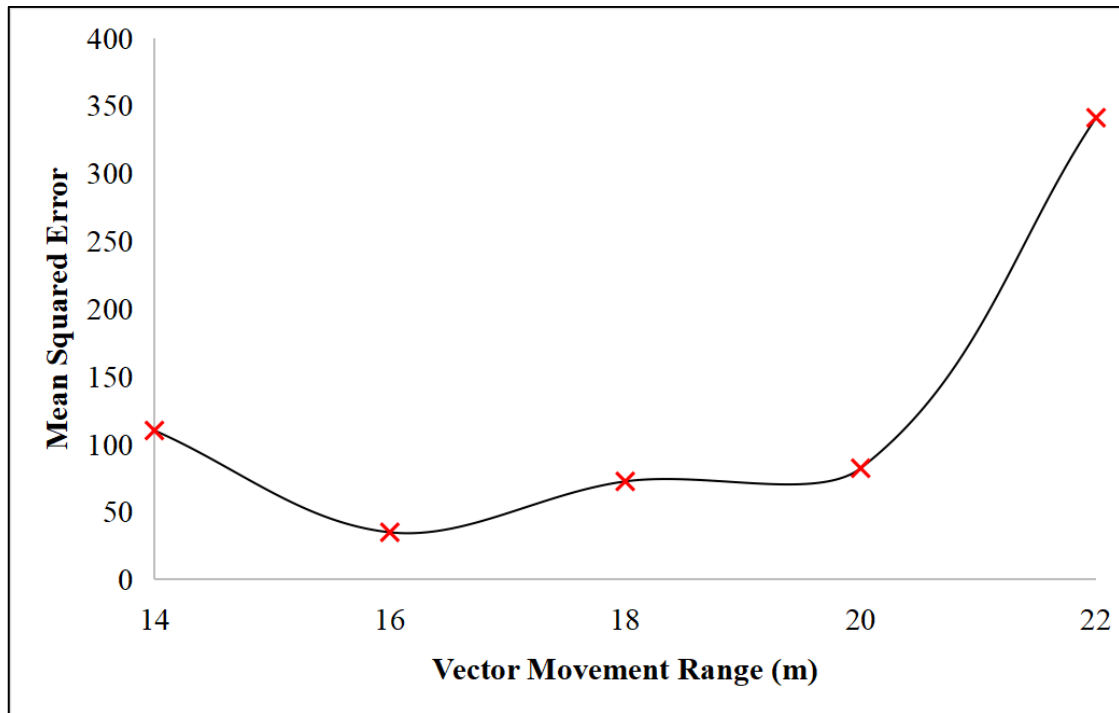


Figure 5.31: MSE of Movement Range of the Vector, η for Week 37 to Week 52

Figure 5.29 to figure 5.31 are the MSE of vector movement range, η for the three waves of leptospirosis outbreaks. The applied range of values for the three outbreaks is different. This is because this parameter is calibrated to obtain the best result for the trend analyses which are shown in Figure 5.14 to Figure 5.16. From Figure 5.29, the error reaches the lowest point when the movement range is 22m and the error inclines afterwards. In addition, Figure 5.30 and Figure 5.31 show the changes in MSE are much alike. The errors decline until the minimum points when the movement range is 19m and 16m respectively. However, the MSE for both outbreaks gets bigger as the movement ranges increase. On the other hand, the MSE show that 22m, 19m and 16m are the best results vector movement range, η as these values have the lowest error of 47.10, 34.82 and 34.95.

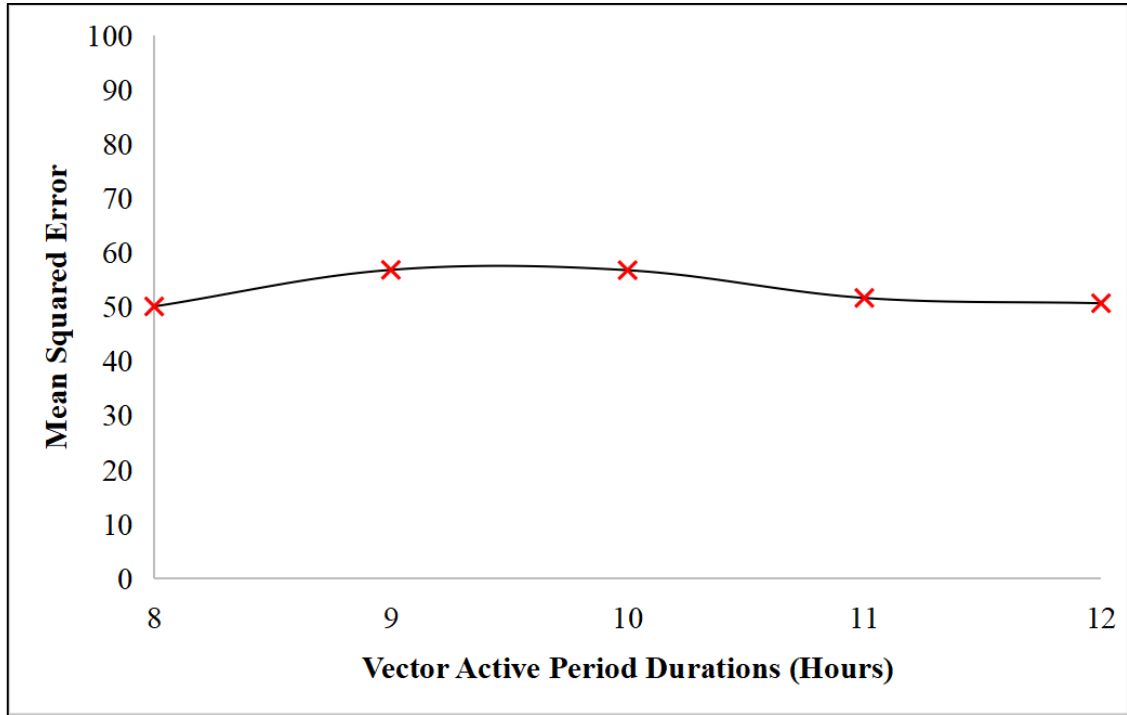


Figure 5.32: MSE of Active Period Durations of the Vector, α_d for Week 1 to Week 16

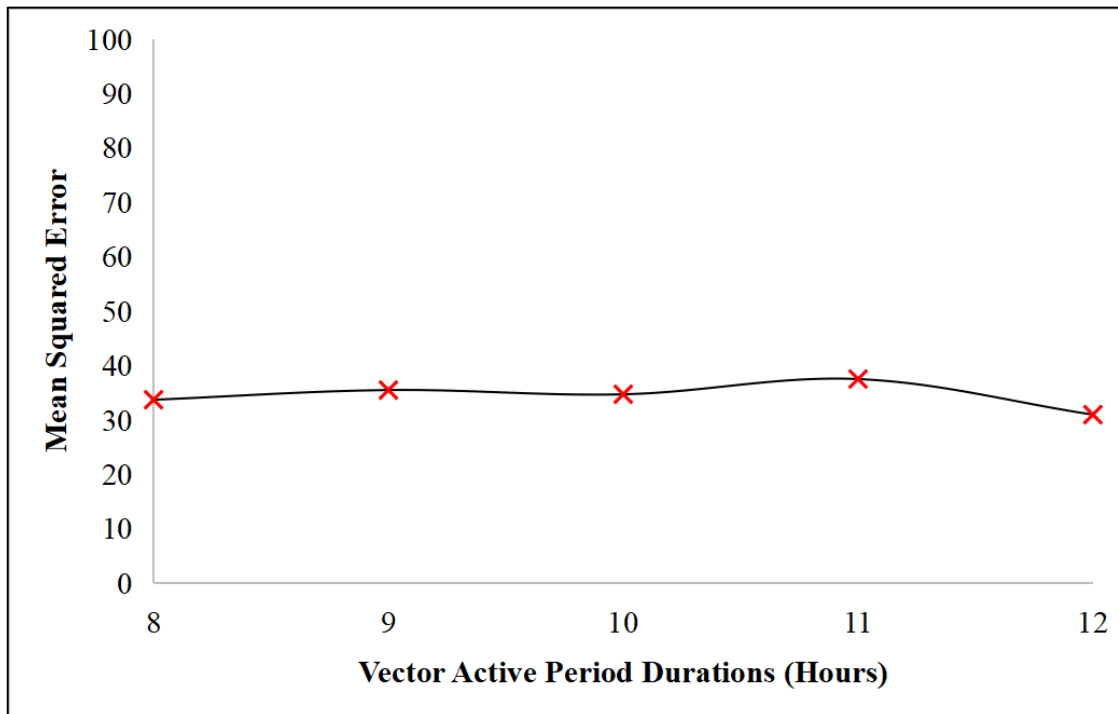


Figure 5.33: MSE of Active Period Durations of the Vector, α_d for Week 17 to Week 36

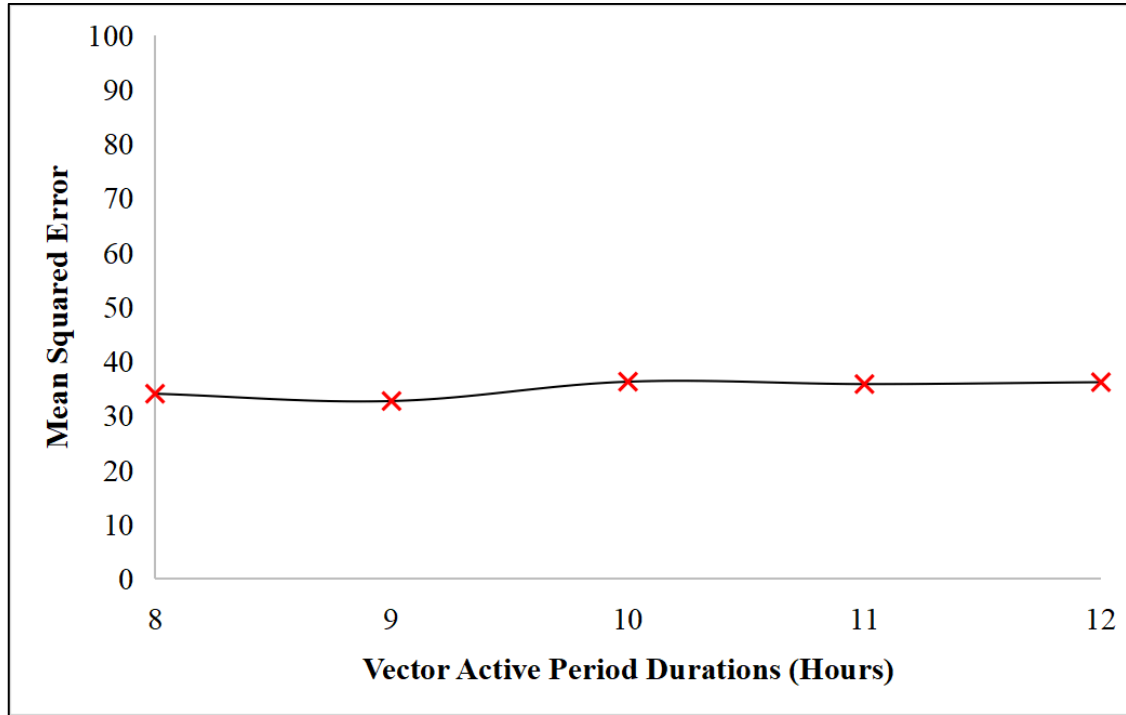


Figure 5.34: MSE of Active Period Durations of the Vector, α_d for Week 37 to Week 52

Figure 5.32 to Figure 5.34 are the MSE of active period durations of the vector, α_d for the three outbreaks. The errors shown in Figure 5.32 are between 50 and 60 for all the active durations. Figure 5.33 and Figure 5.34 have an analogous situation also as the MSE for both outbreaks are between 30 and 40. From the three figures, the errors do not show any significant increase or decrease. These results imply that the active period durations of the vector, α_d is not a sensitive parameter.

5.6.1 Effects of Vector Birth Rate, μ_2

After finding the MSE by performing sensitivity analyses through OLS, the values with the MSE become the interval range of values for the effect of parameters that will be discussed in the following subsections. The first parameter is the natural birth rate of the vector, μ_2 . The first value for showing the effects is 7.10 as this value has the lowest MSE for this parameter. In the interval of 5.10 to 7.10, the value of 5.10 has a higher MSE compared to other values. Meanwhile, 9.10 is another value with a bigger error as well from the interval of 7.10 to 9.10. Therefore, 5.10 and 9.10 are the other values for showing the effects of the natural birth rate of vector, μ_2 . Figure 5.35 and Figure 5.36 visualise the effects of the parameter on the infected subgroups for both populations through the average of 20 IBM simulations by using the selected values of 5.10, 7.10 and 9.10.

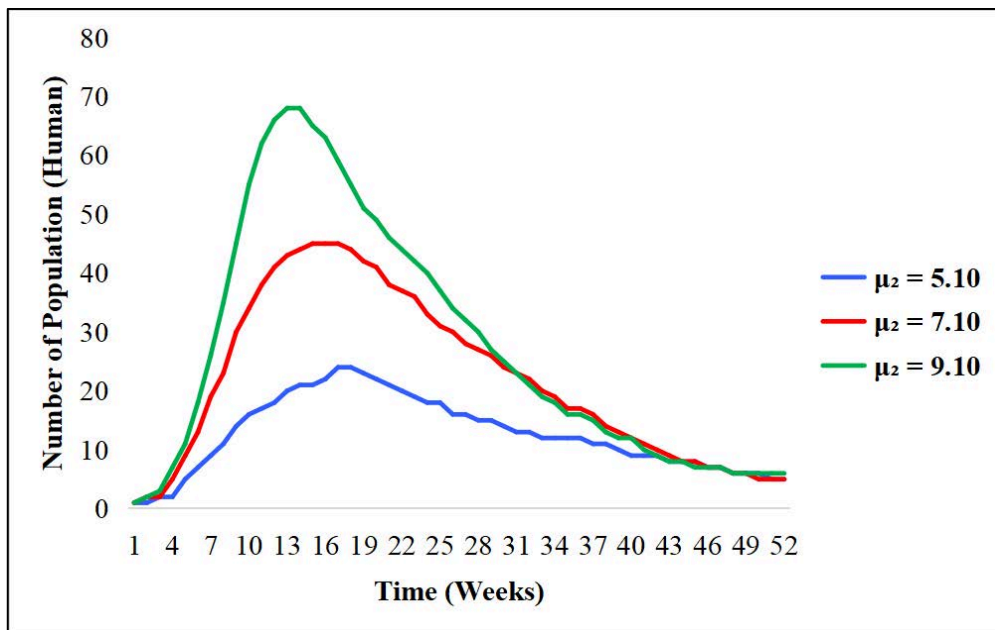


Figure 5.35: Effects of Various Natural Birth Rates of the Vector, μ_2 on Infected Humans

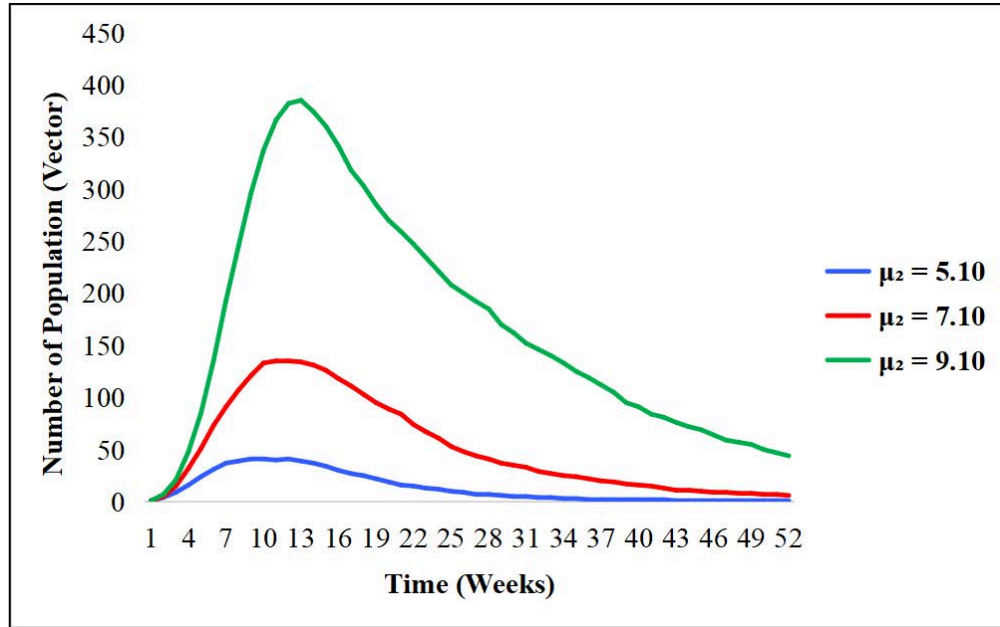


Figure 5.36: Effects of Various Natural Birth Rates of the Vector, μ_2 on Infected Vectors

Figure 5.35 and Figure 5.36 show the effects of various natural birth rates of vectors, μ_2 on the changes of infected humans and vectors. From Figure 5.35, the peak of infection for the infected human is on week fifteen with 45 persons when the birth rate is 7.10. When μ_2 becomes smaller which is 5.10, the number of infected humans diminishes to less than 30 with the infection peak on week seventeen. Conversely, the number of infected humans during the peak of infection on week thirteen increases to nearly 70 as the birth rate rises to 9.10. As for Figure 5.36, the infection peak is in the eleventh week with more than 130 vectors when μ_2 is 7.10. However, the number of infected vectors during the ninth week of infection peak minimises to less than 50 when the birth rate reduces to 5.10. Alternatively, the number of infected vectors reaches the maximum point with more than 350 vectors on week thirteen as if the μ_2 increases to 9.10.

Based on the analyses, a smaller μ_2 or $\mu_2 = 5.10$ would result in fewer numbers of infected humans and vectors. Conversely, more humans and rats have been infected with the

increased vector birth rate of 9.10. These results indicate that if the natural birth rate of the vector is higher, the rats give birth and cause the enlargement of population size. The increasing number of rats serves as the chain of infection as leptospirosis is transmitted from one infected rat to another. Therefore, more infected vectors would boost the disease infection and cause more humans to be infected by the disease.

5.6.2 Effects of Transmission Rate from Susceptible Vector to Infected Vector, θ_2

From the sensitivity analyses, the transmission rate of 0.35 has the lowest MSE. In addition, for the interval of 0.15 to 0.35 and interval of 0.35 to 0.55, the values of 0.15 and 0.55 have higher MSE compared to other values within the intervals. Therefore, 0.15, 0.35 and 0.55 are the ranges of values to show the effects of the parameter. Figure 5.37 and Figure 5.38 represent the average results of the 20 IBM simulations for the effects of transmission rate from susceptible to infected vectors, θ_2 on infected humans and vectors.

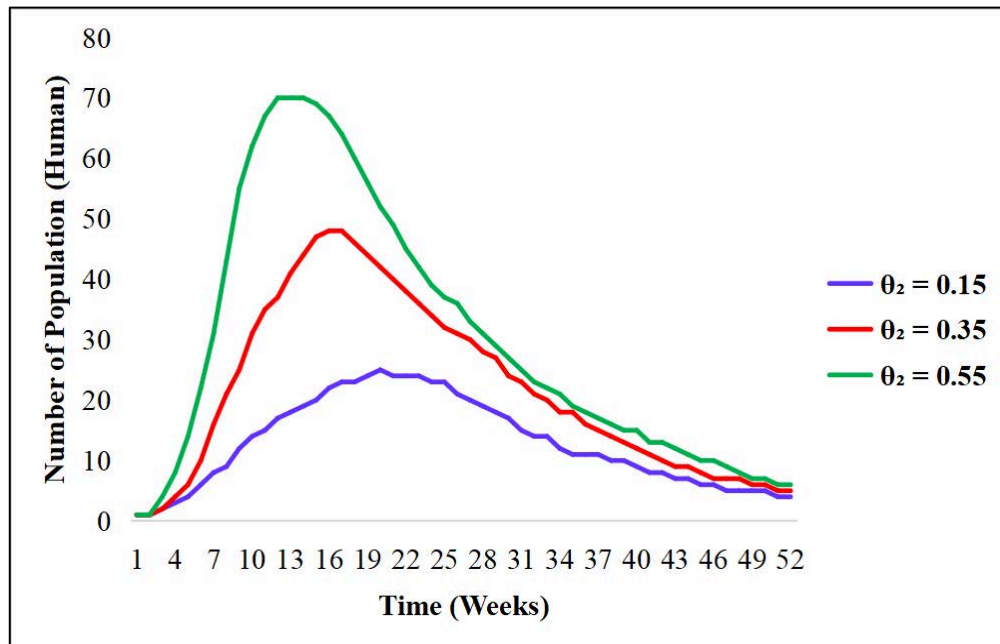


Figure 5.37: Effects of Various Transmission Rates from Susceptible to Infected Vectors, θ_2 on Infected Humans

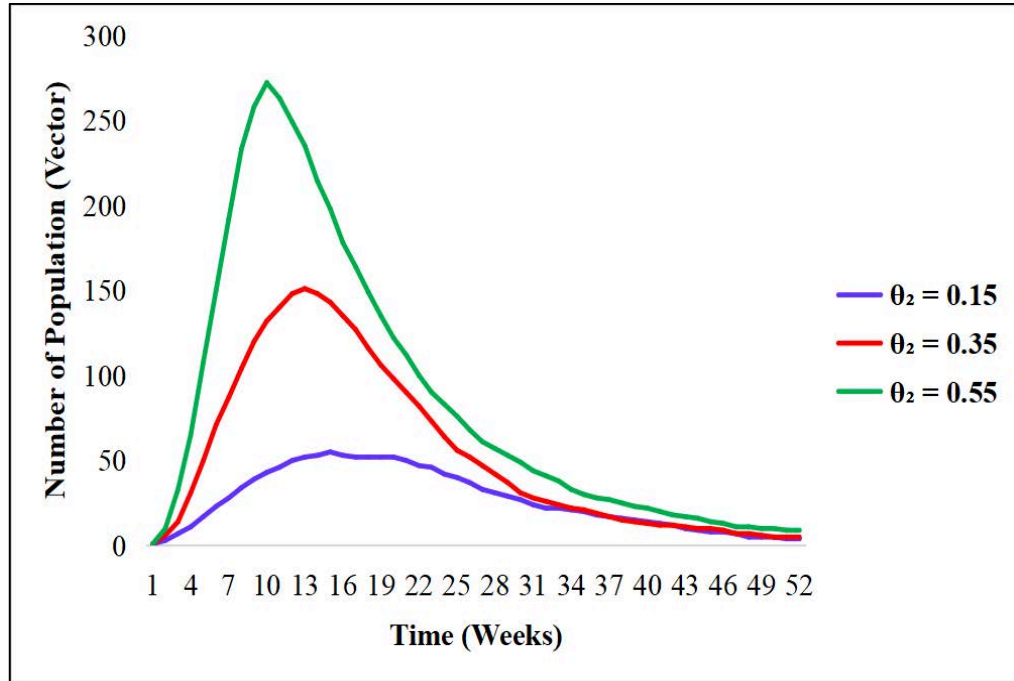


Figure 5.38: Effects of Various Transmission Rates from Susceptible to Infected Vectors, θ_2 on Infected Vectors

Figure 5.37 illustrates the results of the various effects of the transmission rate, θ_2 on infected humans whereas Figure 5.38 shows the influences on the infected vector. Based on Figure 5.37, the infection peak is on week sixteen with nearly 50 individuals when the transmission rate is 0.35. By reducing the θ_2 to 0.15, the peak of infection falls on the twentieth week and in association with less than 30 infected humans. On the contrary, the number of infections increases to the maximum which is week twelve with 70 individuals as if the θ_2 rises to 0.55. In Figure 5.38, the peak of infection during week thirteen shows that there are about 150 infected vectors when the transmission rate is 0.35. In addition, there are more infected vectors during infection peak on week ten if the θ_2 increases to 0.55. However, for $\theta_2 = 0.15$, the situation is opposite when compared with $\theta_2 = 0.35$ and $\theta_2 = 0.55$. On week fifteen which is the peak of infection, the infected vectors become lesser in number. From the figure, 55 vectors are infectious when the parameter value is 0.15.

Based on the analyses, the smaller the transmission rate from susceptible to infected vectors such as $\theta_2 = 0.15$ would result in fewer infected humans. As the parameter value increases, more individuals tend to be infected. The same situation occurs for the vectors as well. The increment of the transmission rate, θ_2 leads to a noticeable rise in the numbers of the infected vector. On the other hand, the decrement of the value of transmission rate minimises the number of infected vectors to become lesser. The results indicate that the transmission rate from susceptible to infected vectors, θ_2 influences the scale of the leptospirosis spreading.

5.6.3 Effects of the Vector Active Period Durations, α_d

This subsection contains the analyses of the effects of the vector active period duration, α_d on both humans and vectors. The sensitivity analyses have shown that the MSE for all the active period durations are consistent whereby there are no significant increases or decreases in the errors. However, the range of value for the sensitivity analysis can be applied as the range of value to show the influences of the parameter. This means that the parameter value for the active period durations starts from 8 hours. With the increment of two hours, the durations increase to 10 hours and reach 12 hours which is the maximum duration of the dark cycle for the vectors to stay active. Figure 5.39 and Figure 5.40 show the effects of the vector active period duration, α_d on infected humans and vectors with an average of 20 IBM simulations.

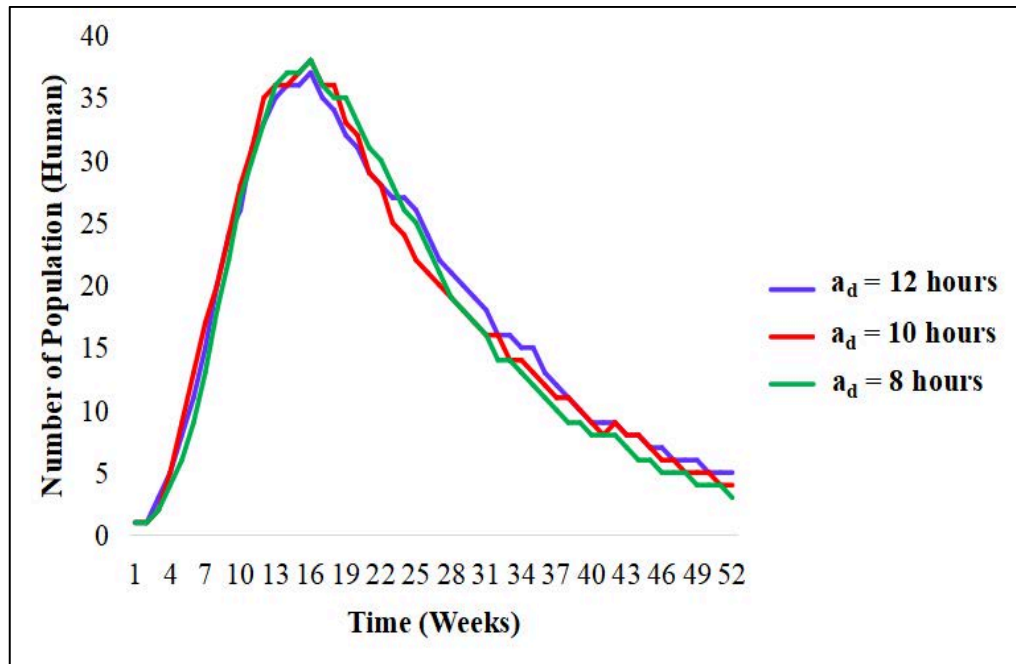


Figure 5.39: Effects of Various Active Period Durations of the Vector, a_d on Infected Humans

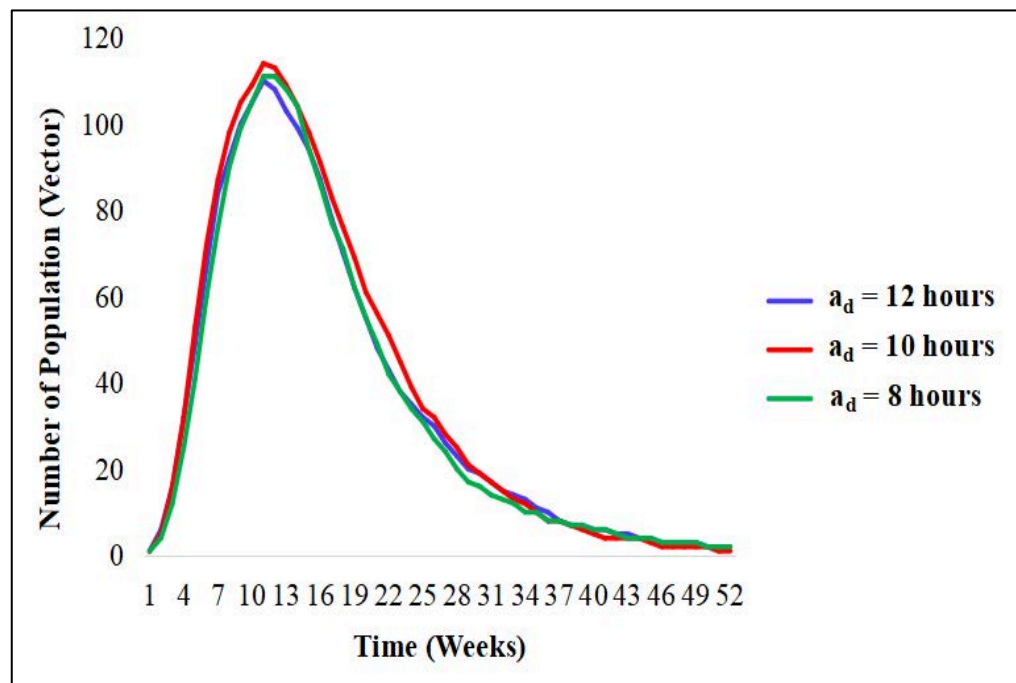


Figure 5.40: Effects of Various Active Period Durations of the Vector, a_d on Infected Vectors

Figure 5.39 illustrate the effects of the active period durations on infected humans and whereas Figure 5.40 is the simulations for the infected vectors. For Figure 5.39, regardless of 8 hours, 10 hours or 12 hours of active period durations, the infection peaks for the three values all are falls on week sixteen with nearly 40 infected individuals. Figure 5.40 shows similar situations as well. The peaks of infection which are on the eleventh week for 8 hours, 10 hours and 12 hours indicate that the number of infected vectors is between 100 and 120.

From the analyses, whether the active period durations is 8 hours, 10 hours or 12 hours, there is no significant increase or decrease in the number of infected humans if the durations are shortened or lengthened. The same case for the infected vectors also. Therefore, there are no clear results are showing the active period durations of vector, α_d would influence the leptospirosis outbreak significantly.

5.6.4 Effects of Vector Movement Range, η

This subsection covers the effects of the movement range of the vectors on the infected humans as well as the infected vectors. Based on the sensitivity analyses through OLS, the ranges of values are applied differently for the three outbreaks. However, it is fine to select one of the ranges for showing the effects of the parameter as the changes of the MSE from the fitted value is the same for the three outbreaks. As the movement range increases from the fitted value, the errors become bigger. Alternatively, if the η becomes smaller, the MSE rises as well. Among the three ranges, the movement range from 18m to 26m is selected as the changes of MSE are more uniform from the fitted value which is shown in Figure 5.29. When η is 22m, it has the lowest error. In addition, the MSE becomes bigger if the range increases to 26m or decreases to 18m.

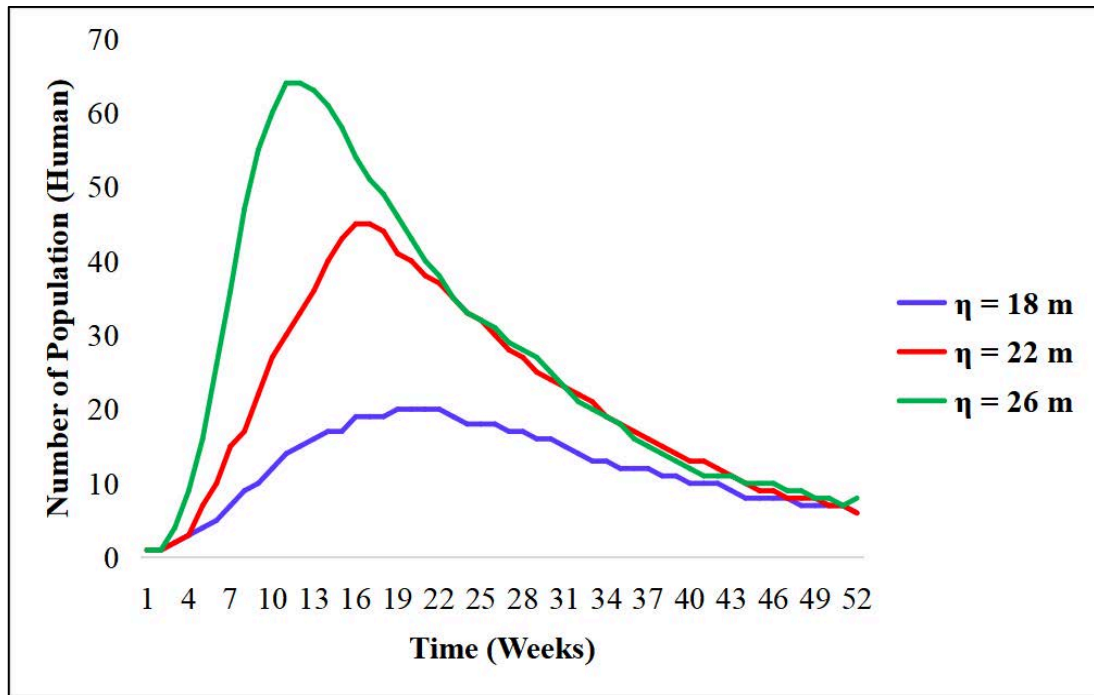


Figure 5.41: Effects of Various Movement Range of the Vector, η on Infected Humans

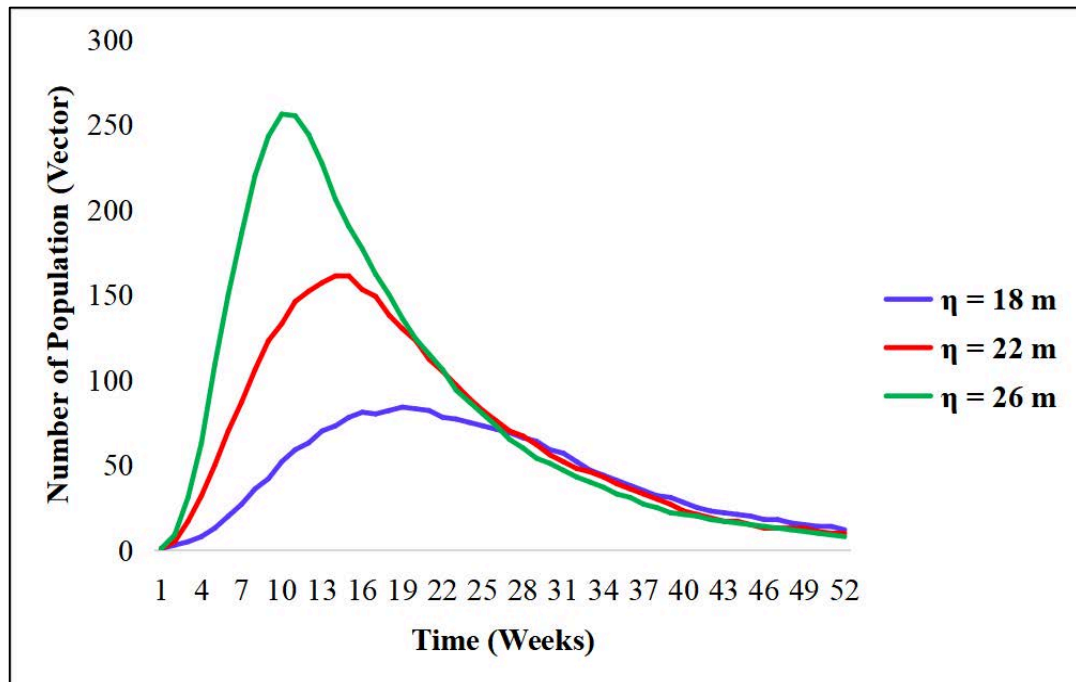


Figure 5.42: Effects of Various Movement Range of the Vector, η on Infected Vectors

Figure 5.41 shows the effects of the movement range of the vectors, η on the infected human whereas Figure 5.42 is for the infected vector. Referring to Figure 5.41, there are 45 infected humans when the infection reaches the maximum point on week sixteen with a movement range of vector of 22m. When η increases to 26m, there are more than 60 infected individuals during the eleventh week of infection peak. Conversely, the number of infected humans declines to 20 during the peak of infection on week nineteen when the η becomes smaller which is 18m. For Figure 5.42, the infection peak on week fourteen shows that there are about 160 infected vectors when the movement range is 22m. As η decreases to 18m, the number of infected vectors diminishes to roughly 80 during the peak of infection on week nineteen. On the other hand, there are more than 250 infected vectors on week ten which is the infection peak when η increases to 26m.

By referring to the analyses, the results deduce the bigger movement range of the vector such as $\eta = 26$ m would cause more numbers of infected humans and vectors. On the contrary, fewer numbers of infected for both groups when the movement range is smaller or $\eta = 18$ m. These results mean that if the infected vector moves from its nest over a long distance, the infected vector has more chances to spread leptospirosis which influences the scale of the disease outbreak.

5.7 Summary

In this chapter, the verification of IBM with the SIR model was performed to ensure that the implementation in NetLogo was correct. The simulation results illustrated the different population behaviours among the subgroups of humans and vectors. In addition, the high coefficient of determination or r^2 and the normally distributed residuals through trend analysis deduced that the IBM was adequate to model the leptospirosis transmission in Sarawak. Additionally, the r^2 of IBM is higher at more than 90% and more consistent for the three outbreaks as compared to the compartmental model shown by Chong et al. (2022). The sensitivity analyses with OLS and the analyses for the effects of the parameters indicated that a few parameters could affect the spread of disease. For example, the higher transmission rate from susceptible to infected vectors, θ_2 and the higher natural birth rate of the vector, μ_2 resulted in more numbers of infected humans and vectors. In terms of behaviours of vectors, the movement range, η influenced the scale of leptospirosis transmission significantly if the η was bigger. As for the active period duration of the vectors or α_d , there were no influences shown from the analyses on the spread of leptospirosis regardless of longer or shorter active period durations.

CHAPTER 6

CONCLUSIONS AND FUTURE WORK

6.1 Outline

This concluding chapter consists of four parts. Section 6.2 describes the summary of the overall research whereas the following Section 6.3 discusses the key contributions of this research. Next, Section 6.4 touches on the possible limitations and the future works of the projects in Section 6.5.

6.2 Discussion and Conclusion

In the general conclusion, this research manages to develop and analyse an epidemiological individual-based model for leptospirosis transmission. As the number of confirmed cases increases in Sarawak, it has become a motivation to conduct this study. Leptospirosis is endemic in many places whereby the disease brings deep impacts on the people and societies in the affected regions. In Sarawak, the number of confirmed cases highlights an increasing trend over the past few years. This situation is worrying as the visible symptoms of leptospirosis are similar to other infectious diseases like dengue, the flu and influenza. For the public health measures enactment against this typical illness, the information and evidence of sciences play significant roles in managing these specific tasks. Disease modelling is one of the practical techniques to enable people to adequately explore the epidemiology of infectious diseases. The obtained results from the model simulation provide valuable information. The outcomes eventually predict the noticeable changes in the population behaviours as well as the disease outbreaks.

The compartmental model is popular in disease modelling. However, the compartmental model that assumes populations to be homogeneous is not adequate for the model that considers the individuals with significant differences (Black & McKane, 2012). The differences among the individuals reflect the existence of heterogeneity. For zoonotic or vector-borne diseases, the heterogeneity of the hosts can influence the disease transmission significantly (Kilpatrick et al., 2006). IBM is a favourable model by the modellers for disease modelling that concerns the heterogeneity among the individuals. Yet, the modelling of leptospirosis transmission by using IBM is limited. Therefore, the limited research on leptospirosis spread by applying IBM becomes a motivation for conducting the related research.

The determination of model assumptions is important before proceeding to the model formulation. Ultimately, these model assumptions represent the behaviours and interactions of the agents. The IBM consists of two populations which are humans and vectors. The model considers the infectious disease dynamics for the populations, whereby three states for humans: susceptible, infected, and recovered, and two states for vectors: susceptible and infected. Furthermore, IBM also considers the heterogeneity of the vectors' behaviours which are active period durations and movement range of vectors. The NetLogo software is a preferable software for IBM implementation as it is simpler for users to apprehend in the development process. As IBM is a stochastic model, it means the results are varying for each simulation. By finding the coefficient of variation or C_v , the simulation number of $n \geq 20$ indicates the C_v for the susceptible, infected, and recovered reaches equilibrium. Therefore, 20 runs are sufficient for the rest of the IBM simulations.

The model verification goes with the comparison between the IBM and SIR model in terms of population behaviours of the subgroups. By comparing both models, IBM can produce similar population behaviours of the subgroups like the SIR model which are shown in Figure 5.1. For the accuracy of the IBM, the calculated MAPE is 7.63%. Unfortunately, the novelty to reflect 7.63% is good or bad for the accuracy of IBM is limited. The reason is most of the researchers do not describe the model verification process or even they have mentioned it, they only compare their models with the SIR models in terms of population behaviours which are described in Section 5.2. As for the model validation, the trend analysis indicates the r -squared (r^2) are 96.08%, 91.01% and 94.68% and the normal probability plots show the errors are in normal distribution for the three outbreaks respectively.

As described in Section 2.9, the r^2 of more than 75% indicates the model to be substantial (Hair et al., 2011) and the r^2 near 1.00 or 100% reflects the model is closely fitted to the data (Chicco et al., 2021). In addition, the residuals of the regression have to follow a normal distribution to imply the model is fitted well with the data (Frost, 2020). As the r^2 for the three outbreaks are more than 90% and the normal probability plots indicate the residuals follow normal distributions, the results are nearly fitted with the actual prevalence data. Compared to the r^2 of 87.40%, 36.09% and 76.06% through the SIRS-SI model by Chong et al. (2022), the r^2 of IBM which is more than 90% and consistent for the three outbreaks indicates the IBM is more preferable in modelling the leptospirosis transmission in Sarawak. On the other hand, the results of trend analysis for the IBM are better when the model considers the heterogeneity of the vectors' behaviour such as the movement range of the vector which the SIRS-SI is not. The improvement in results of trend analysis for IBM is in agreement with Kilpatrick et al. (2006) whereby the heterogeneity of the vectors or hosts can influence the transmission of zoonotic diseases significantly.

Through sensitivity analysis with OLS, the vector birth rate, transmission rate from susceptible to infected vectors and movement range of the vectors are three sensitive parameters as changes of values for these three parameters can affect the number of infected humans and vectors. However, the active period duration of the vector does not show such influences, so it is not a sensitive parameter. For the effects of the parameters, a higher vector birth rate and transmission rate from susceptible to infected vectors resulted in increased numbers of infected humans and vectors. Furthermore, the bigger movement range of the vectors causes more numbers of infected humans and vectors. The results show that the active period duration of the vectors does not influence leptospirosis transmission. This means that the active period of the vector is not necessary to be considered in IBM formation if compared to the movement range of the vector when concerning the vectors' behaviours for disease transmission.

6.3 Contributions of the Research

The formulation of the IBM for leptospirosis transmission represents a significant effort for disease modelling. The model can estimate the changes in the population behaviours of humans and vectors closer to the real data especially the leptospirosis transmission in Sarawak if compared to the compartmental model. In terms of vectors' behaviours, the results indicate that the duration of vectors' active periods does not show any effects on leptospirosis transmission. On the contrary, the movement range of the vector influences the spread of disease, and the results from model validation indicate that 16m to 22m is the range that affects the leptospirosis infection in Sarawak. All these results regarding the influences of the vectors' behaviours in disease transmission are significant for public health management. All this information can serve as guidelines for the public health authorities in the prevention and control of zoonotic or vector-borne diseases through

vector control. Subsequently, the IBM is efficient to model disease transmission that concerns the heterogeneity among the population if compared with the compartmental model which assumes the population to be homogeneous. Applying IBM with considering the heterogeneity of vectors' behaviours produces results that closely fit with the real-world situation in terms of modelling the leptospirosis transmission in Sarawak through trend analysis.

6.4 Limitations of the Research

The simulation results for the respective groups in humans typically reveal the changes in population behaviours when it comes to leptospirosis transmission. However, the evident lack of corresponding data is one of the specific issues for validating the outcomes. For example, the numbers of recovered individuals and deaths because of leptospirosis. More precisely, the published data do not contain all the necessary information that reflects the exact situation of the disease outbreak. Concurrently, the lack of information between leptospirosis transmission and behaviours of vector population is considered another obstacle as well. Many academic studies have mentioned the wide-ranging collection of data from rats is challenging. The key reasons are the rats hide away from human sight and that there is no efficient approach for collecting the data from the vectors demographically and geographically. Therefore, the specific information regarding the possible influences of the behaviours of the rats in the transmission of leptospirosis is unavailable for the moment.

Apart from data unavailability, there are also other limitations. For example, the uses of the trial and error approach in parameter calibration. Although there are advantages as described in Section 5.3.3, the approach will be very time-consuming if the required number of simulations, n is large for the IBM simulations such as $n \geq 40$. When the required number

of simulations, n is large, the alternative method such as the Monte Carlo approach can be applied to calibrate the parameter values in future simulations. Meanwhile, the accuracy of the model when performing model verification is unable to verify. At the moment there are no clear criteria to indicate the error matrix performance for the model verification in disease modelling. The reason is the novelty regarding this particular part is limited as many researchers do not describe their model verification in their studies. Even though some researchers mention the process, they compare their models with the compartmental models in terms of patterns of changes in population behaviours.

6.5 Recommendation for Future Work

The key focus of the research is to introduce an epidemiological model for simulating leptospirosis transmission. Although the formulation of IBM is successful, there are still available spaces for improvement for the model. The amount of rainfall is another perspective that can typically investigate as there is research that states there is a significant correlation between rainfall and the spreading of leptospirosis. Consequently, demographic factors like age or gender can also be in consideration for studying disease transmission among the human population. Moreover, the environmental factor can be a concern as well as there are cases relating to the leptospirosis outbreak that occurs after individuals visited places like rivers. As for the active period of the vectors, it may require other research in terms of zoology to further investigate whether this behaviour of vector can affect the disease transmission or not instead of research through model simulation.

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APPENDICES

Journal Publications

1. **Chong, J. W.,** Tiong, W. K., Labadin, J. & Sahak, N. (2022) Mathematical Modelling of Leptospirosis Spread in Malaysia. *Mathematical Modeling and Computing*, 9(1), 18-25. <https://doi.org/10.23939/mmc2022.01.018>
2. **Chong, J. W.,** Tiong, W. K., Labadin, J. & Phang, P. (2022). Effects of rodents' behaviours on leptospirosis spread: an individual-based modeling approach. *Mathematical Modeling and Computing*, 9(4), 805-815. <https://doi.org/10.23939/mmc2022.04.805>