ASSESSING THE EFFECTS OF TOURISM ON THE SPREAD OF HIV AND AIDS IN MALAYSIA USING SUSCEPTIBLE INFECTED REMOVED MODELS

OFOSUHENE OKOFROBOUR APENTENG

FACULTY OF ECONOMICS AND ADMINISTRATION
UNIVERSITY OF MALAYA
KUALA LUMPUR

2017

ASSESSING THE EFFECTS OF TOURISM ON THE SPREAD OF HIV AND AIDS IN MALAYSIA USING SUSCEPTIBLE INFECTED REMOVED MODELS

OFOSUHENE OKOFROBOUR APENTENG

THESIS SUBMITTED IN FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

FACULTY OF ECONOMICS AND ADMINISTRATION
UNIVERSITY OF MALAYA
KUALA LUMPUR

2017

UNIVERSITI MALAYA

ORIGINAL LITERARY WORK DECLARATION

Name of Candidate:Ofosuhene Okofrobour Apenteng

Registration/Matrix No.:EHA130012

Name of Degree:Doctor of Philosophy

Title of ~~Project Paper/Research Report/Dissertation/~~Thesis ("this Work"):**Assessing the effects of tourism on the spread of HIV and AIDS in Malaysia using susceptible infected removed models**

Field of Study: Mathematical Epidemiology

    I do solemnly and sincerely declare that:

(1) I am the sole author/writer of this Work;
(2) This work is original;
(3) Any use of any work in which copyright exists was done by way of fair dealing and for permitted purposes and any excerpt or extract from, or reference to or reproduction of any copyright work has been disclosed expressly and sufficiently and the title of the Work and its authorship have been acknowledged in this Work;
(4) I do not have any actual knowledge nor do I ought reasonably to know that the making of this work constitutes an infringement of any copyright work;
(5) I hereby assign all and every rights in the copyright to this Work to the University of Malaya ("UM"), who henceforth shall be owner of the copyright in this Work and that any reproduction or use in any form or by any means whatsoever is prohibited without the written consent of UM having been first had and obtained;
(6) I am fully aware that if in the course of making this Work I have infringed any copyright whether intentionally or otherwise, I may be subject to legal action or any other action as may be determined by UM.

   Candidate's Signature   Date

Subscribed and solemnly declared before,

   Witness's Signature   Date

Name:Prof. Dr. Noor Azina Ismail
Designation:Dean

ABSTRACT

The spread of human immunodeficiency virus (HIV) infection and the resulting acquired immune deficiency syndrome (AIDS) is a major health concern in many parts of the world. Tourists may be exposed to health risks before, during and after leaving their countries of origin. Unfortunately, knowledge about the health status of tourists is often limited because they are often excluded from surveys. Tourism has been classified as playing a pivotal role in the spread of HIV and AIDS epidemic. However, it has not been well recognized that tourism is one of the leading activities contributing towards the spread of HIV and AIDS. In this thesis, we developed a mathematical models for HIV and AIDS epidemic to assess how the effect of outbound and inbound tourism have affected the spread of HIV and AIDS incidences in Malaysia. Applying the next generation matrix method to obtain the various basic reproduction numbers, the models were calibrated to HIV and AIDS incidence data in Malaysia using a Markov chain Monte Carlo (MCMC) approach to understand the impact of model-based estimation in light of uncertain parameters on the spread of HIV and AIDS. The models dynamics are analysed under these four scenarios: with the effect of outbound (Model I), inbound tourism (Model II), condom as preventive measure (Model III) and new born babies with HIV through sexual activities which runs through all the three models. The models show distinctive characteristics of positive equilibrium which depicts that both locally and globally are asymptotically stable under particular conditions. These confirmed the basic reproduction numbers that were calculated based on the estimated parameters. The basic reproduction numbers for Model I, Model II and Model III are 1.0262e-06, 7.8060e-01 and 7.1960e-01, respectively. Although, our results show that disease models are stable, this indicates that HIV and AIDS continue to persist at equilibrium level. This is a good

indicator from the public health point of view since the aim is to stabilize the epidemic at the disease-free equilibrium and this will assist public health policy decision makers to forecast and predict HIV/AIDS incidences. We further incorporate the use of condoms as a preventive measure to ascertain its impact on the spread of HIV and AIDS incidence. Thus, if condom as preventive measures are introduced, it reduces the HIV and AIDS incidences. The results indicate that with the persistent inflow of inbound tourists into the country, the disease status has increased. The results also suggest that the government must put more control on illegal prostitution, unprotected sexual activity as well as to emphasize the prevention policies that include safe sexual activity through tourism board campaigns. They should encourage free health care medical examinations for outbound Malaysian tourists after they have returned home. This will assist to reduce the rate of outbound tourists unknowingly spreading HIV.

ABSTRAK

Penyebaran jangkitan virus human immunodeficiency (HIV) dan akibatnya sindrom kurang daya tahan (AIDS) merupakan masalah kesihatan utama di banyak tempat di dunia. Pelancong mungkin terdedah kepada risiko kesihatan sebelum, semasa dan selepas meninggalkan negara asal mereka. Malangnya, pengetahuan mengenai tahap kesihatan pelancong terhad kerana mereka sering dikecualikan daripada kaji selidik. Pelancongan merupakan faktor penyumbang yang penting dalam penyebaran wabak HIV dan AIDS. Walau bagaimanapun, ia tidak diiktiraf sebagai salah satu aktiviti utama yang menyebabkan penyebaran HIV dan AIDS. Dalam tesis ini, kami membina satu model matematik untuk menilai kesan keluar dan masuk pelancong atas insiden penyebaran HIV dan AIDS di Malaysia. Menggunakan kaedah penjanaan matriks seterusnya untuk mendapatkan pelbagai nombor pembiakan asas, model-model telah ditentukurkan kepada data insiden HIV dan AIDS di Malaysia dengan menggunakan pendekatan rantaian Markov Monte Carlo (MCMC) untuk memahami kesan anggaran berdasarkan model, di mana terdapat parameter tidak tentu yang berkaitan dengan penyebaran HIV dan AIDS. Model-model dinamik dianalisis di bawah empat senario: dengan kesan pelancong keluar (Model I), pelancong masuk (Model II), kondom sebagai langkah pencegahan (Model III) dan bayi yang baru lahir dengan HIV melalui aktiviti seksual yang melalui ketiga-tiga model. Model-model menunjukkan ciri tersendiri keseimbangan positif yang menggambarkan kedua-dua tempatan dan global berasimptot stabil di bawah keadaan tertentu. Ini mengesahkan nombor pembiakan asas yang dikira berdasarkan parameter anggaran. Nombor-nombor pembiakan asas untuk Model I, Model II dan III Model adalah 1.0262e-06, 7.8060e-01 dan 7.1960e-01, masing-masing. Walaupun keputusan kami menunjukkan bahawa model penyakit adalah stabil, ini menunjukkan bahawa HIV dan AIDS berterusan pada tahap

keseimbangan. Ini adalah petunjuk yang baik dari sudut pandangan kesihatan awam kerana tujuannya adalah untuk menstabilkan wabak ini pada keseimbangan bebas-penyakit dan ini akan membantu pembuat dasar kesihatan awam untuk meramal dan menjangkakan kejadian HIV/AIDS. Seterusnya, kami menggabungkan penggunaan kondom sebagai langkah pencegahan untuk menentukan kesannya terhadap penyebaran kejadian HIV dan AIDS. Jadi, jika kondom berkesan diperkenalkan sebagai langkah pencegahan, ia mengurangkan kejadian HIV dan AIDS. Keputusan menunjukkan bahawa dengan kemasukan berterusan pelancong asing ke negara ini, status penyakit ini telah meningkat. Keputusan juga menunjukkan bahawa kerajaan perlu meletakkan lebih banyak kawalan ke atas pelacuran haram, aktiviti seksual yang tidak dilindungi di samping menekankan dasar-dasar pencegahan termasuk aktiviti seksual yang selamat melalui kempen oleh lembaga pelancongan. Mereka perlu menggalakkan untuk pemeriksaan kesihatan percuma untuk pelancong Malaysia yang keluar selepas mereka pulang ke negara ini. Ini akan membantu untuk mengurangkan kadar pelancong keluar menyebarkan HIV tanpa disedari.

ACKNOWLEDGEMENTS

Though only my name appears on the cover of this doctoral dissertation, many people have contributed to this thesis. I owe my gratitude to all those people who have made this doctoral dissertation possible and because of whom my graduate experience has been one that I will cherish forever.

I want to express my sincere appreciation and gratitude to my solely supervisor Prof. Dr. Noor Azina Ismail; for her warm encouragement, thoughtful guidance, helpful suggestions increased readability and reduced ambiguity.

My sincere gratitude goes to Dr. Bismark Oduro for reading versions of my dissertation, and for making valuable corrections and instructive remarks. I am very grateful to Sarah Crosswell, Folorunso Obasuyi, Susana Essel, Wong Pui Yi, Gold Kafila Lolah, Juliana Abd Kadir, Najla Abdallah Mohammed and David Ballard for their help and support at stages of this journey and have contributed to the development of my research.

I am greatly indebted to my devoted wife, Jennifer Acheampong, and my son, Ofosuhene Okofrobour Apenteng, that I named after me. They form the backbone and origin of my happiness. Their love and support without any complaint or regret has enabled me to complete this PhD project. Being both a mother and father while I was away was not an easy thing for my wife. She took every responsibility and suffered all the bitterness to take care of my son and my family. Even when my son was ill, both of them would not let me know so as to enable me to concentrate on my research. I owe my every achievement to both of them.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

CHAPTER 1: INTRODUCTION

1.1 Background of Study

Acquired Immunodeficiency Syndrome (AIDS) is caused as a result of Human Immun-odeficiency Virus (HIV), which progressively damages immune system, preventing the body's ability to fight infections. In 2014, 36.9 million people were affected with HIV globally (UNAIDS, 2014). The epidemic is increasing in frequency, magnitude, and greatly increasing globally. HIV/AIDS imposes a substantial economic burden and puts strain on the health care systems in many countries. The severity of HIV/AIDS has also steadily increased, with a substantial increase in severe cases of HIV/AIDS since its emer-gence in 1981. The fatality rate has remained relatively low in some developed countries as compared to the rate in developing countries (UNAIDS, 2009; UNAIDS/WHO, 2010).

In 1993, the United Nations World Tourism Organisation (UNWTO) referred to tourists as "the temporary visitors staying in a place outside their usual place of residence, for a continuous period of at least 24 hours but less than one year, for leisure, business or other purposes" (UNWTO, 1993). Generally, tourism is considered a rapid growing industry across the globe (Bauer, 1999, 2007) and can be classified as domestic and inter-national. International tourism has both incoming and outgoing economic implications on the host country. The benefits promote development of a country. As such, the outgoing represents the outbound tourists while incoming represents inbound tourists in this thesis.

The outbound tourism involves the movement of residents of a particular country traveling to other countries for leisure, business or for other purposes. On the other hand, the inbound tourism involves the activities of non-residents of a country, traveling to other countries for leisure, business or for other purposes. The outbound and inbound tourism stay in a particular country should not exceed a given period of one consecutive

year (March, 1997; Song, Romilly, & Liu, 2000; Jonsson Kvist & Klefsjo, 2006; Peeters, Szimba, & Duijnisveld, 2007).

The use of a mathematical model to determine the effect of tourism on HIV/AIDS cases has not been studied. The few research works did not use mathematical models. Many travellers who traveled during vacations are involved in sexual activity (Oppermann, 1999; Brennan, 2004; T. G. Bauer & McKercher, 2003). As they find these activities more accessible and affordable compared to sexual services in their home country, the spread of HIV and AIDS is equally inevitable (Sinka, Mortimer, Evans, & Morgan, 2003; Abdullah, Ebrahim, Fielding, & Morisky, 2004). Tourism is directly linked to the numerous spread of epidemics worldwide (Chen & Xiao, 2014; Kondgen et al., 2008; Figueroa et al., 1995; Matos et al., 2013; Padilla et al., 2012; Rice et al., 2012).

Millions of children are born with HIV (Sugandhi et al., 2013). The HIV progression rate and the contact rate between the sexually active population and HIV-positive individuals are significant (Nyabadza & Mukandavire, 2011; Steen, Wi, Kamali, & Ndowa, 2009). However, the rate of HIV-positive newborns in Malaysia is negligible (Huang & Hussein, 2004; Azwa & Khong, 2012; Apenteng & Ismail, 2015); thus, this study agrees that HIV is less commonly spread from mother to child during pregnancy, birth or breastfeeding (Vogt et al., 2015; Moreira-Silva, Zandonade, & Miranda, 2015).

Regarding HIV and AIDS, control of the disease is achieved by providing effective control measures and resources necessary to reduce transmission of the virus. Recent evidence shows that HIV/AIDS can be successfully be controlled by using condoms to reduce the transmission of HIV by at least 80–85% (Holmes, Levine, & Weaver, 2004; Steen et al., 2009). Condom use, distribution, and education has played a pivotal role in HIV prevention.

The epidemic models date back to the works of Kermack and McKendrick (1927,

1932, 1933) in the early twentieth century. They formulated the Susceptible-Infected-Removed (SIR) model for the compartmental spread of infectious diseases. On this premise, the SIR model is modified in order to address the fundamental questions raised in this thesis.

1.2 Problem Statement

Globally, Malaysia is positioned 11th and 2nd in the Southeast Asian countries for tourist attractions (MTPB, 2013). For example, in 2014 alone, there were 27,437,315 tourists that arrived in Malaysia which almost corresponded to the population of the country (MTPB, 2013). Over time, the number of tourists in Malaysia has been increasing, hence contributes to steady increase in the Malaysian economy (Tang & Tan, 2015). Though the economy of Malaysia expands through tourism, the large number of tourists that came in during same period brought in infectious diseases (Oppermann, 1992). As the tourists arrived into the country, the Malaysia government was not aware of the HIV/AIDS status of the tourists (Apenteng & Ismail, 2015). There is a need to determine, in clear terms, who among the tourists that has HIV and AIDS.

Moreover, the unavailability of data to identify those who have HIV among the tourists is a constraint to the Malaysia government. This generates concern for the inability of the government to control HIV/AIDS spread. Hence, increase in tourism that increases the spread of HIV/AIDS is a problematic issue in the health sector. To solve the problem will require determination of the parameters that would create data for further studies.

In the meantime, the number of Malaysians who travel abroad has also increased over time. While many traveled with family on business, a proportion of these travellers may be involved in sexual activities (Oppermann, 1992; Anders et al., 1999; Pocock & Phua, 2011). Following the review of the existing literature, to our knowledge, there are no mathematical models developed to investigate the effect of tourism on HIV/AIDS

spread (Dwyer & Forsyth, 1993; Ketshabile, 2007; Bauer, 1999, 2007, 2008b; Padilla et al., 2012). This had been caused by data constraint and over parametrization (Chu, Nie, Cole, & Poole, 2009; Smith et al., 2009). Nevertheless, there are some empirical works that used simulated or calibrated data to investigate the effect of tourism on HIV/AIDS transmission. This has not addressed the issue of lack of data to determine the magnitude of HIV/AIDS in Malaysia.

1.3 Main motivation

The motivation of this thesis is to investigate how tourism has affected the spread of HIV/AIDS. This is because it has become one of the attributes that contributes to the feared and devastating diseases which considerably affected human population. To our best knowledge, no other studies with mathematical models have ever been done before in Malaysia on tourism and HIV/AIDS. As such, this thesis adapted the modified version of the SIR model, taking into account the movement from one compartment to the other. This movement method is not found in panel data and time series analysis. We are equally motivated that data constraints in Malaysia on the inbound tourist have made forecasting of the effect of tourism on HIV/AIDS inconclusive (Apenteng & Ismail, 2015). Since there has been no mathematical modelling on the forecast as well as data limitations, it is presumed that the effect of condoms as a preventive measure and the new born babies likely to be infected, could have been a significant error in the previous studies, requiring an investigation. In so doing, this thesis assessed the effect of tourism on the spread of HIV and AIDS in Malaysia.

1.4 Aims and Objectives

This section discusses aims and objectives which led to the achievement of this thesis. The primary aim of this thesis is to construct mathematical models that can be used to

understand the effect of tourism on the spread of HIV and AIDS. It also demonstrates how time-varying with various SIR models can be extended to include the effect of tourism, HIV-positive newborn babies and condoms as a preventive measure. The available data was used to determine the arbitrary number of parameters that contributes to the spread of the disease in context of population inflows within the model. With the outcome of this thesis, we presented policy recommendations on how to minimise the spread of HIV/AIDS in Malaysia.

To address the aims outlined above, the specific objectives of the study are to:

1. Examine the effect of outbound tourism on the spread of HIV/AIDS in Malaysia.

2. Examine the effect of inbound tourism on the spread of HIV/AIDS in Malaysia.

3. Investigate the effect of implementing condom as prevention policies therapy and HIV control strategy.

4. Investigate the effect of newborn babies HIV-positive on HIV/AIDS transmission.

1.5 Research Questions

The main objectives of this thesis lead us to a major question: Do the dynamics of tourism influence the spread of HIV and AIDS incidences in Malaysia?

Based on the stated objectives, the thesis is designed to answer the following research questions.

1. What are the effects of outbound and inbound tourism on the spread of HIV/AIDS in Malaysia?

2. What is the effect of implementing condom as control strategy on HIV spread in Malaysia?

5

3. What is the effect of newborn babies with HIV-positive on HIV/AIDS transmission in Malaysia?

1.6 Scope of the research

The thesis used data from the Ministry of Health, Malaysia. The first HIV case reported in Malaysia was in 1986 (MoH, 2012a). From this information the thesis used a set of data between (1986-2011). This is to validate the formulated models in this thesis. Why Malaysia? This is because of its strategic place, attractive because of its people, climate and culture which attract a high rate of tourists. As mentioned earlier, in 2010 alone, over 24 million tourists came into Malaysia (MTCM., 2015), as shown in Figure 1.1. The rationale behind studying the effects of tourism on HIV/AIDS spread is because it is among the most increased pattern of tourist trend in Malaysia as depicted in the Figures 1.1 and 1.2 below.
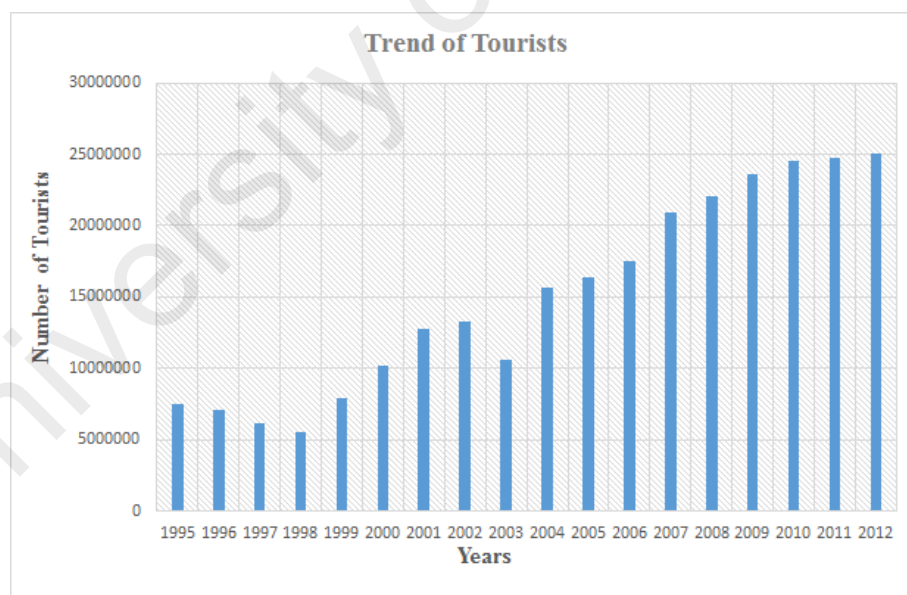
Figure 1.1: Trend of tourists

Figure 1.2, shows the cumulative number of HIV and AIDS incidences in the Malaysia.
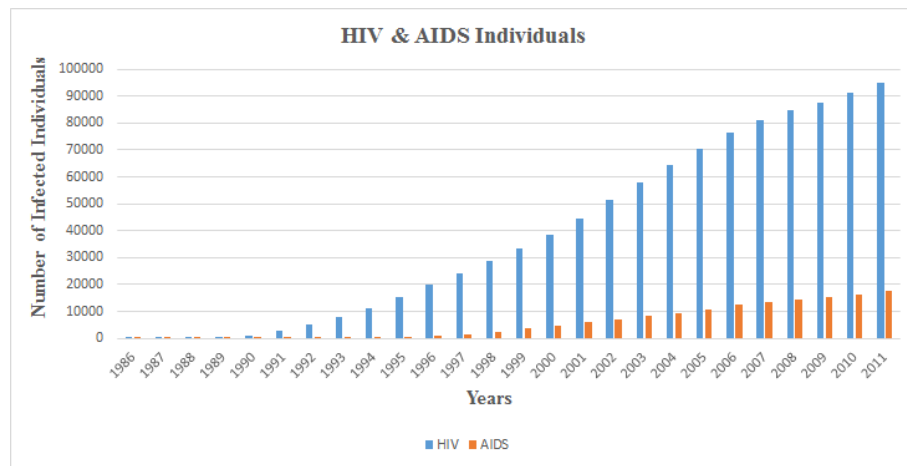
Figure 1.2: Trend of HIV and AIDS individuals in Malaysia

1.7 Justification for research

There are many examples of mathematical modelling of HIV/AIDS in epidemiological modelling (Mukandavire, Garira, & Tchuenche, 2009; Nyabadza, Mukandavire, & Hove-Musekwa, 2011; Apenteng & Ismail, 2015). These have being formulated based on individual behaviour towards how to handle the spread of HIV and AIDS epidemic in different countries as found in Chapter 2. However, none of these have addressed the issues raised in Section 1.5 in the context of Malaysia. We assumed that the approach with Markov chain Monte Carlo (MCMC) has the potential to supplement more mathematical model formulation to eliminate the difficulties in these models. The MCMC technique is employed to model infectious diseases mathematically in terms of parameter estimation (Haario, Laine, Mira, & Saksman, 2006; Laine, 2008; Petzoldt & Soetaert, 2010; Apenteng & Ismail, 2015). However, current models in the literature often do not take into consideration the effects of tourism on HIV and AIDS individuals, HIV/AIDS individuals capable of having children and the possible effective control measure. The outcome from these models could help to plan economic activities in the health sector of the Malaysia economy. In view of this, there is a need to develop mathematical models that would address the impact of tourists on HIV/AIDS transmission, and aimed at reducing HIV

and AIDS disease in Malaysia. Furthermore, there is a need to determine the number of tourists that are infected with HIV and AIDS. This mutually related phenomenon would help to illuminate the various effects of tourism on HIV/AIDS in Malaysia. Finally, the mathematical model formulated as adapted from SIR helped to forecast the trend of inbound tourists and the new born babies infected with HIV/AIDS in Malaysia.

Moreover, this research thesis proceeded to address the research gaps in our epidemiological models. As such, this research would not only benefit Malaysia Tourism Promotion Board (MTPB) but it would provide expert knowledge for other professionals in HIV/AIDS healthcare research forum.

1.8 Overview of thesis

The thesis is classified into six chapters. Figure 1.3 describes the chapters involved in this study.
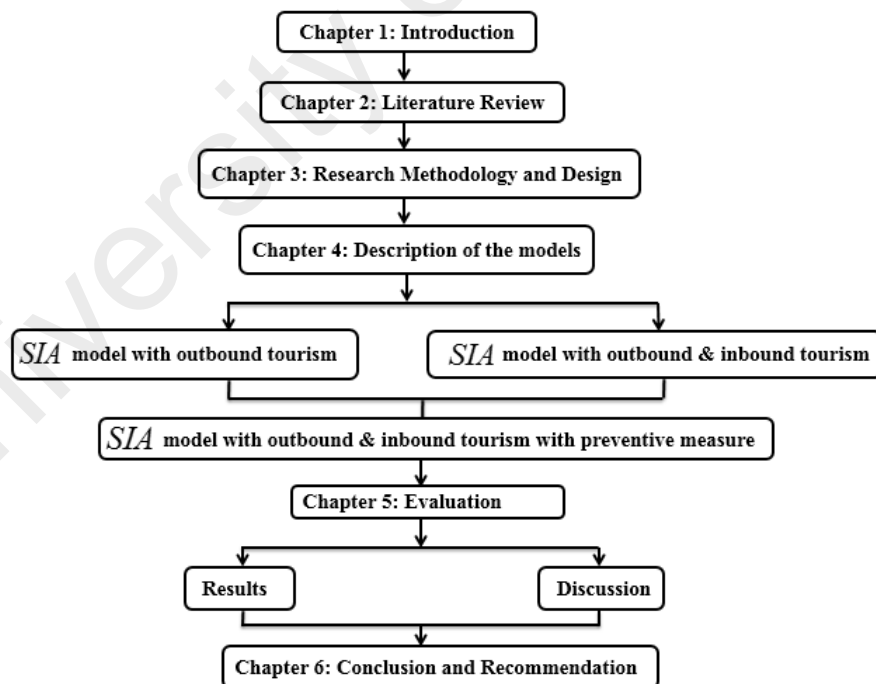
Figure 1.3: Thesis structure

This thesis is organized into six chapters. Chapter one of the thesis presents the introduction to this research study. It contains eight subsections. Section 1.1 presents

the introduction and background for the study. Introduction of HIV/AIDS, definition of inbound and outbound tourism and how they affect the spread of HIV/AIDS in Malaysia through sexual activities, newborn babies transmission, and finally preventive policies. Section 1.2 outlines the problem statement. The main motivations of this research are provided in Section 1.3, including the author's personal motivation of interest and experiences gained while conducting this research, and research questions. Details of the objectives and research goals are provided in Section 1.4. The research design is described in Section 1.5, where the source of data and assumptions of the models are briefly introduced. The challenges in mathematical modelling of HIV/AIDS disease are outlined in Section 1.6. Section 1.7 takes into account the justification for conducting this research work. Finally, the Section 1.8 outlines the structure of the study.

Chapter 2 gives a survey of literature. It focuses on SIR-type mathematical models. Firstly, it gives a general description of HIV/AIDS in Malaysia and tourism. Secondly, how congential transmission of HIV and preventive measures have impacted on the spread of HIV/AIDS. Finally, SIR models and its extension to various mathematical models in term of the HIV/AIDS epidemic.

Chapter 3 presents the methodology and design of this thesis. The various description of SIA models with its theorems, the scope of the data being used, construction of the mathematical models, and finally, the steps involved in the use of MCMC approach to estimate the parameters.

In Chapter 4, we constructed a deterministic mathematical model to reflect the effect of outbound and inbound tourism on HIV and AIDS cases. Conditions for local as well as global stability of the equilibria are derived. The congenital transmission and implementation of condoms as a control strategy on HIV spread were taken into account

Estimation of the models and discussion of findings characterize Chapter 5. Addi-

tionally, all the parameters for each model that influence the spread of HIV and AIDS in Malaysia were estimated.

Finally, Chapter 6 concludes the thesis by discussing the main findings in respect to the parameters and their contributions to the spread of HIV/AIDS in Malaysia. Further, the limitations of the study are discussed and policy recommendations were outlined.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

This chapter reviews prior research and various models that are relevant to the research problems addressed in this work. First, a brief discussion of HIV/AIDS which relates to sexually active and injection drug users (IDU). The effects of tourists in other parts of the world as well in Malaysia, and modelling HIV/AIDS with preventive measures. The general description of mathematical modelling which includes:

- a detail analysis of the *SIR* model with its extensions,

- a vivid description of how *SIR* model had being modified by deterministic approach,

- the used of MCMC techniques to estimate parameters.

2.2 Mathematical modelling on HIV/AIDS study

Prior mathematical models describing HIV transmission have concentrated mainly on populations of specific sexual orientation, that is, homosexual or heterosexual. The HIV/AIDS epidemic has hugely stimulated the use of mathematical models for describing infectious diseases (Punyacharoensin et al., 2016; Silva & Torres, 2017). The dynamic transmission of HIV infection and its eventual development into AIDS, has taken a central role in many mathematical models. Various improvements have been made since the initial HIV and AIDS models by Anderson (1986, 1988).

Many models have been developed to describe people who inject drugs (PWID) (Paraskevis et al., 2013; Wilson & Zhang, 2011; Bramson et al., 2015; Iversen, Page, Madden, & Maher, 2015; Li et al., 2015; Genberg, Astemborski, Vlahov, Kirk, & Mehta, 2015; West et al., 2015). Greenhalgh and Hay (1997) extended Kaplan's model to demonstrate the spread of HIV and AIDS among drug users. The authors assumed that a syringe

used by an HIV-infected person cannot always be infected with HIV infection. Others are iterative, Murray, Law, Gao, and Kaldor (2003) presented the impact of behavioural changes on the prevalence of HIV among injecting drug users. Wilson and Zhang (2011) developed a mathematical transmission model for HIV epidemics among men who have sex with men (MSM) and PWID. They suggested that it would be good to incorporate the evaluation of specific public health programmes in order to provide understanding of the importance of the HIV epidemic. Blower, Hartel, Dowlatabadi, Anderson, and May (1991) developed a mathematical model for heterosexuals and PWID of HIV individuals in New York City. Their study was conducted to ascertain the partial rank correlation coefficients of the key parameters. Wilson, Donald, Shattock, Wilson, and Fraser-Hurt (2015) admitted that there is the need to improve health outcomes for PWID, this included reducing the high and increasing rates of HIV to understand the cost effectiveness of harm reduction programs. Paraskevis et al. (2015) presented how to use molecular epidemiology to understand the outbreak of HIV among IDUs in Athens and Bucharest.

It was found that IDU were the driving force to spread the infections at the early stages of the epidemic in Malaysia, which constituted 70-80% of all the reported cases (Bazazi et al., 2015; MoH, 2012a). In 1994, the highest ratio of IDU/sexual mode of transmission reached 12.2%, this pattern totally shifted sexual mode of transmission with PWID/sexual transmission from 3.9% in 2000 to 0.3% in 2013, (UNGASS, 2010; MoH, 2012a). In 2013 alone, there were 3,393 reported cases of HIV representing nine cases per day. Whereas in 2002, the disease had reached its peak with infected cases of 6,978 (MoH, 2012b).

As in many parts of the world, population movement, including tourism, has become the most universally accepted, supported and lucrative tool for big business. It is a successful business operation, generating considerable revenue and publicity for many

countries worldwide. It is estimated that 50% of travellers engage in sexual practices while abroad (Ericsson, Steffen, Matteelli, & Carosi, 2001). For example, in 2004, Cable News Network (CNN) reported that 16,000 to 20,000 people are estimated to be child sex victims in Mexico, largely in border, urban, and tourist areas (Courson, 2004). In the United Kingdom, a study was conducted by Hawkes, Malin, Araru, and Mabey (1992) involving 258 heterosexual travellers who attended the Hospital for Tropical Diseases in London. Their study revealed that the rate at which foreigners acquired HIV infection was 33.2% as compared to the rate of 1.8% of locally acquired HIV infection.

However, the negative impact of tourism on the host countries, may be either direct or indirect. For instance, the direct impact is the possible transmission of infectious diseases from tourists into the destination countries populace (Bauer, 2008b). The sexual behavior of tourists may impact on the host country in terms of the spread of infectious diseases especially when there are unprotected sexual activities. The direct impact of tourism is mainly to those where diseases are spread into the host country from the tourists who either come with the disease from their home country or pick it up during their stay either sexually or through drug use/share (Bauer, 2007, 2008b).

Tourism per se may not always increase sexual activity of the individual(s) involved, but sexual behavior of the tourists may have an impact on the host country in terms of spread of infectious disease, especially when there are unprotected sexual activities. Child sex tourism is now on the increase, virgin girls are given to tourists for unprotected sex, at times without their knowledge (Bauer, 2008b). Specifically, travellers may not be controlled or restricted in one way or other due to the movement of people coming overseas. The morality of tourists, as a result, has become a problem of serious consequence. However, the ramifications of HIV which trigger AIDS control efforts for international travellers are a growing concern to the world (Lewis, 1989).

Many travellers travel for affordability of sexual services to their travelling destination (Abdullah, Fielding, Hedley, & Luk, 2002) and sex partners who travelled to Thailand (Abdullah et al., 2004) who travelled to Thailand for sex tourism (A. Wilson, 2010; Ocha & Earth, 2013). For instance, in Europe, there has been an increase of new HIV/AIDS cases among immigrants (Sinka et al., 2003). This is no different from Asia and Africa: migrant labourers, long-distance truck drivers, and commercial sex workers with HIV infections travel to other countries for greener pastures. Tourism has brought many benefits such as foreign investment and is a source of income to many countries but it has also caused negative impacts on some countries. For example Thailand (Ocha & Earth, 2013), which is a hot spot for sex tourism, is not dangerous but rather it becomes dangerous when there is unprotected intercourse.

Bauer (1999) analyzed the impact of tourism in developing countries on the health of the local host communities and suggested that there is a need for more research. For example in Peru, Bauer (2007), examined the sexual activities between the local tourists in terms of AIDS. Apenteng and Ismail proposed a mathematical model to study the impact of international travellers (tourists) on the spread of HIV and AIDS epidemic using compartmental differential equation models in Malaysia (Apenteng & Ismail, 2015). According to the authors, mathematical modelling has the potential of improving public health sectors.

Qualitative studies conducted by Greene et al. (2015) have raised the question of how HIV-positive mothers breastfeed their babies in Canada without transmitting the infection to their newborn children. At the same time, the mortality trend of children born with HIV has been increasing. In the case of Brazil, the available data and evidence were presented in studies by Moreira-Silva et al. (2015) found that the cause of death among children born with HIV is due to their late diagnosis. There have been several studies conducted

on mother-to-child infection in HIV/AIDS (Drake, Wagner, Richardson, & John-Stewart, 2014; Gourlay et al., 2015; Mulugeta et al., 2015; Okawa et al., 2015; Palombi et al., 2015; Vogt et al., 2015), and there is a need to rethink how the introduction of treatment for children infected by their mothers is considered (Sugandhi et al., 2013).

2.3 HIV/AIDS in Malaysia and tourism

Since 1986 when the first HIV/AIDS case made its debut in Malaysia, HIV/AIDS has spread widely ever since, becoming a significant problem and one of the country's most serious health and development challenges (MoH, 2012a). According to the population census in 2014, Malaysia's total population was estimated at 30.4 million people and with one of the fastest growing economies in South-East Asia (DoS, 2014). The country is challenged with one of the most deadly diseases in the world with alarming cases of HIV/AIDS incidence (MoH, 2011; UNICEF, 2014). In 2013, World Health Organization (WHO) declared that in Asia-Pacific region, Malaysia hass the fifth fastest-growing infection rate (WHO, 2013). This epidemic is far above 5%, and it is prevalent among Most-at-Risk Populations (MARPs), especially PWID, Sex Workers (SW), Transgender (TG) and Men who have sex with men (MSM) populations (MoH, 2012a).

There are many advantages of tourism to local economies and Malaysia is an increasingly favourite destination in the Southeast Asia. In 2014 alone, there was a total of 27,437,315 tourist arrivals generating MYR 72.0 billion to the Malaysian economy (MTCM., 2015). While there are many advantages of tourism to local communities, studies suggest that tourism areas may become ecologies that heighten HIV vulnerability. Exposure to tourism can promote behaviours such as commercial and transactional sex (Oppermann, 1999). Sexual contact alone does not provide evidence of a higher risk for HIV transmission, alcohol and drug use in tourism areas are also major sources of evidence that such contact may involve a particularly high risk (Bishop & Robinson, 1998).

Clancy (2002) revealed that most of these sex workers prefer foreign tourists due to the money involved. The author further explained that at times, the sexual activities of these tourists involved unprotected sex which had a high risk of HIV infection.

Furthermore, most tourists that are involved in these activities, are from regions where HIV prevalence is high. For example, the rate of sex workers who use condoms is also low given that they come from disadvantaged backgrounds. Due to this activity, there are a lot of children born to foreign travellers, with no financial support and with a high risk of HIV (Bauer, 2008a).

2.4 Congenital transmission of HIV

Congenital transmission is the same as vertical transmission infection, that is, from the mother to the fetus, during pregnancy or after childbirth. HIV-infected mothers transfer HIV to their newborn babies through breastfeeding. Chang et al. (2015) came out that 2.3% infection rate of HIV was attributable to breastfeeding in Malawi. In China the rate of maternal-to-child transmission of HIV is 8.1% alone (Wang et al., 2015). This is not different from South Africa, infected HIV mothers were put on antiretroviral therapy in order to prevent the unborn babies from getting HIV (Manicklal et al., 2014). The risk for mother-to-child transmission of HIV has consistently increased in HIV infected women (King, Ellington, & Kourtis, 2013). The infection rate of mother-to-child in the United States between ages 12-49 is 1.6 representing 1.7 of the basic reproduction number (Colugnati, Staras, Dollard, & Cannon, 2007). Mukandavire and Garira (2007) formulated a sex structured HIV/AIDS model for mother-to-child effects of HIV infection due to breastfeeding. Townsend et al. (2008) analysed the effect of different strategies to prevent mother-to-child transmission in the United Kingdom and Ireland. No other studies of this mother-to-child HIV transmission with mathematical models has ever been done before in Malaysia.

Sharing injecting drug equipment has also contributed to the spread of HIV (Saraswati et al., 2015; Coffin, Rowe, & Santos, 2015). The World Health Organization (WHO) estimated that globally there are 16 million of PWID and out of this, 3 million of them are living with HIV (Burns, 2014). For instance, 80% of all HIV infected cases are a result of drug use, in some parts of Eastern Europe and Central Asia (HRI, 2012).

2.5 Preventive measures

In recent times, advances in treatments in HIV/AIDS have become a major concern to many countries. For instance, the government of Thailand introduced 100% condom program, whereas in Tanzania, a community based education program was introduced to minimize the spread of HIV/AIDS (Bertozzi et al., 2006). The United Nations played an important role in implementing preventive measures on the spread of HIV/AIDS. The UNAIDS held its 38th meeting on 1st July 2016 at Geneva and came out with good development goals to end the HIV/AIDS by 2030 (UNAIDS, 2016).

Many researchers have come out with several preventative measures for HIV (Pinkerton & Abramson, 1997; Adih & Alexander, 1999). One method of HIV prevention is the use of condoms, which prevent individuals who are susceptible from getting HIV (Manhart & Koutsky, 2002). Pickles et al. (2013) proposed a mathematical model of HIV by targeting high-risk groups with prevention programmes in South India. Cabezas, Fornasini, Dardenne, Borja, and Albert (2013) proposed a framework to estimate HIV/AIDS prevalence, by means of a validated questionnaire, and prevention measures with working sectors in Ecuador. However, there has been effective preventive measures against HIV infection (Mclean & Blower, 1993; Schmitz, 2000; Velasco-Hernandez, Gershengorn, & Blower, 2002; Moghadas, Gumel, McLeod, & Gordon, 2003; Blower, Bodine, & Grovit-Ferbas, 2005; Nishimura & Martin, 2011). Nyabadza and Mukandavire (2011) presented a simple deterministic model for HIV/AIDS by incorporating the use of condoms, sexual partner

acquisition, behavior change and treatment. The results suggested that HIV/AIDS could be controlled.

Recently, many mathematical models have been developed to analyse the control strategies in the past (Negredo et al., 2015; Levine, Leskowitz, & Davis, 2015; Sripan et al., 2015; Nyabadza et al., 2011; Abdullah et al., 2002). Mathematical analyses of a different strains of HIV/AIDS at population based levels with antiretroviral treatment have been modeled (Bhunu, Garira, & Magombedze, 2009; Eaton & Hallett, 2014; Falconer, Sandberg, Reichard, & Alaeus, 2009; Jansson, Kerr, & Wilson, 2014; Tamizhmani, Ramani, Grammaticos, & Carstea, 2004; Wilson & Zhang, 2011). Greenhalgh, Doyle, and Lewis (2001) formulated a mathematical model of how the use of condoms can minimize HIV in San Francisco and USA. They suggested that the use of condoms has important implications for control of the disease to reduce the spread of HIV.

Antiretroviral medication (drug treatment) is recommended for all individuals with HIV, irrespective of the duration the individual has been infected with the virus (Eaton & Hallett, 2014; Nosyk et al., 2015; Duber et al., 2015). Kamarulzaman and Altice (2015) admitted that there is a need for taking into account treatment readiness attitudes to reduced HIV spread among PWID in Malaysia. There is evidence showing that when effective treatment is introduced to HIV positive individuals, it delays the progress from HIV to AIDS (Cai, Li, Ghosh, & Guo, 2009; Cai, Guo, & Wang, 2014). In contrast, Eaton and Hallett (2014) proposed that early-stages of HIV treatment does not necessarily mean a long-term individual life span. Huo and Feng (2013) presented how to use the global stability to analysis the spread of HIV model with treatment.

2.6 Modelling with SIR models and extension

The next section addresses some of the modified SIR models. This thesis took into account some of the SIR modified on deterministic models and its importance. Over the past three

hundred years, researchers from various disciplines have used mathematical models to address issues, challenging the understanding of the spread of infectious diseases. This has been beneficial in many ways, for instance, empirical results have helped to improve public-health questions with regard to basic transmission of diseases.

The use of differential equations became important in early 1900s. Ross (1911) developed mathematical a model for malaria. The work of Ross was extended by Kermack and McKendrick in 1926 to obtain epidemic threshold results. Kermack and McKendrick (1927) formulated the SIR model which has become the central fundamental system in epidemiological modelling. The fundamental SIR model was based on deterministic differential equations. Subsequently, the model was given a stochastic dimension by Isham (1988, 1993) with the introduction of natural birth and death rates as demographic features. Since then there have been several modifications of the SIR model that have been developed over the years by changing the assumptions (Inaba, 2007; Bhunu, Mushayabasa, Kojouharov, & Tchuenche, 2011; Mukandavire et al., 2011; Naresh, Tripathi, & Sharma, 2011; Z. Wang, Fan, Jiang, & Li, 2014; Witbooi, 2013; Apenteng & Ismail, 2014; Biswas, Paiva, & de Pinho, 2014).

2.6.1 Stochastic models

Metapopulation gives a good understanding of how to develop spatial models. In spatial models, metapopulation gives a useful description framework by partitioning the population due to the geographical location of the hosts (Keeling, 1999). In all disease modelling the mode of infection is very significant. In case of subpopulations of spatial models the rate of infection can be calculated by summing up the prevalences. The subpopulation of stochastic modelling of infection is always reduced as compared to that of deterministic models. The concept of spatial modelling consists of different methods (Ingemar, 2002). The correlations between subpopulations are also taken into account. For example, posi-

tive correlations are synchronous and negative correlations are asynchronous (Anderson, 1988; Keeling, 1999).

For example, when the interactions between populations are too small the effective dynamic nature of spatial aspect becomes unimportant (Ferguson et al., 2003). In contrast, when the interaction is too large, the effective dynamics are synchronized, which indicates that the subpopulations are well mixed population and once again the spatial aspect becomes unimportant. The degree of knowledge is about the behaviour of the disease and how the scale is chosen. There are two types of scales which play very significant roles in spatial models. These are: 1) the scales of interaction, and 2) the scale of simulation. These two are important because in spatial models the interaction or the neighbourhood is very necessary.

To assess the scale of the individuals who are involved in the interaction, the individuals are then divided and the larger scale at which the simulations are performed can be based on the simulated results (Keeling & Rohani, 2008). Hohle and Feldmann (2007) use stochastic epidemic models to describe how disease transmission can be modelled spatially. On the other hand, deterministic models do not depend on individual randomness.

2.6.2 Deterministic models

Compartmental models are known as deterministic models (Wanduku & Ladde, 2012; Kaddar, Abta, & Alaou, 2011). Deterministic models suit large populations. One of the advantages of deterministic modelling is that it is efficient when it comes to sensitivity analysis as compared to stochastic modelling. For instance, the $SEIR$ model consists of four compartments represented by the Susceptible, Exposed (infected), Infectious, and Recovered or Removal (d'Onofrio, 2002; Biswas et al., 2014; Liu, Bai, & Wang, 2014; Artalejo, Economou, & Lopez-Herrero, 2015).

Numerous studies have examined how to forecast the spread of HIV and AIDS cases from an epidemiological data point of view. De Gruttola and Mayer (1988) assessed how to implement a fitted model of HIV epidemic of heterosexual in the United States. Hyman and Ann Stanley (1989) generated mathematical models based on the underlying transmission mechanisms of AIDS, which were used to understand and anticipate its spread in different populations. Romieu, Sandberg, Mohar, and Awerbuch (1991) presented work demonstrating how to model the spread of AIDS in Mexico City. The goal of their work was to provide a conceptual framework to help understand the transmission dynamics of infection and give a reasonable estimation for the short-term prediction of the cumulative number of AIDS cases. Mathematical modeling of the spread of AIDS has become even more useful in the modern era of AIDS research.

Merli, Hertog, Wang, and Li (2006) presented an exploration of the implications of patterns of sexual behavior for the spread of HIV in China; this model reflected the uncertainty surrounding key parameters, and the analyses used showed a range of possible outcomes. Kakeshashi (1998) formulated a mathematical model to describe the spread of HIV/AIDS among adult commercial sex workers in Japan, which was used to analyze the effect of HIV-infected commercial sex workers introduced into a population without HIV. de Arazoza and Lounes (2002) outlined how a non-linear model could be used to develop an epidemic with contact tracing, specifically in Cuba. The authors suggested that to control the spread of HIV/AIDS, the target group must be in contact with individuals who carry HIV. Nishiura (2007) studied predictions of AIDS incidence in the United States and Japan. The studies failed to predict AIDS incidence in both countries. Similar work was done in South Africa by Nyabadza et al. (2011) to forecast the trend of HIV/AIDS epidemic.

2.6.3 The use of MCMC for parameter estimation

Kim formulated a simple continuous model for the transmission of HIV, although this model failed to take into account the demographical parameters that have a significant impact on modeling the spread of HIV (Kim, 2009). Furthermore, most of these previous models have serious drawbacks. For instance, most of these models have failed to demonstrate how the impact of AIDS causes the death of HIV-infected individuals. These models also typically describe changes in time, therefore are referred to as dynamic models, where time is the independent variable. Similar work was conducted by Haario et al. (2006), the authors proposed various strategies to combine two quite powerful ideas in the MCMC, in which they used adaptive metropolis samplers and delayed rejection to study the spread of algae. Apenteng and Ismail (2015) studied model fitting by using MCMC approach to estimate AIDS after HIV infection in Malaysia. They estimated that without the intervention of antiretroviral medication (drug treatment), the rate at which an individual will fully developed AIDS after HIV infection class is 0.99/year.

There has been several papers about modelling HIV with contributing factors that might have its impact on the spread. Unfortunately, there is little understanding of how to model the impact of tourism on the spread of HIV in public health fields. This makes it necessary to understand the pattern of tourists on the spread of HIV/AIDS.

2.7 Chapter summary

This chapter has provided an adequate survey of important models in support of this research work. Moving forward, evidence will be demonstrated of inadequate modelling of tourists on the spread of HIV and AIDS cases. This has led to a recent shift in the understanding of how to model the impact of tourists on HIV and AIDS mathematically with the MCMC approach to estimate the parameters involved. This move is appropriate, given that, most of these models presented in the literature may be considered epidemiologist

driven.

CHAPTER 3: RESEARCH METHODOLOGY AND DESIGN

3.1 Introduction

The use of mathematical models to examine infectious diseases is of considerable fundamental importance to obtain information such as the underlying mechanisms, which influence the spread of the disease. These models predict and identify the behaviour of the strains of the disease. Therefore, some simplification is needed to reduce the complexity of the models. Our approach here is to formulate mathematical models for the effect of tourists on HIV/AIDS spread. Mathematical models are powerful tools for investigating human infectious diseases, for example, HIV and AIDS. They indeed could contribute to the understanding of the dynamics of disease which can provide valuable information for public health policy makers (Bramson et al., 2015; Luboga, Galukande, Mabweijano, Ozgediz, & Jayaraman, 2010; Padilla et al., 2012).

The mathematical modelling of HIV/AIDS epidemic in this thesis is concerned with the infection processes, mainly from person-to-person contact within a population through sexual activity. It will be interesting to build a simple model to study the effect of tourists on the spread of HIV and AIDS.

Mathematical models assist the understanding of the effects of tourism on the spread HIV and AIDS through the following:

- Empirical results from mathematical models are easily compared with observational data to validate and test for accuracy of the model strengths and weaknesses.

- Models can be used to understand and forecast epidemics according to different scenarios due to intervention programs.

There is a need to model the effects of tourism patterns, babies born with HIV and condom use on the spread of HIV and AIDS to understand how the spread of HIV/AIDS

could be minimized. For example, recent events in Malaysia indicate that there is an increase in tourism issues in the country that could pose a high risk for the spread of disease. Relatively few research has been done on how tourism has impacted on HIV/AIDS in various countries. However, no work had been done in Malaysia.

Against this backdrop, Malaysia has become a tourist destination for people from all over the world. This according to literature, has been attributed to the spate of rapid infrastructure development in Malaysia (Narayanan, 1992; Kassim, 1998; Pillai, 1998; Hugo, 2011; Nah, 2012; Tan & Gibson, 2013; Hafiz, Jamaluddin, Zulkifly, & Othman, 2014; Nair, Chiun, & Singh, 2014; Ramdas & Mohamed, 2014; Shaffril et al., 2015; Tang & Tan, 2015). While the inflow of people has led to improvements in Malaysia's economic development, it has also led to an increased spread of HIV/AIDS in the country.

3.2 Data

The primary data sources for this study was collected from the report produced by Ministry of Health (MoH) (MoH, 2012a). These data were collected and collated by MoH from various resources such as related ministries, universities, NGOs and prisons. The data consist of the number HIV and AIDS yearly incidences reported between 1986 to 2011 for Malaysia. In 1986, the Malaysian population was 16,329,400. There were only 3 HIV cases and 1 AIDS case in 1986, representing $I(0) = 3$ and $A(0) = 1$ respectively (MoH, 2012a). Hence, there were 16,329,396 individuals who are susceptible to infection in 1986. The total number reported case of HIV/AIDS in 2011 alone since 1986 was 94,841, 17,686 and 14,986 are HIV infections, living with AIDS and were deaths related to HIV/AIDS, respectively, thus giving reported number of people living with HIV (PLHIV) of 79,8552. The annual number of reported new HIV cases by the MoH has been on a steady decline from a peak (epidemic) of 6,978 in 2002. In 2011, there were 3,479 new cases reported to the MoH, approximately halve of what was reported in 2002 with an

average of 9 new cases each day (MoH, 2012a). This was repeated in 2013 alone 3,393 new HIV infections detected with an average of 9 new cases per day (MoH, 2014). The trends of HIV and AIDS incidences are shown in Figure 1.2. In 1986, the total number of tourists in Malaysia was 3.2 million (Bujang, 2005). The tourist data an illustrated in Figure 1.1, is used to estimate the number of HIV and AIDS cases of inbound tourists. To simplify our proposed model and due to data availability, we neglect the various stages in HIV infections: acute HIV infection and clinical latency, in order to make the proposed model more tractable.

3.3 Construction of mathematical model

We construct a population-based compartmental epidemic model which integrates knowledge of tourism regarding its effect on HIV and AIDS disease. In a population-based compartmental epidemic model, it is assumed that the total population size in each compartmental level is differentiable with respect to time. Thus, the transformation rates form one compartment level to another compartmental level can be expressed in terms of derivative with respect to time. In view of this, we intend to build a mathematical model that will reflect the effects of tourism on the spread of HIV and AIDS disease. There is a need to estimate the unknown parameters of the model by fitting it into the epidemiological data from Malaysia, with the optimal values of epidemiological parameters, derived from the population based compartmental predictions that give the best-fit to the data. A Bayesian approach was used to estimate the parameters involved (Paraskevis et al., 2003) via the MCMC method (O'Neill, 2002; Xun, Cao, Mallick, Maity, & Carroll, 2013; Xiao et al., 2013). With the reason that every model is based on parameters that have the most effect and least effect on the disease.

As described previously, the mathematical models in this thesis will be formulated by expanding the *SIR* models (Kermack & McKendrick, 1927, 1932; Anderson, 1988,

1986; Kermack & McKendrick, 1991). We replaced the removal class by AIDS class, which then becomes Susceptible-Infected-AIDS as SIA.

When formulating a mathematical model, it is necessary to follow a number of procedures to assure it's suitability for the scientific problem and taking into account all the important information in order to address it. Figure 3.1 depicts the steps that were involved in the formulation of these models that were followed to develop the models in the proceeding chapter.
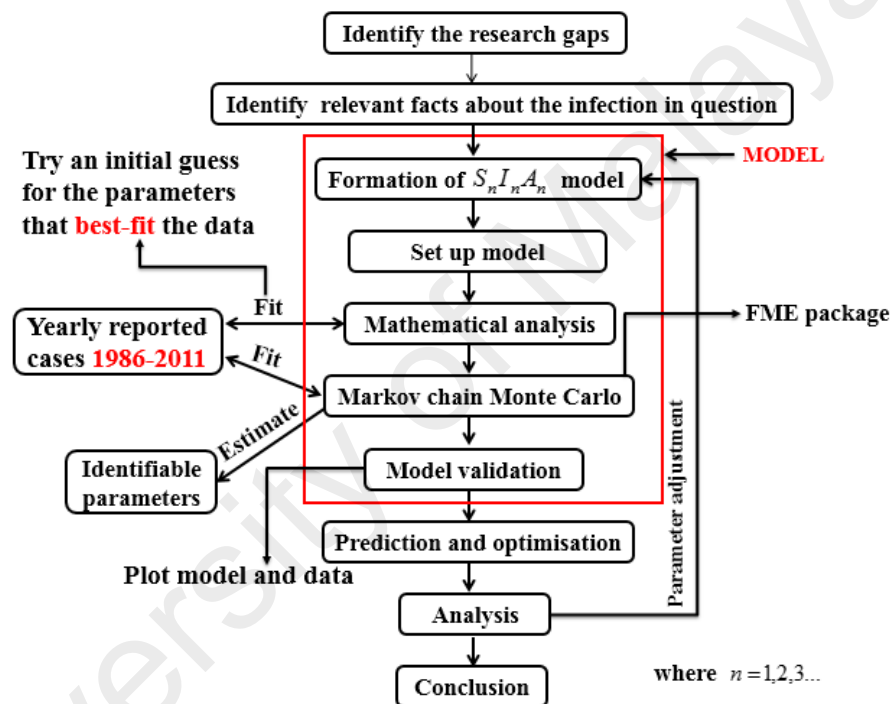
Figure 3.1: Description in the formulation of the models

From Figure 3.1, these models will be proved for mathematical correctness which will be described in Chapter 4. Adjusting and modifying the parameters of the formulated models provides a better understanding that could be used to analyse the problem by fitting into a real data. Bayesian inference plays a very important role when considering the uncertainties in the estimation of unknown parameters. The models that will be presented are meant to fit epidemiological data from Malaysia. It is therefore possible to demonstrate the validity of the models. The models will prove to be mathematically sound

through validations that would be used to test real data. Using mathematical models we can save time. We plot estimated parameters for different scenarios much more quickly than the time the disease might actually take to run its course in the population (Hyman & Ann Stanley, 1989; Romieu et al., 1991; Mukandavire et al., 2011).

In order to calibrate the models, MCMC will be used to estimate the parameters involved (Putter, Heisterkamp, Lange, & de Wolf, 2002). The MCMC approach is more useful in dealing with the non-linearity and interdependency of parameters through their application to a model describing the dynamics of HIV (Petzoldt & Soetaert, 2010). MCMC is one of the most important techniques used to estimate parameters to supplement mathematical modeling in order to calibrate parameter unpredictability (Haario et al., 2006; Apenteng, 2009; Laine, 2008). This has never been done with HIV/AIDS modelling in Malaysia. For more details of these models see Chapter 4 also described in Sections 4.2, 4.5 and 4.7.

3.4 Parameter estimation

The general strategy for model calibration is to define the parameters related to the history of HIV. The empirical results of the analysis will adapt similar approaches used by O'Neill (2002), Haario et al. (2006), Petzoldt and Soetaert (2010) and Apenteng and Ismail (2015) to obtain the posterior probability density for the unknown estimated parameters due to lack of information. Bayesian inference approaches allow the prior information to be inferred from the uncertainties in each of the models.

Construction of an epidemiological model is a very complicated task. As illustrated in Figure 3.1, the problem clearly cannot be statistical solved. However, to validate the model and in order to predict the observations, statistical approaches are able to inform the possible solutions by fitting the set of models into a given epidemiological data set with the prior information that is available. Let's consider a brief description as to how

the concepts of the model would be determined by the Bayesian framework (for details see (Laine, Tamminen, Kyroa, & Haario, 2007)). Let x represent the unknown variable of the main primary interest, and θ^k for the unknown parameters with set of k in the model. The aim is to observe epidemiological data y to estimate the unknowns x, θ^k. In order to apply the Bayesian inference we assign a prior probability by considering all the unknown parameters as, $p(x, \theta^k, k)$. By applying the conditional probabilities rules, the prior probability becomes:

$$p(x, \theta^k, k) = p(x|\theta^k, k)p(\theta^k|k)p(k). \tag{3.1}$$

where $p(x|\theta^k, k)$ is the probability of unknown variables, $p(\theta^k|k)$ is the model parameter in each model, and finally $p(k)$ is the prior probability of the difference models.

There is a need to build the likelihood function $p(y|x, \theta^k, k)$ in order to determine the noise in the distribution of the epidemiological data sets. By using the Bayes formula, the joint posterior distribution is the product of the likelihood and the prior:

$$p(x, \theta^k, k|y) = \frac{p(y|x, \theta^k, k)p(x|\theta^k, k)p(\theta^k|k)p(k)}{p(y)}. \tag{3.2}$$

Where $p(y)$ is the unconditional probability of the epidemiological data set which is the normalizing constant that makes the probability distribution.

3.4.1 Markov Chain Monte Carlo Method

MCMC has become very effective when applied to non-linear models by taking into account both the uncertainty in the model parameters and in the model output. This thesis will discuss its algorithms theories, and give a realistic complexity connection of how the

MCMC could be used to estimate parameters for predictions.

3.4.2   Why use MCMC?

MCMC is a statistical tool that has been in existence since Monte Carlo techniques received considerable attention (Brooks, Gelman, Jones, & Meng, 2011; Rubinstein & Kroese, 2011). It is an established method that enhances samples drawn from a target density that is only known up to proportionality due to the following reasons:

- It permits a huge amount of modelling flexibility that represents the true dependent structures in the data, rather than those that are simple to compute. Analytically it enable one to choose a convenient distributional form or the infectious periods, so that the integrals can be explicitly evaluated (Pritchard, Stephens, & Donnelly, 2000; O'Neill, 2002; Salakhutdinov & Mnih, 2008).

- The second point, the methods enable analysis of very complicated models (of all the model parameters involved) (Huelsenbeck, Ronquist, et al., 2001; O'Neill, 2002).

- The third point of MCMC is that, in combination with the Bayesian approach and MCMC it is unbiased to the sample size (Besag & Green, 1993; Huelsenbeck et al., 2001).

There are many Bayesian inference via MCMC techniques. In this thesis we will adapt the use of Metropolis-Hastings algorithms from Gibbs sampling. Which will represent a good description of this study.

3.4.3   Metropolis-Hastings algorithm

There are many ways to construct a Markov chain with stationary distribution π. Perhaps the simplest is the Metropolis-Hastings algorithm. The algorithms that lie behind MCMC and generate the samples. The Metropolis algorithm was later generalized by Hastings

(1970).

- Initialize by choosing starting point X_1

- Choose a new candidate at $X_n = x$, randomly propose a new position $X_{n+1} = y$ according to a proposal density $q(y|x)$ that depends on the previous point of the chain.

- Accept the candidate with probability

$$min\left(1, \frac{\pi(y)q(x|y)}{\pi(x)q(y|x)}\right).$$
(3.3)

If rejected, repeat $X_{n+1} = x$. Go back to steps 2. The point may still be accepted, with the probability that is given by the ratio of π values.

3.4.4 Why the Metropolis-Hastings algorithm works

We let $p(dx, dy)$ denote the transition kernel of the chain. Then $p(dx, dy)$ is approximately the probability that the chain jumps from a region dx to a region dy. $p(dx, dy)$ is calculated as follows:

$$p(dx, dy) = q(dy|dx)\left(\frac{\pi(dy)q(dx|dy)}{\pi(dx)q(dy|dx)} \wedge 1\right)$$
(3.4)

$$= \frac{\pi(dy)}{\pi(dx)}q(dx|dy) \wedge q(dy|dx)$$
(3.5)

$$\pi(dx)p(dx, dy) = \pi(dy)q(dx|dy) \wedge q(dy|dx)$$
(3.6)

Thus

$$\pi(dx)p(dx, dy) = \pi(dy)p(dy, dx) \tag{3.7}$$

$$\int_{dy \in S} \pi(dx)p(dx, dy) = \int_{dy \in S} \pi(dy)p(dy, dx) \tag{3.8}$$

$$\pi(dx) = \int_{dy \in S} \pi(dy)p(dy, dx) \tag{3.9}$$

This last equation (3.9) shows that π is a stationary distribution for the Markov chain. The choice of proposal $q(y|x) \sim N(0, \sigma^2)$ (Gaussian proposal) is fairly arbitrary. We chose the Metropolis-Hastings, MCMC is almost always used for multi-dimensional problems because it is possible to update each component separately as for example given a target density $\pi(x_1, x_2, \ldots, x_n)$.

Perhaps the most successful of these simulation algorithms is the Metropolis-Hastings algorithm. This algorithm belongs to a set of MCMC approaches that generate samples. A similar approach was performed by Petzoldt and Soetaert, we shall take the prior distribution for the parameters to θ and independent variable t (for details see (Petzoldt & Soetaert, 2010; Apenteng & Ismail, 2015)). Similarly, we set y to represent our system of non-linear equations of our models. We set the prior distribution for the parameters to θ and independent variables to t (for information see (Petzoldt & Soetaert, 2010)). We also assumed that ξ is the additive and the independent Gaussian error, with unknown variance σ^2. These terms can be defined as follows:

$$y = f(t, \theta) + \xi \tag{3.10}$$

$$\xi \sim N(0, \sigma^2) \tag{3.11}$$

The posterior for the parameters is estimated as (Laine, 2008)

$$p\left(\theta|y,\sigma^2\right) \propto exp\left[-0.5\left(\frac{SS(\theta)}{\sigma^2}\right)\right]p_{pri}(\theta) \tag{3.12}$$

where SS is the sum of squares function $SS(\theta) = \sum\left(y_i - f\left(t,\theta\right)_i\right)^2$ and $p_{pri}(\theta)$ is the prior distribution of the parameters. To obtain proper results from the MCMC method, a constrained least squares approach is necessary to provide initial estimates of (θ_i). If the non-informative prior is constant for all of the values of $p_{pri}(\theta)$, this can be ignored. For the reciprocal of the error variance σ^2, a gamma distribution is used:

$$p_{pri}\left(\sigma^{-2}\right) \sim \Gamma\left(\frac{n_0}{2}, \frac{n_0 S_0^2}{2}\right) \tag{3.13}$$

The reciprocal of the error variance at each MCMC step is sampled from a gamma distribution (Gelman et al., 2013) as follow:

$$p\left(\sigma^{-2}|\left(y,\theta\right)\right) \sim \Gamma\left(\frac{n_0 + n}{2}, \frac{n_0 S_0^2 + SS\left(\theta\right)}{2}\right) \tag{3.14}$$

where n_0 and n input arguments to the function and the number of observations, respectively (Petzoldt & Soetaert, 2010).

3.4.5 R package Flexible Modeling Environment (FME)

The set of differential equations are solved using the R package Flexible Modeling Environment (FME) (Petzoldt & Soetaert, 2010). FME is a package designed for inverse modelling, sensitivity and Monte Carlo analysis. This is because starting with good parameters is very important. In this thesis, the potential of FME for inverse modelling is demonstrated by means of three different models: first, a simple three compartment dynamic model from outbound tourists who are infected with HIV and AIDS, and returns

home without the knowledge of their status for Model I; second, the four compartment dynamic model inbound tourists with outbound tourists in order to estimate the number of HIV and AIDS cases of inbound tourists respectively; and finally, condoms as preventive measure intends to reduce infection with outbound and inbound tourists. Also, in order to fit the proposed models to the data, we adapt the following functions approaches from Petzoldt and Soetaert (2010).

- The proposed models are formulated.

- Try an initial guess for the parameters that fits the data best.

- Plot model and data.

- *modCost* estimates residuals of the model output versus the data and calculates model cost (sums of squared residuals).

- *sensFun* calculates the local sensitivity of the model output to the parameter values, which determines the effect on model outcome as a function of an appropriate parameters on a time series probability density function.

- *modFit* it uses the output of *modCost* to find the best-fit parameters for nonlinear model-data fitting. It calls the functions from R's built-in minimization routines such as optim, nls, nlminb, and a pseudo-random search algorithm (Price1977).

- *modMCMC* performs a Markov Chain Monte Carlo simulation (Bayesian analysis) method to derive the data dependent probability distribution of the parameters. It uses the metropolis hastings (MH) algorithm, adaptive metropolis (AM) algorithm and including a delayed rejection (DR) procedure (Haario et al., 2006; Laine, 2008).

- *sensRange* estimates the effect of the parameter uncertainty on the model output which gives predictive envelopes of the proposed model (Petzoldt & Soetaert, 2010).

3.5 Chapter summary

Throughout this chapter we have shown how SIR-type models can be extended to study the spread of HIV/AIDS and how MCMC approach is used to supplement the construction of the models by estimating the parameters involved. For instance, these will help us to examine the following: The effect of outbound and inbound tourists who are infected with HIV/AID. The effect of newborn babies with HIV-positive on HIV/AIDS transmission. And how to implement the use of condoms as a preventive measure. In the proceeding Chapter, we will study how the models will be constructed to analysis all the mathematical models that are involved as well as addressing these matters.

CHAPTER 4: DESCRIPTION OF THE MODELS

4.1 Introduction

In this chapter we present three models by modifying the standard SIR model studied by (Kermack & McKendrick, 1927). That is, we replace the R compartment by an A. This compartment contains individuals that have AIDS. Since there is no cure or recovery for HIV patients, individuals with HIV either remain infected or progress to AIDS. Hence, we constructed three different models for HIV and AIDS cases that capture Malaysian returnees, foreigners and prevention.

Model I considers inclusion of outbound tourism. The outbound tourists are the Malaysian citizens that returned home with an infection of HIV. The Model I focus is to examine the probability of susceptability of the returnees who traveled outside Malaysia for other activities.

While Model I looked at the Malaysian returnees, Model II takes into account the non-Malaysian tourists referred to as inbound tourism. We used the model to examine the effect of the inbound tourism on the spread of HIV/AIDS in Malaysia. As such we focus on quantifying the volume of the susceptible individuals as well as establish number of infected HIV and AIDS of these non-Malaysia tourists. This is necessitated with the fact that Malaysia government was not aware of the infection status during their arrival.

After examination of the objectives relating to Model I and II, we constructed the third model which captures the preventive measure. In this Model III, we introduced the use of condoms as a preventive measure. This is necessary as it will reduce the risk of susceptible individuals from getting HIV. In each of the models, we introduced and estimated the possibility of infected HIV and AIDS individuals having babies. Since the parents of these children are infected with HIV/AIDS, the possibility of spreading the

disease needs be examined. Thus, we added the newborn babies variable into the three models estimated.

4.2 Model I (with outbound tourism)

4.2.1 Key Model I assumptions

In this section, we are only concerned with how outbound tourism is affecting the spread of HIV. These are susceptible outbound tourists who return home with an HIV infection. For HIV/AIDS disease, once an individual becomes infected, that the individual remains infectious for life. Let N be the total population, then individuals can be classified as S representing susceptible, I represents HIV and A represents AIDS. Susceptible stage: The susceptible are at risk of acquiring HIV/AIDS. The susceptible compartment has a recruitment rate b (birth rate). This is independent of vertical transmission and makes it unstable. Let μ be the natural death rate for the all compartments. Infected stage: We subdivide such individual into those diagnosed with HIV ($I(t)$) and AIDS ($A(t)$), at time t and they are assumed to be sexually active. It assumes that infected HIV/AIDS newborn babies enter the HIV class at the rate of $b(I + A)$ for which we assume that I, and A are capable of having children (Apenteng & Ismail, 2015). ρ denote the probability that a susceptible outbound tourist returns home with an HIV infection. The rate that HIV individuals enter the AIDS class is represented by α. β is the contact rate between susceptible individuals and HIV-infected individuals. It is assumed that AIDS individuals are given an additional disease-induced mortality rate: $d > 0$ for $A(t)$.

We present the simplest HIV disease models where individuals classified as a sexually active population. This form of a susceptible–HIV–AIDS (SIA) model can be used to model HIV/AIDS disease based upon the assumption that once an individual becomes infected, that individual remains infectious for life, as shown in Fig.4.1.
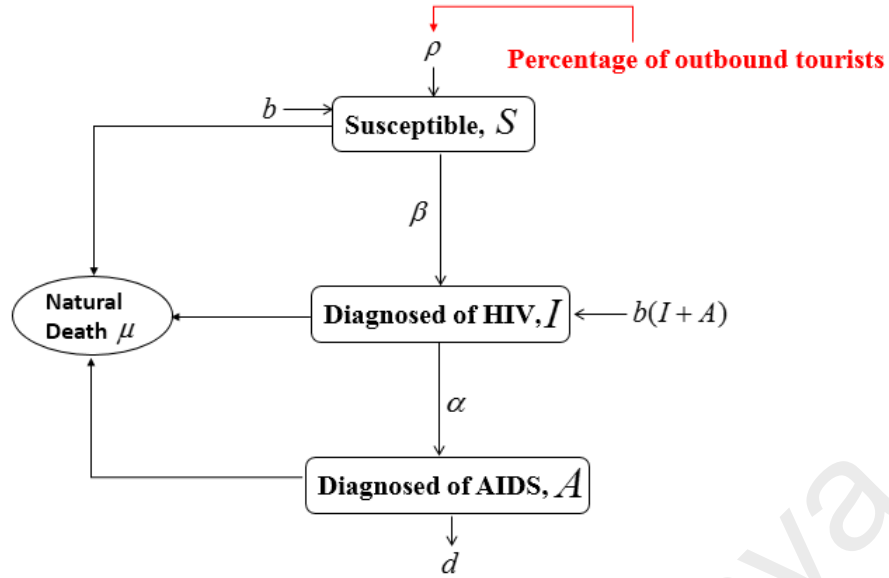
Figure 4.1: Flow diagram of an SIA **model with outbound tourists.**

The deterministic systems of nonlinear differential equations describing the SIA models of HIV/AIDS disease with demographics (birth and death) is of the form:

$$\frac{dS}{dt} = b + \rho S - \beta \frac{I}{N} S - \mu S \tag{4.1}$$

$$\frac{dI}{dt} = b(I + A) + \beta \frac{I}{N} S - (\mu + \alpha)I \tag{4.2}$$

$$\frac{dA}{dt} = \alpha I - (\mu + d)A \tag{4.3}$$

4.3 Basic properties

4.3.1 Invariant region

Since the model is tractable and epidemiologically meaningful in the human population the variables of the various compartments and the parameters are assumed to be positive for all $t \geq 0$. The model system (4.1)-(4.3) will therefore be analysed in a suitable feasible region Ψ of biological interest. From (4.1)-(4.3), we have the following lemma on the region which is restricted to Ψ.

Lemma 4.1. The feasible region Ψ defined by

$\Psi = \left\{ (S(t), I(t), A(t)) \in \mathbb{R}_+^3 : N(t) < \frac{b}{\mu - \rho} \right\}$ with initial condition $S(0) \geq 0$, $I(0) \geq 0$,

$A(0) \geq 0$ is positive for (4.1)-(4.3).

Proof 4.1. By adding (4.1)-(4.3), we obtain

$$\frac{dN}{dt} = b + (\rho - \mu)N + (b - \rho)I + (b - \rho - d)A, \tag{4.4}$$

in the absence of disease free. We assume that $N(t) \leq M$ for all $t \geq 0$, where $M = \frac{b}{\mu - \rho} + \varepsilon$.

ε represents the error, where $\varepsilon > 0$.

Suppose that the assumption is not true then there is a $t_1 \geq 0$, such that

$$N(t_1) = \frac{b}{\mu - \rho} + \varepsilon \tag{4.5}$$

$$N(t) = \frac{b}{\mu - \rho} + \varepsilon \qquad\qquad t < t_1 \tag{4.6}$$

$$\frac{dN(t_1)}{dt_1} \geq 0 \tag{4.7}$$

$$\frac{dN(t_1)}{dt_1} \leq b + (\rho - \mu)N(t_1) \tag{4.8}$$

$$= -b < 0 \tag{4.9}$$

Equation (4.9) is contradiction indicating that the assumption is true. Therefore, $N(t) \leq M$

for all $t \geq 0$.

4.3.2 Positivity of solutions

For (4.1)-(4.3), it is important to show that all the state variables are non-negative so that

the solutions of the system with positive initial conditions remain positive for all $t > 0$.

We state the following lemma (following Lemma of (Huo & Feng, 2013)), we have

Lemma 4.2. If $S(0) \geq 0$, $I(0) \geq 0$, $A(0) \geq 0$, the solutions $S(t)$, $I(t)$, $A(t)$ for

(4.1)-(4.3) are positive for all $t \geq 0$.

Proof 4.2. Under the given conditions, it is easy to prove that the solutions of the (4.1)-(4.3) are positive; if not, we assume a contradiction that there is a first time t_1, such that

$$S(t_1) = 0, \frac{dS}{dt} < 0, I(t) \geq 0, A(t) \geq 0, 0 \leq t \leq t_1, \tag{4.10}$$

there exists a t_2

$$I(t_2) = 0, \frac{dI(t_2)}{dt} < 0, S(t) \geq 0, A(t) \geq 0, 0 \leq t \leq t_2, \tag{4.11}$$

there exists a t_3

$$A(t_3) = 0, \frac{dI(t_2)}{dt} < 0, S(t) \geq 0, A(t) \geq 0, 0 \leq t \leq t_3 \tag{4.12}$$

From (4.10), we have

$$\frac{dS(t_1)}{dt} = (b + \rho) > 0, \tag{4.13}$$

which is a contradiction meaning that $S(t) \geq 0, t \geq 0$.

From (4.11), we have

$$\frac{dI(t_2)}{dt} = b(I(t_2) + A(t_2)) + \beta \frac{I(t_2)}{N} S(t_2) - (\alpha + \mu + d)I(t_2) \geq 0, \tag{4.14}$$

which is a contradiction meaning that $I(t) \geq 0, t \geq 0$. Similar approach can be shown that $A(t) \geq 0$ for all $t \geq 0$.

Therefore, the solutions $S(t)$, $I(t)$, $A(t)$ of (4.1)-(4.3) remain positive for all $t > 0$.

4.4 Analysis of the Model I

In this section, we want to find the existence and stability of the equilibrium points of the model system (4.1)-(4.3). It is important to determine whether the disease is epidemic or endemic; to determine this, the equilibrium point of the disease model where there is disease free equilibrium must be determined. There is one disease free equilibrium E_0 and one endemic equilibrium E^* for (4.1)-(4.3).

4.4.1 Equilibrium solutions

4.4.1.1 Disease free equilibrium and the reproduction number R_0

Model I has a disease free equilibrium given by

$$E_0 = \left(\frac{b}{\mu - \rho}, 0, 0 \right) \tag{4.15}$$

Moreover, to explore whether the disease will continue to spread, we determine the stability of the disease-free equilibrium point. The reproduction number R_0 is a threshold value that can be used to determine the stability of the disease-free equilibrium (van den Driessche & Watmough, 2005; Jones, 2007; Silva & Torres, 2013; Diekmann, Heesterbeek, & Roberts, 2010; Roberts & Heesterbeek, 2007). We write the right-hand side of system (4.1)-(4.3) as $F - V$ with the following equations:

$$F = \begin{bmatrix} \beta \frac{I}{N} S \\ 0 \end{bmatrix} \tag{4.16}$$

$$V = \begin{bmatrix} -b(I + A) + (\mu + \alpha)I \\ -\alpha I + (\mu + d)A \end{bmatrix} \tag{4.17}$$

Then, we consider the Jacobian matrices associated with F and V:

$$J_F = \begin{bmatrix} \beta\frac{S}{N} & 0 \\ 0 & 0 \end{bmatrix} \tag{4.18}$$

$$J_V = \begin{bmatrix} \alpha + \mu - b & -b \\ -\alpha & (\mu + d) \end{bmatrix} \tag{4.19}$$

The spectral radius of the matrix $J_F \times J_V^{-1} = \left\{\frac{\beta S}{N}\right\}\left\{\frac{(\mu+d)}{(\mu+d)(\alpha+\mu-b)-\alpha b}\right\}$. The basic reproduction number of the system for disease free is obtained as

$$R_0 = \left\{\frac{\beta b}{(\mu - \rho)N}\right\}\left\{\frac{(\mu + d)}{(\mu + d)(\alpha + \mu - b) - \alpha b}\right\}. \tag{4.20}$$

4.4.1.2 Existence of the endemic equilibrium

If $R_0 > 1$, then Model I has a unique endemic equilibrium $E^* = (S^*, I^*, A^*)$. From (4.3) we get

$$A^* = \frac{\alpha I^*}{\mu + d} \tag{4.21}$$

By submitting (4.21) into (4.2), and solving for I^*,

$$b\left(I^* + \frac{\alpha I^*}{\mu + d_1}\right) + \beta\frac{I^*}{N}S^* - (\alpha + \mu + d)I^* = 0 \tag{4.22}$$

$$b(\alpha + \mu + d)I^* + \beta\frac{I^*}{N}S^*(\mu + d) - (\mu + d_1)(\alpha + \mu)I^* = 0 \tag{4.23}$$

$$(\mu + d)(\alpha + \mu)I^* - b(\alpha + \mu + d)I^* = \beta\frac{I^*}{N}S^*(\mu + d) \tag{4.24}$$

$$(\mu + d)(\alpha + \mu - b) - \alpha b = \beta\frac{S^*}{N}(\mu + d) \tag{4.25}$$

42

By simple simplification of the algebraic expression,we obtain:

$$S^* = \frac{N\{(\mu + d)(\alpha + \mu - b) - \alpha b\}}{\beta(\mu + d)} \tag{4.26}$$

Substituting (4.26) into (4.3), we obtain I^*:

$$b - \left(\beta\frac{I^*}{N} - (\mu - \rho)\right)S^* = 0 \tag{4.27}$$

$$\left(\beta\frac{I^*}{N} - (\mu - \rho)\right)S^* = b \tag{4.28}$$

$$\beta\frac{I^*}{N} - (\mu - \rho) = \frac{b}{S^*} \tag{4.29}$$

$$\beta\frac{I^*}{N} - (\mu - \rho) = \frac{\beta b(\mu + d)}{\{N(\mu + d)(\alpha + \mu - b) - \alpha b\}} \tag{4.30}$$

$$\beta\frac{I^*}{N} = \frac{\beta b(\mu + d)}{\{N(\mu + d)(\alpha + \mu - b) - \alpha b\}} + (\mu - \rho) \tag{4.31}$$

$$I^* = \frac{N}{\beta}(\mu - \rho) + \frac{\beta b(\mu + d)}{(\mu + d)(\alpha + \mu - b) - \alpha b} \tag{4.32}$$

Substituting (4.33) into (4.21), we obtain A^*:

$$A^* = \left\{\frac{\alpha}{\mu + d}\right\}\left\{\frac{N}{\beta}(\mu - \rho) + \frac{\beta b(\mu + d)}{(\mu + d)(\alpha + \mu - b) - \alpha b}\right\} \tag{4.33}$$

4.4.2 Local stability of the equilibria

Theorem 4.3. The disease free equilibrium E_0 is locally asymptotically stable for $R_0 < 1$ and unstable otherwise.

Proof 4.3. The stability of the endemic equilibrium is determined using the eigenvalues of the characteristic equation of the corresponding Jacobian matrix, $J(S, I, A) = J(E_0)$, which is given by:

$$J(E_0) = \begin{bmatrix} -\beta\frac{I}{N} - \mu & -\beta\frac{S}{N} & 0 \\[2mm] \beta\frac{I}{N} & b(\mu + d + \alpha) + \beta\frac{S}{N}(\mu + d) - (\mu + d)(\alpha + \mu - b) & b \\[2mm] 0 & \alpha & -(\mu + d) \end{bmatrix}$$

(4.34)

$$J(E_0) = \begin{bmatrix} -\mu & -\frac{\beta(b+\rho)}{\mu N} & 0 \\[2mm] 0 & \frac{\beta b}{N(\mu-\rho)} - [(\mu + d_1)(\alpha + \mu - b) - \alpha b] & b \\[2mm] 0 & \alpha & -(\mu + d) \end{bmatrix}$$

(4.35)

The matrix $J(E_0)$ has the following eigenvalues $\lambda_1 = -\mu < 0$, $\lambda_2 = -(\mu + d) < 0$,

$\lambda_3 = \frac{\beta b}{N(\mu-\rho)} - ((\mu + d)(\alpha + \mu - b) - \alpha b)$. For local asymptotically stable, if $\lambda_3 < 0$, that

is, if $\frac{\beta b}{N(\mu-\rho)} < ((\mu + d)(\alpha + \mu - b) - \alpha b)$ holds, which is equivalent to

$$\frac{\beta b}{N(\mu - \rho)\left((\mu + d)(\alpha + \mu - b) - \alpha b\right)} = R_0 < 1$$

(4.36)

4.4.3 Global stability

Theorem 4.4. If $R_0 \leq 1$, then there exist disease free equilibrium E_0 and it is globally

asymptotically stable on Π.

Proof 4.4. Given that $R_0 \leq 1$, then there exists only one disease free equilibrium

$E_0 = \left(\frac{b}{(\mu-\rho)}, 0, 0\right)$. By considering this, we defined our Lyapunov function of $V(S, I, A)$:

$\mathbb{R}^3_+$ as

$$V = \varphi I + A$$

(4.37)

By differentiating (4.38) with respect to time and substituting (4.2)-(4.3), and (4.21), we

obtain:

$$\frac{dV}{dt} = \varphi \frac{dI}{dt} + \frac{dA}{dt} \tag{4.38}$$

$$= \varphi \left\{ b \left(I + \frac{\alpha I}{\mu + d} \right) + \beta \frac{I}{N} S - (\alpha + \mu)I \right\} + \alpha I - (\mu + d)A \tag{4.39}$$

$$= \varphi \left\{ b(\mu + d + \alpha) + \beta \frac{I}{N} S(\mu + d_1) - (\mu + d)(\alpha + \mu)I \right\} + (\mu + d) \left\{ \alpha I - (\mu + d)A \right\} \tag{4.40}$$

$$= \varphi \left\{ \beta \frac{S}{N} (\mu + d) - (\mu + d)(\alpha + \mu - b) - \alpha b \right\} I + (\mu + d) \left\{ \alpha I - (\mu + d)A \right\} \tag{4.41}$$

$$= \varphi \left((\mu + d)(\alpha + \mu - b) - \alpha b \right) \left\{ \frac{\beta S(\mu + d)}{N \left\{ (\mu + d)(\alpha + \mu + d - b) - \alpha b \right\}} - 1 \right\} I$$
$$+ (\mu + d) \left\{ \alpha I - (\mu + d)A \right\} \tag{4.42}$$

Since at disease free equilibrium $S = \frac{b}{\mu - \rho}$ and by using $\varphi = \frac{1}{(\mu + d)(\alpha + \mu - b) - \alpha b}$

$$\frac{dV}{dt} = (R_0 - 1)I + (\mu + d) \left\{ \alpha I - (\mu + d)A \right\} \tag{4.43}$$

$$\leq 0 \tag{4.44}$$

Note that, $\frac{dV}{dt} = 0$ only when $I = A = 0$. Thus, substituting $I = A = 0$ into (4.1) shows

that $S = \frac{b}{\mu - \rho}$ as $t \to \infty$. Hence, the maximum invariant set of $\left\{ S, I, A) \in \Psi | \frac{dV}{dt} \leq 0 \right\}$ is

singleton set $\{E_0\}$. Therefore, the global stability of E_0 when $R_0 \leq 1$ follows from the

LaSalle's invariance principle (see details in (LaSalle, 1968)).

Theorem 4.5. If $R_0 > 1$, then there exists an endemic equilibrium E^* (addition

with the disease free equilibrium) and it is globally asymptotically stable, provided the

following conditions are satisfied.

$$\beta \frac{I^*}{N^*} S^* + (\mu - \rho) S^* = (\mu + d)(\alpha + \mu - b) - \alpha b,$$

$$\beta \frac{I^*}{N^*} S^* + (\mu - \rho) S^* = b(\mu + d) + (1 - b)(\alpha + \mu) I^*,$$

$$\alpha I^* = (\mu + d) A^*,$$

$$A^* = \frac{\alpha I^*}{\mu + d}.$$

Proof 4.5. Let us consider the following positive definite function about E^*

$$V = \frac{1}{2}(S - S^*)^2 + x\left(I - I^* - I^* \ln \frac{I}{I^*}\right) + \frac{1}{2}(A - A^*)^2 \tag{4.45}$$

$$\frac{dV}{dt} = (S - S^*)\frac{dS}{dt} + x\left(\frac{I - I^*}{I}\right)\frac{dI}{dt} + (A - A^*)\frac{dA}{dt} \tag{4.46}$$

$$= (S - S^*)\left\{b + \rho - \beta\frac{I}{N}S - \mu S\right\}$$

$$+ x\left(\frac{I - I^*}{I}\right)\left\{b(I + A) + \beta\frac{I}{N}S - (\mu + \alpha)I\right\} + (A - A^*)\left\{\alpha I - (\mu + d)A\right\}$$

$$\tag{4.47}$$

$$= (S - S^*)\left\{b(\mu + d) - (\mu + d)\beta\frac{I}{N}S - (\mu + d)(\mu - \rho)S\right\}$$

$$+ x\left(\frac{I - I^*}{I}\right)\left\{b(\mu + \alpha)I + (\mu + d)\beta\frac{I}{N}S - (\mu + d)I(\mu + \alpha)I\right\} \tag{4.48}$$

$$+ (\mu + d)(A - A^*)\left\{\alpha I - (\mu + d)A\right\}$$

$$= (S - S^*)\left\{b(\mu + d) - (\mu + d)\beta\frac{I}{N}S - (\mu + d)(\mu - \rho)S\right\}$$

$$+ x\left(\frac{I - I^*}{I}\right)\left\{(\mu + d)\beta\frac{I}{N}S - (\mu + d)(\mu + \alpha - b)I + \alpha bI\right\} \tag{4.49}$$

$$+ (\mu + d_1)(A - A^*)\left\{\alpha I - (\mu + d)A\right\}$$

$$= (S - S^*)\left\{(\mu + d)\beta\frac{I}{N}S^* + (\mu + d)(\mu - \rho)S^* - (\mu + d_1)\beta\frac{I}{N}S - (\mu + d)(\mu - \rho)S\right\}$$

$$+ x(I - I^*)\left\{(\mu + d)\beta\frac{S^*}{N} - (\mu + d)\beta\frac{S^*}{N}\right\} - (\mu + d)^2(A - A^*)^2$$

$$\tag{4.50}$$

$$\frac{dV}{dt} = -(2\mu + d)(S - S^*)^2 + \frac{\beta}{N}(S - S^*)^2(I^* - I) + x(\mu + d_1)\frac{\beta}{N}(I - I^*)(S - S^*)$$
$$- (\mu + d_1)^2(A - A^*)^2$$

$$\tag{4.51}$$

$$= -(2\mu + d - \frac{\beta}{N})(S - S^*)^2(I^* - I) + x(\mu + d)\frac{\beta}{N}(I - I^*)(S - S^*)$$
$$- (\mu + d)^2(A - A^*)^2$$

$$\tag{4.52}$$

$$\leq 0 \tag{4.53}$$

Note that, $\frac{dV}{dt} = 0$ only at $\{E^*\}$, when $S \leq S^*$, $I \leq I^*$ and $A \leq A^*$. By applying LaSalle's invariance principle (LaSalle, 1968), with the initial conditions in Ψ, every solution of (4.1)-(4.3) approaches E^* at as $t \rightarrow \infty$ whenever $R_0 > 1$. Therefore, the endemic equilibrium E^* is globally asymptotically stable in Ψ whenever $R_0 > 1$.

4.5 Model II (Inbound with outbound tourists)

We extend the simplest HIV and AIDS model of Model I (outbound tourists) with the impact of inbound tourism, international tourists who visit Malaysia and are sexually active as shown in Figure 4.2.

4.5.1 Key Model II assumptions

Let T denote the inbound tourism compartment of individuals who come from different parts of the world to Malaysia. This is necessary because, their HIV/AIDS status is unknown upon their arrival. Although there is a need for real demographic data for one to know the proportion of tourists recruited into each of the aforementioned compartmental levels (Figure 4.2) due to their susceptability, HIV and AIDS status. In view of this, there is a need to know the percentage of inbound tourists who are susceptible, infected with HIV and AIDS. We assumed that some of them are susceptible, infected with HIV and

AIDS, and here δ, δ_1, and δ_2 are the fractions of these individuals recruited into $S(t)$, $I(t)$ and $A(t)$, respectively (as indicated by red line in Figure 4.2). It is also assumed that the number of days inbound tourists stay in Malaysia at the rate of σ from $S(t)$, $I(t)$ and $A(t)$.
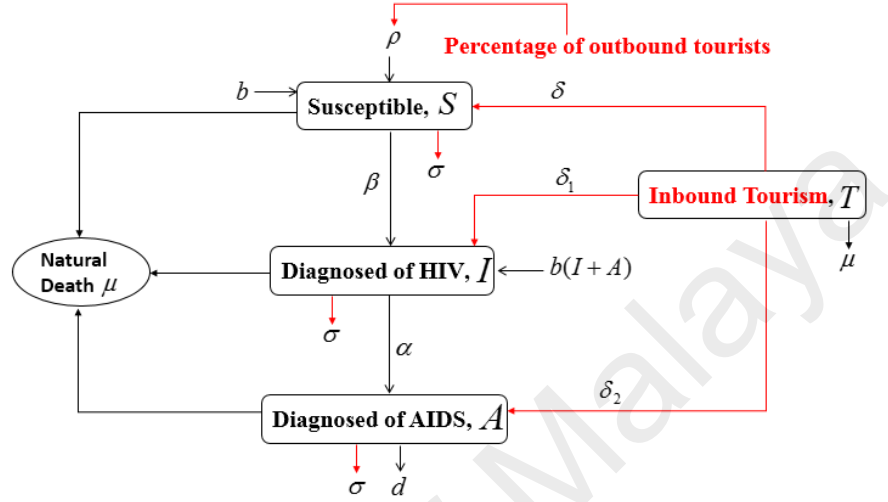
Figure 4.2: Flow diagram of HIV transmission with inbound tourism.

The model takes the following form

$$\frac{dS}{dt} = b + \rho S + \delta T - \beta \frac{I}{N} S - (\mu + \sigma) S \tag{4.54}$$

$$\frac{dI}{dt} = b(I + A) + \delta_1 T + \beta \frac{I}{N} S - (\mu + \alpha + \sigma) I \tag{4.55}$$

$$\frac{dA}{dt} = \alpha I + \delta_2 T - (\mu + \sigma + d) A \tag{4.56}$$

$$\frac{dT}{dt} = -(\delta + \delta_1 + \delta_2) T - \mu T \tag{4.57}$$

Lemma 4.6. The feasible region Π defined by

$\Pi = \left\{ (S(t), I(t), A(t), T(t)) \in \mathbb{R}_+^4 : N(t) < \frac{b}{\mu + \sigma - \rho} \right\}$ with initial condition $S(0) \geq 0$, $I(0) \geq 0$, $A(0) \geq 0$, $T(0) \geq 0$ is positive.

Proof 4.6. By adding (4.55)-(4.58), we obtain

$$\frac{dN}{dt} = b - (\mu + \sigma - \rho)N + (b - \rho)I + (b - \rho - d)A, \qquad (4.58)$$

The proof is similar to the simple model I. In the absence of HIV/AIDS, the feasible region for inbound tourists Π of (4.55)-(4.58) is defined by $\Pi = \frac{b}{\mu+\sigma-\rho}$. This region is positively invariant under model (4.55)-(4.58), hence the system is both epidemiologically and mathematically well-posed. Therefore, it is sufficient to study the dynamics of the model in Π.

4.6 Analysis of the Model II

Similarly, it is important to determine whether the disease is epidemic or endemic. There is one disease-free equilibrium E_{01} and one endemic equilibrium E_1^* for (4.55)-(4.58).

4.6.1 Equilibrium solutions

4.6.1.1 Disease free equilibrium and the reproduction number R_{01}

Model II has a disease-free equilibrium given by

$$E_{01} = \left(\frac{b + \delta T}{\mu + \sigma - \rho}, 0, 0, 0 \right) \qquad (4.59)$$

We calculate the reproduction number R_{01} for Model II. We write the right-hand side

of system (4.55)-(4.58) as $F - V$ with the following equations:

$$F = \begin{bmatrix} \beta \frac{I}{N} S \\ 0 \end{bmatrix} \qquad (4.60)$$

$$V = \begin{bmatrix} -b(I + A) + (\mu + \alpha + \sigma)I \\ -\alpha I + (\mu + \sigma + d)A \end{bmatrix} \qquad (4.61)$$

Then, we consider the Jacobian matrices associated with F and V:

$$J_F = \begin{bmatrix} \beta \frac{S}{N} & 0 \\ 0 & 0 \end{bmatrix} \qquad (4.62)$$

$$J_V = \begin{bmatrix} \alpha + \mu + \sigma - b & -b \\ -\alpha & (\mu + \sigma + d) \end{bmatrix} \qquad (4.63)$$

The spectral radius of the matrix $J_F \times J_V^{-1} = \left\{ \frac{\beta S}{N} \right\} \left\{ \frac{(\mu+\sigma+d)}{(\mu+d)(\alpha+\mu+\sigma-b)-\alpha b} \right\}$. The basic reproduction number of the system for disease free is obtained as

$$R_{01} = \left\{ \frac{\beta(b + \delta T)}{(\mu + \sigma - \rho)N} \right\} \left\{ \frac{(\mu + \sigma + d)}{(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b} \right\}. \qquad (4.64)$$

4.6.1.2   Existence of the endemic equilibrium

If $R_{01} > 1$, system (4.55)-(4.58) has a unique endemic equilibrium $E_1^* = (S^*, I^*, A^*, T^*)$.

From (4.58) we get

$$b(\mu + \sigma + d + \alpha)I + b\delta_2 T + \delta_1 T(\mu + \sigma + d) + \beta\frac{I}{N}S(\mu + \sigma + d)$$

$$-(\mu + \sigma + d)(\mu + \alpha + \sigma)I = 0$$

$$\text{(4.65)}$$

$$b\delta_2 T + \delta_1 T(\mu + \sigma + d) + \beta\frac{I}{N}S(\mu + \sigma + d) - (\mu + \sigma + d)(\mu + \alpha + \sigma - b)I + \alpha bI = 0$$

$$\text{(4.66)}$$

$$b\delta_2 T + \delta_1 T(\mu + \sigma + d) + \beta\frac{I}{N}S(\mu + \sigma + d) - \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b) - \alpha b\}I = 0$$

$$\text{(4.67)}$$

$$\left\{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \frac{\beta S}{N}) - \alpha b\right\}I = b\delta_2 T + \delta_1 T(\mu + \sigma + d) \qquad \text{(4.68)}$$

From (4.55), we have

$$I^* = \frac{N}{\beta}\left\{\frac{(b + \delta T)}{S} - (\mu + \sigma - \rho)\right\} \qquad \text{(4.69)}$$

By substituting (4.69) into (4.68)

$$b\delta_2 T + \delta_1(\mu + \sigma + d)T = \left\{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \frac{\beta S}{N}) - \alpha b\right\}\frac{N}{\beta}\left\{\frac{(b + \delta T)}{S} - (\mu + \sigma - \rho)\right\}$$

$$\text{(4.70)}$$

$$b\delta_2 T + \delta_1(\mu + \sigma + d)T = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{\beta}\left\{\frac{(b + \delta T)}{S} - (\mu + \sigma - \rho)\right\}$$
$$- (b + \delta T) - S(\mu + \sigma - \rho)$$

$$(4.71)$$

$$b\delta_2 T + \delta_1(\mu + \sigma + d)T = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{\beta S}(b + \delta T)$$
$$- (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{\beta}$$
$$- (b + \delta T) - S(\mu + \sigma - \rho)$$

$$(4.72)$$

$$(\mu + \sigma - \rho)S^2 + (b + \delta T)S - b\delta_2 TS - \delta_1(\mu + \sigma + d)TS$$
$$- (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{\beta}S$$
$$+ \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{\beta}(b + \delta T) = 0$$

$$(4.73)$$

Equation (4.73) become quadratic equation

$$\mathcal{X} = \frac{-\mathcal{B} \pm \sqrt{\mathcal{B}^2 - 4\mathcal{A}C}}{2\mathcal{A}}$$

$$(4.74)$$

From (4.74) where

$$\mathcal{A} = (\mu + \sigma - \rho),$$

$$\mathcal{B} = (b + \delta T) - b\delta_2 T - \delta_1(\mu + \sigma + d)T - (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{\beta},$$

$$C = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{\beta}(b + \delta T)$$

Now S^* becomes,

$$S^* = \frac{F + Y - (b + \delta T) + \sqrt{(F + Y - (b + \delta T))^2 - 4D(\mu + \sigma - \rho)}}{2(\mu + \sigma - \rho)} \tag{4.75}$$

where

$$Y = b\delta_2 T - \delta_1(\mu + \sigma + d)T,$$

$$D = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{\beta}(b + \delta T),$$

$$F = \delta_1(\mu + \sigma + d)T - (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{\beta}$$

By substituting (4.75) into (4.69) and (4.58), we obtain I^* and A^*, respectively

$$I^* = \frac{N}{\beta}\left\{\frac{(b + \delta T)2(\mu + \sigma - \rho)}{F + Y - (b + \delta T) + \sqrt{(F + Y - (b + \delta T))^2 - 4D(\mu + \sigma - \rho)}} - (\mu + \sigma - \rho)\right\}$$

$$\tag{4.76}$$

$$A^* = \frac{\alpha I^*}{(\mu + \sigma + d)} + \frac{\delta_2 T}{(\mu + \sigma + d)} \tag{4.77}$$

$$T^* = \frac{(\mu + \sigma + d)A^* + \alpha I^*}{\delta_2} \tag{4.78}$$

4.6.2 Local stability of the equilibria

In this section we determine the local equilibrium of Model II. Note that at equilibrium, equation (4.56) becomes

$$A = \frac{\alpha I + \delta_2 T}{\mu + \sigma + d} \tag{4.79}$$

Theorem 4.7. The disease free equilibrium E_{01} is locally asymptotically stable for $R_{01} < 1$ and unstable otherwise.

Proof 4.7. The stability of the endemic equilibrium is determined using the eigenvalues of the characteristic equation of the corresponding Jacobian matrix, $J(S, I, A, T) = J(E_{01})$, which is given by:

$$J(E_{01}) = \begin{bmatrix} -\beta\frac{I}{N} - \mu & -\beta\frac{S}{N} & 0 & -\delta \\ \beta\frac{I}{N} & \beta\frac{S}{N}(\mu + \sigma + d) - H & 0 & -\delta_1 \\ 0 & \alpha & -(\mu + \sigma + d) & -\delta_2 \\ 0 & 0 & 0 & -(\delta + \delta_1 + \delta_2 + \mu) \end{bmatrix}$$

(4.80)

where $H = [(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b]$

$$J(E_{01}) = \begin{bmatrix} -\mu & -\frac{\beta b}{(\mu+\sigma-\rho)N} & 0 & -\delta \\ 0 & \frac{\beta b}{N(\mu+\sigma-\rho)} - H & b & -\delta_1 \\ 0 & \alpha & -(\mu + \sigma + d) & -\delta_2 \\ 0 & 0 & 0 & -(\delta + \delta_1 + \delta_2 + \mu) \end{bmatrix}$$

(4.81)

The matrix $J(E_{01})$ has the following eigenvalues $\lambda_1 = -\mu < 0$, $\lambda_2 = -(\mu + \sigma + d < 0$, $\lambda_3 = -(\delta + \delta_1 + \delta_2 + \mu) < 0$, $\lambda_4 = \frac{\beta b}{N(\mu+\sigma-\rho)} - \{(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b\}$. For local asymptotically stable, if $\lambda_4 < 0$, that is, if

$\frac{\beta b}{N(\mu+\sigma-\rho)} < \{(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b\}$ holds, which is equivalent to

$$\frac{\beta b(\mu + \sigma + d)}{N(\mu + \sigma - \rho)\{(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b\}} = R_{01} < 1 \qquad (4.82)$$

4.6.3 Global stability

Theorem 4.8. If $R_{01} \leq 1$, then there exist disease free equilibrium E_{01} is globally asymptotically stable on Π.

Proof 4.8. Given that $R_{01} \leq 1$, then there exist only one disease free equilibrium $E_{01} = \left(\frac{b}{\mu + \sigma - \rho}, 0, 0, 0 \right)$. By considering this, we define a Lyapunov function of $V(S, I, A, T) : \mathbb{R}_+^4$ as

$$V = \phi I + A \tag{4.83}$$

$$\frac{dV}{dt} = \phi \frac{dI}{dt} + \frac{dA}{dt} \tag{4.84}$$

$$= \phi \left\{ b(I + A) + \delta_1 T + \beta \frac{I}{N} S - (\alpha + \mu + \sigma + d)I \right\} + \alpha I + \delta_2 T - (\mu + \sigma + d_1)A \tag{4.85}$$

$$= \phi \left\{ b(\mu + \sigma + \alpha + d)I + b\delta_2 T + (\mu + \sigma + d)\delta_1 T + \beta \frac{I}{N} S(\mu + \sigma + d) - (\alpha + \mu + \sigma + d)I \right\}$$
$$+ \alpha I + (\mu + \sigma + d)A - \alpha I - (\mu + \sigma + d)A \tag{4.86}$$

$$\frac{dV}{dt} = \phi \left\{ (\alpha + \mu + \sigma - b) - \alpha b \right\} \left\{ \frac{b\{(\mu + \sigma + \alpha + d)\delta_1 + \delta_2\}T}{(\alpha + \mu + \sigma + d - b) - \alpha b} \right. \tag{4.87}$$

$$\left. + \left(\frac{\beta S(\mu + \sigma + d)}{N\left[(\alpha + \mu + \sigma - b) - \alpha b\right]} - 1 \right) I \right\} \tag{4.88}$$

$$= \phi \left\{ (\alpha + \mu + \sigma - b) - \alpha b \right\} \left\{ \frac{b\{(\mu + \sigma + \alpha + d_1)\delta_1 + \delta_2\}T}{(\alpha + \mu + \sigma - b) - \alpha b} + (R_0 - 1)I \right\} \tag{4.89}$$

$$= \phi \left\{ (\alpha + \mu + \sigma - b) - \alpha b \right\} \left\{ \frac{b\{(\mu + \sigma + \alpha + d)\delta_1 + \delta_2\} \left\{ \frac{(\mu + \sigma + d)A - \alpha I}{\delta_2} \right\}}{(\alpha + \mu + \sigma - b) - \alpha b} + (R_{01} - 1)I \right\} \tag{4.90}$$

Since at disease free equilibrium $S = \frac{b+\delta T}{\mu+\sigma-\rho}$ and by letting $\phi = \frac{1}{(\mu+d_1)(\alpha+\mu-b)-\alpha b}$

$$\frac{dV}{dt} = (R_0 - 1)I + \frac{b\{(\mu + \sigma + \alpha + d)\delta_1 + \delta_2\}\left\{\frac{(\mu+\sigma+d_1)A-\alpha I}{\delta_2}\right\}}{(\alpha + \mu + \sigma - b) - \alpha b} \tag{4.91}$$

$$\leq 0 \tag{4.92}$$

Note that, $\frac{dV}{dt} = 0$ only when $I = A = 0$. Thus, substituting $I = A = 0$ into (4.55) shows that $S = \frac{b}{\mu+\sigma-\rho}$ as $t \to \infty$. Hence, the maximum invariant set of $\left\{S, I, A, T\right) \in \Pi | \frac{dV}{dt} \leq 0\right\}$ is singleton set $\{E_0\}$. Therefore, the global stability of E_{01} when $R_{01} \leq 1$ follows from the LaSalle's invariance principle (see details in (LaSalle, 1968)).

Theorem 4.9. If $R_{01} > 1$, then there exists an endemic equilibrium E_1^* (addition with the disease-free equilibrium) and it is globally asymptotically stable, provided the following conditions are satisfied.

$$\beta\frac{I^*}{N^*}S^* + \mu + \sigma S^* = b(\mu + \sigma + d),$$

$$\beta\frac{I^*}{N^*}S^* = (\mu + d)(\alpha + \mu - b) - \alpha b - b\delta_2 T^*,$$

$$\alpha I^* = (\mu + d)A^*.$$

Proof 4.9. Let us consider the following positive definite function about E_1^*

$$V = \frac{1}{2}(S - S^*)^2 + \frac{1}{2}(T - T^*)^2 + x\left(I - I^* - I^*\ln\frac{I}{I^*}\right) + \frac{1}{2}(A - A^*)^2 \tag{4.93}$$

$$\frac{dV}{dt} = (S - S^*)\frac{dS}{dt} + (T - T^*)\frac{dT}{dt} + x\left(\frac{I - I^*}{I}\right)\frac{dI}{dt} + (A - A^*)\frac{dA}{dt} \tag{4.94}$$

$$= (S - S^*)\left\{b + \rho - \beta\frac{I}{N}S - \mu S\right\} + (T - T^*)\{-(\delta + \delta_1 + \delta_2 + \mu)\}$$

$$+ x\left(\frac{I - I^*}{I}\right)\left\{b(I + A) + \beta\frac{I}{N}S - (\mu + \alpha + d)I\right\} + (A - A^*)\{\alpha I - (\mu + d)A\}$$

$$\tag{4.95}$$

$$\frac{dV}{dt} = (S - S^*) \left\{ b(\mu + \sigma + d) - (\mu + \sigma + d)\beta \frac{I}{N} S \right.$$

$$\left. - (\mu + \sigma + d)(\mu + \sigma)S \right\}$$

$$+ (S - S^*)(\mu + \sigma + d)\delta T + (T - T^*)(\mu + \sigma + d)\left\{ -(\delta + \delta_1 + \delta_2 + \mu) \right\} \quad (4.96)$$

$$+ x(\mu + \sigma + d)\left(\frac{I - I^*}{I}\right)\left\{ b\delta_2 T + \beta \frac{I}{N} S - ((\mu + \alpha + \sigma - b) - \alpha b) I \right\}$$

$$+ (\mu + \sigma + d_1)(A - A^*)\left\{ \alpha I - (\mu + \sigma + d)A \right\}$$

$$= (S - S^*)(\mu + \sigma + d)\left\{ \beta \frac{I^*}{N} S^* + (\mu + \sigma - \rho)S^* - (\mu + \sigma + d)\beta \frac{I}{N} S - (\mu + \sigma - \rho)S \right\}$$

$$+ (\mu + \sigma + d)T \left\{ (S - S^*)\delta - (T - T^*)(\delta + \delta_1 + \delta_2 + \mu) \right\}$$

$$+ x(\mu + \sigma + d)\left(\beta \frac{I}{N} S - \beta \frac{I^*}{N} S^* \right)$$

$$+ (\mu + \sigma + d)(A - A^*)\left\{ (\mu + \sigma + d)A* - (\mu + \sigma + d)A \right\}$$

$$(4.97)$$

$$= -(\mu + \sigma)(S - S^*)^2(\mu + \sigma + d) + \frac{\beta}{N} S^*(I^* - I)(S - S^*)(\mu + \sigma + d)$$

$$+ (\mu + \sigma + d)T \left\{ (S - S^*)\delta - (T - T^*)(\delta + \delta_1 + \delta_2 + \mu) \right\}$$

$$\qquad (4.98)$$

$$x(\mu + \sigma + d)\frac{\beta}{N}(I - I^*)(S - S^*) - x(\mu + \sigma + d)\frac{\beta}{N}(S - S^*)^2$$

$$- (\mu + \sigma + d)^2(A - A^*)^2$$

$$= -(S - S^*)^2(\mu + \sigma + d)\left\{ (\mu + \sigma) - x\frac{\beta}{N} \right\} - (\mu + \sigma + d)^2(A - A^*)^2$$

$$+ \frac{\beta}{N} S^*(I^* - I)(S - S^*)(\mu + \sigma + d)(1 + x) \qquad (4.99)$$

$$+ (\mu + \sigma + d_1)T \left\{ (S - S^*)\delta - (T - T^*)(\delta + \delta_1 + \delta_2 + \mu) \right\}$$

$$\leq 0 \qquad (4.100)$$

Note that, $\frac{dV}{dt}$ is negative definite showing that V is a Lyapunov function only at $\left\{ E_1^* \right\}$, when $S \leq S^*$, $I \leq I^*$, $A \leq A^*$ and $T \leq T^*$. By applying LaSalle's invariance principle (LaSalle, 1968), with the initial conditions in Π, every solution (4.55)-(4.58) approaches

E_1^* at as $t \to \infty$ whenever $R_{01} > 1$. Therefore, the endemic equilibrium E_1^* is globally asymptotically stable in Π whenever $R_{01} > 1$.

4.7 Model III (condom as preventive measure with inbound and outbound tourism)

We extend Model II (inbound with outbound tourists) by incorporating preventive measures, as shown in Figure 4.3. Since as at now there is no specific cure for HIV/AIDS we introduced condoms as a preventive measure. Why condoms? This is because when a condom is correctly used it gives 100% protection against HIV infection. It serves as a physical barrier that assists an individual to minimize the risk of getting the HIV infection sexually (Adih & Alexander, 1999; Holmes et al., 2004; Wilton, 2013).

4.7.1 Key Model III assumptions

Taking into consideration that we are modelling disease transmission, assume that we put condoms as an intervention with protection η then the reduction in risk becomes $\beta_p = (1 - \eta)\beta$. The main point here is to protect the susceptible population who are not infected since they are capable of reducing the risk of infection. In this context we further assumed that the range is between $0 < \eta < 1$, depicting that this does not include 0 and 1 because 0 would mean that condoms as a preventive measure become useless or meaningless and 1 implies that condoms as a preventive measure are comprehensively effective (Nyabadza et al., 2011). In view of this they need to be protected.

The model takes the following form

$$\frac{dS}{dt} = b + \rho S + \delta T - (1 - \eta)\beta \frac{I}{N} S - (\mu + \sigma)S \tag{4.101}$$

$$\frac{dI}{dt} = b(I + A) + \delta_1 T + (1 - \eta)\beta \frac{I}{N} S - (\mu + \alpha + \sigma)I \tag{4.102}$$

$$\frac{dA}{dt} = \alpha I + \delta_2 T - (\mu + \sigma + d)A \tag{4.103}$$

$$\frac{dT}{dt} = -(\delta + \delta_1 + \delta_2)T - \mu T \tag{4.104}$$
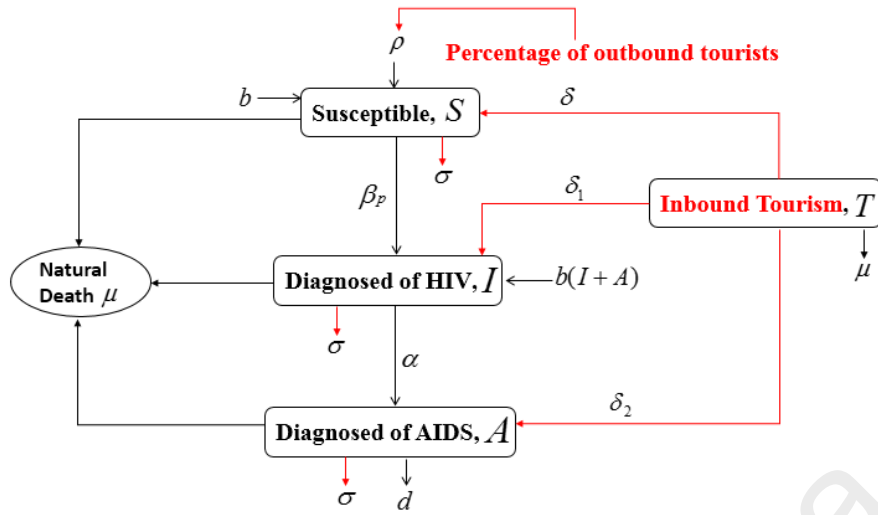
Figure 4.3: Flow diagram of HIV transmission with tourism and condom as intervention.

From (4.101)-(4.104) depict the similar property of (4.1)-(4.3) and (4.55)-(4.58) that all the compartment and the parameters are non-negative for all time. We now prove the positivity of (4.101)-(4.104).

Theorem 4.10. The solutions for $S(t)$, $I(t)$, $A(t)$, $T(t)$ of (4.101)-(4.101) with the initial condition $S(0) > 0, I(0) > 0, A(0) > 0, T(0) > 0$ are positive for all $t > 0$.

Proof 4.10. We use similar approach by (Mukandavire et al., 2009). Assume that $T = sup\{t \geq 0 : S > 0, I > 0, A > 0, T > 0 \text{in}[0, t]\}$. When $T > 0$, and if $T < \infty$ then one of $S(T), I(T), A(T), T(T)$ must be equal to zero. From (4.105), we have

$$
\frac{d}{dt}\left\{ S \exp\left[\int_0^t (1 - \eta)\frac{\beta}{N}du + (\mu + \sigma - \rho)t \right] \right\} = \\
[b + \delta T] \exp\left[\int_0^t (1 - \eta)\frac{\beta}{N}du + (\mu + \sigma - \rho)t \right]
$$
(4.105)

Hence,

$$
S(T) \exp\left[\int_0^T (1 - \eta)\frac{\beta}{N}du + (\mu + \sigma - \rho)T \right] - S(0) = \\
\int_0^T [b + \delta T] \exp\left[\int_0^u (1 - \eta)\frac{\beta}{N}dv + (\mu + \sigma - \rho)u \right] du
$$
(4.106)

59

Therefore,

$$
\begin{aligned}
S(T) = & S(0) \exp\left[-\int_0^t (1-\eta)\frac{\beta}{N} du + (\mu + \sigma - \rho)T \right] \\
& + \left\{ \exp\left[-\int_0^t (1-\eta)\frac{\beta}{N} du + (\mu + \sigma - \rho)T \right] \right\} \\
& \times \left\{ \int_0^T [b + \delta T] \exp\left[\int_0^u (1-\eta)\frac{\beta}{N} dv + (\mu + \sigma - \rho)u \right] du \right\} > 0.
\end{aligned}
\tag{4.107}
$$

For $I(t)$, we obtain,

$$
\begin{aligned}
& \frac{d}{dt} \left\{ I \exp\left[\int_0^t (1-\eta)\frac{\beta}{N} du + (\alpha + \mu + \sigma)t \right] \right\} = \\
& [b(I+A) + \delta_1 T] \exp\left[\int_0^t (1-\eta)\frac{\beta}{N} du + (\alpha + \mu + \sigma)t \right]
\end{aligned}
\tag{4.108}
$$

Hence,

$$
\begin{aligned}
& I(T) \exp\left[\int_0^T (1-\eta)\frac{\beta}{N} du + (\mu + \sigma - \rho)T \right] - I(0) = \\
& \int_0^T [b(I+A) + \delta_1 T] \exp\left[\int_0^u (1-\eta)\frac{\beta}{N} dv + (\alpha + \mu + \sigma)u \right] du
\end{aligned}
\tag{4.109}
$$

Therefore,

$$
\begin{aligned}
I(T) = & I(0) \exp\left[-\int_0^t (1-\eta)\frac{\beta}{N} du + (\alpha + \mu + \sigma)T \right] \\
& + \left\{ \exp\left[-\int_0^t (1-\eta)\frac{\beta}{N} du + (\alpha + \mu + \sigma)T \right] \right\} \\
& \times \left\{ \int_0^T [b(I+A) + \delta_1 T] \exp\left[\int_0^u (1-\eta)\frac{\beta}{N} dv + (\alpha + \mu + \sigma)u \right] du \right\} > 0.
\end{aligned}
\tag{4.110}
$$

Similarly, it can be shown that $T > 0$, and $A > 0$ for all $t > 0$ and this completes this proof.

4.8 Analysis of the Model III

Similarly, it is important to determine whether the disease is epidemic or endemic. There is one disease free equilibrium E_{02} and one endemic equilibrium E_2^* for (4.101)-(4.104).

4.8.1 Equilibrium solutions

4.8.1.1 Disease free equilibrium and the reproduction number R_{02}

The Model III has a disease-free equilibrium given by

$$E_{02} = \left(\frac{b + \delta T}{\mu + \sigma - \rho}, 0, 0, 0 \right) \tag{4.111}$$

We calculate the reproduction number R_{02} for Model III. We write the right-hand side of system (4.101)-(4.104) as $F - V$ with the following equations:

$$F = \begin{bmatrix} (1 - \eta)\beta \frac{I}{N} S \\ \\ 0 \end{bmatrix} \tag{4.112}$$

$$V = \begin{bmatrix} -b(I + A) + (\mu + \alpha + \sigma)I \\ \\ -\alpha I + (\mu + \sigma + d)A \end{bmatrix} \tag{4.113}$$

Then, we consider the Jacobian matrices associated with F and V:

$$J_F = \begin{bmatrix} (1 - \eta)\beta \frac{S}{N} & 0 \\ \\ 0 & 0 \end{bmatrix} \tag{4.114}$$

$$J_V = \begin{bmatrix} \alpha + \mu + \sigma - b & -b \\ \\ -\alpha & (\mu + \sigma + d) \end{bmatrix} \tag{4.115}$$

The spectral radius of the matrix $J_F \times J_V^{-1} = \left\{ \frac{(1-\eta)\beta S}{N} \right\} \left\{ \frac{(\mu+\sigma+d)}{(\mu+\sigma+d)(\alpha+\mu+\sigma-b)-\alpha b} \right\}$. The basic

reproduction number of the system for disease-free is obtained as

$$R_{02} = \left\{ \frac{(1-\eta)\beta(b+\delta T)}{(\mu+\sigma-\rho)N} \right\} \left\{ \frac{(\mu+\sigma+d)}{(\mu+\sigma+d)(\alpha+\mu+\sigma-b)-\alpha b} \right\}. \qquad (4.116)$$

4.8.1.2 Existence of the endemic equilibrium

If $R_{02} > 1$, from (4.101)-(4.104) has a unique endemic equilibrium $E_2^* = (S^*, I^*, A^*, T^*)$

by solving (4.101)-(4.104) simultaneously. From (4.104) we get

$$b(\mu+\sigma+d+\alpha)I + b\delta_2 T + \delta_1 T(\mu+\sigma+d) + (1-\eta)\beta \frac{I}{N} S(\mu+\sigma+d)$$
$$-(\mu+\sigma+d)(\mu+\alpha+\sigma)I = 0 \qquad (4.117)$$

$$b\delta_2 T + \delta_1 T(\mu+\sigma+d) + (1-\eta)\beta \frac{I}{N} S(\mu+\sigma+d)$$
$$-(\mu+\sigma+d)(\mu+\alpha+\sigma-b)I + \alpha b I = 0 \qquad (4.118)$$

$$b\delta_2 T + \delta_1 T(\mu+\sigma+d) + (1-\eta)\beta \frac{I}{N} S(\mu+\sigma+d)$$
$$-\{(\mu+\sigma+d)(\mu+\alpha+\sigma-b) - \alpha b\} I = 0 \qquad (4.119)$$

$$\left\{ (\mu+\sigma+d)(\mu+\alpha+\sigma-b-(1-\eta)\beta\frac{S}{N}) - \alpha b \right\} I = b\delta_2 T + \delta_1 T(\mu+\sigma+d)$$
$$(4.120)$$

From (4.103), we have

$$I = \frac{N}{(1-\eta)\beta} \left\{ \frac{(b+\delta T)}{S} - (\mu+\sigma-\rho) \right\} \qquad (4.121)$$

By substituting (4.69) into (4.120)

$$\left\{ (\mu + \sigma + d)(\mu + \alpha + \sigma - b - (1 - \eta)\beta \frac{S}{N}) - \alpha b \right\} \frac{N}{(1 - \eta)\beta} \left\{ \frac{(b + \delta T)}{S} - (\mu + \sigma - \rho) \right\}$$

$$= b\delta_2 T + \delta_1(\mu + \sigma + d)T$$

(4.122)

$$b\delta_2 T + \delta_1(\mu + \sigma + d)T = \frac{\{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\} N}{(1 - \eta)\beta} \left\{ \frac{(b + \delta T)}{S} - (\mu + \sigma - \rho) \right\}$$

$$- (b + \delta T) - S(\mu + \sigma - \rho)$$

(4.123)

$$b\delta_2 T + \delta_1(\mu + \sigma + d)T = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}(1 - \eta)\beta \frac{N}{S}(b + \delta T)$$

$$- (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{(1 - \eta)\beta}$$

$$- (b + \delta T) - S(\mu + \sigma - \rho)$$

(4.124)

$$(\mu + \sigma - \rho)S^2 + (b + \delta T)S - b\delta_2 TS - \delta_1(\mu + \sigma + d)TS$$

$$- (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{(1 - \eta)\beta}S$$

(4.125)

$$+ \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\} \frac{N}{(1 - \eta)\beta}(b + \delta T) = 0$$

Equation (4.125) become quadratic equation

$$\mathcal{X} = \frac{-\mathcal{B} \pm \sqrt{\mathcal{B}^2 - 4\mathcal{A}C}}{2\mathcal{A}}$$

(4.126)

From (4.126) where

$$\mathcal{A} = (\mu + \sigma - \rho),$$

$$\mathcal{B} = (b + \delta T) - b\delta_2 T - \delta_1(\mu + \sigma + d)T - (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{(1 - \eta)\beta},$$

$$C = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{(1 - \eta)\beta}(b + \delta T)$$

Now S^* becomes,

$$S^* = \frac{F + Y - (b + \delta T) + \sqrt{(F + Y - (b + \delta T))^2 - 4D(\mu + \sigma - \rho)}}{2(\mu + \sigma - \rho)} \qquad (4.127)$$

where

$$Y = b\delta_2 T - \delta_1(\mu + \sigma + d)T,$$

$$D = \{(\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\}\frac{N}{(1 - \eta)\beta}(b + \delta T),$$

$$F = \delta_1(\mu + \sigma + d)T - (\mu + \sigma + d)(\mu + \alpha + \sigma - b - \alpha b)\frac{N}{(1 - \eta)\beta}$$

By substituting (4.127) into (4.103) and (4.104), we obtain I^* and A^*, respectively

$$I^* = \frac{N}{(1 - \eta)\beta}\left\{\frac{(b + \delta T)2(\mu + \sigma - \rho)}{F + Y - (b + \delta T) + \sqrt{(F + Y - (b + \delta T))^2 - 4D(\mu + \sigma - \rho)}} - (\mu + \sigma - \rho)\right\}$$

$$(4.128)$$

$$A^* = \frac{\alpha I^*}{(\mu + \sigma + d)} + \frac{\delta_2 T}{(\mu + \sigma + d)} \qquad (4.129)$$

$$T^* = \frac{(\mu + \sigma + d)A^* + \alpha I^*}{\delta_2} \qquad (4.130)$$

4.8.2 Local stability of the equilibria

Equation (4.101)-(4.104) becomes

$$\frac{dS}{dt} = b + \rho S + \delta T - (1 - \eta)\beta \frac{I}{N}S - (\mu + \sigma)S \tag{4.131}$$

$$\frac{dI}{dt} = b(\mu + \sigma + \alpha)I + b\delta_2 T + \delta_1 T + (1 - \eta)\beta \frac{I}{N}S(\mu + \sigma) - (\mu + \sigma)(\mu + \alpha + \sigma)I \tag{4.132}$$

$$\frac{dA}{dt} = \alpha I + \delta_2 T - (\mu + \sigma + d)A \tag{4.133}$$

$$\frac{dT}{dt} = -(\delta + \delta_1 + \delta_2)T - \mu T \tag{4.134}$$

Note that at equilibrium, equation (4.104) becomes

$$A = \frac{\alpha I + \delta_2 T}{\mu + \sigma + d} \tag{4.135}$$

Theorem 4.11. The disease-free equilibrium E_{02} is locally asymptotically stable for $R_{02} < 1$ and unstable otherwise.

Proof 4.11. The stability of the endemic equilibrium is determined using the eigenvalues of the characteristic equation of the corresponding Jacobian matrix, $J(S, I, A, T) = J(E_{02})$, which is given by:

$$J(E_{02}) = \begin{bmatrix} -\beta\frac{I}{N} - \mu & -(1-\eta)\beta\frac{S}{N} & 0 & -\delta \\ \beta\frac{I}{N} & (1-\eta)\beta\frac{S}{N}(\mu + \sigma + d) - H & 0 & -\delta_1 \\ 0 & \alpha & -(\mu + \sigma + d) & -\delta_2 \\ 0 & 0 & 0 & -(\delta + \delta_1 + \delta_2 + \mu) \end{bmatrix} \tag{4.136}$$

where $H = [(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b]$

$$J(E_{02}) = \begin{bmatrix} -\mu & -\frac{\beta b}{\mu N} & 0 & -\delta \\[2mm] 0 & \frac{(1-\eta)\beta b}{N\mu} - H & b & -\delta_1 \\[2mm] 0 & \alpha & -(\mu + \sigma + d_1) & -\delta_2 \\[2mm] 0 & 0 & 0 & -(\delta + \delta_1 + \delta_2 + \mu) \end{bmatrix} \qquad (4.137)$$

The matrix $J(E_{02})$ have the following eigenvalues $\lambda_1 = -\mu < 0$, $\lambda_2 = -(\mu + \sigma + d < 0$, $\lambda_3 = -(\delta + \delta_1 + \delta_2 + \mu) < 0$, $\lambda_4 = \frac{(1-\eta)\beta b}{N(\mu+\sigma-\rho)} - \{(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b\}$. For local

asymptotically stable, if $\lambda_4 < 0$ that is $\frac{(1-\eta)\beta b}{N(\mu+\sigma-\rho)} < \{(\mu + \sigma + d_1)(\alpha + \mu + \sigma - b) - \alpha b\}$

holds, which is equivalent to

$$\frac{(1 - \eta)\beta b(\mu + \sigma + d)}{N(\mu + \sigma - \rho)\{(\mu + \sigma + d)(\alpha + \mu + \sigma - b) - \alpha b\}} = R_{02} < 1 \qquad (4.138)$$

4.8.3 Global stability

Theorem 4.12. If $R_{02} \leq 1$, then there exists disease-free equilibrium E_{02} is globally asymptotically stable on Ω.

   Proof 4.12. Given that $R_{02} \leq 1$, then there exists only one disease-free equilibrium $E_{02} = \left(\frac{b}{\mu+\sigma-\rho}, 0, 0, 0\right)$. By considering this, we define a Lyapunov function of $V(S, I, A, T) : \mathbb{R}_+^4$ as

$$V = \phi I + A \qquad (4.139)$$

$$\frac{dV}{dt} = \phi\frac{dI}{dt} + \frac{dA}{dt} \qquad (4.140)$$

$$\frac{dV}{dt} = \phi \left\{ b(I + A) + \delta_1 T + (1 - \eta)\beta\frac{I}{N}S - (\alpha + \mu + \sigma + d)I \right\}$$
$$+ \alpha I + \delta_2 T - (\mu + \sigma + d_1)A \tag{4.141}$$

$$= \phi \left\{ b(\mu + \sigma + \alpha + d)I + b\delta_2 T + (\mu + \sigma + d)\delta_1 T + (1 - \eta)\beta\frac{I}{N}S(\mu + \sigma + d) \right\}$$
$$- \phi(\alpha + \mu + \sigma + d)I + \alpha I + (\mu + \sigma + d)A - \alpha I - (\mu + \sigma + d)A$$

$$\tag{4.142}$$

$$= \phi \left\{ (\alpha + \mu + \sigma - b) - \alpha b \right\} \left\{ \frac{b\{(\mu + \sigma + \alpha + d)\delta_1 + \delta_2\}T}{(\alpha + \mu + \sigma + d - b) - \alpha b} \right.$$
$$\left. + \left(\frac{(1 - \eta)\beta S(\mu + \sigma + d)}{N\left[(\alpha + \mu + \sigma - b) - \alpha b \right]} - 1 \right) I \right\} \tag{4.143}$$

$$= \phi \left\{ (\alpha + \mu + \sigma - b) - \alpha b \right\} \left\{ \frac{b\{(\mu + \sigma + \alpha + d_1)\delta_1 + \delta_2\}T}{(\alpha + \mu + \sigma - b) - \alpha b} + (R_{02} - 1)I \right\} \tag{4.144}$$

$$= \phi \left\{ (\alpha + \mu + \sigma - b) - \alpha b \right\} \left\{ \frac{b\{(\mu + \sigma + \alpha + d)\delta_1 + \delta_2\}\left\{ \frac{(\mu+\sigma+d)A - \alpha I}{\delta_2} \right\}}{(\alpha + \mu + \sigma - b) - \alpha b} + (R_{02} - 1)I \right\}$$

$$\tag{4.145}$$

Since at disease free equilibrium $S = \frac{b + \delta T}{\mu + \sigma - \rho}$ and by letting $\phi = \frac{1}{(\mu + \sigma + d)(\alpha + \mu - b) - \alpha b}$

$$\frac{dV}{dt} = (R_{02} - 1)I + \frac{b\{(\mu + \sigma + \alpha + d)\delta_1 + \delta_2\}\left\{ \frac{(\mu+\sigma+d)A - \alpha I}{\delta_2} \right\}}{(\alpha + \mu + \sigma - b) - \alpha b} \tag{4.146}$$

$$\leq 0 \tag{4.147}$$

Note that, $\frac{dV}{dt} = 0$ only when $I = A = 0$. Thus, substituting $I = A = 0$ into (4.55) shows that $S = \frac{b}{\mu + \sigma - \rho}$ as $t \to \infty$. Hence, the maximum invariant set of $\left\{ S, I, A, T \right\} \in \Pi | \frac{dV}{dt} \leq 0 \right\}$ is singleton set $\{E_{02}\}$. Therefore, the global stability of E_{02} when $R_{02} \leq 1$ which follows the LaSalle's invariance principle (see details in (LaSalle, 1968)).

Theorem 4.13. If $R_{02} > 1$, then there exists an endemic equilibrium E_2^* (addition with the disease-free equilibrium) and it is globally asymptotically stable, provided the

conditions are satisfied by using the following:

$$(1 - \eta)\beta\frac{I^*}{N^*}S^* + \mu + \sigma S^* = b(\mu + \sigma + d) + (1 - b)(\alpha + \sigma + \mu + d)I^*,$$

$$\beta\frac{I^*}{N^*}S^* = (\mu + d)(\alpha + \mu - b) - \alpha b - b\delta_2 T^*,$$

$$\alpha I^* = (\mu + d)A^*.$$

Proof 4.13. Let us consider the following positive definite function about E_2^*

$$V = \frac{1}{2}(S - S^*)^2 + \frac{1}{2}(T - T^*)^2 + x\left(I - I^* - I^*\ln\frac{I}{I^*}\right) + \frac{1}{2}(A - A^*)^2 \tag{4.148}$$

$$\frac{dV}{dt} = (S - S^*)\frac{dS}{dt} + (T - T^*)\frac{dT}{dt} + x\left(\frac{I - I^*}{I}\right)\frac{dI}{dt} + (A - A^*)\frac{dA}{dt} \tag{4.149}$$

$$= (S - S^*)\left\{b + (1 - b)(I + A) - (1 - \eta)\beta\frac{I}{N}S - (\mu + \sigma - \rho)S\right\}$$

$$+ (T - T^*)\{-(\delta + \delta_1 + \delta_2 + \mu)\}$$

$$+ x\left(\frac{I - I^*}{I}\right)\left\{b(I + A) + (1 - \eta)\beta\frac{I}{N}S - (\mu + \alpha + d)I\right\} \tag{4.150}$$

$$+ (A - A^*)\{\alpha I - (\mu + d)A\}$$

$$= (S - S^*)\{b(\mu + \sigma + d) + (1 - b)(\mu + \sigma + d + \alpha)I + (1 - b)\delta_2 T\}$$

$$- (S - S^*)\left\{(\mu + \sigma + d)\beta\frac{I}{N}S - (\mu + \sigma + d)(\mu + \sigma - \rho)S\right\}$$

$$+ (S - S^*)(\mu + \sigma + d)\delta T + (T - T^*)(\mu + \sigma + d)\{-(\delta + \delta_1 + \delta_2 + \mu)\}$$

$$+ x(\mu + \sigma + d)\left(\frac{I - I^*}{I}\right)\left\{b\delta_2 T + (1 - \eta)\beta\frac{I}{N}S - ((\mu + \alpha + \sigma - b) - \alpha b)I\right\}$$

$$+ (\mu + \sigma + d_1)(A - A^*)\{\alpha I - (\mu + \sigma + d)A\}$$

$$\tag{4.151}$$

$$\frac{dV}{dt} = (S - S^*)(\mu + \sigma + d)\left\{(1 - \eta)\beta\frac{I^*}{N}S^* + (\mu + \sigma - \rho)S^*\right.$$

$$\left. - (\mu + \sigma + d)(1 - \eta)\beta\frac{I}{N}S - (\mu + \sigma - \rho)S\right\}$$

$$+ (\mu + \sigma + d)T\left\{(S - S^*)\delta - (T - T^*)(\delta + \delta_1 + \delta_2 + \mu)\right\} \qquad (4.152)$$

$$+ x(\mu + \sigma + d_1)\left(\beta\frac{I}{N}S - (1 - \eta)\beta\frac{I^*}{N}S^*\right)$$

$$+ (\mu + \sigma + d_1)(A - A^*)\left\{(\mu + \sigma + d)A* - (\mu + \sigma + d)A\right\}$$

$$= -(\mu + \sigma)(S - S^*)^2(\mu + \sigma + d) + \frac{\beta}{N}S^*(I^* - I)(S - S^*)(\mu + \sigma + d)$$

$$+ (\mu + \sigma + d_1)T\left\{(S - S^*)\delta - (T - T^*)(\delta + \delta_1 + \delta_2 + \mu)\right\}$$

$$x(\mu + \sigma + d)\frac{(1 - \eta)\beta}{N}(I - I^*)(S - S^*) - x(\mu + \sigma + d_1)\frac{(1 - \eta)\beta}{N}(S - S^*)^2 \qquad (4.153)$$

$$- (\mu + \sigma + d)^2(A - A^*)^2$$

$$= -(S - S^*)^2(\mu + \sigma + d)\left\{(\mu + \sigma) - x\frac{(1 - \eta)\beta}{N}\right\} - (\mu + \sigma + d)^2(A - A^*)^2$$

$$+ \frac{\beta}{N}S^*(I^* - I)(S - S^*)(\mu + \sigma + d)(1 + x) \qquad (4.154)$$

$$+ (\mu + \sigma + d_1)T\left\{(S - S^*)\delta - (T - T^*)(\delta + \delta_1 + \delta_2 + \mu)\right\}$$

$$\leq 0 \qquad (4.155)$$

Note that, $\frac{dV}{dt}$ is a negative definite showing that V is a Lyapunov function only at $\left\{E_2^*\right\}$, when $S \leq S^*$, $I \leq I^*$, $A \leq A^*$ and $T \leq T^*$. By applying LaSalle's invariance principle (LaSalle, 1968), with the initial conditions in Ω, every solution in (4.101)-(4.104) approaches E_2^* at as $t \to \infty$ whenever $R_{02} > 1$. Therefore, the endemic equilibrium E_2^* is globally asymptotically stable in Ω whenever $R_{02} > 1$.

4.9 Chapter summary

This chapter provided mathematical analysis by determining the disease-free equilibrium, the various basic reproduction numbers, by performing the sensitivity analysis on the basic reproduction numbers showing existence and stability of the endemic equilibrium for both

local and global stability. The proceeding chapter will analyse the results based on the estimated parameters by performing the simulations using the HIV and AIDS incidence data between 1986 and 2011 in order to vilify the proposed models.

CHAPTER 5: MODEL VALIDATION

5.1 Introduction

This chapter illustrates how the models are calibrated to the Malaysia incidence data of HIV and AIDS from 1986 to 2011 (MoH, 2012a), as described in Section 3.2. The calibration of these models are based on the parameters relating to the assumptions in Model I, Model II and Model III (see details in Chapter 4). The parameters relating to modeling of the disease, the start time of the epidemic, the trend and magnitude of spread of the disease are estimated using Bayesian approach by MCMC (Robert & Casella, 2011; Apenteng & Ismail, 2015) see details in Chapter 3. These techniques enable analyse of very complicated models that give posterior summaries such as means, medians, variances, credible intervals and are all easily obtained for individual parameters involved in the joint distributions of the parameters (O'Neill, 2002). All the models are subject to assumptions relating to the effects of tourists on HIV and AIDS.

5.2 Estimated model parameters

In this section, we estimate the unknown parameters involved in Model I, Model II and Model III by using the details in Chapter 3. There are 6, 10 and 11 parameters estimated for Model I, Model II and Model III, respectively. The parameters that described the proposed models are taken into account. After the fitting the model into the data to obtain the approximate best-fit parameters by optimizer (Section 3.4.5) that uses. In order to determine the estimated parameters the proposed models were linearized to obtain the approximate best-fit parameters by optimizer (Section 3.4.5). MCMC was used to get the uncertainty in the estimated parameters. The MCMC chain length perform 40000 iterations, with different initial parameter starting points. In order to minimize the correlation it is necessary to ensure that constraints on parameters are commonly satisfied.

5.3 Analysis of the results for Model I

This section discusses Model I, investigating the spread of HIV and AIDS incidences, taking into account citizens of Malaysia who leave the country and who upon returning are infected with HIV. Six parameters were estimated in this model.

5.3.1 Sensitivity analysis

There are various parameters present in the proposed Model I and the values of these parameters will directly affect the dynamics of the HIV and AIDS, taking into account outbound tourism. We carry out a sensitivity analysis to determine which parameters are more important by finding which parameter has the higher sensitivity value as shown in Table 5.1. Based on these summary statistics shown in Table 5.1, it is clear that parameter β, the contact rate has the highest sensitivity value. This is due to the flow of outbound tourism that moved to the susceptible compartment as compared to the remaining four parameters. When $L1 = \frac{\sum |S_{ij}|}{n}$ and $L2 = \sqrt{\frac{\sum (S_{ij}^2)}{n}}$ are the $L1$ norm, this condition is referred to as the least absolute deviation, and the $L2$ norm is known as the least square. The mean represents the mean of the sensitivity functions, the Min represents the minimal value of the sensitivity functions, and Max represents the maximum value of the sensitivity functions.

Table 5.1: Summary of sensitivity values

	Value	Scale	$L1$	$L2$	Mean	Min	Max
β	2.0e+00	2.0e+00	7.4e+00	1.1e+00	7.4e+00	0.0000	9.8e+00
α	5.0e-02	5.0e-02	4.9e-01	7.5e-02	3.1e-02	-0.7549	8.3e-01
μ	2.0e-01	2.0e-01	8.0e+00	1.3e-01	-8.0e+00	-14.3613	0.0e+00
b	1.3e-01	1.3e-01	1.6e+00	2.6e-01	1.6e+00	0.0000	3.6e+00
ρ	9.0e-08	9.0e-08	2.4e-06	3.8e-07	2.4e-06	0.0000	4.1e-06
d	1.0e-03	1.0e-03	1.5e-03	3.1e-04	-1.5e-03	-0.0057	0.0e+00

Table 5.2 shows all the six estimated parameters involved in Model I. The transmission coefficient of susceptible individuals and HIV-infected individuals β is 1.9704 for a portion

of susceptible individuals being infected with HIV. The progression rate α is 8.376159e-02/year which gives an average of 12 years. It is estimated that the percentage of outbound tourists that are in the susceptible group who returns home with an infection of HIV without the knowledge of their status, ρ is 3.569704e-06.

Table 5.2: Model I parameters definitions and their estimated parameters

Parameter	Definition	Estimated Parameter
β	Contact rate between S and I	1.970413e+00
α	Rate of progression to AIDS	8.376159e-02
μ	Natural death rate	1.732356e-02
b	Natural birth rate	1.593382e-02
ρ	Percentage of outbound tourists	3.569704e-06
d	Disease-induced mortality due to AIDS	1.724533e-01

Figure 5.1 depicts an overlay of annually reported HIV case counts and simulations with fitted parameters during the 25-year (1986-2011) calibration period. The black line incorporates the estimated parameters. The highest peak infection rate occurred during year 16, which corresponded to 2002, when there were 6978 infected individuals. The reported data was used to parameterize Model I in order to obtain a good fit. We did not obtain a better fit, however, Figure 5.1 gives a good indication for public health that the disease is under control with the basic reproduction number of 1.026218e-06. This result shows that the spread of HIV/AIDS is stable.
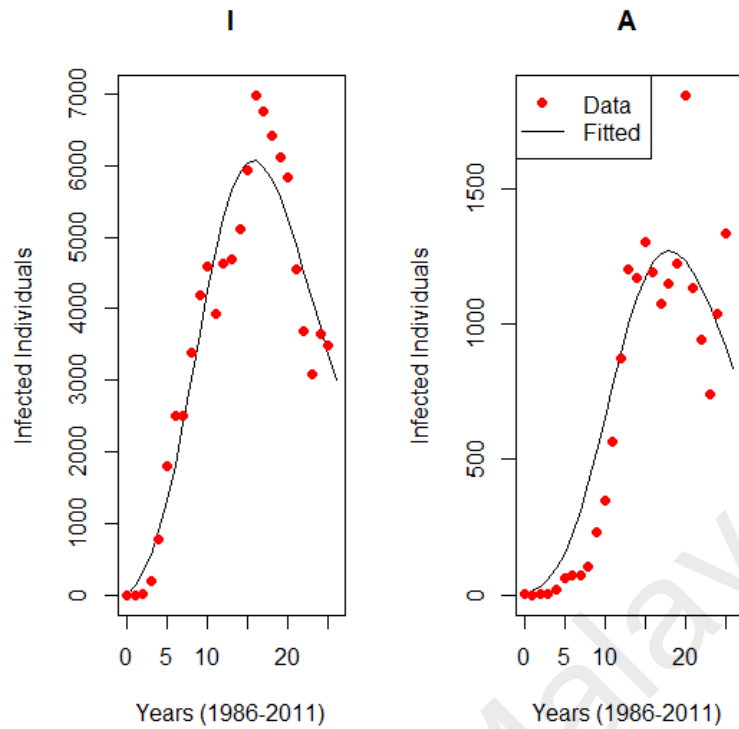
Figure 5.1: The fitted growth curve to the incidence values of HIV and AIDS populations with ρ.

The following figures show the simulations from the MCMC approach for each parameter. From Figure 5.2, the trace of the MCMC chain (grey line) show that the chain has converged. The last figure also shows the error variances for each observed variable.
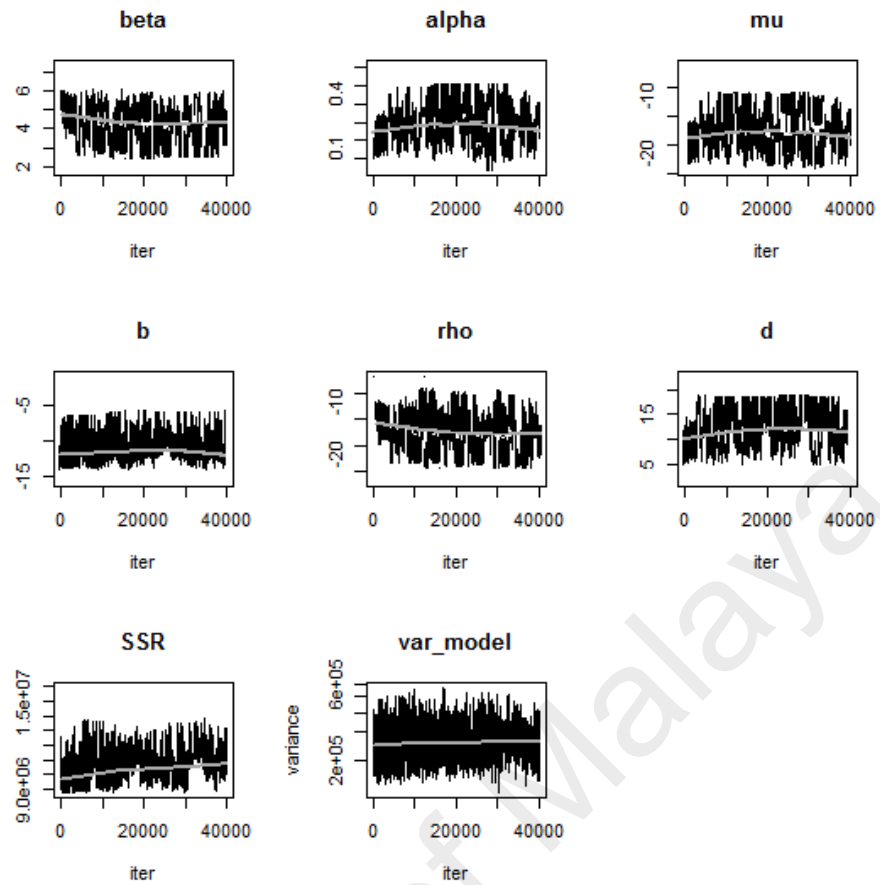
Figure 5.2: MCMC parameter values.

Table 5.3 shows a summary of mean, 25, 50 and 75% percentiles of the posterior distributions representing the 95% credible intervals.

Table 5.3: Summary of MCMC

	β	α	μ	b	ρ	d	var model
mean	1.9929407	0.1887909	0.08305449	0.1560183	-0.1313195	0.8432826	418220.06
sd	0.1000459	0.1384636	0.78231898	0.6512615	0.8104748	0.9965722	86834.39
min	1.7627714	0.0424479	-2.04250655	-1.5451292	-2.3363577	-1.0869920	215918.15
max	2.3163534	0.7693753	2.033380725	1.7355278	1.8952311	4.1269374	837621.35
q025	1.9322349	0.1151575	-0.24768540	-0.1451738	-0.4697421	0.1950808	354594.51
q050	1.9605085	0.1521775	0.08552304	0.1358938	-0.1303218	0.6405053	404625.22
q075	2.0430190	0.2129700	0.39760852	0.4240753	0.1998647	1.1524405	461969.40

Plotted pairs of the MCMC samples for the six parameters show a pairwise relationship of correlation coefficient between the upper panel, the lower panel, and the marginal distribution for each six parameters showing on the diagonal. In Figure 5.3, the pair plots show a strong relation between parameters ρ and b, and μ with $r^2 > 0.85$.
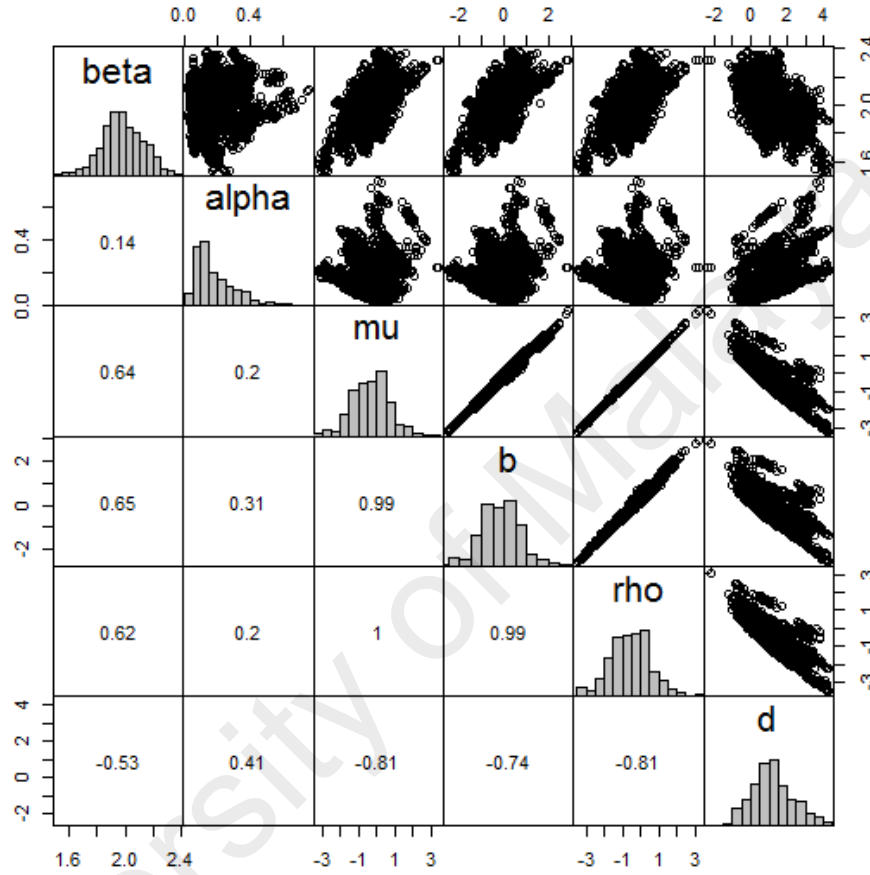
Figure 5.3: Pairs plot of the MCMC samples for the six parameters.

Figure 5.4 shows the sensitivity range of annually reported HIV cases based on parameter distribution as generated with the MCMC method during the 25-year calibration period (1986-2011). The light grey area represents the minimum and maximum model response at each time step, and the dark grey area (Mean ±sd) illustrates the mean model response plus/minus one standard deviation. Among the compartment populations, the variance increases in the following order: $I > S > A$. The large variance is due to either the uncertainties in the model or noise in data collection.
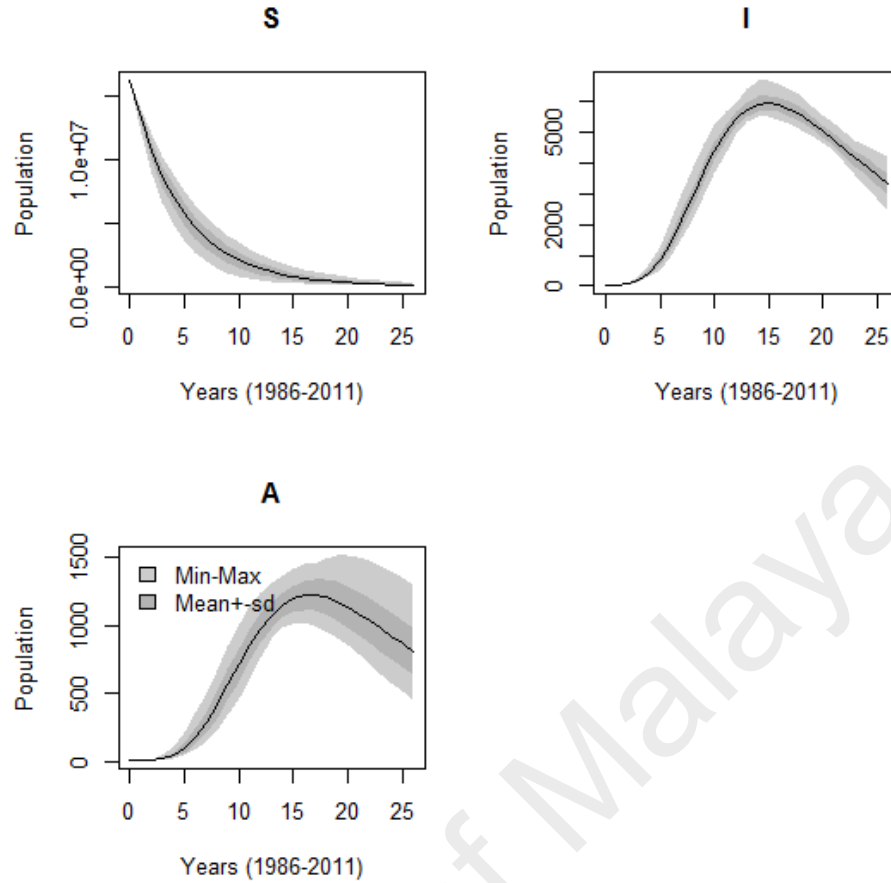
Figure 5.4: Sensitivity range of yearly reported HIV and AIDS cases. Predictions take the form of credible regions.

5.4 Summary of Model I

Model I shows how a mathematical model can be used to model the effect of outbound tourists on the spread of HIV/AIDS. The results suggest that the percentage of outbound tourists ρ, and individuals who are infected with HIV after returning home increases the HIV persistence in Malaysia.

5.5 Analysis of the results for Model II

This section discusses the extension of Model I with the inflow of inbound tourists who arrive in Malaysia. In Model I, there were six parameters involved. An additional four parameters are added to make a total of ten parameters. These are a fraction of inbound tourists δ, δ_1, and δ_2 that are recruited into $S(t)$, $I(t)$ and $A(t)$, respectively, and to ascertain the number of days the tourists stay in Malaysia which is represented by σ at the $S(t)$,

$I(t)$ and $A(t)$.

5.5.1 Sensitivity analysis

There are ten parameters in Model II in relation to the inflow of inbound tourists, which directly affect the HIV and AIDS incidence. We carried out a sensitivity analysis to determine which parameter is more important by finding the parameter that has the highest sensitivity value as show in Table 5.4 below. It is clear that parameter b (natural birth rate) has the least effect on the output variables while the transmission coefficient of susceptible individuals and HIV-infected individuals, β has the highest sensitivity value. This result suggests that even with the inflow of tourists and outflow of citizens to other countries the contact rate between S and I remains the most significant parameter.

Table 5.4: Summary of sensitivity values

	Value	Scale	$L1$	$L2$	Mean	Min	Max
β	1.7e+00	1.7e+00	7.9e+00	1.2e+00	7.9e+00	0.0e+00	1.2e+01
α	3.9e-02	3.9e-02	4.7e-01	7.4e-02	-2.2e-02	-1.0e+00	7.1e-01
μ	1.4e-01	1.4e-01	7.0e+00	1.2e+00	-7.0e-01	-1.4e+01	0.0e+00
σ	1.0e-05	1.0e-05	4.8e-04	8.0e-05	-4.8e-04	-9.9e-04	0.0e+00
δ	9.0e-04	9.0e-04	6.2e-03	1.0e-03	6.2e-03	-6.0e-04	1.3e-02
δ_1	1.0e-07	1.0e-07	5.9e-02	8.6e-03	5.9e-02	0.0e+00	6.9e-02
δ_2	1.0e-06	1.0e-06	5.9e-02	2.4e-02	5.9e-02	-8.2e-07	7.2e-01
ρ	1.0e-04	1.0e-04	3.6e-03	5.9e-04	3.6e-03	0.0e+00	7.4e-03
d	1.0e-03	1.0e-03	1.3e-03	3.1e-04	-1.3e-03	-6.0e-03	1.8e-09
b	9.0e-08	9.0e-08	1.1e-06	1.9e-07	1.1e-06	0.0e+00	2.7e-06

The Table 5.5 below shows the results of the ten estimated parameters used in Model II. Among the parameters, the contact rate between susceptible individuals and HIV-infected individual β is 7.442e-01 for a portion of susceptible individuals being infected with HIV. This is due to the fraction inflow of inbound tourists δ, that of 9.976e-02 were recruited into the susceptible stage. The progression rate α is 9.076e-02/year which gives an average of 11 years. The fraction rate of inbound tourist recruited to HIV and AIDS, δ_1 is 3.189e-05 and δ_2 is 2.781e-06, gives the estimated number of HIV and AIDS cases of inbound tourists that came to Malaysia from 1995-2011 as shown in Table 5.7 and 5.8, respectively.

Table 5.5: Model II parameters definitions and their estimated parameters

Parameter	Definition	Estimated Parameter
β	Contact rate between S and I	7.442e-01
α	Rate of progression to AIDS	9.076e-02
μ	Natural death rate	1.387e-02
σ	Number of days inbound tourists leave Malaysia	8.297e-04
δ	Fraction of inbound tourists recruited into S	9.976e-02
δ_1	Fraction of inbound tourists recruited into I	3.189e-05
δ_2	Fraction of inbound tourists recruited into A	2.781e-06
ρ	Percentage of outbound tourists	5.860e-02
d	Disease-induced mortality due to AIDS	7.200e-01
b	Natural birth rate	1.304e-02

Figure 5.5 depicts a fitted graph of Model II for reported HIV and AIDS incidence in Malaysia. Although we did not obtain a better fit. The basic reproduction number for Model II is 0.7806267. However, the result shows that the spread of HIV/AIDS is stable. There is an increase in the basic reproduction number from 1.026218e-06 in Model I to 0.7806267 in Model II. This is due to the inflow of inbound tourists who are not citizens of Malaysia but contributed to spread of HIV/AIDS.
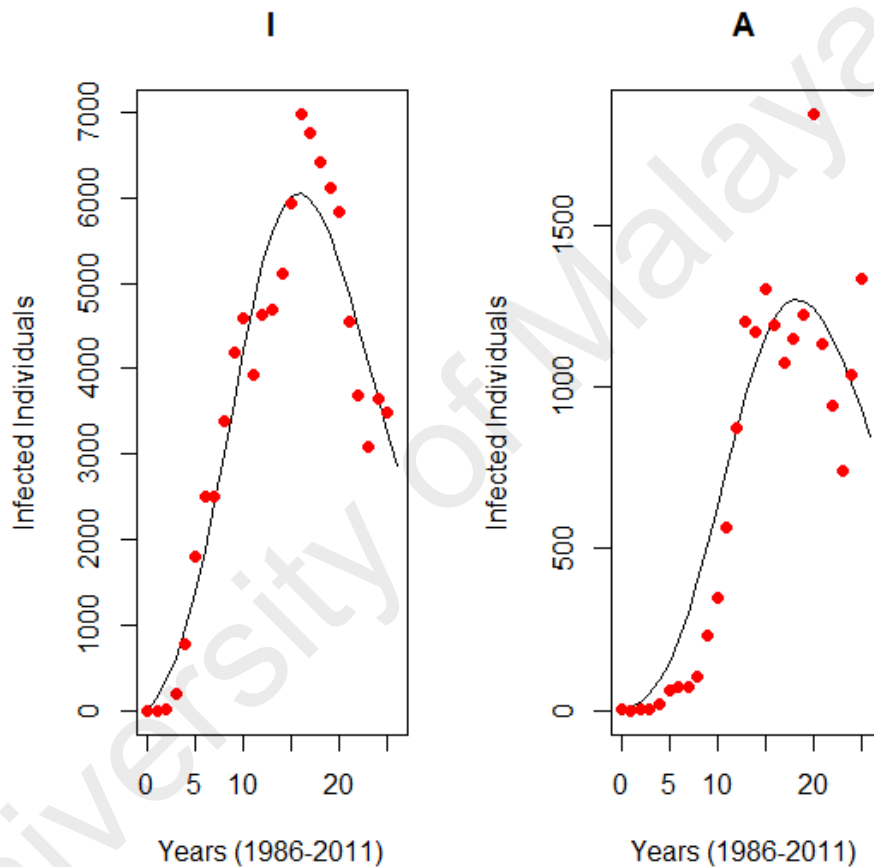
Figure 5.5: The fitted growth curve to the incidence values of HIV and AIDS populations with $\delta, \delta_1 \& \delta_2$.

The following figures show the simulations from the MCMC approach for each parameter.
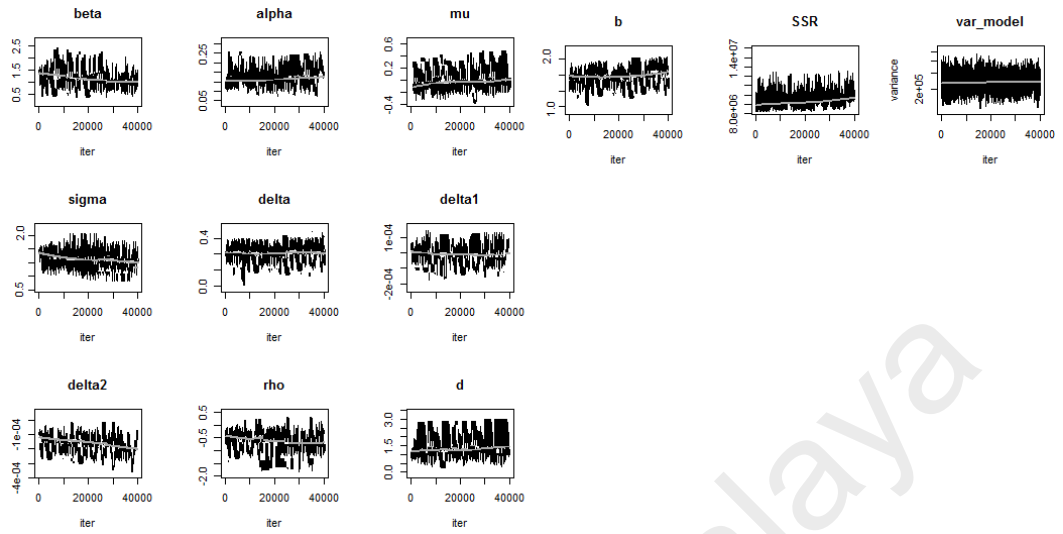
Figure 5.6: MCMC parameter values.

From Figure 5.6, the trace of the MCMC chain (grey line) show that the chain has converged. The last figure also shows the error variances for each observed variable.

Table 5.6 show a summary of mean, 25, 50 and 75% percentiles of the posterior distributions representing the 95% credible intervals of each of the estimated parameters.

Table 5.6: Summary of MCMC

	β	α	μ	σ	δ	δ_1	δ_2	ρ	d	b	var model
mean	0.7065	0.0680	0.0069	-0.0198	-0.0980	7.093e-05	-9.897e-06	0.0270	0.1707	-0.6646	209730
sd	0.1168	0.0155	0.0207	0.0134	0.0184	7.540e-06	5.356e-06	0.0137	0.0362	0.1028	42506
min	0.4406	0.0313	-0.0368	-0.0525	-0.1488	5.580e-05	-2.210e-05	-0.0031	0.0829	-0.9889	115562
max	1.0765	0.1212	0.0653	0.0112	-0.0580	9.536e-05	3.663e-06	0.0727	0.2855	-0.4259	415448
q025	0.6273	0.0578	-0.0108	-0.0306	-0.1118	6.517e-05	-1.323e-05	0.0164	0.1446	-0.7344	178451
q050	0.6999	0.0664	0.0057	-0.0195	-0.0963	7.041e-05	-9.979e-06	0.02491	0.1699	-0.6577	205184
q075	0.7794	0.0769	0.0227	-0.0090	-0.0838	7.620e-05	-6.858e-06	0.0377	0.1897	-0.5920	235446

Figure 5.7, pairs plotted of the MCMC samples for the ten parameters. Which shows a pairwise relationship of correlation coefficient between the upper panel, the lower panel, and the marginal distribution for each ten parameters showing on the diagonal. The pairs plotted show a strong relation between parameters ρ and σ, and μ and σ, δ and δ_1 with $r^2 > 0.85$.
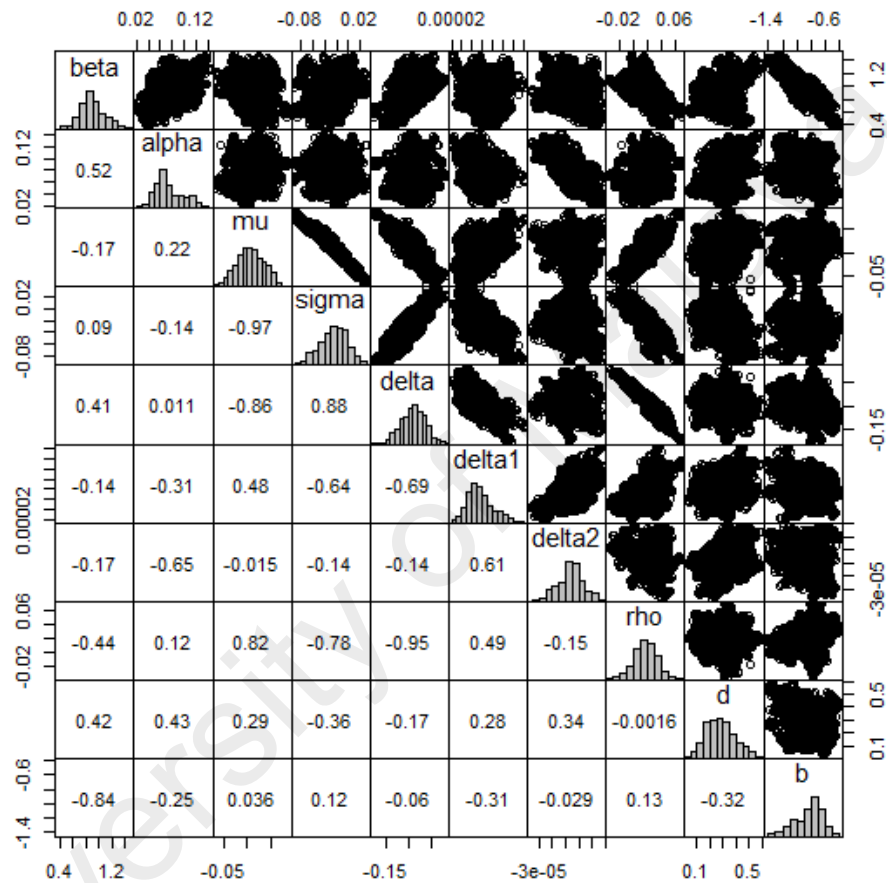
Figure 5.7: Pairs plot of the MCMC samples for the ten parameters.

Figure 5.8 shows the sensitivity range of annually reported HIV cases based on parameter distribution as generated with the MCMC method during the 25-year calibration period (1986-2011). The light grey area represents the minimum and maximum model response at each time step, and the dark grey area (Mean±sd) illustrates the mean model response plus/minus one standard deviation. Among the compartment population, the variance increases in the following order: $I > A > T > S$. The large variance is due to either the uncertainties in the model or noise in data collection.
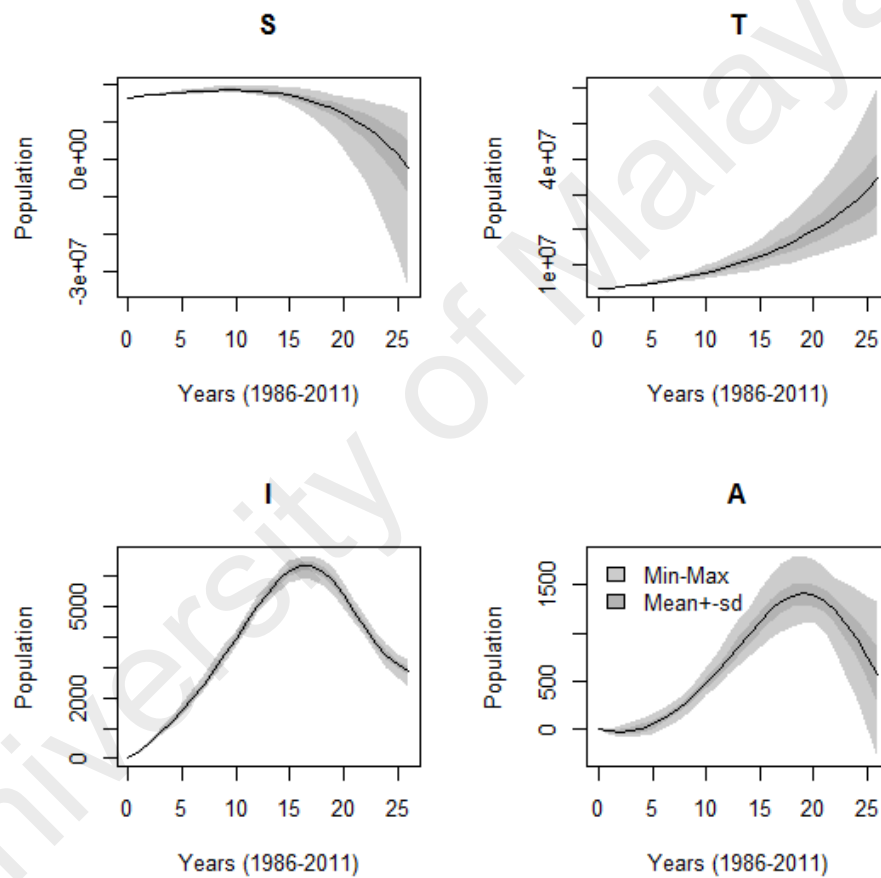
Figure 5.8: Sensitivity range of yearly reported HIV and AIDS cases. Predictions take the form of credible regions.

5.6 Summary of Model II

Model II demonstrates how to model the effects of the inflow of tourists on the spread of HIV/AIDS in Malaysia. From the estimated parameters of δ_1 and δ_2 obtained from Model II, we are able to estimate the numbers of tourists who come to Malaysia with HIV and AIDS. Prior to the estimation of Model II, there was no available data to explain the status of inbound tourists in Malaysia. Consequently, we have been able to estimate the status of HIV and AIDS in Model II as presented in Table 5.7 and 5.8 below. We use parameter values of δ_1 and δ_2 to indicate the rate of tourists recruited to HIV and AIDS compartments respectively to calculate the number of tourists according to their health status (HIV/AIDS).

Table 5.7: Estimated number of HIV cases

Years	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
*Malaysia	4198	4597	3924	4624	4692	5107	5938	6978	6756	6427	6120	5830	4549	3692	3080	3652	3479
Tourists	305	292	254	227	324	418	522	543	432	642	671	717	857	901	966	1004	1010
Total	4503	4889	4178	4851	5016	5525	6460	7521	7188	7069	6791	6547	5406	4593	4046	4656	4489

* Actual number of cases

Table 5.8: Estimated number of AIDS cases

Years	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
*Malaysia	233	347	568	875	1200	1168	1302	1193	1076	1148	1221	1842	1130	941	741	1035	1334
Tourists	4	3	3	3	4	5	6	6	5	8	8	9	10	11	11	12	12
Total	237	350	571	878	1204	1173	1308	1199	1081	1156	1229	1851	1140	951	752	1047	1346

* Actual number of cases

5.7 Analysis of the results for Model III

This section discusses the extension of Model II with the addition of condoms as a preventive measure. There is an additional parameter, making a total of eleven parameters in Model III. This is η as the rate of sexually active people using condoms, which is used to investigate the effect of the control strategy between susceptible and infected HIV/AIDS population. This is because the susceptible individuals are at risk of HIV infection.

5.7.1 Sensitivity analysis

We carried out a sensitivity analysis to determine the most important parameter that is used in the model. This can be achieved by finding the parameter that has the highest value of sensitivity. It is clear that b (birth rate) has the least effect on the output variables while β (the contact rate) has the highest sensitivity value. This means that it has more impact on the spread of HIV/AIDS as shown in Table 5.9 below.

Table 5.9: Summary of sensitivity values

	Value	Scale	$L1$	$L2$	Mean	Min	Max
β	1.7e+00	1.7e+00	7.6e+00	1.1e+00	7.6e+00	0.0e+00	1.1e+01
α	3.9e-02	3.9e-02	4.7e-01	7.3e-02	-1.9e-02	-9.7e-01	7.0e-01
μ	1.4e-01	1.4e-01	6.8e+00	1.1e+00	-6.8e+00	-1.4e+01	0.0e+00
σ	1.0e-05	1.0e-05	4.7e-04	7.7e-05	-4.7e-04	-9.4e-04	0.0e+00
δ	9.0e-04	9.0e-04	5.9e-03	9.8e-04	5.9e-03	-6.2e-04	1.2e-02
δ_1	1.0e-07	1.0e-07	6.0e-02	8.8e-03	6.0e-02	0.0e+00	6.9e-02
δ_2	1.0e-06	1.0e-06	6.2e-02	2.5e-02	6.2e-02	-1.2e-06	7.2e-01
ρ	1.0e-04	1.0e-04	3.4e-03	5.7e-04	3.4e-03	0.0e+00	6.9e-03
d	1.0e-03	1.0e-03	1.4e-03	3.1e-04	-1.4e-03	-6.2e-03	2.4e-09
b	9.0e-08	9.0e-08	1.1e-06	1.8e-07	1.1e-06	0.0e+00	2.6e-06
η	3.0e-02	3.0e-02	2.3e-01	3.5e-02	-2.3e-01	-3.4e-01	0.0e+00

Table 5.10 shows all the eleven estimated parameters used in Model III. The inclusion of the use of condoms as a preventive measure helped us to observe the effectiveness in the control of HIV and AIDS in Model III. The results show that the introduction of condoms as a preventive measure produces 0.35 which represents 35% of the susceptible individuals. The 35% are individuals that are protected from HIV infection as a result

of the use of condoms during sexual activity. In addition, the contact rate between the susceptible and infected individuals changed in Model III as a result of the introduction of the condoms. The contact rate between the susceptible and the HIV infected individuals in Model II is 7.442e-01 while in Model III, it is 1.196e+00. This implies that the condoms introduced, allow for increase in safe sexual activity among the HIV/AIDS infected and the susceptible.

From Table 5.10 above, we wish to report the fraction of the inbound tourists with HIV which reduces the spread of HIV when condoms are introduced. The results show a fraction of inbound tourists δ_1 of 4.079e-05 in Model II which reduces to 3.89e-05 in Model III. This gives a total of 19% decrease for the inbound tourists in Malaysia. Similarly, the results of the inbound tourists infected with AIDS gives the fraction δ_2 of 5.900e-07 in Model II reducing to 2.781e-06 in Model III. This represents a 2.191e-04 reduction of HIV and AIDS. This has positive impact by minimizing the risk of getting the HIV infection sexually of the use of condom as preventive measure rate η by 3.475e-01, as shown in Figures 5.13 and 5.14, respectively.

Table 5.10: Model III parameters definitions and their estimated parameters

Parameter	Definition	Estimated Parameter
β	Contact rate between S and I	1.196e+00
α	Rate of rate progression to AIDS	9.494e-02
μ	Natural death rate	1.345e-02
σ	Number of days inbound tourists leave Malaysia	7.017e-04
δ	Fraction of inbound tourists recruited into S	8.575e-02
δ_1	Fraction of inbound tourists recruited into I	4.079e-05
δ_2	Fraction of inbound tourists recruited into A	5.900e-07
ρ	Percentage of outbound tourists	3.646e-02
d	Disease-induced mortality due to AIDS	2.985e-01
b	Natural birth rate	1.340e-02
η	The use of condom as preventive measure	3.475e-01

Figure 5.9 depicts a fitted graph of Model III for reported HIV and AIDS incidence in Malaysia. The basic reproduction number calculated for Model II is 0.7806267. Indicating

that the spread of HIV/AIDS is stable. This gives a good indication for public health that the disease is under control. There is a decrease in the basic reproduction number of Model II from 0.7806267 to 0.7195585 for Model III.
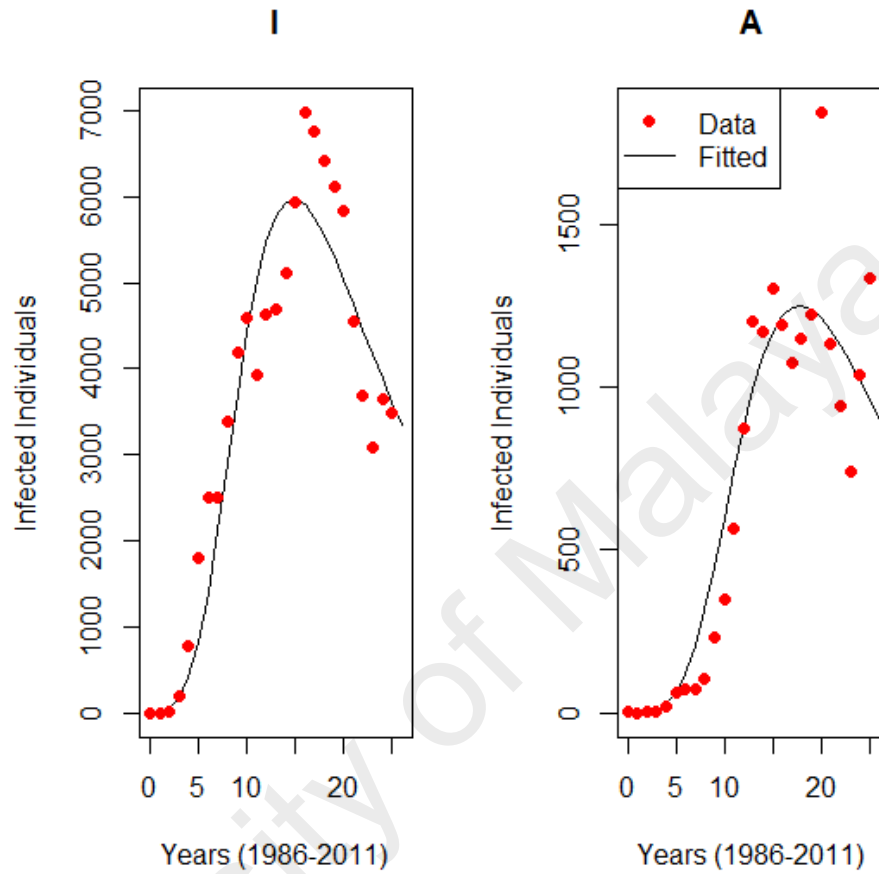
Figure 5.9: The fitted growth curve to the incidence values of HIV and AIDS populations with condom, η.

The following figures show the simulations from the MCMC approach for each parameter.
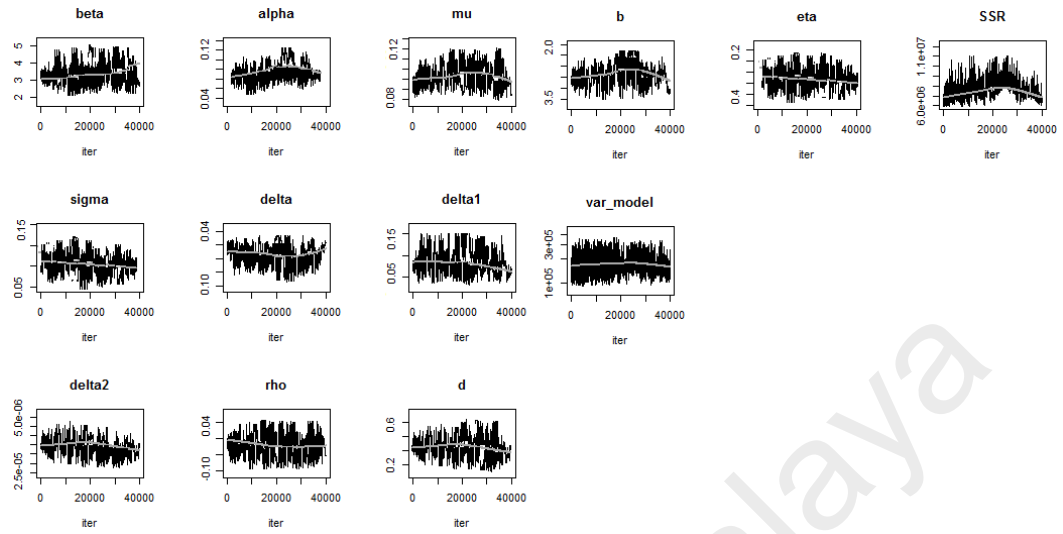
Figure 5.10: MCMC parameter values.

From Figure 5.10, the trace of the MCMC chain (grey line) show that the chain has converged. The last figure also shows the error variances for each observed variable.

Table 5.12 shows a summary of mean, 25, 50 and 75% percentiles of the posterior distributions representing the 95% credible intervals of each of the estimated parameters.

Table 5.11: Summary of MCMC

|	β	α	μ	σ	δ	δ_1	δ_2	ρ	d	b	η	var model
mean	2.8005	0.0691	-0.0640	-0.0258	-0.0351	6.3540e-05	-1.0464e-05	-0.0646	0.2315	-2.6261	0.1007	1580
sd	0.1098	0.0107	0.0141	0.0079	0.0077	2.0227e-05	4.8630e-06	0.0219	0.0280	0.1835	0.0661	3222
min	2.3256	0.0417	-0.0939	-0.0452	-0.0546	1.2320e-05	-1.9824e-05	-0.1062	0.1583	-3.0779	-0.0721	8328
max	3.0591	0.0909	-0.0366	-0.0077	-0.0233	1.1410e-04	-1.3530e-06	-0.0222	0.2752	-2.1331	0.2850	3149
q025	2.7373	0.0613	-0.0748	-0.0316	-0.0412	4.7100e-05	-1.4232e-05	-0.0803	0.2226	-2.7583	0.0485	1359
q050	2.8069	0.0695	-0.0651	-0.0261	-0.0326	6.2407e-05	-1.0148e-05	-0.0683	0.2386	-2.6195	0.1121	1563
q075	2.8813	0.0762	-0.0509	-0.0206	-0.0290	8.0442e-05	-6.8932e-06	-0.0507	0.2508	-2.5124	0.1486	1766
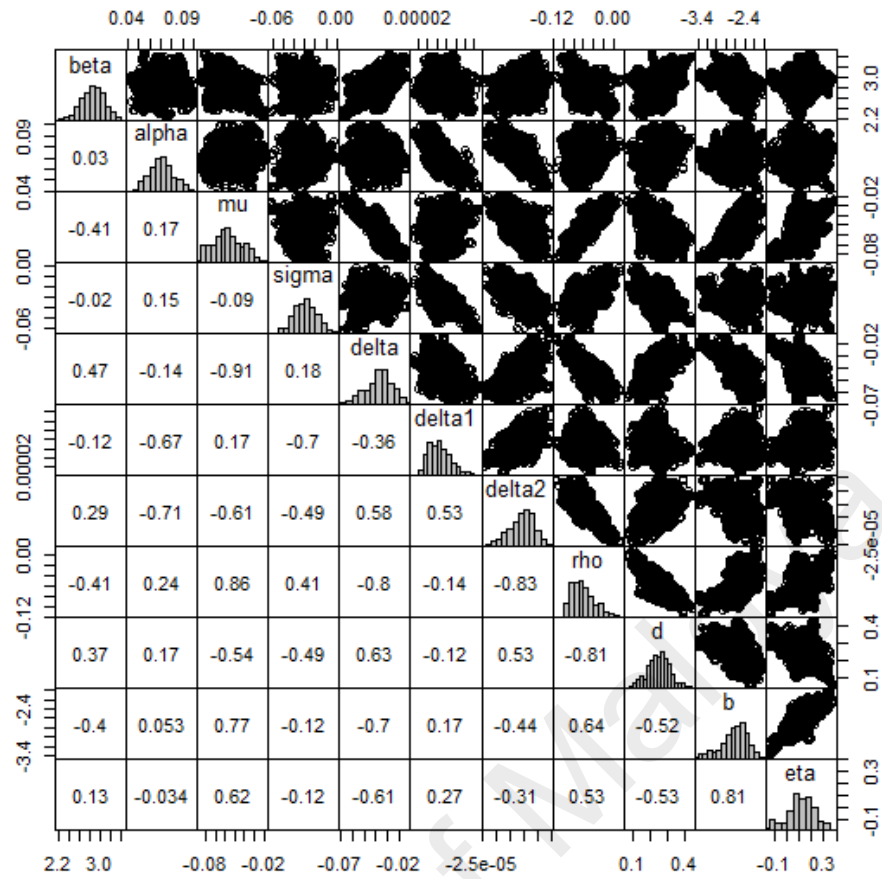
Figure 5.11: Pairs plot of the MCMC samples for the eleven parameters.

Figure 5.11 shows plotted pairs of the MCMC samples for the eleven parameters with a strong relation between parameters ρ and μ, and σ and δ, and between α and δ_2, and finally between β and η with $r^2 > 0.85$.
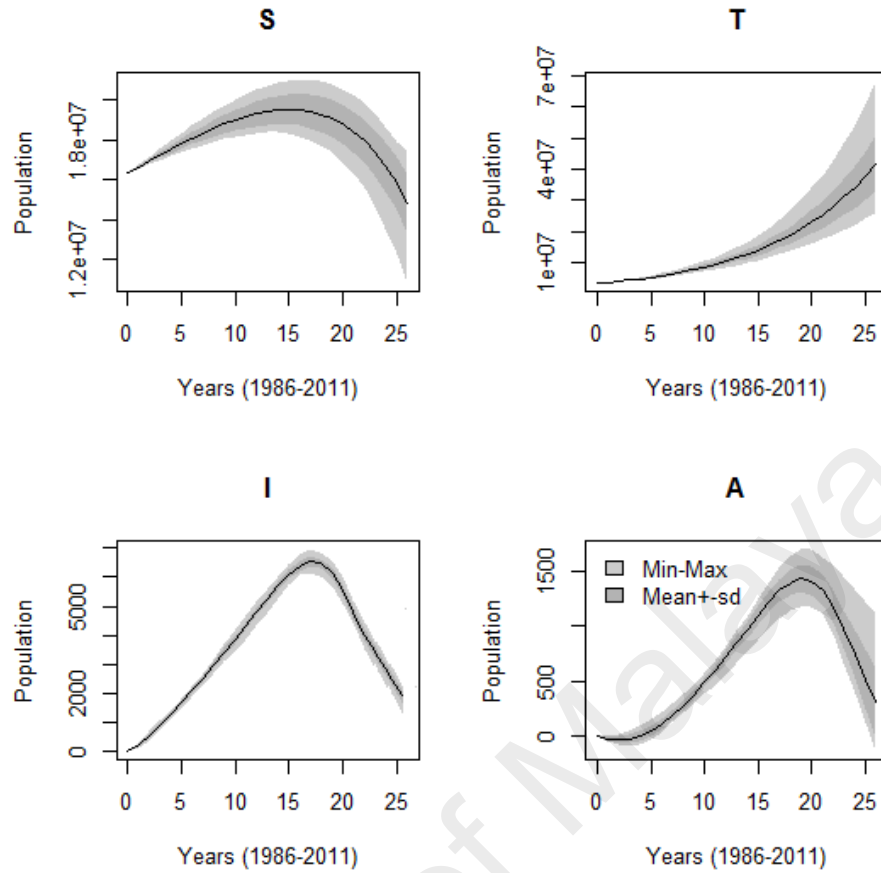
Figure 5.12: Sensitivity range of yearly reported HIV and AIDS cases. Predictions take the form of credible regions.

Figure 5.12 shows the sensitivity range of annually reported HIV cases based on parameter distribution as generated by the MCMC method during the 25-year calibration period (1986-2011). The light grey area represents the minimum and maximum model response at each time step, and the dark grey area (Mean±sd) illustrates the mean model response plus/minus one standard deviation. Among the compartment populations, the variance increases in the following order: $I > A > T > S$. The large variance is due to either the uncertainties in the model or noise in data collection.

5.8 Summary of Model III

Model III demonstrates how important it is to include a preventive measure such as the use of condoms in modeling HIV/AIDS (Greenhalgh et al., 2001; Moghadas et al., 2003; Wilton, 2013; Holmes et al., 2004; Deb et al., 2009). Before a comparison is made between

the results of the control of the Model II (without the inclusion of the use of condoms as a preventive measure) and Model III to show the use of condoms as a preventive measure for HIV and AIDS individuals in Model III. These are shown in Figure 5.13 and 5.14, respectively.
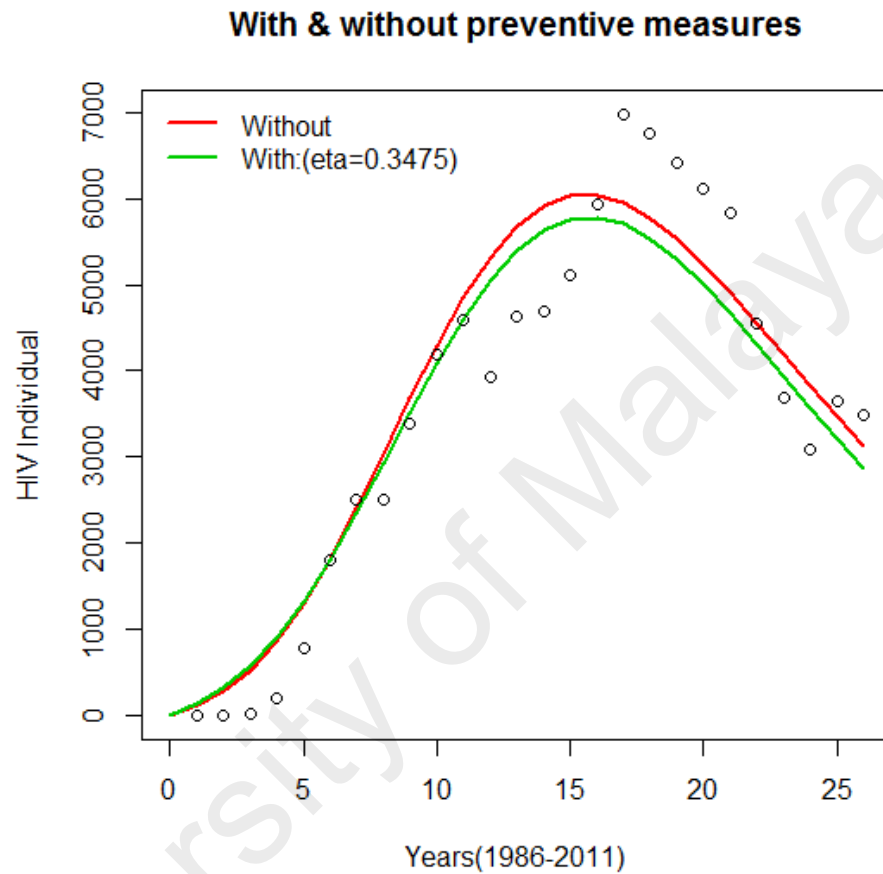

Figure 5.13: A graph of HIV individuals with and without condom as preventive measure.

The curves of the compartments in Figure 5.13 show the effect of condoms in reducing the number of HIV individuals and the period of infection, by decreasing the number of susceptible individuals who are getting infected with HIV.
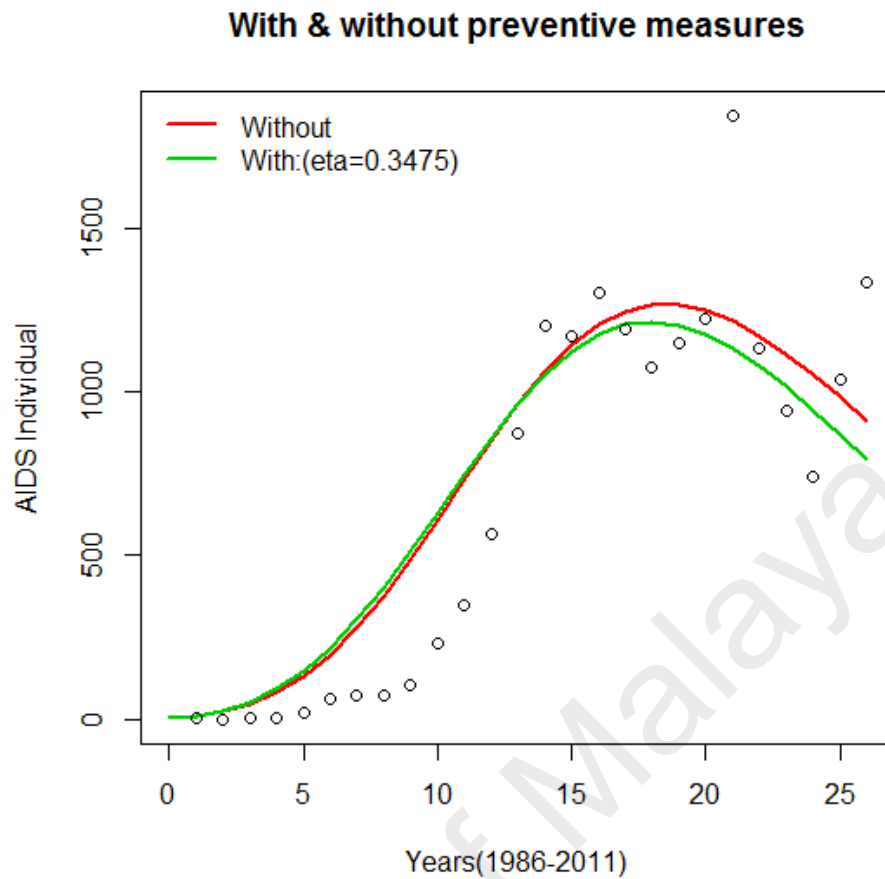
Figure 5.14: A graph of AIDS individuals with and without condom as preventive measure.

The curves of the compartments in Figure 5.14 depict the effect of the condoms in reducing the number of HIV individuals and the period of infection, there is a decrease in the number of AIDS individuals since there is a reduction of susceptible individuals getting HIV.

It is important to note that in the Model III, there is a reduction in the spread of the HIV as compared to the output of Model II. The Figure 5.12 shows that the use of condoms of the Model III starts at 1995. The condoms were more effective in 2004 which led to the reduction in the spread of HIV in the country. Similarly, Figure 5.13 shows that the introduction of condoms in Model II that produces model III has efficient results. Starting with 2004, there is a reduction in the death rate among individuals with AIDS.

5.8.1 Results and discussion of the newborn babies of HIV

In reality, we observed that both the inbound and outbound tourists are likely to have children in the course of entry into Malaysia. To enhance the robustness of the three models (Model I, II and III), we estimated for the children born with HIV/AIDS in all the three models. As such, we take parameter values of b from Table 5.2, 5.5 and 5.10 and we calculate the newborn babies with HIV ($b(I + A)$) by using the infected individuals of HIV and AIDS (MoH, 2012a). Figure 5.15, shows the results of newborn babies with HIV.
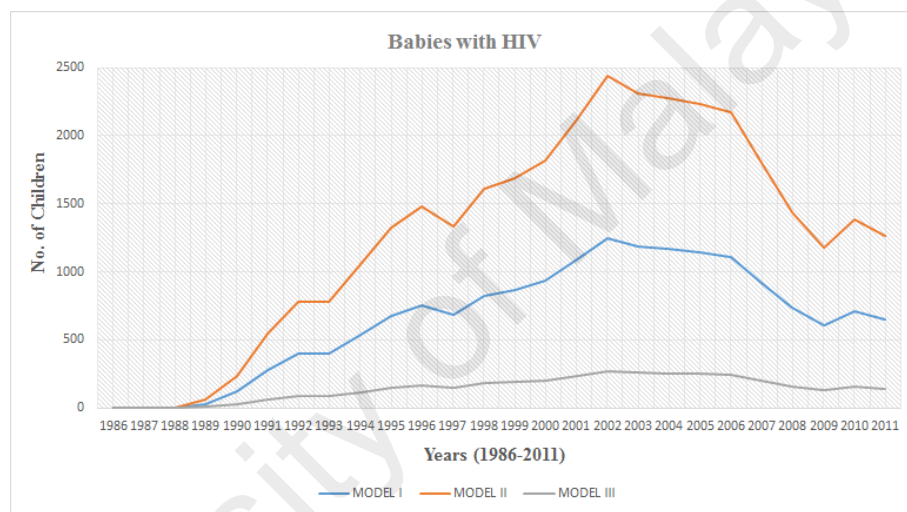
Figure 5.15: Different level of newborn babies of HIV.

Figure 5.15 reports the trends of the number of children born with infected HIV for Model I, Model II and Model III. We can observe that in 1986, there was not much prevalence of HIV. The trend begins to grow exponentially from 1989 to 2002. By 1990, the number of children born with HIV was 239 in Model I, 122 in Model II and 26 in Model III. However, there was a drastic decline of infection of HIV/AIDS from 2003 to 2010. This might be due to the implementation of the harm reduction program by Malaysian government (Wolfe, Carrieri, & Shepard, 2010; Kamarulzaman, 2009) . In conclusion, the inflow of inbound tourists (Model II) shows that there was a higher rate of newborn babies with HIV as compared to outbound tourists (Model I) followed by

preventive measure (Model III). This indicates that the inflow of inbound tourists has more effect on the spread of HIV/AIDS than outbound tourists and when there is the introduction of condoms in Malaysia.

CHAPTER 6: DISCUSSIONS AND CONCLUSIONS

6.1 Introduction

This chapter presents the summary of findings as estimated in the formulated model in this thesis. It covers the discussion of the findings of the models' estimated parameters. Finally, it presents the conclusion and policy recommendation for the Malaysia public healthcare sector.

6.2 Discussions

This thesis assessed the effects of tourism on the spread of HIV and AIDS in Malaysia using the SIA model. In the previous work such as in the work of Bauer (1999, 2007, 2008b) and Ketshabile (2007), mathematical modelling were not applied in the estimation of HIV/AIDS. In our case, we developed mathematical modeling to analyse different factors that contribute to the spread of HIV and AIDS subject to potential control strategies. We conducted comprehensive sensitivity analysis in order to find the global and local parameters that have highest attribute impact on HIV and AIDS disease. Modeling a complex system like HIV and AIDS, several assumptions are required to make the analysis tractable. As such, we assumed that there were sexual interactions between the susceptible and HIV-infected populations. We also assume that a fraction of infected newborn babies moved directly to the HIV class to increase the growth of the total population. If $R_0 < 1$, then an endemic of HIV/AIDS occurs, and if $R_0 > 1$, then the disease becomes epidemic.

From the analysis of the estimated models, the reproduction numbers are used to determine whether the disease is epidemic or endemic. The three estimated models have the basic reproduction numbers of 1.0262e-06, 0.7806 and 0.7196 respectively. The implication of the outcome is that the number of HIV and AIDS cases is still stable within the Malaysian population. This is a good indicator from the public health point

of view since the aim is to stabilize the epidemic at the disease-free equilibrium. It also indicates that the rate of HIV infection will increase faster than expected. The disease stability further implies that HIV will continue to infect the susceptible population because the rate of transmission was very high among HIV- and AIDS-infected tourists. Furthermore, Model III compromises of inbound tourists, outbound tourists and condoms as a preventive measure with less reproduction numbers, which is good for prediction as compared to Model II which excludes condoms. Whereas the result from Apenteng and Ismail (2015) without preventive measure, inbound and outbound tourists show that the number of HIV cases and AIDS cases is still epidemic within the Malaysian population.

In Model I, there were some significant differences in the estimated parameters relevant to the public health sector. Potentially, the inclusion of the parameters provides a practical and more effective way to explain an epidemiological model of outbound tourism. On the other hand, our results further suggest that the percentage of outbound tourists ρ, individuals who are not aware of their HIV status after returning home, increased thereby increasing the HIV spread in Malaysia. In addition, we estimated the numbers of inbound tourists with HIV and AIDS, (Table 5.7 and 5.8 respectively) in Model II. We evaluated the various stages of inflow of inbound tourists in respect of HIV and AIDS status and found that HIV and AIDS in Malaysia which increased the incidence cases. Firstly, we estimated the inbound tourists for HIV. The result shows a proportion of 4.079e-05 that carry the HIV infection each year. This proportion contributed significantly to the spread of HIV in Malaysia. Secondly, we estimated the inbound tourists for AIDS. There is a proportion of 5.9006e-07 representing the actual AIDS carriers among the inbound tourists. Estimating the proportion of tourists who enter into each of the aforementioned compartmental levels as well as their level of susceptibility to HIV and AIDS is important, however, there is need to obtain real demographic data. This will provide necessary knowledge regarding

the total number of inbound tourists who arrive in Malaysia annually.

We have ascertained that the inbound tourism that has a significant impact on the spread of HIV and AIDS in Malaysia, the outcome of the estimated model indicates fractions of inbound tourists of δ_1 and δ_2 recruited into HIV and AIDS respectively. It is also important to note that an addition of inbound tourists had the highest reproduction number of 0.78060 which is closed to 1 which would make it epidemic/unstable. This means that the inflow of inbound tourists has increased the spread of HIV/AIDS in the order of Model II, Model III, then followed by Model I.

In Model III, we introduced condoms used as an preventive variable to establish effectiveness. Condoms were incorporated as a preventive measure. The rationale is to project considerable reduction among the susceptible population contacting HIV. One can see that the control strategy is more important in our estimated Model III. The Model III result indicates an preventive measure rate of 3.475e-01. This requires an immediate campaign of condoms as a control against HIV/AIDS. With this intervention, the basic reproduction number value of 0.7806 in Model II brought the spread of HIV/AIDS to 0.7196 in Model III. In our estimation, sensitivity analysis of the three models is examined to ascertain the importance of each of the estimated parameters. It turns out that the transmission coefficient β has the highest sensitivity value and the most sensitive parameter. This indicates that there is a higher contact rate between susceptible and confirmed HIV individuals and that the susceptible individuals are easily infected with virus.

Specifically, this thesis has some key strengths to contribute to the body of knowledge. First, we developed mathematical models on HIV and AIDS epidemic to assess the effect of outbound and inbound tourism on the spread of HIV and AIDS incidence in Malaysia. Second, we conducted a comprehensive sensitivity analysis using the epidemiological

incidence data. The sensitivity analysis helped to address the inherent uncertainties associated with the parameter values which in turn helped to determine the parameters that have the highest effect on the spread of HIV and AIDS disease. Outbound tourism have impact on the spread of HIV/AIDS, since this will give an idea of their status to the policy makers. Inbound tourism have impact on the spread of HIV/AIDS, which gives insightful idea, since the Malaysia government do not know their status. Use of condom have reduced the spread of HIV. It is important to put newborn babies with HIV on treatment therapy. It also helped us to determine the HIV and AIDS status of the inbound and outbound tourists with necessary models. Based on the analysis, a number of conclusions are drawn which are useful for public health and policy makers. For example, Model I, Model II and Model III provide a useful illustration of the effect of tourism on the spread of HIV and AIDS.

As such, the continuous lines in Figure 5.1, 5.5 and 5.9 in Chapter 5 represent the outputs for Models I, II and III. The small red-like dots represent the data points in each of the models. There were few data points that fit poorly to the models' outcome. However, the overall models' solutions and the data are a good fit, suggesting that the estimated parameters as shown in Table 5.2, 5.5 and 5.9 are reliable (Samsuzzoha, Singh, & Lucy, 2013).

Although we acknowledge the strengths of this research thesis, there are number of challenges regarding the controlling and preventing travelers spreading HIV/AIDS. These challenges have contributed to the spread of HIV/AIDS epidemic in Malaysia. The main limitation of our study is the simplifying assumptions, which are a typical characteristic of modeling that does not come from the statistical domain. We acknowledge the absence of movements of tourism of multiple entries to infected HIV individuals as well as AIDS individuals. We did not consider the proportion of newborn babies with HIV/AIDS

who are susceptible. Equally, we did not take into account the most-at-risk populations (MARPs) for the target group of susceptible individuals who could easily become infected by sex workers and their clients, men who have sex with men, and prisoners, due to lack of epidemiological data. The available data was used, that is, annual data and very limited with only 26 data points and therefore very difficult to get good estimates to establish statistical significance. Although, the use of condoms is considered, the cost-effectiveness was not. Based on the insights gained during the period of this research work, the limitations that are outlined in this thesis are all interesting future research areas.

6.3   Conclusion and recommendation

As per the preceding discussions in this chapter, the inbound and outbound tourists have impacted on the spread of HIV and AIDS in Malaysia. There is significant contribution from the children born with HIV to the spread of HIV and AIDS in Malaysia. Finally, we conclude that the use of condoms among the inhabitants of Malaysia reduces the spread of the disease.

Consequentially, mathematical models applied in this research work can be used not only to understand tourism patterns on HIV/AIDS dynamics but also to predict epidemiological parameter values in Malaysia. Based on the findings, the estimated models helped to predict the spread of HIV/AIDS incidence in Malaysia based on the inflow of tourists to Malaysia and citizens of Malaysia to other countries on. Furthermore, we recommend that national based HIV/AIDS support and healthcare programmes should be implemented by the government in collaboration with the Malaysian Tourism Board to reduce HIV/AIDS. Educating the general public on the importance of safe sexual activities.

We equally recommend that there should be an intensive campaign about the use of condoms. This will control the spread of the disease among the susceptible population. In addition to condom as preventive measure, there should be other effective measures

that could aid the minimization of the spread of the HIV and AIDS epidemic among the inbound tourists. Finally, the public healthcare policy makers need to be proactive towards introducing more control strategies to curtail the epidemic.

This research thesis will be of benefit to the tourism board and HIV/AIDS healthcare professionals. While this research work presents a consolidation of the aforementioned contributions above, more finely detailed outputs are found in the following published and submitted works as outlined in the LIST OF PUBLICATIONS AND PAPERS PRE-SENTED.

REFERENCES

Abdullah, A. S. M., Ebrahim, S. H., Fielding, R., & Morisky, D. E. (2004). Sexually transmitted infections in travelers: Implications for prevention and control. *Clinical Infectious Diseases*, *39*(4), 533-538. Retrieved from http://cid.oxfordjournals.org/content/39/4/533.abstract doi: 10.1086/422721

Abdullah, A. S. M., Fielding, R., Hedley, A. J., & Luk, Y. K. (2002). Risk factors for sexually transmitted diseases and casual sex among chinese patients attending sexually transmitted disease clinics in hong kong. *Sexually Transmitted Diseases*, *29*, 360-365.

Adih, W. K., & Alexander, C. S. (1999). Determinants of condom use to prevent hiv infection among youth in ghana. *Journal of Adolescent Health*, *24*(1), 63 - 72. Retrieved from http://www.sciencedirect.com/science/article/pii/S1054139X98000627 doi: http://dx.doi.org/10.1016/S1054-139X(98)00062-7

Anders, J. T., Antonius-Smits, C., Cabezas, A. L., Campbell, S., Davidson, J. O., Fernandez, N., . . . others (1999). *Sun, sex, and gold: Tourism and sex work in the caribbean*. Rowman & Littlefield Publishers.

Anderson, R. M. (1986). A preliminary study of the transmission dynamics of the human immunodeficiency virus (hiv), the causative agent of aids [Journal Article]. *Mathematical medicine and biology*, *3*(4), 229.

Anderson, R. M. (1988). The epidemiology of hiv infection: Variable incubation plus infectious periods and heterogeneity in sexual activity [Journal Article]. *Journal of the Royal Statistical Society. Series A (Statistics in Society)*, *151*(1), 66-98. Retrieved from http://www.jstor.org/stable/2982185

Apenteng, O. O. (2009). Demographic modelling of human population growth. Retrieved from https://www.doria.fi/xmlui/bitstream/handle/10024/59850/nbnfi-fe201004151672.pdf?sequence=1

Apenteng, O. O., & Ismail, N. A. (2014). The impact of the wavelet propagation distribution on SEIRS modeling with delay. *PLoS ONE*, *9*(6), e98288. Retrieved from http://dx.doi.org/10.1371%2Fjournal.pone.0098288 doi: 10.1371/journal.pone.0098288

Apenteng, O. O., & Ismail, N. A. (2015). Modelling the impact of international travellers on the trend of hiv/aids epidemic. In *In transactions on engineering technologies*

(p. 381-389). Springer Netherlands. Retrieved from `http://link.springer.com/chapter/10.1007/978-94-017-7236-5_27#page-1`

Artalejo, J., Economou, A., & Lopez-Herrero, M. (2015). The stochastic seir model before extinction: Computational approaches. *Applied Mathematics and Computation*, *265*, 1026 - 1043. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0096300315007729` doi: http://dx.doi.org/10.1016/j.amc.2015.05.141

Azwa, I., & Khong, S. Y. (2012). Human immunodeficiency virus (hiv) in pregnancy: a review of the guidelines for preventing mother-to-child transmission in malaysia. *Ann Acad Med Singapore*, *41*(12), 587–94.

Baue, I. (1999). The impact of tourism in developing countries on the health of the local host communities: the need for more research. *Journal of Tourism Studies*, *10*(2), 2–17.

Bauer, I. (2007, September). Understanding sexual relationships between tourists and locals in cuzco/peru. *Travel Medicine and Infectious Disease*, *5*, 287–294. Retrieved from `http://researchonline.jcu.edu.au/2528/`

Bauer, I. (2008a). The health impact of tourism on local and indigenous populations in resource-poor countries. *Travel Medicine and Infectious Disease*, *6*, 276–291. Retrieved from `http://researchonline.jcu.edu.au/8356/`

Bauer, I. (2008b). They don't just come for machu picchu: locals' views of tourist-local sexual relationships in cuzco, peru. *Culture, Health & Sexuality*, *10*, 611–624. Retrieved from `http://researchonline.jcu.edu.au/6170/`

Bauer, T. G., & McKercher, B. (2003). *Sex and tourism: journeys of romance, love, and lust*. Routledge.

Bazazi, A. R., Zelenev, A., Fu, J. J., Yee, I., Kamarulzaman, A., & Altice, F. L. (2015). High prevalence of non-fatal overdose among people who inject drugs in malaysia: Correlates of overdose and implications for overdose prevention from a cross-sectional study. *International Journal of Drug Policy*, *26*(7), 675–681.

Bertozzi, S., Padian, N. S., Wegbreit, J., DeMaria, L. M., Feldman, B., Gayle, H., . . . Isbell, M. T. (2006). Hiv/aids prevention and treatment. *Disease control priorities in developing countries*, *2*, 331–370.

Besag, J., & Green, P. J. (1993). Spatial statistics and bayesian computation. *Journal of the Royal Statistical Society. Series B (Methodological)*, 25–37.

Bhunu, C., Garira, W., & Magombedze, G. (2009). Mathematical analysis of a two strain hiv/aids model with antiretroviral treatment. *Acta biotheoretica*, *57*(3), 361–381.

Bhunu, C., Mushayabasa, S., Kojouharov, H., & Tchuenche, J. (2011). Mathematical analysis of an hiv/aids model: Impact of educational programs and abstinence in sub-saharan africa [Journal Article]. *Journal of Mathematical Modelling and Algorithms*, *10*(1), 31-55. Retrieved from http://dx.doi.org/10.1007/s10852 -010-9134-0 doi: 10.1007/s10852-010-9134-0

Bishop, R., & Robinson, L. S. (1998). *Night market: Sexual cultures and the thai economic miracle*. Psychology Press.

Biswas, M. H. A., Paiva, L. T., & de Pinho, M. (2014). A seir model for control of infectious diseases with constraints. *Mathematical Biosciences and Engineering*, *11*(4), 761-784. Retrieved from http://aimsciences.org/journals/displayArticlesnew .jsp?paperID=9738 doi: 10.3934/mbe.2014.11.761

Blower, S. M., Bodine, E. N., & Grovit-Ferbas, K. (2005). Predicting the potential public health impact of disease-modifying hiv vaccines in south africa: the problem of subtypes. *Current drug targets-infectious disorders*, *5*(2), 179-192.

Blower, S. M., Hartel, D., Dowlatabadi, H., Anderson, R., & May, R. (1991). Drugs, sex and hiv: a mathematical model for new york city. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *331*(1260), 171–187.

Bramson, H., Des Jarlais, D. C., Arasteh, K., Nugent, A., Guardino, V., Feelemyer, J., & Hodel, D. (2015). State laws, syringe exchange, and hiv among persons who inject drugs in the united states: History and effectiveness. *Journal of public health policy*, *36*(2), 212–230.

Brennan, D. (2004). *What's love got to do with it?: Transnational desires and sex tourism in the dominican republic*. Duke University Press.

Brooks, S., Gelman, A., Jones, G., & Meng, X.-L. (2011). *Handbook of markov chain monte carlo*. CRC press.

Bujang, N. (2005). *The impact of the existence of ulu skrang roads upon tourism*

activities and rural livelihood (Unpublished doctoral dissertation). Faculty of Social Sciences.

Burns, L. (2014). World drug report 2013 by united nations office on drugs and crime new york: United nations, 2013isbn: 978-92-1-056168-6, 151 pp. grey literature. *Drug and Alcohol Review*, *33*(2), 216–216.

Cabezas, M. C., Fornasini, M., Dardenne, N., Borja, T., & Albert, A. (2013). A cross-sectional study to assess knowledge about hiv/aids transmission and prevention measures in company workers in ecuador. *BMC public health*, *13*(1), 1.

Cai, L., Guo, S., & Wang, S. (2014). Analysis of an extended hiv/aids epidemic model with treatment. *Applied Mathematics and Computation*, *236*, 621–627.

Cai, L., Li, X., Ghosh, M., & Guo, B. (2009). Stability analysis of an hiv/aids epidemic model with treatment. *Journal of computational and applied mathematics*, *229*(1), 313–323.

Chang, T. S., Wiener, J., Dollard, S. C., Amin, M. M., Ellington, S., Chasela, C., . . . others (2015). Effect of cytomegalovirus infection on breastfeeding transmission of hiv and on the health of infants born to hiv-infected mothers. *AIDS (London, England)*, *29*(7), 831–836.

Chen, C., & Xiao, Y. (2014). Modeling saturated diagnosis and vaccination in reducing hiv/aids infection. In *Abstract and applied analysis* (Vol. 2014).

Chu, H., Nie, L., Cole, S. R., & Poole, C. (2009). Meta-analysis of diagnostic accuracy studies accounting for disease prevalence: alternative parameterizations and model selection. *Statistics in medicine*, *28*(18), 2384–2399.

Clancy, M. (2002). The globalization of sex tourism and cuba: A commodity chains approach. *Studies in Comparative International Development*, *36*(4), 63–88.

Coffin, P. O., Rowe, C., & Santos, G.-M. (2015). Novel interventions to prevent hiv and hcv among persons who inject drugs. *Current HIV/AIDS Reports*, *12*(1), 145–163.

Colugnati, F. A., Staras, S. A., Dollard, S. C., & Cannon, M. J. (2007). Incidence of cytomegalovirus infection among the general population and pregnant women in the united states. *BMC infectious diseases*, *7*(1), 1.

Courson, P. (2004). *Japan put on sex-trade watch list.* CNN International.

de Arazoza, H., & Lounes, R. (2002). A non-linear model for a sexually transmitted disease with contact tracing [Journal Article]. *Mathematical Medicine and Biology*, *19*(3), 221-234. Retrieved from `http://imammb.oxfordjournals.org/content/19/3/221.abstract` doi: 10.1093/imammb/19.3.221

Deb, A., Deb, M., Saha, M., Chakraborty, S., Bhattacharya, S., & Detels, R. (2009). Hiv transmission potential among local and migrant factory workers in kolkata, india. *AIDS and Behavior*, *13*(5), 928-938. Retrieved from `http://dx.doi.org/10.1007/s10461-009-9542-1` doi: 10.1007/s10461-009-9542-1

De Gruttola, V., & Mayer, K. H. (1988). Assessing and modeling heterosexual spread of the human immunodeficiency virus in the united states. *Review of Infectious Diseases*, *10*(1), 138-150.

Diekmann, O., Heesterbeek, J. A. P., & Roberts, M. G. (2010). The construction of next-generation matrices for compartmental epidemic models. *Journal of The Royal Society Interface*, *7*(47), 873–885. doi: 10.1098/rsif.2009.0386

d'Onofrio, A. (2002). Stability properties of pulse vaccination strategy in seir epidemic model [Journal Article]. *Mathematical Biosciences*, *179*(1), 57-72. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0025556402000950` doi: http://dx.doi.org/10.1016/S0025-5564(02)00095-0

DoS. (2014). The population census in 2014 [Computer software manual]. Department of Statistics, Malaysia.

Drake, A. L., Wagner, A., Richardson, B., & John-Stewart, G. (2014). Incident hiv during pregnancy and postpartum and risk of mother-to-child hiv transmission: a systematic review and meta-analysis. *PLoS Med*, *11*(2), e1001608.

Duber, H. C., Dansereau, E., Masters, S. H., Achan, J., Burstein, R., DeCenso, B., . . . others (2015). Uptake of who recommendations for first-line antiretroviral therapy in kenya, uganda, and zambia. *PloS one*, *10*(3), e0120350.

Dwyer, L., & Forsyth, P. (1993). Assessing the benefits and costs of inbound tourism. *Annals of Tourism Research*, *20*(4), 751–768.

Eaton, J. W., & Hallett, T. B. (2014). Why the proportion of transmission during early-stage

hiv infection does not predict the long-term impact of treatment on hiv incidence. *Proceedings of the National Academy of Sciences*, *111*(45), 16202–16207.

Ericsson, C. D., Steffen, R., Matteelli, A., & Carosi, G. (2001). Sexually transmitted diseases in travelers. *Clinical Infectious Diseases*, *32*(7), 1063-1067. Retrieved from `http://cid.oxfordjournals.org/content/32/7/1063.abstract` doi: 10 .1086/319607

Falconer, K., Sandberg, J. K., Reichard, O., & Alaeus, A. (2009). Hcv/hiv co-infection at a large hiv outpatient clinic in sweden: Feasibility and results of hepatitis c treatment [Journal Article]. *Scandinavian Journal of Infectious Diseases*, *41*(11-12), 881-885. Retrieved from `http://informahealthcare.com/doi/abs/10.3109/00365540903214272` doi: doi:10.3109/00365540903214272

Ferguson, N. M., Keeling, M. J., John Edmunds, W., Gani, R., Grenfell, B. T., Anderson, R. M., & Leach, S. (2003). Planning for smallpox outbreaks [Journal Article]. *Nature*, *425*(6959), 681-685. Retrieved from `http://dx.doi.org/10.1038/nature02007` (10.1038/nature02007)

Figueroa, J. P., Brathwaite, A., Ward, E., DuCasse, M., Nembhard, I. T. O., & Williams, E. (1995). The hiv/aids epidemic in jamaica. *Aids*, *9*(7), 761–768.

Gelman, A., Carlin, J., Stern, H., Dunson, D., Vehtari, A., & Rubin, D. (2013). Bayesian data analysis, third edition.

Genberg, B. L., Astemborski, J., Vlahov, D., Kirk, G. D., & Mehta, S. H. (2015). Incarceration and injection drug use in baltimore, maryland. *Addiction*.

Gourlay, A., Wringe, A., Todd, J., Cawley, C., Michael, D., Machemba, R., . . . Zaba, B. (2015). Factors associated with uptake of services to prevent mother-to-child transmission of hiv in a community cohort in rural tanzania. *Sexually transmitted infections*, sextrans–2014.

Greene, S., Ion, A., Elston, D., Kwaramba, G., Smith, S., Carvalhal, A., & Loutfy, M. (2015). "why aren't you breastfeeding?": How mothers living with hiv talk about infant feeding in a "breast is best" world. *Health care for women international*, *36*(8), 883–901.

Greenhalgh, D., Doyle, M., & Lewis, F. (2001). A mathematical treatment of aids and condom use. *Mathematical Medicine and Biology*, *18*(3), 225–262.

Greenhalgh, D., & Hay, G. (1997). Mathematical modelling of the spread of hiv/aids amongst injecting drug users. *Mathematical Medicine and Biology*, *14*(1), 11–38.

Haario, H., Laine, M., Mira, A., & Saksman, E. (2006). Dram: Efficient adaptive mcmc. *Statistics and Computing*, *16*(4), 339-354. Retrieved from `http://dx.doi.org/10.1007/s11222-006-9438-0` doi: 10.1007/s11222-006-9438-0

Hafiz, M., Jamaluddin, M., Zulkifly, M., & Othman, N. (2014). Exploring responsible tourism development facet. *Theory and Practice in Hospitality and Tourism Research*, 173.

Hastings, W. K. (1970). Monte carlo sampling methods using markov chains and their applications. *Biometrika*, *57*(1), 97–109.

Hawkes, S., Malin, A., Araru, T., & Mabey, D. (1992). Hiv-infection among heterosexual travelers attending the hospital-for-tropical-diseases, london. *Genitourinary Medicine*, *68*, 309-311.

Hohle, M., & Feldmann, U. (2007). Rladybug—an r package for stochastic epidemic models [Journal Article]. *Computational Statistics and amp; Data Analysis*, *52*(2), 680-686. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0167947306004221` doi: 10.1016/j.csda.2006.11.016

Holmes, K. K., Levine, R., & Weaver, M. (2004). Effectiveness of condoms in preventing sexually transmitted infections. *Bulletin of the World Health Organization*, *82*(6), 454-461.

HRI. (2012). *The global state of harm reduction 2012: Towards an integrated response.* Harm Reduction International (HRI) London.

Huang, M., & Hussein, H. (2004). The hiv/aids epidemic country paper: Malaysia. *AIDS Education and Prevention*, *16*(Supplement A), 100–109.

Huelsenbeck, J. P., Ronquist, F., et al. (2001). Mrbayes: Bayesian inference of phylogenetic trees. *Bioinformatics*, *17*(8), 754–755.

Hugo, G. (2011). Migration and development in malaysia. *Asian Population Studies*, *7*(3), 219-241. Retrieved from `http://dx.doi.org/10.1080/17441730.2011.608983` doi: 10.1080/17441730.2011.608983

Huo, H.-F., & Feng, L.-X. (2013). Global stability for an hiv/aids epidemic model with different latent stages and treatment. *Applied Mathematical Modelling*, *37*(3), 1480–1489.

Hyman, J. M., & Ann Stanley, E. (1989). Using mathematical models to understand the aids epidemic [Journal Article]. *Mathematical and Computer Modelling*, *12*(9), 1180. Retrieved from `http://www.sciencedirect.com/science/article/pii/0895717789902525` doi: 10.1016/0895-7177(89)90252-5

Inaba, H. (2007). Age-structured homogeneous epidemic systems with application to the mseir epidemic model. *Journal of Mathematical Biology*, *54*(1), 101-146. Retrieved from `http://dx.doi.org/10.1007/s00285-006-0033-y` doi: 10.1007/s00285-006-0033-y

Ingemar, N. (2002). Stochastic models of some endemic infections [Journal Article]. *Mathematical Biosciences*, *179*(1), 1-19. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0025556402000986` doi: 10.1016/s0025-5564(02)00098-6

Isham, V. (1988). Mathematical modelling of the transmission dynamics of hiv infection and aids: A review [Journal Article]. *Journal of the Royal Statistical Society. Series A (Statistics in Society)*, *151*(1), 5-49. Retrieved from `http://www.jstor.org/stable/2982179`

Isham, V. (1993). Stochastic models for epidemics with special reference to aids [Journal Article]. *The Annals of Applied Probability*, *3*(1), 1-27. Retrieved from `http://www.jstor.org/stable/2959726`

Iversen, J., Page, K., Madden, A., & Maher, L. (2015). Hiv, hcv, and health-related harms among women who inject drugs: Implications for prevention and treatment. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *69*, S176-S181.

Jansson, J., Kerr, C. C., & Wilson, D. P. (2014). Predicting the population impact of increased hiv testing and treatment in australia. *Sexual health*, *11*(2), 146–154.

Jones, J. H. (2007). *Notes on r0.*

Jonsson Kvist, A.-K., & Klefsjo, B. (2006). Which service quality dimensions are important in inbound tourism? a case study in a peripheral location. *Managing Service Quality: An International Journal*, *16*(5), 520-537.

Kaddar, A., Abta, A., & Alaou, H. T. (2011). A comparison of delayed sir and seir epidemic models [Journal Article]. , *16*(2).

Kakeshashi, M. (1998). A mathematical analysis of the spread of hiv/aids in japan [Journal Article]. *Mathematical Medicine and Biology*, *15*(4), 299-311. Retrieved from `http://imammb.oxfordjournals.org/content/15/4/299.abstract` doi: 10.1093/imammb/15.4.299

Kamarulzaman, A. (2009). Impact of hiv prevention programs on drug users in malaysia. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *52*, S17–S19.

Kamarulzaman, A., & Altice, F. L. (2015). Treatment readiness, attitudes toward, and experiences with methadone and buprenorphine maintenance therapy among people who inject drugs in malaysia.

Kassim, A. (1998). International migration and its impact on malaysia. *A Pacific Peace: Issues and Responses, Kuala Lumpur, ISIS, Kossoudji, SA.*

Keeling, M. J. (1999). The effects of local spatial structure on epidemiological invasions. [Journal Article]. *Proceedings of the Royal Society of London B*, *266*, 859–867.

Keeling, M. J., & Rohani, P. (2008). Modeling infectious diseases in humans and animals [Journal Article]. , 1-366.

Kermack, & McKendrick, A. (1991). Contributions to the mathematical theory of epidemics—iii. further studies of the problem of endemicity. *Bulletin of Mathematical Biology*, *53*(1-2), 89-118. Retrieved from `http://dx.doi.org/10.1007/BF02464425` doi: 10.1007/BF02464425

Kermack, & McKendrick, A. G. (1927). A contribution to the mathematical theory of epidemics [Journal Article]. *Proceedings of the Royal Society of London. Series A*, *115*(772), 700-721. Retrieved from `http://rspa.royalsocietypublishing.org/content/115/772/700.short` doi: 10.1098/rspa.1927.0118

Kermack, & McKendrick, A. G. (1932). Contributions to the mathematical theory of epidemics. ii. the problem of endemicity. *Proceedings of the Royal Society of London A: Mathematical, Physical and Engineering Sciences*, *138*(834), 55–83. doi: 10.1098/rspa.1932.0171

Kermack, & McKendrick, A. G. (1933). Contributions to the mathematical theory of

epidemics. iii. further studies of the problem of endemicity. *Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character*, 94–122.

Ketshabile, L. (2007). *Hiv and aids as a threat to southern african tourism.* Cape Peninsula University of Technology.

Kim, J.-H. (2009). *Dynamic partnerships and hiv transmissions by stage* (3392859). Retrieved from `http://ezproxy.aut.ac.nz/login?url=http://search.proquest.com/docview/89183960?accountid=8440`

King, C., Ellington, S., & Kourtis, A. (2013). The role of co-infections in mother-to-child transmission of hiv. *Current HIV research*, *11*(1), 10–23.

Kondgen, S., Kuhl, H., N'Goran, P. K., Walsh, P. D., Schenk, S., Ernst, N., . . . others (2008). Pandemic human viruses cause decline of endangered great apes. *Current Biology*, *18*(4), 260–264.

Laine, M. (2008). *Adaptive mcmc methods with applications in environmental and geophysical models.* Finnish Meteorological Institute.

Laine, M., Tamminen, J., Kyroa, E., & Haario, H. (2007). Aerosol model selection and uncertainty modeling by rjmcmc.

LaSalle, J. (1968). Stability theory for ordinary differential equations. *Journal of Differential Equations*, *4*(1), 57-65.

Levine, B., Leskowitz, R., & Davis, M. (2015). Personalized gene therapy locks out hiv, paving the way to control virus without antiretroviral drugs. *Expert opinion on biological therapy*(0), 1–13.

Lewis, N. (1989). Aids and tourism: implications for pacific island states. *AIDS and tourism: implications for Pacific Island States.*.

Li, J., Gu, J., Lau, J. T., Chen, H., Mo, P. K., & Tang, M. (2015). Prevalence of depressive symptoms and associated factors among people who inject drugs in china. *Drug and alcohol dependence*, *151*, 228–235.

Liu, M., Bai, C., & Wang, K. (2014). Asymptotic stability of a two-group stochas-

tic seir model with infinite delays. *Communications in Nonlinear Science and Numerical Simulation*, *19*(10), 3444 - 3453. Retrieved from `http://www.sciencedirect.com/science/article/pii/S1007570414000938` doi: http://dx.doi.org/10.1016/j.cnsns.2014.02.025

Luboga, S., Galukande, M., Mabweijano, J., Ozgediz, D., & Jayaraman, S. (2010). Key aspects of health policy development to improve surgical services in uganda. *World journal of surgery*, *34*(11), 2511–2517.

Manhart, L. E., & Koutsky, L. A. (2002). Do condoms prevent genital hpv infection, external genital warts, or cervical neoplasia?: A meta-analysis. *Sexually transmitted diseases*, *29*(11), 725–735.

Manicklal, S., Van Niekerk, A., Kroon, S., Hutto, C., Novak, Z., Pati, S. K., . . . Boppana, S. (2014). Birth prevalence of congenital cmv among infants of hiv-infected women on prenatal antiretroviral prophylaxis in south africa. *Clinical Infectious Diseases*, ciu096.

March, R. (1997). Diversity in asian outbound travel industries: a comparison between indonesia, thailand, taiwan, south korea and japan. *International Journal of Hospitality Management*, *16*(2), 231–238.

Matos, M. A. d., Caetano, K. A. A., Francca, D. D. d. S., Pinheiro, R. S., Moraes, L. C. d., & Teles, S. A. (2013). Vulnerability to sexually transmitted infections in women who sell sex on the route of prostitution and sex tourism in central brazil. *Revista latino-americana de enfermagem*, *21*(4), 906–912.

Mclean, A. R., & Blower, S. M. (1993). Imperfect vaccines and herd immunity to hiv. *Proceedings of the Royal Society of London B: Biological Sciences*, *253*(1336), 9-13.

Merli, M. G., Hertog, S., Wang, B., & Li, J. (2006). Modelling the spread of hiv/aids in china: The role of sexual transmission [Journal Article]. *Population Studies*, *60*(1), 1-22. Retrieved from `http://www.jstor.org/stable/27643362`

Moghadas, S. M., Gumel, A. B., McLeod, R. G., & Gordon, R. (2003). Could condoms stop the aids epidemic? *Journal of Theoretical Medicine*, *5*(3-4), 171-181.

MoH. (2011). National strategic plan on hiv and aids 2011-2015.

MoH. (2012a). Global aids response country progress report 2012. [Computer software manual]. HIV/STI Section, Disease Control Division, Ministry of Health (MoH) Malaysia, Government of Malaysia.

MoH. (2012b). *The global aids response progress report 2014, malaysia.* (Tech. Rep.).

MoH. (2014). Global aids response country progress report 2014. [Computer software manual]. HIV/STI Section, Disease Control Division, Ministry of Health (MoH) Malaysia, Government of Malaysia.

Moreira-Silva, S. F., Zandonade, E., & Miranda, A. E. (2015). Mortality in children and adolescents vertically infected by hiv receiving care at a referral hospital in vitoria, brazil. *BMC infectious diseases*, *15*(1), 1.

MTCM. (2015). *Malaysia tourism statistics in brief* (Vol. 2013) [Web Page]. Ministry of Tourism and Culture of Malaysia. Retrieved from http://www.tourism.gov .my/statistics

MTPB. (2013). Tourist arrivals by country of residence, malaysia. [Computer software manual]. Malaysia Tourism Promotion Board (MTPB).

Mukandavire, Z., Das, P., Chiyaka, C., Gazi, N., Das, K., & Shiri, T. (2011). Hiv/aids model with delay and the effects of stochasticity [Journal Article]. *Journal of Mathematical Modelling and Algorithms*, *10*(2), 181-191. Retrieved from http:// dx.doi.org/10.1007/s10852-010-9148-7 doi: 10.1007/s10852-010-9148-7

Mukandavire, Z., & Garira, W. (2007). Age and sex structured model for assessing the demographic impact of mother-to-child transmission of hiv/aids. *Bulletin of mathematical biology*, *69*(6), 2061–2092.

Mukandavire, Z., Garira, W., & Tchuenche, J. (2009). Modelling effects of public health educational campaigns on hiv/aids transmission dynamics. *Applied Mathematical Modelling*, *33*(4), 2084–2095.

Mulugeta, A., Endale, S., Yesuf, J., Yehbyo, H., Bilal, A., & Gelan, Y. (2015). Effectiveness of interventions for prevention of mother-to-child transmission of hiv/aids in five governmental health institutions in mekelle city, northern ethiopia: a prospective follow up study. *Contraception*, *92*(4), 395–396.

Murray, J. M., Law, M. G., Gao, Z., & Kaldor, J. M. (2003). The impact of behavioural

changes on the prevalence of human immunodeficiency virus and hepatitis c among injecting drug users. *International Journal of Epidemiology*, *32*(5), 708-714.

Nah, A. M. (2012). Globalisation, sovereignty and immigration control: The hierarchy of rights for migrant workers in malaysia. *Asian Journal of Social Science*, *40*(4), 486-508. Retrieved from `http://booksandjournals.brillonline.com/content/journals/10.1163/15685314-12341244`

Nair, V., Chiun, L. M., & Singh, S. (2014). The international tourists' perspective on malaysia's economic transformation programme (etp). *Procedia - Social and Behavioral Sciences*, *144*, 433 - 445. Retrieved from `http://www.sciencedirect.com/science/article/pii/S1877042814042414` (5th Asia-Euro Conference 2014 in Tourism, Hospitality and amp; Gastronomy) doi: http://dx.doi.org/10.1016/j.sbspro.2014.07.313

Narayanan, S. (1992). Impact of international migration on malaysia: the positive and negative aspects. In *Conference on industrial relations, japan institute of labour and japan industrial relations research association, march* (p. 10-11).

Naresh, R., Tripathi, A., & Sharma, D. (2011). A nonlinear hiv/aids model with contact tracing. [Journal Article]. *Applied Mathematics and Computation*, *217*(23), 9575-9591. Retrieved from `http://www.sciencedirect.com/science/article/pii/S009630031100590X` doi: 10.1016/j.amc.2011.04.033

Negredo, E., Bonjoch, A., Perez-Alvarez, N., Ornelas, A., Puig, J., Herrero, C., . . . others (2015). Comparison of two different strategies of treatment with zoledronate in hiv-infected patients with low bone mineral density: single dose versus two doses in 2 years. *HIV medicine*.

Nishimura, Y., & Martin, M. A. (2011). The acute hiv infection: implications for intervention, prevention and development of an effective aids vaccine. *Current Opinion in Virology*, *1*(3), 204 - 210. Retrieved from `http://www.sciencedirect.com/science/article/pii/S1879625711000125` (Viral pathogenesis) doi: http://dx.doi.org/10.1016/j.coviro.2011.05.007

Nishiura, H. (2007). Lessons from previous predictions of hiv/aids in the united states and japan: epidemiologic models and policy formulation [Journal Article]. *Epidemiologic Perspectives and Innovations*, *4*(1), 3. Retrieved from `http://www.epi-perspectives.com/content/4/1/3`

Nosyk, B., Min, J. E., Evans, E., Li, L., Liu, L., Lima, V. D., . . . Montaner, J. S. (2015). The effects of opioid substitution treatment and highly active antiretroviral therapy

on the cause-specific risk of mortality among hiv-positive people who inject drugs. *Clinical Infectious Diseases*, civ476.

Nyabadza, F., & Mukandavire, Z. (2011). Modelling hiv/aids in the presence of an hiv testing and screening campaign [Journal Article]. *Journal of Theoretical Biology*, *280*(1), 167-179. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0022519311002219` doi: 10.1016/j.jtbi.2011.04.021

Nyabadza, F., Mukandavire, Z., & Hove-Musekwa, S. D. (2011). Modelling the hiv/aids epidemic trends in south africa: Insights from a simple mathematical model [Journal Article]. *Nonlinear Analysis: Real World Applications*, *12*(4), 2091-2104. Retrieved from `http://www.sciencedirect.com/science/article/pii/S1468121810003342` doi: 10.1016/j.nonrwa.2010.12.024

Ocha, W., & Earth, B. (2013). Identity diversification among transgender sex workers in thailand's sex tourism industry. *Sexualities*, *16*(1-2), 195-216. Retrieved from `http://sex.sagepub.com/content/16/1-2/195.abstract` doi: 10.1177/1363460712471117

Okawa, S., Chirwa, M., Ishikawa, N., Kapyata, H., Msiska, C. Y., Syakantu, G., . . . Yasuoka, J. (2015). Longitudinal adherence to antiretroviral drugs for preventing mother-to-child transmission of hiv in zambia. *BMC pregnancy and childbirth*, *15*(1), 1.

O'Neill, P. D. (2002). A tutorial introduction to bayesian inference for stochastic epidemic models using markov chain monte carlo methods. *Mathematical biosciences*, *180*(1), 103–114.

Oppermann, M. (1992). Intranational tourist flows in malaysia. *Annals of Tourism Research*, *19*(3), 482–500.

Oppermann, M. (1999). Sex tourism. *Annals of Tourism Research*, *26*(2), 251–266.

Padilla, M. B., Reyes, A. M., Connolly, M., Natsui, S., Puello, A., & Chapman, H. (2012). Examining the policy climate for hiv prevention in the caribbean tourism sector: a qualitative study of policy makers in the dominican republic. *Health policy and planning*, *27*(3), 245–255.

Palombi, L., Galluzzo, C. M., Andreotti, M., Liotta, G., Jere, H., Sagno, J.-B., . . . others (2015). Drug resistance mutations 18 months after discontinuation of nevirapine-based art for prevention of mother-to-child transmission of hiv in malawi. *Journal*

of Antimicrobial Chemotherapy, dkv171.

Paraskevis, D., Lemey, P., Salemi, M., Suchard, M., Van de Peer, Y., & Vandamme, A.-M. (2003). Analysis of the evolutionary relationships of hiv-1 and sivcpz sequences using bayesian inference: implications for the origin of hiv-1. *Molecular biology and evolution*, *20*(12), 1986–1996.

Paraskevis, D., Nikolopoulos, G., Fotiou, A., Tsiara, C., Paraskeva, D., Sypsa, V., ... others (2013). Economic recession and emergence of an hiv-1 outbreak among drug injectors in athens metropolitan area: a longitudinal study. *PLoS One*, *8*(11), e78941.

Paraskevis, D., Paraschiv, S., Sypsa, V., Nikolopoulos, G., Tsiara, C., Magiorkinis, G., ... others (2015). Enhanced hiv-1 surveillance using molecular epidemiology to study and monitor hiv-1 outbreaks among intravenous drug users (idus) in athens and bucharest. *Infection, Genetics and Evolution*, *35*, 109–121.

Peeters, P., Szimba, E., & Duijnisveld, M. (2007). Major environmental impacts of european tourist transport. *Journal of Transport Geography*, *15*(2), 83–93.

Petzoldt, T., & Soetaert, K. (2010). Inverse modelling, sensitivity and monte carlo analysis in r using package fme. *Journal of Statistical Software*, 1–28.

Pickles, M., Boily, M.-C., Vickerman, P., Lowndes, C. M., Moses, S., Blanchard, J. F., ... Alary, M. (2013). Assessment of the population-level effectiveness of the avahan hiv-prevention programme in south india: a preplanned, causal-pathway-based modelling analysis. *The Lancet Global Health*, *1*(5), 289 - 299. Retrieved from http://www.sciencedirect.com/science/article/pii/S2214109X13700834 doi: http://dx.doi.org/10.1016/S2214-109X(13)70083-4

Pillai, P. (1998). The impact of the economic crisis on migrant labor in malaysia: policy implications. *Asian and Pacific Migration Journal*, *7*(2-3), 255-280.

Pinkerton, S. D., & Abramson, P. R. (1997). Effectiveness of condoms in preventing hiv transmission. *Social science and medicine*, *44*(9), 1303–1312.

Pocock, N. S., & Phua, K. H. (2011). Medical tourism and policy implications for health systems: a conceptual framework from a comparative study of thailand, singapore and malaysia. *Globalization and health*, *7*(1), 12.

Pritchard, J. K., Stephens, M., & Donnelly, P. (2000). Inference of population structure using multilocus genotype data. *Genetics*, *155*(2), 945–959. Retrieved from http://www.genetics.org/content/155/2/945

Punyacharoensin, N., Edmunds, W. J., De Angelis, D., Delpech, V., Hart, G., Elford, J., . . . White, R. G. (2016). Effect of pre-exposure prophylaxis and combination hiv prevention for men who have sex with men in the uk: a mathematical modelling study. *The lancet HIV*, *3*(2), e94–e104.

Putter, H., Heisterkamp, S. H., Lange, J. M. A., & de Wolf, F. (2002). A bayesian approach to parameter estimation in hiv dynamical models. *Statistics in Medicine*, *21*(15), 2199–2214. Retrieved from http://dx.doi.org/10.1002/sim.1211 doi: 10.1002/sim.1211

Ramdas, M., & Mohamed, B. (2014). Visitor perceptions on the impacts of tourism activities, development and infrastructure on the environment of perhentian islands. *SHS Web of Conferences*, *12*, 01081. Retrieved from http://dx.doi.org/10.1051/shsconf/20141201081 doi: 10.1051/shsconf/20141201081

Rice, B., Gilbart, V., Lawrence, J., Smith, R., Kall, M., & Delpech, V. (2012). Safe travels? hiv transmission among britons travelling abroad. *HIV medicine*, *13*(5), 315–317.

Robert, C., & Casella, G. (2011). A short history of markov chain monte carlo: Subjective recollections from incomplete data. *Statist. Sci.*, *26*(1), 102–115. Retrieved from http://dx.doi.org/10.1214/10-STS351 doi: 10.1214/10-STS351

Roberts, M., & Heesterbeek, J. (2007). Model-consistent estimation of the basic reproduction number from the incidence of an emerging infection [Journal Article]. *Journal of Mathematical Biology*, *55*(5), 803-816. Retrieved from http://dx.doi.org/10.1007/s00285-007-0112-8 doi: 10.1007/s00285-007-0112-8

Romieu, I., Sandberg, S., Mohar, A., & Awerbuch, T. (1991). Modeling the aids epidemic in mexico city [Journal Article]. *Human biology*, *63*(5), 683 - 695.

Ross, R. (1911). Some quantitative studies in epidemiology [Journal Article]. *Nature*, *87*, 466-467.

Rubinstein, R. Y., & Kroese, D. P. (2011). *Simulation and the monte carlo method* (Vol. 707). John Wiley & Sons.

Salakhutdinov, R., & Mnih, A. (2008). Bayesian probabilistic matrix factorization using markov chain monte carlo. In *Proceedings of the 25th international conference on machine learning* (pp. 880–887).

Samsuzzoha, M., Singh, M., & Lucy, D. (2013). Parameter estimation of influenza epidemic model. *Applied Mathematics and Computation*, *220*(0), 616 - 629. Retrieved from http://www.sciencedirect.com/science/article/pii/S009630031300790X doi: http://dx.doi.org/10.1016/j.amc.2013.07.040

Saraswati, L. R., Sarna, A., Sebastian, M. P., Sharma, V., Madan, I., Thior, I., . . . Tun, W. (2015). Hiv, hepatitis b and c among people who inject drugs: high prevalence of hiv and hepatitis c rna positive infections observed in delhi, india. *BMC public health*, *15*(1), 1.

Schmitz, S.-F. H. (2000). Effects of treatment or/and vaccination on hiv transmission in homosexuals with genetic heterogeneity. *Mathematical biosciences*, *167*(1), 1-18.

Shaffril, H. A. M., Hamzah, A., Yassin, S. M., Samah, B. A., D'Silva, J. L., Tiraieyari, N., & Muhammad, M. (2015). The coastal community perception on the socio-economic impacts of agro-tourism activities in coastal villages in malaysia. *Asia Pacific Journal of Tourism Research*, *20*(3), 295-313. Retrieved from http://dx.doi.org/10.1080/10941665.2013.877048 doi: 10.1080/10941665.2013.877048

Silva, C. J., & Torres, D. F. (2013). Optimal control for a tuberculosis model with reinfection and post-exposure interventions. *Mathematical Biosciences*, *244*(2), 154 - 164. Retrieved from http://www.sciencedirect.com/science/article/pii/S0025556413001296 doi: http://dx.doi.org/10.1016/j.mbs.2013.05.005

Silva, C. J., & Torres, D. F. (2017). A sica compartmental model in epidemiology with application to hiv/aids in cape verde. *Ecological Complexity*, *30*, 70–75.

Sinka, K., Mortimer, J., Evans, B., & Morgan, D. (2003). Impact of the hiv epidemic in sub-saharan africa on the pattern of hiv in the uk. *AIDS*, *17*, 1683-1690. Retrieved from http://journals.lww.com/aidsonline/Fulltext/2003/07250/Impact_of_the_HIV_epidemic_in_sub_Saharan_Africa.13.aspx

Smith, G. J., Vijaykrishna, D., Bahl, J., Lycett, S. J., Worobey, M., Pybus, O. G., . . . others (2009). Origins and evolutionary genomics of the 2009 swine-origin h1n1 influenza a epidemic. *Nature*, *459*(7250), 1122.

Song, H., Romilly, P., & Liu, X. (2000). An empirical study of outbound tourism demand in the uk. *Applied Economics*, *32*(5), 611-624.

Sripan, P., Le Coeur, S., Amzal, B., Ingsrisawang, L., Traisathit, P., Ngo-Giang-Huong, N., . . . others (2015). Correction: Modeling of in-utero and intra-partum transmissions to evaluate the efficacy of interventions for the prevention of perinatal hiv. *PloS one*, *10*(8), e0137368.

Steen, R., Wi, T. E., Kamali, A., & Ndowa, F. (2009). Control of sexually transmitted infections and prevention of hiv transmission: mending a fractured paradigm. *Bulletin of the World Health Organization*, *87*(11), 858-865.

Sugandhi, N., Rodrigues, J., Kim, M., Ahmed, S., Amzel, A., Tolle, M., . . . others (2013). Hiv exposed infants: Rethinking care for a lifelong condition. *AIDS (London, England)*, *27*(0 2), S187.

Tamizhmani, K. M., Ramani, A., Grammaticos, B., & Carstea, A. S. (2004). Modelling aids epidemic and treatment with difference equations [Journal Article]. *Advances in Difference Equations*, *2004*(3), 183-193.

Tan, P.-L., & Gibson, J. (2013). Impact of foreign maids on female labor force participation in malaysia. *Asian Economic Journal*, *27*(2), 163-183. Retrieved from `http:// dx.doi.org/10.1111/asej.12008` doi: 10.1111/asej.12008

Tang, C. F., & Tan, E. C. (2015). Does tourism effectively stimulate malaysia's economic growth? *Tourism Management*, *46*, 158–163.

Townsend, C. L., Cortina-Borja, M., Peckham, C. S., de Ruiter, A., Lyall, H., & Tookey, P. A. (2008). Low rates of mother-to-child transmission of hiv following effective pregnancy interventions in the united kingdom and ireland, 2000–2006. *Aids*, *22*(8), 973–981.

UNAIDS. (2009). *The global economic crisis and hiv prevention and treatment programmes: Vulnerabilities and impact* (Report). Retrieved from `http://www.unaids.org/en/media/unaids/contentassets/dataimport/ pub/report/2010/20100204_summary_intro_final_040210_en.pdf`

UNAIDS. (2014). *Unaids report on the global aids epidemic* (Report). Author. Retrieved from `http://www.unaids.org/globalreport/Global_report.htm`

UNAIDS. (2016). *Press relance: Unaids board underlines the need for accelerated action and increased investment to end the aids epidemic by 2030* (Tech. Rep.). Retrieved from `http://www.unaids.org/sites/default/files/20160701_PR_PCB38_en.pdf`

UNAIDS/WHO. (2010). *Adult (15-49) hiv prevalence percent by country, 1990-2007,in 2008 report on the global aids epidemic.* (Report). Author. Retrieved from `http://www.unaids.org/globalreport/Global_report.htm`

UNGASS. (2010). Country progress report malaysia 2010.

UNICEF. (2014). *Aids in malaysia.* (Report).

UNWTO. (1993). *Definitions concerning tourism statistics.* Madrid, Spain: United Nations World Tourism Organisation.

van den Driessche, P., & Watmough, J. (2005). Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. [Journal Article]. *Mathematical Biosciences*, *180*(1-2), 29-48. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0025556402001086` doi: 10.1016/s0025-5564(02)00108-6

Velasco-Hernandez, J., Gershengorn, H., & Blower, S. (2002). Could widespread use of combination antiretroviral therapy eradicate hiv epidemics? *The Lancet infectious diseases*, *2*(8), 487-493.

Vogt, F., Ferreyra, C., Bernasconi, A., Ncube, L., Taziwa, F., Marange, W., . . . Becher, H. (2015). Tracing defaulters in hiv prevention of mother-to-child transmission programmes through community health workers: results from a rural setting in zimbabwe. *Journal of the International AIDS Society*, *18*(1).

Wanduku, D., & Ladde, G. S. (2012). Global properties of a two-scale network stochastic delayed human epidemic dynamic model [Journal Article]. *Nonlinear Analysis: Real World Applications*, *13*(2), 794-816. Retrieved from `https://www.scopus.com/inward/record.url?eid=2-s2.0-80054938816&partnerID=40&md5=2c09573ac6a6306679e1a3f0084e6a03` (Export Date: 1 January 2012 Source: Scopus)

Wang, Qiao, Y.-P., Wang, L.-H., Fang, L.-W., Wang, F., Jin, X., . . . others (2015). Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis b virus in china. *Bulletin of the World Health Organi-*

zation, *93*(1), 52–56.

Wang, Z., Fan, X., Jiang, F., & Li, Q. (2014). Dynamics of deterministic and stochastic multi-group msirs epidemic models with varying total population size. *Advances in Difference Equations*, *2014*(1), 1–25.

West, B. S., Pouget, E. R., Tempalski, B., Cooper, H. L., Hall, H. I., Hu, X., & Friedman, S. R. (2015). Female and male differences in aids diagnosis rates among people who inject drugs in large us metro areas from 1993 to 2007. *Annals of epidemiology*, *25*(4), 218–225.

WHO. (2013). World health statistics 2013.

Wilson, Donald, B., Shattock, A. J., Wilson, D., & Fraser-Hurt, N. (2015). The cost-effectiveness of harm reduction. *International Journal of Drug Policy*, *26*, S5–S11.

Wilson, & Zhang, L. (2011). Characteristics of hiv epidemics driven by men who have sex with men and people who inject drugs. *Current Opinion in HIV and AIDS*, *6*(2), 94-101.

Wilson, A. (2010). Post-fordist desires: The commodity aesthetics of bangkok sex shows. *Feminist Legal Studies*, *18*(1), 53–67.

Wilton, J. (2013). Condoms for the prevention of hiv and sti transmission.

Witbooi, P. J. (2013). Stability of an seir epidemic model with independent stochastic perturbations. *Physica A: Statistical Mechanics and its Applications*, *392*(20), 4928 - 4936. Retrieved from http://www.sciencedirect.com/science/article/pii/S0378437113005232 doi: http://dx.doi.org/10.1016/j.physa.2013.06.025

Wolfe, D., Carrieri, M. P., & Shepard, D. (2010). Treatment and care for injecting drug users with hiv infection: a review of barriers and ways forward. *The Lancet*, *376*(9738), 355–366.

Xiao, Y., Tang, S., Zhou, Y., Smith, R. J., Wu, J., & Wang, N. (2013). Predicting the hiv/aids epidemic and measuring the effect of mobility in mainland china. *Journal of theoretical biology*, *317*, 271–285.

Xun, X., Cao, J., Mallick, B., Maity, A., & Carroll, R. J. (2013). Parameter estima-

tion of partial differential equation models. *Journal of the American Statistical Association*, *108*(503), 1009–1020.

LIST OF PUBLICATION AND PAPERS PRESENTED

Journal Article

1. **A**penteng O.O. and Noor Azina Ismail. 2017. 'Modelling the spread of HIV and AIDS epidemic trends in male and female populations.' *World Journal of Modelling and Simulation* Vol. 13 (2017) No. 3, pp. 183-192.

2. **Apenteng O.O.** and Ismail N.A. 2015. 'A markov chain monte carlo approach to estimate AIDS after HIV infection.' *PLoS One* 10(7): e0131950. doi:10.1371/journal.pone.0131950.

3. **Apenteng O.O.** and Noor Azina Ismail. 2014. 'The impact of the wavelet propagation distribution on SIERS modelling with delay.' *PLoS One* 9(6): e98288. doi:10.1371/ journal.pone.0098288.

Book Chapter

1. **Apenteng, O.O.** and Noor Azina Ismail. Modeling the impact of international travellers on the trend of the HIV/AIDS epidemic. In. Kim, Haeng Kon; Amouzegar, Mahyar A.; Ao, Sio-long (eds). Transcations on Engineering Technologies: World Congress on Engineering and Computer Science 2014. Springer.

2. Noor Azina Ismail , Herlianna Naning, **Ofosuhene O. Apenteng**, Adeeba Kamaruzzaman, and Haider A. A. Al-Darraji.2014. Challenges Facing Modelling The Spread Of Infectious Diseases In The Community And Congregate Settings. In Ainin Sulaiman and M. Muzamil Naqshbandi, Social Media: Dynamism, issues and challenges. Partridge.

Conference Proceeding

1. **Apenteng, O.O.** and Ismail, N. A. 'Analyzing the impact of infected new born of HIV babies on HIV/AIDS incidence cases in Malaysia using with Markov Chain Monte Carlo Method.' Fifth International Conference on Infectious Disease Dynamics. Clearwater, Florida from 1-4 December 2015.

2. **Apenteng, O.O.** and Ismail, N. A. 'Analysing the impact of tourists on Human Immunodeficiency Virus prevalence cases in Malaysia.' The annual 5th World Congress on Virology. December 7-9, 2015 at Atlanta, USA.

3. Nur Sabrina Che Soh, Karuthan Chinna, Jonathan Inbaraj Dass, Rafdzah Ahmad Zaki and **Ofosuhene O.Apenteng.**. 'Vertical transmission of dengue fever.' 46th APACPH Conference, At Kuala Lumpur, Malaysia, October 17-19, 2014.

   item **Apenteng, O.O.** and Ismail, N. A. 'Statistical Data Analysis of Migration Impact on the Spread of HIV Epidemic Model using Markov Chain Monte Carlo Method.' The 17th International Conference on Virology and Infectious Diseases. London, United Kingdom, September 25 - 26, 2015.

4. **Apenteng, O.O.** and Ismail, N. A. 'Modelling the Impact of International Travellers on the trend of HIV epidemic.' Proceedings of the World congress on Engineering and Computer Science 2014 Vol II WCECS 2014,pp 776 - 780. 22-24 October 2014 San Francisco, USA.

Abstract

1. **Apenteng, O.O.** and Ismail, N. A. Assessing and modelling individual failure to administer HIV antiretroviral therapy of People Who Inject Drugs in Malaysia. 2nd International Conference on Statistical Distributions and Applications, Crowne Plaza, Niagara Falls, Canada, October 1416, 2016.

2. **Apenteng, O.O.** and Ismail, N. A. Impact of Tourists on HIV (Human Immunodeficiency Virus) Incidence. International Journal of Mathematical and Computational Sciences Vol:2, No:11, 2015.

3. **Apenteng, O.O.** and Ismail, N. A. Analysing the impact of tourists on Human Immunodeficiency Virus prevalence cases in Malaysia. 5th World Congress on Virology.