A stage structured model for HIV/AIDS in the presence of vertical transmission: The case of Ghana

by

Raima Carol Appaw

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Department of Mathematical Sciences,
University of Stellenbosch,
Private Bag X1, Matieland 7602, South Africa.

Supervisor: Prof. Farai Nyabadza

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Abstract

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Raima Carol Appaw

Department of Mathematical Sciences,
University of Stellenbosch,
Private Bag X1, Matieland 7602, South Africa.

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Vertical transmission remains a global problem with respect to HIV infection dynamics. It refers to the transmission of HIV from the mother to child during pregnancy, delivery and breastfeeding soon after birth. In this thesis, we formulated a mathematical model to determine the transmission dynamics of HIV/AIDS and the general impact vertical transmission of the disease will have on the spread of HIV/AIDS in Ghana, given that, horizontal transmission is the only well documented mode of transmission. The model incorporates treatment of juveniles, adults and both vertical and horizontal transmission of HIV/AIDS. The infection free state and the persistent state are examined. The analysis of the model is done through the basic reproduction number $\mathfrak{R}_o$. We proved that, the infection free state is globally stable when the reproduction number is less than one. The model is fitted to data obtained on HIV/AIDS from the Ghana Health Service in order to estimate, determine and predict current and future prevalence of the HIV/AIDS epidemics. We also determined that, without treatment, pregnant women have high risk of transmitting HIV to their babies. However,

with treatment, even if the reproduction number of vertical transmission R_v increases, the disease can still be kept under control and less babies will be born with the disease. Numerical analysis are carried out as well as sensitivity analysis to determine the parameters that influences the model output. Results from the sensitivity analysis showed that, the parameters that have most influence on the model were, effective transmission rate β and treatment rate τ_2. We noticed that increasing β increases $\mathfrak{R}_o$ and increasing τ_2 decreases $\mathfrak{R}_o$. This suggests that, efforts must be intensified by the health policy makers for continuous sustainability and implementation of the disease protocols to reduce the transmission rate and to enrol more people into treatment. This will lead to the reduction of HIV/AIDS burden in the population.

Uittreksel

'n Stadium-Gestruktureerde Model vir MIV/VIGS in die teenwoordigheid van vertikale oordrag: die geval van Ghana

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Raima Carol Appaw

Departement Wiskuudige Wetenskappe,
Universiteit van Stellenbosch,
Privaatsak X1, Matieland 7602, Suid Afrika.

Tesis: MSc

Desember 2018

Vertikale transmissie bly 'n globale probleem ten opsigte van MIV-infeksie dinamika. Dit verwys na die oordrag van MIV van die moeder na die kind tydens swangerskap, aflewering en borsvoeding kort na geboorte. In hierdie tesis het ons 'n wiskundige model geformuleer om die transmissiedinamika van MIV/-VIGS en die algemene impak van die vertikale oordrag van die siekte sal hÃł op die verspreiding van MIV/VIGS in Ghana aangesien horisontale oordrag die enige goed gedokumenteerde modus van oordrag is. Die model sluit behandeling in van jongmense, volwassenes en beide vertikale en horisontale oordrag van MIV/vigs. Die infeksie-vry toestand en die aanhoudende toestand word ondersoek. Die analise van die model word gedoen deur die basiese voortplantingsnommer $\mathfrak{R}_o$. Ons het bewys dat die infeksie-vry toestand wÃłreldwyd stabiel is wanneer die voortplantingsnommer minder as een is. Die model is gebaseer op data wat op MIV/VIGS verkry word uit die Ghana Gesondheidsdiens ten einde die huidige en toekomstige voorkoms van MIV te bepaal en

te voorspel. Ons het ook vasgestel dat, sonder behandeling, swanger vroue 'n hoÃń risiko het om MIV oor te dra aan hulle babas. Maar met behandeling, selfs al neem die voortplantingsnommer van vertikale oordrag, R_v, toe, kan die siekte steeds onder beheer gehou word en minder babas gebore word met die siekte. Numeriese analise word uitgevoer sowel as sensitiwiteitsanalise om die parameters te bepaal wat die uitset van die model beinvloed. Resultate uit die sensitiwiteitsanalise het getoon dat die parameters wat die grootste invloed op die model gehad het die effektiewe oordrag tempo en behandeling koers τ_2 is. Ons het opgemerk dat toenemende β die $\mathfrak{R}_o$ laat toeneem en toenemende τ_2 die $\mathfrak{R}_o$ laat afneem. Dit dui daarop dat die gesondheidsbeleidmakers die intensiteit van die omgewing moet verbeter vir volgehoue volhoubaarheid en implementering van die siekte protokolle om oordragtempo te verminder en meer mense behandeling gee. Hierdie sal lei tot die vermindering van die MIV/VIGS las in die bevolking

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Dedications

To my family, friends and all my loved ones.

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Chapter 1

Introduction

1.1 HIV/AIDS

HIV (Human immuno-deficiency virus) is a deadly viral disease that destroys the immune system and leaves the immune system prone to many other acute, chronic and fatal diseases and disorders. HIV is one of the many viruses that can be transmitted by physical contact including sexual contact (horizontal transmission) and by other means (sharing of infected needles used for injection, injecting drugs, tattooing and body piercing). Transmission through sexual and other physical contacts are as a result of contacts between susceptible and infected individuals. HIV is also tramitted vertically. Vertical transmission of HIV occurs when the disease is transmitted directly by an infected mother to an unborn baby. Vertical transmission occurs during pregnancy, through delivery and after childbirth via breastfeeding by an infected mother to the juvenile (children under 15 years). Example of diseases transmitted vertically include rubella, chickenpox, chlamydia, syphilis, hepatitis B, zika fever, HIV/AIDS, etc.

Intervention strategies against vertical transmission of HIV have significantly lead to the improvement in the lives of individuals in the past decade in developed countries. Consequently, the tendency of infected fertile women to give birth have increased. In the study conducted by [20], it was noted that individuals are living longer, productive and healthier lives and as a result, their parenting goals and tendency to give birth is likely to be ultered to become more

similar to those of uninfected individuals. Consequently, in the United States, the rates of pregnancy and live-birth among women living with HIV have increased, with rates now being similar to those of uninfected women [20]. However, in developing countries, this is not necessarily the case. Despite increasing access to anti-retroviral therapy (ART) in sub-Saharan Africa, diagnosis and treatment of HIV-positive infants has been very poor. For example, it has been noted in Uganda [47] that out of a total of 78 000 infected HIV-positive juveniles (aged 0-14 years) eligible for ART in 2010 in Uganda, only 24 031 (31%) were diagnosed and started on ART.

The impact of vertical transmission of HIV/AIDS in Africa will persist to be more severe without appropriate anti-retroviral therapy. Due to the low level of literacy, poor health care system and various issues with respect to our health care system, vertical transmission of HIV/AIDS with or without treatment will continue to be a burden in our African continent. Generally, HIV-positive juveniles must be given early diagnosis and treatement to boost their chances of survival, since HIV/AIDS progresses more faster in infected juveniles than adults due to their underdeveloped immune system. For HIV-positive juveniles not initiated on ART, 35% are likely to die within the first year of life and 52% by 2 years of age. Early initiation of HIV-positive juveniles into treatment slows disease progression, suppresses viral load, and dramatically reduces mortality rates [47].

It has been noted in [47] that the number of infants newly infected with HIV globally has declined in recent years, from 370 000 in 2009 to 150 000 in 2015. In 2005, a total estimated amount of 630 000 - 820 000 infants were newly infected, of whom breastfeeding accounts for around 280 000 - 360 000 [23]. Similarly, in the year 2006, almost 530 000 infants were newly infected with the HIV virus. Mother-to-child transmission (MTCT) before, during or after delivery accounts for about 90% of them [11, 24, 26]. According to Kgosimore and Lungu [46], maternal viral load and type of delivery are some factors that influence the transmission during delivery. Globally, about 1.8 million juveniles (0-14) are approximated to be living with HIV (UNICEF, 2016) [33]. The second leading cause of death for adolescents worldwide and the leading cause of death for

adolescents in Africa is now HIV/AIDS (WHO, 2014) [34].

Since 2005, the availability of new antiretroviral drugs/therapy (ART) which offer high efficacy and acceptability and less toxicity, has led to a decrease of HIV related deaths worldwide [39, 54, 68]. Although progress has been substantial, uncertainties persist concerning the best way to manage the HIV/AIDS disease [30]. For instance in 2011, there were approximately 330 000 new childhood infections, representing a reduction of 43% since 2003. This however, remains unacceptably high. Unfortunately, increased childhood infection rates were observed in Angola, Congo, Equatorial Guinea, and Guinea-Bissau [67].

The impact of HIV in many cases has been linked to areas where there is poverty, poor health care services and illiteracy, especially in sub-Saharan Africa and Asia where the disease is endemic. The treatment of HIV infected mothers in sub-Saharan Africa and other places has however, revealed that, when the mothers infected with the HIV virus are treated with Zidovudine or Nevirapine or receiving dual antiretroviral therapy with no or one highly active drug (Multi-ART), the number of juveniles born infected reduces drastically [22, 25, 27, 37, 52]. Most of this significant reduction in vertical transmission is noted among non breastfeeding women in developed countries.

HIV/AIDS, accounts for mortality of millions of individuals and expenditure of huge amount of money in health care and control of the disease [56]. A lot of countries where this disease persist are economically disadvantaged. Their economic growth and productivity is low. HIV/AIDS continues to affect economic growth especially in developing countries where there is no proper education, prevention and proper health care systems.

1.2 HIV/AIDS in Ghana

When the HIV/AIDS epidemic in Ghana was first reported in the country in the mid 1980s, it was thought to be a disease for prostitutes and people with a his-

tory of travelling abroad [3]. Although the original HIV/AIDS cases in Ghana were diagnosed in 1986, attempt to track prevalence were not established until 1990, when the Ministry of Health in Ghana, implemented the national HIV Sentinel Surveillance (HSS) system. From 1994, an annual HIV sentinel survey have been conducted at antenatal care (ANC) clinics for women who are pregenant and also, sexually transmitted infection (STI) centers for patients with sexually transmitted infections (STIs) [4].

HIV/AIDS in Ghana like most countries in the world, is generally prevalent among the sexually active age groups. Various factors such as traditional beliefs, religious beliefs and ethnic norms play a notable role in the spread of HIV/AIDS in Ghana. The mode of transmission of HIV/AIDS is both sexual and vertical from a mother-to-child. Gyimah et *al*. [38], in their work reported that although the HIV/AIDS state in Ghana is not as severe as in some eastern and southern African countries, data from sentinel sites in the country indicate that prevalence has somewhat stalled at 3.4%, mostly due to high infection rates among young people.

1.2.1 Epidemiology of HIV/AIDS in Ghana

The main mode of transmission of the virus in Ghana is through heterosexual intercourse, which accounts for 75 - 80 % of all HIV/AIDS infections. Vertical transmission from a mother-to-child transmission (MTCT) accounts for 15%, and transmission through blood and blood product accounts for 5% [4]. In Ghana since the inception of ART in 2003, a juvenile who is HIV positive in Ghana must be stabilized in accordance with good medical practices before being initiated on ART. The treatment reccommendation for an HIV sero-positive juvenile < 18 month is treat and/or request HIV antibody test at 18 month or a virological test is done to confirm infection, and juveniles between 18 month to 18 years with HIV antibody positive are treated [65]. Likewise all HIV infected juveniles irrespective of their feeding behaviour are provided within two days of birth with Zidovudine at every 12 hours for six weeks. It has been noted in [73], that in the absence of anti-retroviral therapy and/or co-trimozole prophy-

laxis in sub-Saharan Africa, about 35% of HIV-positive infected juveniles die in just their first year of life, and 53% of the infected juveniles die before the onset of age two. Though early initiation of juveniles on ART is said to reduce their mortality and mobidity rate, the rate of juvenile death continue to increase due to late enrollment of juveniles on treatment as of 2010 [73]. The most prevalent infecting agent of HIV/AIDS in Ghana is HIV-1 (94.4 %); 5.1% of cases are dual infections with HIV-1 and HIV-2; and only 0.5% of all infections in 2003 were HIV-2 alone [4].

In Ghana, economic factors mostly tend to influence the sexual behaviours of adolescents in their reproductive ages, and they constitute more than 50% of the population [31]. Qualitative and quantitative studies conducted in Ghana suggested that the lifestyles of university students are placing them at risk of contracting HIV [62, 72]. Similarly, influential peer norms to gain access to luxury items, such as cars, expensive shoes, clothing, jewellery, fashionable hairstyles, makeup and other accessories drives young women to engage in transactional sex in Ghana exposing them to high risk of sexually transmitted diseases [9, 50, 72, 74] .

Ghana Demographic and Health Survey (GDHS) in 2003 indicated that 9% of women and 4% of men had sex at age 15 [36], while the Ghana Statistical Service (GSS) report indicated that 27% of men and 44% of women had first sex at age 18 (GSS, 2004) [35]. Sexual intercourse with non-married or non-cohabiting partners is widely understood to be associated with an increase in the risk of contracting sexually transmitted diseases. In 2003, according to GDHS, 20% of women and 66% of men between age 15-49 had indulged in higher-risk sexual behaviour in the preceding 12 months of the survey. In addition, another 25% of women and 45% of men between age 15-49 were found to have had unprotected sex or sex without the use of condoms. More predominant among young people aged 15-24 was higher-risk sexual behaviour (sex without protection), i.e. 75% of men and more than 50% of women (GSS, 2004) [35]. Less than one-third of women and half of men aged 15-24 among those who engage in high-risk sex used a condom during their last episode of unsafe sex. Sexual intercourse with more than one partner is associated with a high risk of exposure to sexu-

ally transmitted diseases. In addition, 10% of men and 1% of women aged 15-49 had sexual intercourse with more than one partner in the 12 months prior to the survey in 2004 [31].

1.2.2 Stigmatization and education of HIV/AIDS in Ghana

HIV/AIDS is a stigmatized disease and a discussion about it is often avoided in Africa [12]. In addition to devastating the familial, social, and economic lives of individuals, HIV/AIDS stigma is cited as a major barrier to accessing prevention, care, and treatment services [15, 19, 45, 51].

In the Ghanaian community, certain illnesses and behaviours have traditionally been regarded as despicable and are therefore stigmatized. Tuberculosis, mental illness, leprosy, and sexually transmitted diseases are among those illnesses. Specific behaviours such as prostitution are also considered despicable, and people practicing prostitution are similarly condemned. The original association of AIDS with prostitution, together with the reality that most of the AIDS cases in Ghana are acquired through sexual transmission, provided fuel for the stigmatization of the disease and those who are infected by it [9,13,53]. The families of AIDS victims are also identified and regarded as a disgrace to society [55].

Various forms of educational platforms have been used to communicate the dangers and risks associated with getting HIV/AIDS in Ghana. Generally, girls from the senior high school were aware of the nature, modes of transmission, and prevention of HIV/AIDS. However, some other students displayed limited comprehension on some issues including the treatment and causes of the HIV/AIDS virus, contacts and involvement with infected persons, and determination of HIV infection from appearances rather than testing [10]. Appiah *et al*. [10], also raised significant concerns about the unwillingness of senior high school girls to use condoms as a preventive measure and the need to reestablish awareness interventions of HIV/AIDS in Ghana. Hence, more education and information needs to be spread across about the stigmatization of the dis-

ease. Due to the significant religious and cultural values in Ghana, Amoako [5], suggested that, increasing HIV prevention information and incorporating culturally relevant and socially acceptable values might lend support to improve adolescent school-based HIV/AIDS prevention programs.

1.2.3 National AIDS Control Program

The National AIDS/Sexual transmitted disease (STI) Control Program (NACP) is responsible for the coordination and implementation of the HIV and AIDS related aspects of the Ghana Health Sector Strategic Framework. It is a Program under the Disease Control and Prevention Department of the Public Health Division of the Ghana Health Service (GHS).

The Program started as the National Technical Committee on AIDS and later became National Advisory Council on HIV and AIDS in 1985. The Council evolved into NACP in 1987. NACP has since then been the technical lead agency in the health sector's response to HIV and AIDS in Ghana. In order to ensure a systematic approach to the national response, NACP first developed a short term plan to avert and control HIV/AIDS in 1987, and went on to develop two Medium Term Plans; one from 1989 to 1993 and the other from 1996 to 2000. Subsequently, the NACP implemented the health sector component of the National HIV Strategic Framework (NSF I 2001-2005 & NSF II 2006-2010) and is presently accountable for implementing the health sector aspects of the National HIV and AIDS Strategic Plan (NSP 2011-2015). Additionally, the Program has been guided by the Health Sector Program of Work.

The National AIDS/STI Control Program is mandated to undertake the following activities:

- The delivery of a package of interventions to reduce HIV transmission.

- The delivery of a package of support and care services for Persons Living with HIV (PLHIV).

- The delivery of strategic information on HIV and AIDS and other STIs.

- The provision of essential technical support to all Ministries, Departments and Agencies (MDAs) in the implementation of their HIV programs.

1.2.4 HIV Sentinel Survey in Ghana

The HIV Sentinel Survey (HSS) has for twenty three years provided important data on the trends of infections from the HIV virus in Ghana. The HSS was established in 1992. The main data for the estimation and projection of the HIV and AIDS impact in the overall population was provided by the HSS report. The report also serves as a reference document for the design, implementation and monitoring of programs within the national response. Despite global efforts to explore new alternatives for monitoring HIV prevalence using routine Antenatal Clinic (ANC) data, the annual HSS remains the most robust and authentic primary data source for tracking HIV prevalence trends in Ghana.

The HSS is a cross sectional survey directed at women attending antenatal clinics in specific antenatal clinic sites in Ghana. HIV sentinel surveillance system was initiated annually in Ghana. It was based on the reasoning that, prevalence of HIV among pregnant women is a good representation and indicator of the extent to which the HIV infection spreads among the population. The HSS data have also been the main source of data for the National HIV and AIDS estimate over the last 10 years in Ghana. Prevalence among pregnant women is represented by the HSS Report while the National HIV Prevalence estimates that is derived from HSS data calibrated with Demographic and Health Surveys geographic data (DHS+), indicates the national HIV prevalence rates for Ghana.

As at the reporting time, forty sentinel sites have been initiated across the country with at least three sites in each region of the total ten regions. This represent a total of seventeen rural sites and twenty three urban sites. The number of sites in the rural areas were increased from one in 2002 to seven in 2003 and to a total

of seventeen cites by 2005. The increment ensures a balanced representation of urban and rural areas in the determination of the prevalence of HIV in Ghana. Since 2005, the total number of sites established have remained the same [59].

In view of this, HIV trends, national HIV and AIDS estimate in Ghana are estimated using the HIV sentinel survey reports. According to the HSS report 2015, the 2015 median HIV prevalence among antenatal clients is still below the 2% mark for the third consecutive year, despite, the marginal increment from 1.6% to 1.8%. Similarly, according to the National HIV prevalence and AIDS estimates reports from 2009-2015 for Ghana, prevalence of HIV among antenatal clients in 2009 was 2.9%, representing a 31 % increase over the past years. In 2009, the estimated adult national HIV prevalence was 1.9% with an estimated 267,069 people made up of 112,457 males and 154,612 females living with HIV and AIDS. There were 22,177 new infections and 20,313 AIDS deaths. Twenty five thousand six hundred and sixty six (25,666) juveniles were living with HIV; 12,579 being girls according to the HSS report 2015 [59].

Regional HIV prevalence ranged from 1.2% in the Northern region to 3.2% in the Greater Accra region, and site prevalence ranged from 0.0% in Kintampo and Builsa (rural) to 6.2% in Agormanya (urban). The Northern region had a 100% increment in prevalence over the previous year. The increase of HIV in the region is driven mainly by the 350% and 600% increments in Adibo (rural) and Nalerigu (urban) respectively. Greater Accra has overtaken the Eastern region as the region with the highest prevalence. Out of the seven sites with prevalences of 3% and above, Adabraka, Dangme East, Maamobi and Korle-bu is accounted for by Greater Accra. This is reflected in the linear trend analysis of region-specific prevalence. Consistent reductions in the Agormanya and Koforidua sites accounted for the overall Eastern regional prevalence. It is noteworthy that prevalence in Fanteakwa (rural) also dropped in the 2015 survey.

A summary of the 2016 HSS report by the Ghana Aids Commission (GAC), indicated that HIV prevalence among pregnant women attending antenatal clinics in 2016 was 2.4 % which represents a second continuous upsurge from the 2014 prevalence of 1.6% and 1.8 % in 2015 [2]. HIV prevalence was lower in rural

areas (1.9 %) than urban areas (1.9 %) while HIV prevalence among the young population (15-24), a proxy for new infections remained unchanged at 1.1 % [2]. HIV prevalence by age group 45-49 is the highest at 5.6%, followed by 35-39 at 3.5% with 15-19 being the lowest at 0.6% [2, 21]. The regional HIV prevalence ranged from 0.7% in the in the Northern region as the region with the lowest prevalence, Volta and Brong Ahafo regions as the regions with the highest prevalence 2.7% [2]. With respect to sites, HIV prevalence ranged from 0.4% in Nalerigu to 4.2% in Agomanya and Sunyani. The highest prevalence within urban sites were 4.2% in Agormanya and Sunyani followed by Wa 3.7% [21]. Rural prevalence in 2016 ranged from 0.5% in Builsa, Salaga and Kintampo to 3.3% in Fanteakwa. A linear trend analysis of antenatal clinic HIV prevalence since 2001 shows a reduction in the epidemic, despite, the increase from last year's prevalence of 1.8% [21]. Comparatively, HIV prevalence is higher in urban areas while Syphilis is higher in rural areas (HSS, 2016) [21]. The table below shows the prevalence of HIV in the ten regions in Ghana for 2016 .

Table 1.1: **HIV Regional prevalence in Ghana, 2016, [21]**

Region	Prevalence
Volta region	2.7%
Brong Ahafo region	2.7%
Eastern region	2.6%
Ashanti region	2.6%
Western region	2.5%
Upper West region	2.5%
Greater Accra region	2.4%
Central region	1.8%
Upper East region	1.7%
Northern region	0.7%

1.3 Mathematical modelling of HIV/AIDS

Mathematical models have increasingly been used to analyze the spread and the control of infectious diseases. Linear and non-linear ordinary or partial differential equations have been used to study and analyze the transmission dynamics of HIV/AIDS, see for example, [6, 16, 38, 40, 46].

Deterministic and stochastic epidemic models are the models mostly used to analyze HIV/AIDS dynamics. Many extensions of the epidemic models were based on the special case of the famous Kermack and McKendrick Susceptible Infected and Recovered (SIR) deterministic model in 1927. Kermack and McKendrick were the pioneers in the field of mathematical epidemiology. Between World War I and II, they published a series of papers on deterministic structured population models for the spread of infectious diseases, which have been used by many researchers [42]. Thieme and Castillo-Chavez [76], extended their work based on this SIR epidemic model to formulate an epidemic model with variable infectivity of HIV/AIDS transmission in a homogeneously mixing population. Similarly, epidemic models studied by Anderson and May [7], Anderson et *al*. [8], Bongaarts [16] with demographic characteristics are also extensions of the SIR epidemic model by Kermack and McKendrick.

Some other models widely capture important parameters such as the evolution, progression, transmission and treatment of HIV/AIDS. Wordaz and Nowak [81], introduced a basic model of virus infection in VIVO (in the living) and demonstrated how it can be used to study HIV dynamics and to measure crucial parameters that lead to a new understanding of the disease process.

Models which are compartmental in structure, with differential equations describing the changes in the dynamics among the compartments were also based on the special form of the classical Kermack and McKendrick deterministic epidemic model [42]. Some of these models with compartmental structure such as [6, 40] seeks to determine and comprehend the transmission dynamics among the compartments. They also endeavour to determine which factors and variables control and drive the disease within and among different susceptible groups

of the population under study. These models also try to determine the long-term effects of the disease on each compartment.

1.4 Motivation

Most models for HIV/AIDS in Ghana do not incorporate vertical transmission and as a consequence, may fail to capture the effect of vertical transmission and the actual impact of HIV/AIDS in the Ghanaian population. Furthermore, HIV infected juveniles surviving into early adulthood were considered rarely, but now possible for them to survive due to the availability of antiretroviral treatments (ARTs). However, survival to older childhood with untreated vertically acquired HIV infection which was previously considered unusual was noted in Harare, Zimbabwe [28] and a substantial epidemic of HIV/AIDS in older survivors from vertical transmission is emerging in Southern Africa [29]. Since Ghana is located in the sub Saharan like most of these countries, we are intrigued to ask the questions: What will be the long-term transmission dynamics of HIV/AIDS in Ghana in the presence of vertical transmission and what effect will progression from juvenile stage (under or not under treatment) to adulthood have on the transmission dynamics of HIV/AIDS in the long run?, what will be the future trend of HIV/AIDS transmission in the presence of vertical and horizontal transmission in Ghana given current estimates?

Stage structured model are better to use when one wants to identify and determine particular parameters such as maturation rate, survival rate, progression rate, etc. A stage structured model is also a better predictor of demographic rates within a population experiencing lots of demographic changes. This is useful especially when dealing with intervention strategies for epidemics within a changing or varying population. As a consequence, in our study, we proposed a non-linear compartmental stage structured mathematical model of HIV/AIDS infection which includes both the juvenile and adult stage and is different from other models about this disease in Ghana. First, our model is applied to Ghana. It is fitted to data on infected juveniles and adults from Ghana who are under

treatment and not under treatment which has not been done to the best of our knowledge. Second, it captures the vertical transmission of HIV/AIDS and the proportion of infected juveniles who are not under treatment, but survive to early adulthood based on studies by Ferrand et *al*. [28, 29]. This is under the assumption that though they are symptomatic and survive the maturation age, they mature into early adulthood to take part in the transmission of the virus. Models with HIV/AIDS dynamics that disregard the effects of vertical transmission may not truly show the impact of HIV/AIDS in a population [46].

1.5 Objectives

A thorough investigation of the transmission dynamics of HIV/AIDS in Ghana requires the analysis of the modes of transmission, quantification of estimates, comprehension of the dynamics of the diseae spread in the varying Ghanaian population. Mathematical modeling plays a significant role in predicting, assessing, controlling potential outbreaks of diseases as well as analyzing social, demographical and ecomomic factors of diseases. Therefore, the main aim of this study is to formulate a mathematical model with both modes of transmission of HIV (horizontal and vertical), to quantify results and together with computer simulations investigate the behaviour of our model. To also fit the model to data obtained from Ghana to determine and predict the trends and progression of HIV/AIDS epidemic in Ghana which has not been done to the best of our knowledge.

1.5.1 Specific objectives

Specific objectives include:

- To carry out steady states analysis of the resulting mathematical model.
- To carry out sensitivity and numerical analysis of the model.

- To fit the model to data obtained from Ghana to test for the general robustness of the model, draw out consequences of assumptions we have made and to predict future trends of the epidemics.
- Draw out conclusion on the epidemics based on the evaluated infection and progression rates.

1.6 Mathematical preliminaries

1.6.1 Lyapunov functions and stability

We first consider some stability definitions.

Definition 1.6.1. Let $\dot{y} = f(y)$ be a non-linear time invariant system, where, $f : R^n \to R^n$.
A point $y_e \in R^n$ is an equilibrium point of the system, if $y_e = 0$. This implies, $y(t) = y_e$ is a trajectory.

Suppose y_e is the equilibrium point, then

- the system is locally asymptotically stable (l.a.s) near or at the point y_e if there exist an $h > 0$ such that $\| y(0) - y_e \| \leq h$. Therefore, $y(t) \to y_e$ as $t \to \infty$,
- the system is globally asymptotically stable (g.a.s) if for every trajectory $y(t)$, we get, $y(t) \to y_e$ as $t \to \infty$.

Definition 1.6.2. A function $V : R^n \to R$ is positive definite if

- $V(y) \geq 0 \quad \forall y$,
- $V(y) = 0$ if and only if $y = 0$,
- All sublevel sets of V are bounded,
- $V(y) \to \infty$ as $y \to \infty$.

If there exist a function V that satisfies the above condition, we call V a lyapunov function.

Theorem 1.6.3. (Lyapunov boundedness theorem) Suppose that that there is a function V that satisfies

- All sublevel sets of V are bounded,
- $\mathrm{V}(y) \leq 0 \; \forall y$,

then all trajectories are bounded. Thus, for each trajectory y, there exist an $h > 0$ such that $\| \; y(t) \; \| \leq h \quad \forall t \geq 0$.

Theorem 1.6.4. (Lyapunov global asymptotic stability theorem [18]) Suppose that there is a function V such that

- V is positive definite,
- $\dot{\mathrm{V}}(y) < 0 \; \forall \; y \neq 0$ and $\dot{\mathrm{V}}(y) = 0$, then, every trajectory of $\dot{\mathrm{V}}(y) = f(y) \to 0$ as $t \to \infty$. Hence, the system is globally asymptotically stable.

Proof. We first assume that the trajectory $y(t)$ does not converge to zero. $\mathrm{V}(y(t))$ is decreasing and non-negative so it converges to an ϵ_1 as $t \to \infty$. Now since, $y(t)$ does not converge to zero, we have $\epsilon_1 > 0$. Therefore, $\forall t$, $\epsilon_1 \leq \mathrm{V}(y(t)) \leq \mathrm{V}(y(0))$. $\mathrm{D} = \{g | \epsilon_1 \leq \mathrm{V}(g) \leq \mathrm{V}(y(0))\}$ is closed and bounded hence compact. We assume $\dot{\mathrm{V}}$ is continuous and that it attains it supremum on D. Thus, $sup_{g \in \mathrm{D}}$ $\dot{\mathrm{V}}(g) = -c < 0$, where $c > 0$. Since, $\dot{\mathrm{V}}(y(t)) \leq -c$ for all t, we have

$$\mathrm{V}(y(t^*)) = \mathrm{V}(y(0)) + \int_0^{t^*} \dot{\mathrm{V}}(y(t))dt \leq \mathrm{V}(y(0)) - ct^*,$$

which for $t^* > \dot{\mathrm{V}}(y(0))/c$ implies $\mathrm{V}(y(0)) < 0$ a contradiction. So every trajectory $\dot{y} = f(y)$ is globally asymptotically stable (g.a.s).

□

Using Lasalle's theorem, we can conclude that the system is (g.a.s). Lets consider our trajectory $\dot{y} = f(y)$.

Theorem 1.6.5. (Lasalle's theorem [18]) Suppose that there is a fuction V : $R^n \rightarrow R$ such that

- V is positive definite,
- $\dot{V}(g) \leq 0$,
- The only solution of $\dot{u} = f(u), \dot{V}(u) = 0$ is $u(t) = 0\ \forall t$, then the system $\dot{y} = f(y)$ is (g.a.s).

1.6.2 Routh-Hurwitz criterion for higher order degree polynomials

The Routh-Hurwitz criteria are important criterion based on mathematical test that gives the necessary and sufficient conditions for all the zeros of a characteristic polynomial with real coefficients to lie in the left half of the complex plane. The criterion is applied also in the determination of the local asymptotic stability of an equilibrium of non-linear differential equation. Lets consider the following polynomial,

$$P(\theta) = a_0\theta^n + a_1\theta^{n-1} + a_2\theta^{n-2} + ... + a_{n-1}\theta + a_n.$$

The coefficients a_i, $i = 1, 2, 3, 4, 5, ..., n$ are all real constants and define the matrices of the Hurwitz criterion. Let $a_0 \neq 0$ and $a_n > 0$. To determine the number of eigen values θ of an nxn matrix, the condition $G_1 > 0$, $G_2 > 0$, $G_3 > 0$, $G_4 > 0$,....,$G_n > 0$ must be met for θ to have negative real parts, where

$$G_1 = [a_1],$$

$$G_2 = \begin{vmatrix} a_1 & a_0 \\ a_3 & a_2 \end{vmatrix}, G_3 = \begin{vmatrix} a_1 & a_0 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{vmatrix},$$

$$G_m = \begin{vmatrix} a_1 & a_0 & . & . & . & 0 \\ a_3 & a_2 & . & . & . & 0 \\ . & . & . & . & . & . \\ . & . & . & . & . & . \\ . & . & . & . & . & 0 \\ a_{2n-1} & a_{2n-2} & . & . & . & a_n \end{vmatrix}.$$

We have a stable steady states if the real part of θ is negative for all θ, that is $G_m > 0$ for all $m = 1, 2, 3, 4, ..., n$.

Thus, for our eigen values to be all negative

- $a_1 \neq 0$ and $a_n > 0$,
- $a_1, a_2, a_3, a_4 > 0$,
- $a_1a_2 - a_3, a_3a_2 - a_1a_4, a_1a_2a_3 - a_3^2 - a_1^2a_4 > 0$.

Determinant calculus operation/polynomial division are mainly used to determine the eigen values θ of high order degree polynomials.

1.6.3 Reproduction number

We use the next generation matrix approach to determine the basic reproduction number. The reproduction number will help in analyzing the stability of the equilibria for our model.
We define x_t to be the set containing our infection-free states given by

$$x_t = \{x \geq 0 | x_i = 0, i = 1, 2, 3, ..., n\}$$

Let $F_i(x)$ represent the rate of appearance of newly infected in compartment i and $V_i^-(x)$ represent the rate of transfer of individual into compartment i by

all other means and $V_i^+(x)$ represent the rate of transfer of individual out of compartment i. So, we can write,

$$\frac{dx_i}{dt} = F_i(x) - V_i(x), \ \ 1 \leq i \leq m,$$

where $V_i(x) = V_i^-(x) - V_i^+(x)$. If the disease-free equilibrium/infection-free state is (x_0), then subsequently, we find the reproduction number by taking the spectral radius of our matrix FV^{-1} at the disease-free equilibrium/infection-free state, where

$$F = \left[\frac{dF_i(x_0)}{dx_j}\right], \text{and } V = \left[\frac{dV_i(x_0)}{dx_j}\right], 1 \leq i, j \leq n.$$

F is a non-negative matrix and V is a non singular matrix that can be invertible. Thus, the reproduction number is the maximum of all the eigenvalues given by

$$\mathfrak{R}_o = \rho(FV^{-1}),$$

where $\rho(FV^{-1})$ the spectral radius of $FV^{-1} = \max|\lambda_i|_{1\leq i\leq n}$.

1.7 Structure of thesis

The research thesis is organized into four chapters. Chapter one, consist of the introduction of the transmission dynamics of HIV/AIDS in Ghana. Literature review is considered in Chapter two, where, we look at a number of mathematical models of HIV/AIDS. Chapter three details the main model formulated in the thesis and its analysis. The assumptions governing the model are stated in this chapter. Local and global stability of the model are established, the basic reproduction number of HIV/AIDS infection in Ghana was determined to study the dynamics of the disease. The model was fitted to data obtained from Ghana. Parameters of the model were estimated, numerically and sensitivity analysis of

parameters were performed to determine the parameters which have the most influence on the model output. The project is concluded in Chapter four with important discussions and recommendations.

Chapter 2

Literature review

Mathematical models have countlessly been used to study the epidemiology of HIV/AIDS, the transmission dynamics, the role of demographics on the transmission patterns, the impact of vertical transmission on the disease as well as the long and short-term impact of a disease on a population. These models in one way or another make use of ordinary differential equations (ODEs) or partial differential equations (PDEs) to describe the dynamics of their systems. Many of these mathematical models used are: deterministic/compartmental models, stochastic models, models with delays, network models and models with vertical transmission.

To ascertain, fully comprehend the true nature of HIV/AIDS and to accurately estimate, assess and predict the HIV/AIDS epidemics in a population, it is important to include vertical and horizontal transmission in any model developed or formulated. A model without the vertical transimmion will fail to trully capture the impact of the HIV epidemics in a changing population.

Özalp and Demirci [64], developed a fractional order differential equation with vertical transmission in a varying population. They employed quantitative research method with underlying assumptions for their studies. They divided the model formulated into four compartment given as, susceptible (S(t)), exposed (E(t)), infectious (I(t)) and recovered (R(t)). They stated fractional order differential equations to be generalizations of integer order differential equations as

a reason for their choice of model. They assumed that horizontal transmission of disease is by direct physical contact between the susceptible population and the infectious population. They further assumed that juveniles coming from the exposed and infected populations are born into an exposed population with probabilities p and q respectively.

They analyzed the equilibrium point and stability of the model developed and in addittion, determined the positivity of the model. This is very important since it shows the model is biologically, mathematically and epidemiologically well posed. They went on to determine the reproduction number which serves as a threshold quantity in disease epidemics and is used to measure the transmission potential of infectious diseases. Graphical representations was used to show their analytically obtained results.

This model could have been better improved and extended if it had included vertical transmission in the presence of treatment as well as the juvenile and adult stage which our model has done.

In conclusion, they cited the importance of using mathematical model for prediction of the dynamics of an epidemic and for quantification of estimates to be compared with observed patterns. This I belive is also one of the relevant key point our research considered.

Vertical transmission models contains information to public health personnel as well as other stake holders. They will help them with information on how to regulate disease spread since a cure is still to be found. While Özalp and Demirci [64], developed a fractional order differential equation with vertical transmission in a varying population, Ogala et *al*. [61], in their work described the mother-juvenile pair characteristic that contribute to the vertical transmission on HIV and to propose remedies. They assessed the various factors responsible for increasing the chance of HIV transmission in juveniles born to positive HIV infected mothers in western Kenya. Descriptive analysis was used for their studies. A retrospe ctive studies on data collected from January to December 2015 on 1028 medical records of mother-juvenile pairs enrolled in prevention

of mother-to-child transmission (PMTC) was used. They compared the transmission rate amongst positive mothers known to be HIV-positive before birth versus transmission amongst those who were newly detected to be HIV-positive during maternal and child health care.

Statistical analysis such as chisquared and kruskal-wallis with a confidence interval of 95% was used by them to compare the socio-demographic and clinical characteristic of mothers. In order to study the factors asociated with juveniles HIV-positive status, a logistic regression was used to analyzed the relationship between mother and juvenile characteristics with juvenile HIV status. The logistic regression they performed showed no connection between juveniles HIV status and mother's age, WHO stage, ART at conception and juveniles sex, but that juveniles HIV status were crucially connected to the age of their enrolment on ART, mothers' HIV status at conception, and juveniles feeding type.

They noted in their results that 60% of mothers were known to be HIV-positive before giving birth and that those who knew they were HIV-positive before birth and infected mothers who were newly diagnosed of HIV through clinical attendance had mother-to-child transmission (MTCT) rates of 5-5% and 20.7% respectively. They also noted that an estimated 90% of newly diagnosed HIV infected mothers were at an initial HIV clinical stage at the beginning and 40% were enrolled after conception. Furthermore, mothers HIV status and juveniles age at conception were related to juveniles HIV status. Also, most mothers enrolling into prevention of mother-to-child transmission (PMTCT) knew their HIV status. Newly diagnosed HIV infected mothers are mostly responsible for mother-to-child transmission (MTCT) of HIV in western Kenya. Also, a significant proportion of mothers who were initiated into the prevention of mother-to-child transmission (PMTCT) program were newly identified during pregnancy and lactation. Finally, they noted that none of the HIV infected juveniles were given nevirapine prophylaxis during the period the routine data was collected in 2015.

They concluded that the most important HIV-positive class that continuously increase MTCT in the region understudied are the newly diagnosed HIV-positive

mothers. Their justification was that this newly diagnosed class detect their HIV status at a very later stage leading to delay and late initiation into the PMTCT program. However, it has been noted by them that HIV-positive women who already know their status are becoming pregnant at a high rate, and although the test and start guidelines will enrol more of them into treatment (ART treatment), more effort will be required to improve other factors affecting mother-to-child transmission if eliminination of mother-to-child transmission is to be attained.

The authors noted that their studies was limited by the absence of qualitative data which made them not able to particularly account for the various findings reported in the study. Also, they noted the study solely depended on information obtained from the electronic medical record (EMR) system-backed health facilities and that data from non-EMR facilities which was exempted would have improved upon the analysis made in the study. Although the analysis was basically statistical, their study could have benefited from a mathematical point of view. Estimatation, assessment of cetain vital parameters and future prediction of the number of infected mothers and juveniles enrolled in PMTCT care in western Kenya could have been better assessed and attained by the use of a mathematical model. However, the study outlined the importance of intervention programs such as making sure all pregnant women have knowledge about their HIV status very early and encouraging constant check-ups for HIV-negative mothers in case of any change, increased infant prophylaxis uptake, and informing HIV-positive mothers on appropriate infant feeding practices such as exclusive feeding of juveniles for six month. These intervention strategies which was adopted in western Kenya and outlined by the authors in the study support the assumption stated in our study on survival of HIV infected juveniles into adulthood.

Intervention and control programs and strategies for prevention of vertical transmission of HIV and elimination of vertical transmission have been heavily embarked upon by world authorities to drastically reduce vertical transmission or mother-to-child transmission of HIV globally. Unlike the retrospective studies carried out by Ogala et *al*. [61], Afolabi et *al*. [1], carried out a study to assess the risk of transmission of HIV among HIV-exposed juveniles on follow up

at a PMTCT clinic in an antiretroviral health facility service in western Nigeria. The study was basically a descriptive one performed among HIV-positive mother-juvenile pair receiving treatment and health care service for PMTCT intervention program at a referral health care institution in Ibadan in Nigeria. In the study conducted, the timing of the first HIV-1 PCR-positive test for juveniles was used to determine the means by which the viral transmission of HIV for every mother-juvenile transmission took place. Juvenles who demonstrated a PCR-positive test at birth was concluded to obtain the HIV virus in utero, whiles juveniles were characterized to be infected via breastfeeding if they potrat a PCR-negative at birth and exactly a month of age but PCR-positive after six weeks. A follow-up was carried was carried out on HIV-positive juveniles t six hours after child birth, on the sixth day after birth, and at week six,ten, and fourteen of early life in accordance with WHO guidlines [1]. Surveillance was also carried out on monthly basis until sixth month of age and for every three months untill the the child is 18 month. This is done for juveniles not showing any symptoms. Routine follow-ups are however performed periodically on HIV-negative juveniles to detect any changes in their HIV status. At each ART clinical visits by the paticipants (HIV-positive pregnant women who agreed to this study), blood samples were obtained. Demographical informtion of participants such as age, gestation age, the extent of drug usage, HIV test results, and the occupation of participant were recorded on a structured questionnaire by an attending midwife. Initially, a total of 66 mother-juvnile participants were enrolled for the studies, but a final total of 44 mother-juvenile pairs were present for analysis through out the study carried.

Results from the study showed no correlation between the age of mothers with HIV viral load before and after delivery. It has been noted however that there was an important connection with the year enrolled on ARV and at enrollment to the exposed juveniles follow-up clinic. There was also a strong significant correlation existing between the virl load before and after delivery which was exclusively connected to the mother-to-child transmission of HIV In the study they conducted. The risk of vertical transmission was 50% among juveniles with no prophylaxis in the study conducted. They concluded that there was high HIV prevalence among the exposed juveniles who attended the HIV-exposed

juvenile ARV clinic, and that the determinant factors leading to high risk of HIV infection to juveniles from infected mothers are; late enrollment on PMTCT intervention program, practice of mixed infant feeding as a replacement for exclusive feeding, rural residency and delivery at home. This tends to suggest that better health care services and intervention programs exist and are better sustained and maintained in urban settings than rural settings. Also, due to little education and lack of information in rurral areas on infants feeding practices by infected mothers, the risk of HIV transmission to juveniles is high in this rural areas compared to urban areas where information in widely spread. A child delivered at home by an HIV infected mother without proper health care before and after delivery also have a higher risk of HIV transmission.

The authors contrast, compared and criticized their results with other studies and findings to show the consistency of their work to other studies, however, the use of a low sample space was one of their limitations, they noted that some risk factors which were not clearly captured by the study and therefore neither included nor assessed made it difficult for the generalization of determinants of MTCT of HIV in the study. It could also be argued that a study to assess the burden of HIV infection in the Nigerian population inorder to determine the risk of vertical transmission of HIV to juveniles from infected mothers could have provided proper quantification, estimatation and prediction of the disease burden in the Nigerian population by using a mathematical model which our research has. Also, I believe a mathematical model could have been adopted to reproduce or simulate the ART and prophylaxis uptake by both mother and juveniles for the study. However, Afolabi et *al*. [1], emphasized on the PMTCT intervention strategies by the Nigerian government to prevent vertical transmission such as; providing free tests including ARV certified drugs which will cater for mother and juveniles during child birth at PMTCT health service centers in Nigeria, and enrolling all infected HIV-positive mothers and their familes into antiretroviral treatment as well as monitoring of their immune respond to therapy. This I believe further substantiate the assumption and results in our research work of survival of infected juveniles into adulthood and the control of vertical transmission in the presence of treatment even if the reproduction number through vertical transmission increased.

At first trimester of pregnancy, pregnant women in Ghana are enrolled into antenatal care at a health service facilities. Women with simple pregnancies without complications in Ghana have the opportunity to go for at least four antenatal care visits [79]. Vandeusen et *al*. [78], reported that the various services provided at antenatal visits for expecting mothers include; assessment provision to detect complications such as anemia, hypertension, and bleeding during pregnancy, provision of advice on nutrition whiles execting, provision of immunization, HIV disease testing and counselling, pregnancy progress monitoring, and provision of assessment of the over all welfare of expecting mothers and their fetal state. During each visit by pregnant HIV-positive women, health personnel monitor ART side effects on these women and further assess compliance to treatment by these infected pregnant women.

Vandeusen et *al*. [78], developed a state transition compartmental model consisting of five different stages or states of women and juveniles given as women pregnant for nine months, juveniles who are HIV-positive and breastfeeding, HIV-negative juveniles breastfeeding, women not pregnant and women dead. This model was developed to assess the cost effectiveness of option B+ for prevention of vertical transmission of HIV in Kumasi-Ghana. Pregnant HIV-positive women were the population considered for the study. Each compartment in their model they developed consist of the five states of health associated with either women or juveniles. A time period indicating the amount of time spent in each compartment is indicated below them. Transition from one state to another state is indicated with an arrow associated with key probablity rates of transition. Motivation for the choice of the model was that the model they developed incuded several pregnancies in the economic evaluation of option B+ needed to fully record the extent of the significance of continuous therapy regimens in areas characterized by multiple juveniles which no study have done as to the best of their knowlegde in Ghana. In addition, they stated their work will aid in HIV therapy recommendations for women pregnant in resource limited areas. Transmission rate, life expectancy and compliance rates to ART were obtained from the Ghana Health Service for the study. Estimates for the other parametrs in the model were obtained from published work. The data mainly

used for the study was from patient patronage of two government hospitals in Kumasi-Ghana.

Results from the study indicated that the percentage of women who accessed health care services during the first, second and third trimester were 12%, 40%, and 48% respectively. Through a sensitivity analysis carried out in the research, it has been noted that the most sensitive parameter to the cost of antiretroviral therapy for the infected mother on Option B+ is cost-effectiveness. They noted that option B+ has a projected rate of HIV transmission by the model as 1% during pregnancy, delivery and during breastfeeding compared to option B of projected vertical transmission rate of 10.2% during pregnancy, delivery and 1% through breastfeeding. Consequently, 146 projected juveniles per year would have been infected with option B+ as compared to 841 juveniles infected per year. The authors significantly compared their result which was consistent with other studies on estimating the cost-effectiveness of option B+ as compared to option B.

They concluded that in a deprived or limited resource country as Ghana, Option B+ represents a good value and can potentially provide significant health benefits to HIV-positive women and juveniles particularly in the case where women become pregnant multiple times. They estimated that a total number of 668 newly born juveniles would not be infected yearly in Ghana by HIV, and that intervention strategies against these infections will ultimately reduce the future burden of HIV in the Ghana.

Many models such as [17, 41, 43, 75] considered different factors such as age-structure, sex-structures, incubation period (period from getting the disease and development of symptoms), population density, mixing patterns, variable infectivity, genetic variation, time from infection to AIDS. These models were equipped with these characteristic so as to answer different questions and address important issues associated with the transmission dynamics of HIV / AIDS especially in developing countries and communities where the health care systems are poor.

In this research project, we formulate a model that aims to determine the transmission dynamics of HIV/AIDS and the general impact vertical transmission of the disease will have on HIV/AIDS spreading in Ghana given that horizontal transmission is the only well documented mode of transmission. A non-linear deterministic model that incorporates the vertical and horizontal transmission is formulated. The disease free state and the state at which the disease persists in the population are examined. The analysis of the model is done through the basic reproduction number. The model is fitted to data obtained on HIV/AIDS from the Ghana Health Service in order to estimate, determine and predict current and future trends of the HIV/AIDS epidemics in Ghana. Numerical analysis are carried out as well as sensitivity analysis to determine the parameters that influences the model outputs or the parameters that have major effect on the evasion and invasion of the disease.

Chapter 3

A stage structured model for HIV/AIDS in the presence of vertical transmission. The case of Ghana

3.1 Introduction

In 2017, it was noted that people living with HIV globally was 36.9 million. The total number of infected new HIV cases was 1.8 million (UNAIDS, 2017) [77]. HIV is one of the many viruses that can be transmitted by either horizontal or vertical means. Vertical transmission, occurs during pregnancy, through delivery and after childbirth via breastfeeding by an infected mother to the juvenile (children under 15 years). Horizontal transmission however, occurs via physical contact including sexual contact and by other means (sharing of infected needles used for injection, injecting drugs, tattooing and body piercing). Transmission through sexual and other physical contacts are mainly as a result of contacts between susceptible and infected individuals. HIV strongly affect the economic and social lives of infected individuals and the nation as a whole.

Mother-to-child transmission or vertical transmission have been a mode of transmission of HIV to juveniles for many years. In the absence of any intervention, the transmission rates range from 15% to 45% [63]. In 2005, an estimated 630 0000 - 820 000 infants were newly infected, of whom around 280 000 - 360 000

were infected through breastfeeding [23]. Similarly, in 2006, almost 530 000 infants became newly infected with HIV, 90% of them occured via transmission from mother-to-child (MTCT) before, during or after delivery [11, 24, 26]. Between the period of 2001 and 2012 an estimated 52% reduction of vertical transmission occuring amongst newly born juveniles was recorded [78]. According to Kgosimore and Lungu, [46], maternal viral load and type of delivery are some factors that influence the transmission during delivery. Transmission can also occur through breastfeeding. Globally, 1.8 million juveniles (aged 0-14) are estimated to be having the HIV virus (UNICEF, 2016) [33]. Vertical transmission has accounted for a total of 90% pediatric AIDS cases [1]. The second most common primary cause of death for adolescents in the world is HIV/AIDS. It is also the leading cause of death for adolescents in Africa (WHO, 2014) [34].

The overall number of HIV victims on antiretroviral drugs (ARTs) were 21.7 million in 2017 (UNAIDS, 2017) [77]. Since 2005, the availability of new antiretroviral drugs (ARTs) which offer high efficacy and acceptability and less toxicity, has led to a decrease of HIV related deaths worldwide [39, 54, 68]. Although, progress has been substantial, uncertainties persist concerning the best way to manage the HIV/AIDS disease [30]. For instance in 2011, there were approximately 330 000 new childhood infections, representing a reduction of 43% since 2003. This however, remains unacceptably high. Unfortunately, increased childhood infection rates were observed in Angola, Congo, Equatorial Guinea, and Guinea-Bissau [67].

HIV/AIDS in Ghana was first discovered in the mid 1980s [3]. The disease is generally prevalent among the sexually active age groups. Factors such as traditional beliefs, religious beliefs and ethnic norms play a dtermining role in the how HIV/AIDS is spread in Ghana. The mode of transmission of HIV/AIDS is both sexual and vertical from a mother-to-child [38]. Sexual transmission of the virus in Ghana is via heterosexual intercourse, which accounts for 75 - 80 % of all HIV/AIDS infections. Vertical transmission from a mother-to-child transmission (MTCT) accounts for 15%, and transmission through blood, and blood product accounts for 5% [4]. The primary infecting agent is HIV-1 (94.4 %); 5.1% of all reported cases are with HIV-1 and HIV-2; and in 2003, only 0.5% of all in-

fections were mainly HIV-2 (GHS, 2003) [4]. Although the state of HIV/AIDS in Ghana is not as grievous as in some southern and eastern African countries, data from sentinel sites in the country indicate that prevalence has somewhat stalled at 3.4%, mostly due to high infection rates among young people [38]. The Ministry of Health in Ghana in 2001 established PMTCT intervention program using single-dose nevirapine. However, Option B was adopted in 2011, with a total of 1656 PMTCT sites being started as at December 2012, and about 90% of expecting mothers having access to antenatal health care services in Ghana [78].

Models for HIV/AIDS in Ghana do not incorporate vertical transmission and as a result, may omit the effect of vertical transmission which is significant to the actual impact of HIV/AIDS in the Ghanaian population. In addition, HIV infected juveniles surviving into early adulthood were rarely considered, but now possible for them to survive due to the availability of antiretroviral treatments (ARTs). However, survival to older childhood with untreated vertically acquired HIV infection which was previously considered unusual was noted in Harare, Zimbabwe [28] and a substantial epidemic of HIV/AIDS in older survivors from vertical transmission is emerging in Southern Africa [29]. Consequently, we are intruiged to ask: What will be the long-term transmission dynamics of HIV/AIDS in Ghana in the presence of vertical transmission and what effect will progression from juvenile stage (under or not under treatment) to adulthood have on the transmission dynamics of HIV/AIDS in the long run?, what will be the future trend of HIV/AIDS transmission in the presence of vertical and horizontal transmission in Ghana given current estimates?

Mathematical models have been used to analyze the spread and the control of infectious diseases [69]. Mathematical models with linear and non-linear ordinary or partial differential equations have been formed to analyze the transmission dynamics of HIV/AIDS; see for example [6, 16, 38, 40, 46]. Vertical transmission models or models that incorporate vertically transmission have also been recently used for cost effective studies with regards to intervention strategies, to assess risk of HIV transmission among HIV-exposed juveniles, to identify characteristics leading to vertical transmission HIV from and infected mother to a susceptible juvenile, and to develop a care model for prevention of

vertical transmission to juveniles; see for example [1, 49, 61, 78]. Nyabadza [60] noted that the process of formulating a model to explain the HIV epidemic is usually followed by underlying assumptions and the importance for acquiring data to estimate parameter values for both qualitative and quantitative predictions or projections that can be ultimately compared with observed patterns. The outcomes are significant for health planing purposes and disease management.

In this chapter, we proposed a non-linear deterministic/compartmental stage structured mathematical model of HIV/AIDS infection that is different from other models about this disease in Ghana. First, our model is applied to Ghana. It is fitted to data on infected juveniles and adults from Ghana who are under treatment and not under treatment which has not been done to the best of our knowledge. Second, it captures the vertical transmission of HIV/AIDS and the proportion of infected juveniles who are not under treatment, but survive to early adulthood supported by Ferrand et *al*. [28, 29]. This is under the assumption that, though they are symptomatic and survive the maturation age, they mature into early adulthood to take part in the transmission of the virus. In deprived or resource-limited countries, almost more than 50% of the infeted juveniles die before their second birthday, but with PMTCT intervention programs and control strategies such as early diagnosis of juveniles, early enrollment on anteretroviral prophylaxis and treatment will ultimately prevent opportunistic disease leading to reduction in the mobidity, mortality of juveniles, and consequently increasing their life expectancy [49].

Models with HIV/AIDS dynamics that disregard the overall effects of vertical transmission may not be able to trully take into account the impact of HIV/AIDS in a population [46].

3.2 Model formulation

We consider a mathematical model that describes the dynamics of HIV/AIDS infection between two populations of adults and juveniles.

The juvenile population is made up of susceptible juveniles (S_j), infected juveniles not under treatment (I_j) and those under treatment (T_j) .

Similarly, the adult population is made up of susceptible adults (S_a), infected adults not under treatment (I_a) and those under treatment (T_a) .

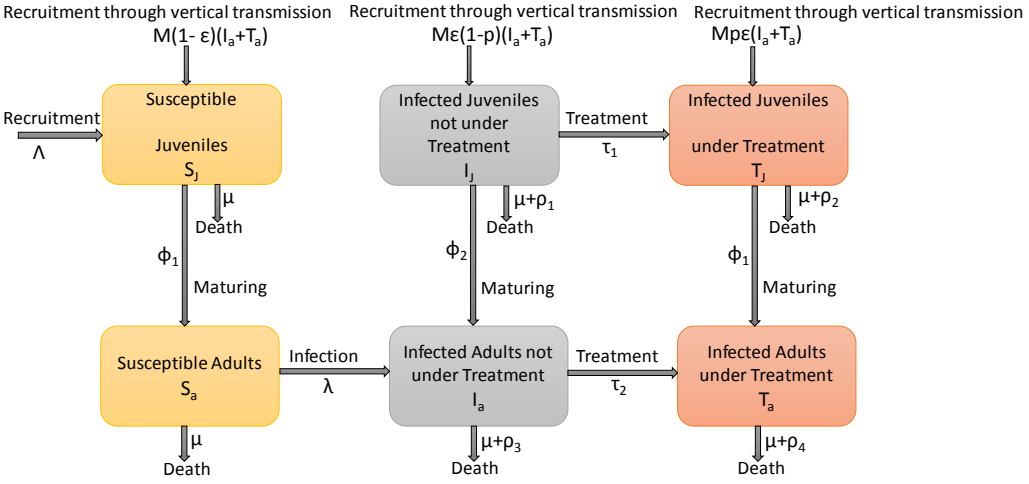

Figure 3.1: Schematic diagram of the stage structure model.

The total adult and juvenile populations N_a and N_j respectively are,

$$N_a = S_a + I_a + T_a, \tag{3.1}$$

$$N_j = S_j + I_j + T_j. \tag{3.2}$$

The susceptible juvenile class is generated by the initial juvenile population Λ. The susceptible juveniles are also generated by recruitment through birth at the rate $\Pi e^{-\mu_0\phi_1}(1-\epsilon)(I_a+T_a)$, where Π is the natural birth rate, ϵ is the fraction of juveniles born with the virus and $e^{-\mu_0\phi_1}$ is the probability of surviving the juvenile stage, taken to be (0-15) years, with μ_0 the natural death rate of juveniles.

We assume the susceptible juveniles after surviving the maturation age, ϕ_1 (15 years) matures to the susceptible adult population and also die naturally at per capita death rate μ. The dynamics of the susceptible juvenile class are given by

$$\dot{S}_j = \Lambda + \Pi e^{-\mu_0 \phi_1}(1-\epsilon)(I_a + T_a) - (\mu + \phi_1)S_j. \tag{3.3}$$

We assume that a proportion p of juveniles born with the virus are subjected to treatment straight after birth, and given they survive the maturation age, progress to the class of infected juveniles under treatment. The infected juveniles under treatment class are recruited at the rate $\Pi e^{-\mu_0 \phi_1} p\epsilon(I_a + T_a)$ and also by the rate τ_1 at which infected juveniles not under treatment move to be under treatment. Like the susceptible juveniles, individuals leave this class by maturing into the infected adults under treatment class at a rate ϕ_1 and also die naturally at per capita death rate μ. The infected juveniles under treatment are assumed to also progress to AIDS with a rate ρ_2. The dynamics of the infected juvenile under treatment class is given by

$$\dot{T}_j = \Pi e^{-\mu_0 \phi_1} p\epsilon(I_a + T_a) + \tau_1 I_j - (\mu + \phi_1 + \rho_2)T_j. \tag{3.4}$$

The infected juveniles not under treatment class is generated by the recruitment rate $\Pi e^{-\mu_0 \phi_1}\epsilon(1-p)(I_a + T_a)$, where $(1-p)$ are the proportion born with the virus, but not subjected to treatment. We assume that susceptible juveniles are not sexually active. We also assume that a significant proportion n of infected juveniles not under treatment though symptomatic, progress to early adulthood to cause infection. Therefore the maturation rate of infected juveniles not under treatment $\phi_2 = n\phi_1$, where $0 < n < 1$. This assumption is supported by [28, 29], where $0 \leq \phi_2 \leq 1$. Juveniles in this class also die naturally at per capita death rate μ. The infected juveniles not under treatment are assumed to also progress to AIDS with a rate ρ_1 . The dynamics of the infected juvenile not under treatment class is given by

$$\dot{I}_j = \Pi\epsilon e^{-\mu_0 \phi_1}(1-p)(I_a + T_a) - (\mu + \phi_2 + \rho_1)I_j. \tag{3.5}$$

Adults are assumed to transmit the infection horizontally and vertically. Infected adults not on treatment and on treatment are assumed to be infectious. Let c be the average number of sexual contacts susceptible adults makes with individuals from both infected adult classes per unit time. Not all contacts might

result in an infection. Suppose $\bar{p}$ is the probability that an infection occurs per contact with an individual from either of the infected adult groups, then the effective transmission rate β is the product $c\bar{p}$. Thus, β is called the effective transmission rate and is given by $\beta = c\bar{p}$. Sexual transmitted diseases like HIV/AIDS are usually driven by a standard incidence force of infection. The force of infection λ is given by $\lambda = \frac{\beta(I_a + \eta T_a)}{N_a}$, where η is the relative infectivity of T_a with respect to I_a.

The susceptible adult class is generated by maturation of susceptible juveniles at the rate ϕ_1. Individuals also leaves this class via per capita natural death rate μ and also by transition into the infected adult class I_a at a rate λS_a, where $\lambda = \frac{\beta(I_a + \eta T_a)}{N_a}$. The dynamics of the susceptible adult class is therefore given by

$$\dot{S}_a = \phi_1 S_j - (\mu + \lambda) S_a. \tag{3.6}$$

The class of the infected adults not under treatment I_a is generated by the maturation of infected juveniles not under treatment at the rate ϕ_2 and the infection of the adults in S_a. Similarly, the infected adults under treatment class are generated by the maturation of infected juveniles under treatment at the rate ϕ_1. Adults not under treatment are treated at a rate τ_2. Both infected adult classes have per capital natural death rate μ. The infected adults not under treatment and under treatment are assumed to also progress to AIDS with a rate ρ_3 and ρ_4, respectively. The dynamics of both infected adult classes are given by

$$\dot{I}_a = \lambda S_a + \phi_2 I_j - (\mu + \tau_2 + \rho_3) I_a, \tag{3.7}$$

$$\dot{T}_a = \tau_2 I_a + \phi_1 T_j - (\mu + \rho_4) T_a. \tag{3.8}$$

The infected individuals (both from I_a and T_a) progress to the AIDS class, which is assumed not to be involved with disease transmission, and thus, taken as redundant.

Let $M = \Pi e^{-\mu_0 \phi_1}$, from the description of the dynamics of each class, the following ordinary differential equations are used to describe the transmission dy-

namics of HIV/AIDS in the presence of vertical transmission.

$$\left.\begin{aligned}
\dot{S}_j &= \Lambda + M(1-\epsilon)(I_a + T_a) - (\mu + \phi_1)S_j, \\
\dot{I}_j &= M\epsilon q(I_a + T_a) - (\phi_2 + \mu + \tau_1 + \rho_1)I_j, \\
\dot{T}_j &= p\epsilon M(I_a + T_a) + \tau_1 I_j - (\phi_1 + \mu + \rho_2)T_j, \\
\dot{S}_a &= \phi_1 S_j - (\mu + \lambda)S_a, \\
\dot{I}_a &= \lambda S_a + \phi_2 I_j - (\mu + \tau_2 + \rho_3)I_a, \\
\dot{T}_a &= \tau_2 I_a + \phi_1 T_j - (\mu + \rho_4)T_a,
\end{aligned}\right\} \tag{3.9}$$

with initial conditons $S_j(0) = S_{j(0)}$, $I_j(0) = I_{j(0)}$, $T_j(0) = T_{j(0)}$, $S_a(0) = S_{a(0)}$, $I_a(0) = I_{a(0)}$, $T_a(0) = T_{a(0)}$, where

$$0 < \eta < 1, \;\; \mu_0 < \mu, 0 < \epsilon < 1, \;\; q = 1 - p, \;\; (1-\epsilon) + \epsilon q + \epsilon p = 1,$$

$$0 < p < 1, \;\; N = S_j + I_j + T_j + S_a + I_a + T_a, \;\; 0 \leq n \leq 1, \;\; \phi_2 = n\phi_1.$$

3.3 Basic properties

Let us define,

$$\begin{aligned}
&Q_1 = \mu + \phi_1, \;\; Q_2 = \mu + \phi_2 + \tau_1 + \rho_1, \;\; Q_3 = \mu + \phi_1 + \rho_2, \\
&Q_4 = \mu + \tau_2 + \rho_3, \;\; Q_5 = \mu + \rho_4.
\end{aligned}$$

We can rewrite the system (3.9) as

$$\left.\begin{aligned}
\dot{S}_j &= \Lambda + M(1-\epsilon)(I_a + T_a) - Q_1 S_j, \\
\dot{I}_j &= M\epsilon q(I_a + T_a) - Q_2 I_j, \\
\dot{T}_j &= p\epsilon M(I_a + T_a) + \tau_1 I_j - Q_3 T_j, \\
\dot{S}_a &= \phi_1 S_j - (\mu + \lambda)S_a, \\
\dot{I}_a &= \lambda S_a + \phi_2 I_j - Q_4 I_a, \\
\dot{T}_a &= \tau_2 I_a + \phi_1 T_j - Q_5 T_a.
\end{aligned}\right\} \tag{3.10}$$

3.3.1 Continuity, positivity, uniqueness and boundedness of solution

For the model system (3.10) to be biologically, mathematically and epidemiologically meaningful, we prove that all the state variables of the model system will remain positive and that the solutions with positive initial conditions will remain positive for all $t > 0$.

Theorem 3.3.1. There exist a unique and bounded solution of the system in a positive invariant set that remains finite $\forall\ t \geq 0$. Thus, the unique solution

$$(S_j(t)I_j(t)T_j(t)S_a(t)I_a(t)T_a(t))$$

of the model system (3.10) defined in the open interval $(0, T)$ with positive initial data will remain positive for all $T > 0$ for the set of initial data

$$(S_j(0), I_j(0), T_j(0), S_a(0), I_a(0), T_a(0)).$$

We now consider the biological feasible region for the system (3.10) which is in $\mathbb{R}^6_+$ and is represented by the invariant region

$$\Omega = \left\{(S_j,\ I_j,\ T_j,\ S_a,\ I_a,\ T_a) \in \mathbb{R}^6_+ : 0 \leq\ N \leq \frac{\Lambda}{\mu - M}\right\},$$

in which the usual local existence, uniquenes and continuity of solutions holds. We note that here, M is always less than μ_0. This result is established by Lemma 3.3.2. The positive invariant can be established given that

$$\begin{aligned}\dot{N} &= \Lambda + M(I_a + T_a) - \mu N \\ &\leq \Lambda + MN - \mu N \\ &= \Lambda + (M - \mu)N.\end{aligned}$$

Integration yields,

$$N(t) \leq \left(N_0 + \frac{\Lambda}{M - \mu}\right)e^{(M-\mu)t} + \frac{\Lambda}{\mu + M}.$$

Lemma 3.3.2. $M < \mu$.

Proof. Suppose $M > \mu$, then

$$\begin{aligned}
\frac{\Pi}{e^{\mu_0\phi_1}} &> \mu, \text{ but } \mu_0 < \mu, \\
\mu &< \frac{\Pi}{e^{\mu_0\phi_1}}, \\
e^{\mu_0\phi_1} &< \frac{\Pi}{\mu} \Rightarrow \mu e^{\mu_0\phi_1} < \Pi \text{ but,} \\
M &= \Pi e^{-(\mu_0\phi_1)} > \Pi e^{-(\mu\phi_1)}, \text{ since } \mu_0 < \mu, \\
N(t) &\leq \frac{\Lambda}{\mu - M} + \left(N_0 - \frac{\Lambda}{\mu - M}\right) e^{-(\mu - M)t},
\end{aligned}$$

we note, as

$$\lim_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu - M}.$$

This means

$$\lim_{t\to\infty} N(t) \leq \frac{\Lambda}{\mu - M} < 0,$$

which is a contradiction, therefore $M < \mu$.

□

Proposition 3.3.3. The domain Ω is positively invariant. That is, the solution of system (3.10) is positive and remains or stays in Ω for all positive time, given initial conditions in Ω.

Proof. Applying Birkhoff's theorem [14], the right hand side (R.H.S) of the model system (3.10) is continuous and therefore, the partial derivtives exist and are continuous. Hence, our model has a unique solution in $\mathbb{R}^6_+$ for $t \in [0, \infty)$ and

the positive initial conditions.

We thus have

$$\left.\begin{aligned}
\dot{S}_j &\geq S_j(0)e^{-Q_1 t} > 0,\\
\dot{I}_j &\geq I_j(0)e^{-Q_2 t} > 0,\\
\dot{T}_j &\geq T_j(0)e^{-Q_3 t} > 0,\\
\dot{S}_a &\geq S_a(0)e^{-(\mu+\lambda)t} > 0,\\
\dot{I}_a &\geq I_a(0)e^{-Q_4 t} > 0,\\
\dot{T}_a &\geq T_a(0)e^{-Q_5} > 0.
\end{aligned}\right\} \tag{3.11}$$

It follows that

$$\lim_{t\to\infty} S_j(t) \geq 0,$$

and therefore

$$S_j(t) \geq 0, \ \ \forall t > 0.$$

Similarly, as $\lim_{t\to\infty}$, $I_j(t)$, $T_j(t)$, $S_a(t)$, $I_a(t)$ and $T_a(t)$ are all positive for all $t > 0$ as likewise, $\lim_{t\to\infty}$, $I_j(t)$, $T_j(t)$, $S_a(t)$, $I_a(t)$ and $T_a(t) \geq 0\ \forall t > 0$. Thus, for all time $t > 0$, the solution exist. Therefore the solutions of the model system remains in Ω for all positive time. The model system (3.10) is, therefore mathematically, epidemiologically and biologically well posed.

□

3.4 Steady states

To obtain the steady states, we set the right hand side of the model system (3.10) to zero. It is easy to note that the model system (3.10) has one infection-free state (i.f.s) in the positive feasible region $\mathbb{R}^6_+$ given as

$$E^0 = \Big(\frac{\Lambda}{Q_1}, \frac{\phi_1\Lambda}{\mu Q_1}, 0, 0, 0, 0\Big).$$

From the second and third equation of the model system (3.10), we obtain

$$I_j^* = \nu_1(I_a^* + T_a^*), \text{ where } \nu_1 = \frac{M\epsilon q}{Q_2},$$
$$T_j^* = \nu_2(I_a^* + T_a^*), \text{ where } \nu_2 = \frac{M\epsilon p + \nu_1\tau 1}{Q_3},$$
$$\text{we can rewrite } \nu_2 \text{ as } \nu_2 = \frac{M\epsilon(pQ_2 + q\tau 1)}{Q_2Q_3}.$$

From the sixth equation of the model system (3.10),

$$T_a^* = \nu_3 I_a^*, \text{ where } \nu_3 = \frac{\tau_2 + \phi_1\nu_2}{Q_5 - \phi_1\nu_2}.$$

Rewritting ν_3, we have

$$\nu_3 = \frac{Q_2Q_3\tau 2 + M\epsilon(pQ_2 + q\tau_1)\phi_1}{Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2 + q\tau 1)},$$

and hence

$$\nu_3 = \frac{Q_2Q_3\tau 2 + M\epsilon(pQ_2 + q\tau_1)\phi_1}{Q_2Q_3Q_5(1 - R_v)},$$

where

$$R_v = \frac{\phi_1(p\epsilon MQ_2 + \tau_1 M\epsilon q)}{Q_2Q_3Q_5} \text{ with } 0 < R_v < 1. \tag{3.12}$$

R_v is referred to as the reproduction number that drives vertical transmission. It can be noted from equation (3.12) that R_v is always less than unity. Thus, $R_v < 1$, therefore the epidemiological explanation to $R_v < 1$ is that the reproduction number through vertical transmission of HIV/AIDS cannot lead to the disease invasion in a population. That is, no epidemics will occur as long as $R_v < 1$. The goal therefore is to study the over all impact R_v has on the spread of HIV/AIDS in a population.

We can rewrite I_j^*, T_j^*, S_j^* in terms of I_a^* as

$$\begin{aligned} I_j^* &= \nu_1(1+\nu_3)I_a^*, \\ T_j^* &= \nu_2(1+\nu_3)I_a^*, \\ S_j^* &= \frac{\Lambda}{Q_1} + \nu_4 I_a^*, \end{aligned}$$

where

$$\nu_4 = \frac{M(1-\epsilon)(1+\nu_3)}{Q_1},$$

that is

$$\nu_4 = \frac{M(1-\epsilon)}{Q_1(1-R_v)} + \frac{M(1-\epsilon)\tau_2}{Q_1Q_5(1-R_v)}.$$

The force of infection of the model system (3.10) can be expressed as

$$\lambda^* = \frac{\beta(1+\eta\nu_3)I_a^*}{S_a^* + (1+\eta\nu_3)I_a^*},$$

that is

$$\lambda^* = \psi\frac{I_a^*}{N_a^*}, \text{ where } \psi = \beta(1+\eta\nu_3).$$

From $\dot{I}_a^*$, $I_a^* = 0$, corresponding to the infection-free state, or

$$\begin{aligned}\psi\frac{S_a^*}{N_a^*} &= Q_4 - \phi_2\nu_1(1+\nu_3),\\ \frac{S_a^*}{N_a^*} &= \frac{Q_4 - \phi_2\nu_1(1+\nu_3)}{\psi},\\ S_a^* &= \frac{(1+\nu_3)}{\mathfrak{R}_o - 1}I_a^*,\end{aligned}$$

where

$$\mathfrak{R}_o = \frac{\psi}{Q_4 - \phi_2\nu_1(1+\nu_3)},$$

that is

$$\mathfrak{R}_o = \frac{\beta(Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2+q\tau_1)) + \eta\beta(Q_2Q_3\tau 2 + M\epsilon\phi_1(pQ_2+q\tau_1))}{Q_4(Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2+q\tau_1)) - M\epsilon qQ_3(Q_5+\tau_2)\phi_2}.$$

We can rewrite the equation $\dot{S}_a$ and solve for I_a^*. Thus

$$\phi\left(\frac{\Lambda}{Q_1}\right) + \phi_1\nu_4 I_a^* - \frac{\psi}{\mathfrak{R}_o}I_a^* = 0, \tag{3.13}$$

$$I_a^* = \frac{\mathfrak{R}_o(\mathfrak{R}_o - 1)\phi_1\Lambda}{Q_1(\mu\mathfrak{R}_o(1+\nu_3) + (\mathfrak{R}_o - 1)\beta(1+\eta\nu_3)(1-\theta_2))}, \tag{3.14}$$

where

$$\theta_2 = \frac{M(1-\epsilon)\phi_1}{Q_1Q_4(1-\omega)} + \frac{M(1-\epsilon)\tau_2\phi_1}{Q_1Q_4Q_5(1-\omega)}, \text{ and,}$$

$$\omega = \frac{M\epsilon p\phi_1}{Q_1Q_3Q_5} + \frac{M\epsilon q\tau_1\phi_1}{Q_1Q_2Q_3Q_5} + \frac{M\epsilon q\phi_2}{Q_1Q_2Q_4} + \frac{M\epsilon q\tau_2\phi_2}{Q_1Q_2Q_4Q_5}.$$

We can note that ω and θ_2 are all positive fractions. Hence, $0 < \omega < 1$, $0 < \theta_2 < 1$.

The endemic steady state expressed in terms of I_a^* are given by the following components.

$$\begin{aligned}
S_j^* &= \frac{\Lambda}{Q_1} + \frac{\nu_4(1+\nu_3)\Re_o(\Re_o-1)\phi_1\Lambda}{Q_1(\mu\Re_o(1+\nu_3)+(\Re_o-1)\beta(1+\eta\nu_3)(1-\theta_2))},\\
S_a^* &= \frac{\phi_1\Lambda\Re_o(1+\nu_3)}{Q_1(\mu\Re_o(1+\nu_3)+(\Re_o-1)\beta(1+\eta\nu_3)(1-\theta_2))},\\
I_a^* &= \frac{\Re_o(\Re_o-1)\phi_1\Lambda}{Q_1(\mu\Re_o(1+\nu_3)+(\Re_o-1)\beta(1+\eta\nu_3)(1-\theta_2))},\\
T_a^* &= \frac{\phi_1\Lambda\Re_o(\Re_o-1)\nu_3}{Q_1(\mu\Re_o(1+\nu_3)+(\Re_o-1)\beta(1+\eta\nu_3)(1-\theta_2))},\\
I_j^* &= \frac{\phi_1\Lambda\Re_o(\Re_o-1)\nu_1(1+\nu_3)}{Q_1(\mu\Re_o(1+\nu_3)+(\Re_o-1)\beta(1+\eta\nu_3)(1-\theta_2))},\\
T_j^* &= \frac{\phi_1\Lambda\Re_o(\Re_o-1)\nu_2(1+\nu_3)}{Q_1(\mu\Re_o(1+\nu_3)+(\Re_o-1)\beta(1+\eta\nu_3)(1-\theta_2))}.
\end{aligned} \tag{3.15}$$

We have

$$\lambda^* = \frac{Q_4Q_5(1-R_v)(1-\theta_3)(\Re_o-1)}{\Re_o(Q_5+\tau_2)},$$

where $\theta_3 = \dfrac{M\epsilon q(Q_5+\tau_2)\phi_2}{Q_2Q_4Q_5(1-R_v)}$, and $0 < \theta_3 < 1$ with $R_v < 1$.

The model system (3.10), therefore has exactly two steady states, the infection-free state (i.f.s), given by

$$E^0 = \left(S_j^0, I_j^0, T_j^0, S_a^0, I_a^0, T_j^0\right) = \left(\frac{\Lambda}{Q_1},\ 0,\ 0,\ \frac{\phi\Lambda}{\mu Q_1},\ 0,\ 0\right), \tag{3.16}$$

and the persistent state also commonly known as the endemic state, given as

$$E^* = \left(S_j^*,\ I_j^*,\ T_j^*,\ S_a^*,\ I_a^*,\ T_j^*\right). \tag{3.17}$$

We thus have the following result on the persistent equilibrium.

Theorem 3.4.1. The persistent equilibrium E^* exist if $\mathfrak{R}_o > 1$.

The basic reproduction number $\mathfrak{R}_o$ is computed in the next section.

3.5 Basic reproduction number with next generation matrix

Considering the next generation method for analysis with the model system (3.10), we have

$$F = \begin{bmatrix} 0 \\ 0 \\ \Lambda S_a \\ 0 \end{bmatrix}, V = \begin{bmatrix} Q_2 I_j - M\epsilon q(I_a + T_a) \\ Q_3 T_j - \tau_1 I_j - p\epsilon M(I_a + T_a) \\ Q_4 I_a - \phi_2 I_j \\ Q_5 T_a - \phi_1 T_j - \tau_2 I_a \end{bmatrix}.$$

Rewritting F and V with $\lambda = \dfrac{\beta(I_a + \eta T_a)}{N_a}$,

$$F = \begin{bmatrix} 0 \\ 0 \\ \dfrac{\beta(I_a + \eta T_a)}{N_a} \\ 0 \end{bmatrix}, V = \begin{bmatrix} Q_2 I_j - M\epsilon q(I_a + T_a) \\ Q_3 T_j - \tau_1 I_j - p\epsilon M(I_a + T_a) \\ Q_4 I_a - \phi_2 I_j \\ Q_5 T_a - \phi_1 T_j - \tau_2 I_a \end{bmatrix}.$$

Finding the derivate of the F and V matrices with respect to the state variables and at the infection-free state (3.16), we have the F and V matrices as

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & \beta & \eta\beta \\ 0 & 0 & 0 & 0 \end{bmatrix}, V = \begin{bmatrix} Q_2 & 0 & -M\epsilon q & -M\epsilon q \\ -\tau_1 & Q_3 & -p\epsilon M & -p\epsilon M \\ -\phi_2 & 0 & Q_4 & 0 \\ 0 & -\phi_1 & -\tau_2 & Q_5 \end{bmatrix}.$$

We note that FV^{-1} is given by

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ e_1 & e_2 & e_3 & e_4 \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

The effective reproduction number is the spectral radius of FV^{-1} given by

$$\mathfrak{R}_o = \rho(FV^{-1}) = e_3,$$

and

$$e_3 = \frac{\beta(Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2 + q\tau_1)) + \eta\beta(Q_2Q_3\tau 2 + M\epsilon\phi_1(pQ_2 + q\tau_1))}{Q_4(Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2 + q\tau_1)) - M\epsilon qQ_3(Q_5 + \tau_2)\phi_2}.$$

Therefore

$$\mathfrak{R}_o = \frac{\beta(Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2 + q\tau_1)) + \eta\beta(Q_2Q_3\tau 2 + M\epsilon\phi_1(pQ_2 + q\tau_1))}{Q_4(Q_2Q_3Q_5 - M\epsilon\phi_1(pQ_2 + q\tau_1)) - M\epsilon qQ_3(Q_5 + \tau_2)\phi_2}. \tag{3.18}$$

Simplifying $\mathfrak{R}_o$ gives us

$$\mathfrak{R}_o = \frac{\beta}{Q_4(1-\theta_3)} + \frac{\eta\beta(\tau_2 + Q_5\theta_1)}{Q_4Q_5(1-R_v)(1-\theta_3)}, \tag{3.19}$$

where

$$\theta_3 = \frac{M\epsilon q\phi_2}{Q_2Q_4(1-R_v)} + \frac{M\epsilon q\tau_2\phi_2}{Q_2Q_4Q_5(1-R_v)}, \text{ and } 0 < \theta_3 < 1.$$

The reproduction number $\mathfrak{R}_o$ is hence expressed as a function of R_v in (3.19). Clearly if R_v increases $\mathfrak{R}_o$ also increases.

3.5.1 Reproduction numbers of the model

3.5.1.1 Sexual transmission (Horizontal transmission)

We adopt similar approach by Kgosimore and Lungu, [46], to analyse the reproduction numbers of the model system (3.10).

Without mother-to-child transmission (MTCT), $\epsilon = 0$. Which means that $R_v = 0$ and $\theta_3 = 0$. Therefore $\mathfrak{R}_o$ becomes

$$\mathfrak{R}_o = \frac{\beta}{Q_4} + \frac{\eta\beta\tau_2}{Q_4Q_5}. \tag{3.20}$$

Here, $\mathfrak{R}_o$ is the basic reproduction number for horizontal transmission.

Let the average number individuals in the infected class I_a infects during their duration of infectiousness be denoted as $R_1 = \frac{\beta}{\mu+\rho_3}$ and the average number individuals in the infected class T_a infects during their duration of infectiousness be denoted as $R_2 = \frac{\eta\beta}{\mu+\rho_4}$.

From equation (3.20), we have that

$$\frac{d\mathfrak{R}_o}{d\beta} = \frac{1}{Q_4(1-\theta_3)} + \frac{\eta(\tau_2 + Q_5R_v)}{(Q_4Q_5(1-R_v)(1-\theta_3))^2},$$

$$\frac{d\mathfrak{R}_o}{d\tau_2} = \frac{-(\mu+\rho_3)(\beta-R_2)}{(\mu+\tau_2+\rho_3)^2}.$$

This informs us that $\mathfrak{R}_o$ is monotonic increasing function of β and a decreasing function of τ_2 if and only if $\beta - R_2 > 0$, which implies, $\beta > R_2$. Therefore $\mathfrak{R}_o > \beta > R_2$ is a prerequisite condition that needs to be satisfied in order to slow the spread of the disease.

The optimal treatment value to reduce the reproduction number below unity is given as

$$\tau_2^* = \frac{(\mu+\rho_4)(\beta-(\mu+\rho_3))}{(\mu+\rho_4)-\eta\beta},$$

that is

$$\tau_2^* = \frac{(\mu+\rho_3)(R_1-1)}{(1-R_2)}.$$

We have that $\tau_2^* > 0$ provided $R_1 > 1$ and $R_2 < 1$. We can therefore find $\tau_2^* > \tau_2$ such that, as long as $R_1 > 1 > R_2$, the intervention strategy (treatment) can be applied to reduce the disease burden in the population.

3.5.1.2 Mother-to-child transmission (MTCT) (Vertical transmission)

Since MTCT is mainly from infected mothers by some factors during and after child birth, the impact of MTCT can be investigated by looking at the dependence of the basic reproduction number on the reproduction number through vertical transmission. Thus the dependence of $\mathfrak{R}_o$ on R_v. Finding the derivative of $\mathfrak{R}_o$ in equation (3.19) with respect to R_v, we have

$$\frac{d\mathfrak{R}_o}{dR_v} = \frac{(Q_5+\tau_2)}{Q_4(1-\theta_3)(1-R_v)^2}\mathfrak{R}_2.$$

This implies $\mathfrak{R}_o$ is strictly a monotonic increasing function of R_v.

Let

$$R_v{}^* = \frac{Q_4((1-\theta_3) - \mathfrak{R}_o)}{Q_4(1-\theta_3) + (\eta\beta - \beta)},$$

be the critical vertical transmission threshold number which must not be surpass if we want to control the disease. We note that $\eta\beta - \beta > 0$ and $(1-\theta_3) > 0$, since $R_v < 1$. By assymption, it can be seen that there is an $R_v{}^*$ for $\mathfrak{R}_o < 1$ and $\eta\beta > \beta$ such that the impact of MTCT would be negligible for values $R_v < R_v{}^*$.

3.5.2 Local stability of infection free state

Local asymptotic stability of the infection-free equilibrium can be deduced by computing the model system (3.10) at the infection-free state E^0 using the jacobian matrix J. We therefore have

$$J_{E^0} = \begin{pmatrix} -Q_1 & 0 & 0 & 0 & M(1-\epsilon) & M(1-\epsilon) \\ 0 & -Q_2 & 0 & 0 & M\epsilon q & M\epsilon q \\ 0 & \tau_1 & -Q_3 & 0 & p\epsilon M & p\epsilon M \\ \phi_1 & 0 & 0 & -\mu & -\beta & -\eta\beta \\ 0 & \phi_2 & 0 & 0 & \beta - Q_4 & \eta\beta \\ 0 & 0 & \phi_1 & 0 & \tau_2 & -Q_5 \end{pmatrix}$$

After expanding the determinant of the characterisitc equation $|J_{E^0} - \lambda l| = 0$ around column 1 row 1 and column 4 row 4, we have two eigenvalues $\lambda_1 = -Q_1$ and $\lambda_2 = -\mu$. The remaining of the eigenvalues are determined by the 4

x 4 matrix, given by the jacobian matrix with the infected classes only, namely $I_a,\ T_a,\ I_j,\ T_j$. Hence, the 4 x 4 matrix is

$$\begin{pmatrix} -Q_2 & 0 & M\epsilon q & M\epsilon q \\ \tau_1 & -Q_3 & p\epsilon M & p\epsilon M \\ \phi_2 & 0 & \beta - Q_3 & \eta\beta \\ 0 & \phi_1 & \tau_2 & -Q_5 \end{pmatrix},$$

whose characteristic equation is given by $|J_{E^0} - \lambda|$,

$$\begin{vmatrix} -Q_2 & 0 & M\epsilon q & M\epsilon q \\ \tau_1 & -Q_3 & p\epsilon M & p\epsilon M \\ \phi_2 & 0 & \beta - Q_3 & \eta\beta \\ 0 & \phi_1 & \tau_2 & -Q_5 \end{vmatrix} = 0.$$

The remaining eigenvalues are given by the quartic polynomial equation

$$P(\lambda) = a_0\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0,$$

where

$$\begin{aligned} a_0 &= 1, \\ a_1 &= Q_2 + Q_3 + Q_4 + Q_5 - \beta, \\ a_2 &= w_1 - (\beta(Q_2 + \mu + Q_1 + \eta\tau_2), \\ a_3 &= w_2 - \beta(\eta\tau_2(Q_2 + Q_3) - Q_2Q_3 + Q_5(Q_2 + Q_3), \\ a_4 &= k(1 - \mathfrak{R}_o), \end{aligned}$$

and

$$w_1 = Q_3Q_5(1-\psi_1) + Q_2Q_4(1-\psi_2) + (Q_2+Q_4)(Q_3+Q_5),$$

where

$$\psi_1 = \frac{M\epsilon p\phi_1}{Q_3Q_5},$$

$$\psi_2 = \frac{M\epsilon q\phi_2}{Q_2Q_4},$$

and $0 < \psi_1 < 1, 0 < \psi_1 < 1,$

$w_2 = Q_2Q_3Q_5(1-R_v)Q_2Q_4Q_5(1-\theta_3) + Q_4(Q_3Q5(1-\psi_1)) + Q_3(Q_2Q_4(1-\psi_2)) + p\epsilon M(\beta-\eta\beta)\phi_1.$

We notice from w_2 that $\beta > \eta\beta$ since $0 < \eta < 1$.

$$K = Q_2Q_3Q_4Q_5(1-R_v)(1-\theta_3).$$

To show that the infection-free state is locally asymptotically stable, we show that $P(\lambda) = 0$ lies in the left half plane (has only negative roots) using the Routh-Hurwitz conditions for dimension four. We notice that $\Re_o < 1$ correspond to $a_4 > 0$, where k is positive given $R_v < 1$. Thus when $\Re_o < 1$, $a_4 > 0$.

The condition $\Re_o < 1$ also gives $Q_2 + Q_3 + Q_4 + Q_5 + \mu > \beta$, hence $a_1 > 0$. Similarly, the condition $\Re_o < 1$ also gives $w_1 > \beta(Q_2 + \mu + Q_1 + \eta\tau_2)$. We also note that $w_2 > \beta(\eta\tau_2(Q_2 + Q_3) - Q_2Q_3 + Q_5(Q_2 + Q_3))$ when $R_v < 1$ with the condition $\Re_o < 1$. It means that $a_2 > 0$ and $a_3 > 0$.

We use the Routh-Hurwitz conditions for quartic equations to make our analysis, thus $a_i > 0$ for $i = 0, 1, 2, 3, 4$, $a_1a_2 - a_0a_3 > 0$ and $a_1a_2a_3 - a_1^2a_4 - a_0a_3^2 > 0$. We note here that all the coefficients of the polynomial $P(\lambda) = 0$ are greater than zero. That is $a_1 > 0$, $a_2 > 0$, $a_3 > 0$ and $a_4 > 0$. We now state the theory of local stability of the infection-free state E^0 using the Routh-Hurwitz conditions.

Theorem 3.5.1. Let $R_v < 1$. The infection-free state E^0, whenever it exists, is locally asymptotically stable (l.a.s) for $\Re_o < 1$ provided that $a_1a_2 - a_0a_3 > 0$ and $a_1a_2a_3 - a_1^2a_4 - a_0a_3^2 > 0$ otherwise it is unstable.

It can also be established by considering the fact that the reproduction number was determined by the next generation matrix approach.

3.5.2.1 Global stability of infectious free state

We show that the infectious-free state (3.16) of the model system (3.10) is globally asymtotically stable (g.a.s). We adapt the concept of Lyapunov in (1.6.4).

Theorem 3.5.2. If $\Re_o \leq 1$, then the infectious-free state is globally asymptotically stable (g.a.s) on Ω.

Proof. Let us define a lyapunov function **v** as

$$\mathbf{v}(I_j, T_j, I_a, T_a) = I_a + b_1I_j + b_2T_j + b_3T_a.$$

Where

$$b_1 = \frac{\beta\eta\tau_1\phi_1(Q_3Q_5(1-\psi_1))\phi_2}{Q_2Q_3Q_5(1-R_v)},$$

$$b_2 = \frac{\phi_1(\eta\beta Q_2 + M\epsilon q\phi_2)}{Q_2Q_3Q_5(1-R_v)},$$

$$b_3 = \frac{Q_3(\eta\beta Q_2 + Mq\epsilon\phi_2)}{Q_2Q_3Q_5(1-R_v)}.$$

Since, the state solutions of the model system (3.10) are positive, we have that $Q_2Q_3Q_5(1-R_v) > 1$. Therefore constants b_1, b_2, b_3, are all positive for $R_v < 1$ at the infection-free state.

We take the partial derivative of $\mathbf{v}$ with respect to t. Thus,

$$\frac{\partial \mathbf{v}}{\partial t} = \frac{\partial \mathbf{v}}{\partial I_a}\dot{I}_a + \frac{\partial \mathbf{v}}{\partial I_j}\dot{I}_j + \frac{\partial \mathbf{v}}{\partial T_j}\dot{T}_j + \frac{\partial \mathbf{v}}{\partial T_a}\dot{T}_a.$$

We therefore have

$$\dot{\mathbf{v}} = \lambda S_a + \phi_2 I_j - Q_4 Ia + b_1(M\epsilon q(I_a + T_a) - Q_2 I_j) + b_2(P\epsilon M(I_a + T_a) + \tau_1 I_j - Q_3) + b_3(\tau_2 I_a + \phi_1 T_j - Q_5 T_a),$$

$$\dot{\mathbf{v}} = \frac{\beta(I_a + \eta T_a)}{N_a} S_a + \phi_2 I_j - Q_3 Ia + b_1(M\epsilon q(I_a + T_a) - Q_2 I_j) + b_2(P\epsilon M(I_a + T_a) + \tau_1 I_j - Q_3) + b_3(\tau_2 I_a + \phi_1 T_j - Q_5 T_a),$$

Given that at the infection-free state, $\frac{S_a}{N_a} \leq 1$, we have

$$\dot{\mathbf{v}} = I_a(\beta + b_1 M\epsilon q + b_2 M\epsilon p + b_3\tau_2 - Q_4) + T_a(\eta\beta + b_1 M\epsilon q + b_2 p\epsilon M - b_3 Q_5)$$

we have an expression in only I_a after simplifying and substituting b_1, b_2, b_3,

$$\dot{\mathbf{v}} = \left[\frac{\beta(Q_2Q_3Q_5 - M\epsilon\phi_1(q\tau_1 + pQ_2))}{Q_2Q_3Q_5 - M\epsilon(pQ_2 + q\tau_1)\phi_1} + \frac{\eta\beta(Q_2Q_3\tau_2 + M\epsilon\phi_1(q\tau_1 + pQ_2))}{Q_2Q_3Q_5 - M\epsilon(pQ_2 + q\tau_1)\phi_1} - \left(\frac{Q_4(Q_2Q_3Q_5 - M\epsilon\phi_1(q\tau_1 + pQ_2)) - M\epsilon qQ_3(Q_5 + \tau_2)\phi_2}{Q_2Q_3Q_5 - M\epsilon(pQ_2 + q\tau_1)\phi_1}\right)\right] I_a,$$

$$\dot{\mathbf{v}} = \left[\beta + \frac{\eta\beta(\tau_2 + Q_5R_v)}{Q_5(1 - R_v)} - Q_4(1 - \theta_3)\right] I_a,$$

$$\dot{\mathbf{v}} = \Gamma(\mathfrak{R}_o - 1)I_a,$$

where $\Gamma = Q_4(1 - \theta_3)$.

Γ is positive since, $0 < \theta_3 < 1$, when $R_v < 1$. All the model parameters are positive and the state variables are non-negative, therefore it follows that $\dot{\mathbf{v}} \leq 0$ for $\mathfrak{R}_o \leq 1$ with $\dot{\mathbf{v}} = 0$ if and only if $I_a = 0$ or $\mathfrak{R}_o = 1$. Therefore $\dot{\mathbf{v}}$ is a lyapunov function on Ω. Since, the set is compact, positively invariant, we deduce by LaSalle's Invariance Principle (1.6.5) that

$$(I_a,\ T_a,\ I_j,\ T_j) \to (0,\ 0,\ 0,\ 0), \tag{3.21}$$

therefore the infectious-free state in globally asymptotically stable.

We know that since

$$\lim_{t\to\infty} \sup I_a = 0,$$

and

$$\lim_{t\to\infty} \sup T_a = 0,$$

it suffice that for adequately small $\bar{\gamma} > 0$ there exist constant A_1 and A_2 such that

$$\lim_{t\to\infty} \sup I_a \leq \bar{\gamma}$$

for all $t > A_1$ and

$$\lim_{t\to\infty} \sup T_a \leq \bar{\gamma}$$

for all $t > A_2$. Hence, from the second equation in the model system (3.10), we have that for $t > \max\{A_1, A_2\}$

$$\dot{I}_j \leq 2M\epsilon q\bar{\gamma} - Q_1 I_j, \tag{3.22}$$

thus by comparison theorem [70],

$$I_j^{\infty} = \lim_{t\to\infty} \sup I_j \leq \frac{2M\epsilon q\bar{\gamma}}{Q_1}, \tag{3.23}$$

so that if $\bar{\gamma} \to 0$,

$$I_j^{\infty} = \lim_{t\to\infty} \sup I_j \leq 0. \tag{3.24}$$

Similarly, it can be shown that

$$I_{j\infty} = \lim_{t\to\infty} \sup I_j \geq 0, \tag{3.25}$$

by (3.24) and (3.25),

$$I_j^{\infty} \leq 0 \leq I_{j\infty}, \tag{3.26}$$

which implies

$$\lim_{t\to\infty} I_j = 0. \tag{3.27}$$

It can also be shown that

$$T_j^{\infty} \leq 0 \leq T_{j\infty}, \tag{3.28}$$

and that

$$\lim_{t\to\infty} T_j = 0, \tag{3.29}$$

likewise

$$\lim_{t\to\infty} S_{j(t)} = \frac{\Lambda}{Q_1}, \tag{3.30}$$

$$\lim_{t\to\infty} S_{a(t)} = \frac{\phi\Lambda}{\mu Q_1}. \tag{3.31}$$

Therefore it suffice that from (3.21), (3.27), (3.29), (3.30), (3.31) as $\lim_{t\to\infty}$ (for $\Re_o < 1$), all solution of the model system (3.10) with positive initial conditions in Ω approaches the infection-free state E^0.

3.5.3 Existence of persistent state

The model system (3.10) is said to be uniformly or consistently persistent if there exist a constant c such that

$$\lim_{t\to\infty} S_{j(t)} > c, \quad \lim_{t\to\infty} I_{j(t)} > c,$$

$$\lim_{t\to\infty} T_{j(t)} > c, \quad \lim_{t\to\infty} S_{a(t)} > c,$$

$$\lim_{t\to\infty} I_{a(t)} > c, \quad \lim_{t\to\infty} T_{a(t)} > c,$$

provided $(S_j(0),\ S_a(0),\ I_j(0),\ T_j(0),\ I_a(0),\ T_a(0) \in \Omega^o)$, where Ω^o is the interior of Ω. The constant c does not depend on the initial conditions in Ω.

Theorem 3.5.3. Assume that $\mathfrak{R}_o > 1$ then the model system (3.10) is persistent in Ω^o

Proof. The theorem can be proved by applying a persistence result in [32] and by using the approach use to prove Proposition 3.3 of [48]. Given that $\mathfrak{R}_o > 1$, it follows that the model system (3.10) is persistent ; by applying Theorem 2.8.6 in [71], we have that the model system (3.10), has at least one persistent state in Ω^o. We establish the following result.

Lemma 3.5.4. Whenever $\mathfrak{R}_o > 1$, we have at least one persistent state given by E^*.

□

3.6 Numerical simulations

3.6.1 Estimation of Parameters

In this section, we give the results of numerical simulations for the model system (3.10). The life expectancy of Ghana from [66] is 62.4 giving us the death rate μ as 0.016. Only a handful of parameters are known, it is therefore imperative to estimate the others. The estimation process seeks to find the best concordance between the observed and computed data. To illustrate the usefulness of the model system (3.10), we determined the population dynamics of the juvenile and adult population when the reproduction number $\mathfrak{R}_o$ is less than

one and when it is greater than one. These simulations were done in Matlab. Least squares-curve fitting method in Matlab was used to estimate parameters that gave the best fit. The unknown parameter values in the Matlab codes are allocated upper and lower bounds. Parameter values that gave the best fit were obtained from within the bounds. The range of the parameter values and their sampled values used in the simulations and data fitting are shown in Table 3.1. The initial populations for juveniles and adult were estimated close to the population of Ghana [66]. That is, $SJ0 = 10000000$, $SA0 = 18000000$. Recruitment Λ was taken to be 1600000.

In Figure 3.2, we note that the model approaches the stable infection free HIV state. The infected populations asymptotically converge to zero while the susceptible adult population increases and susceptible juvenile population decreases as a result of progression to adulthood (susceptible adult population). This is a graphical description of the fact that the infection-free state is locally stable for $\mathfrak{R}_o < 1$ and unstable otherwise.

We observe in Figure 3.3 that the populations are at a stable endemic state where both susceptible populations decreases asymptotically to zero. This is also a graphical description of the fact that the persistent state is locally stable for $\mathfrak{R}_o > 1$ and unstable otherwise.

From Figure 3.4, we can notice that the population variables of the model system (3.10) bifurcates from the stable infection free state to the persistent state as the effective transmission rate β is maximized. This confirms result from the analysis on the model reproduction number that in the absence of vertical transmission 3.20, $\mathfrak{R}_o$ is an increasing function of β and a decreasing function of τ_2. Biologically, this makes sense as one would expect the reproduction number $\mathfrak{R}_o$ to increase as the transmission rate increases. Thus, in this abscence of these intervention programs, the graphical representation shows the disease will continue to rise. This may be due to a number of reasons such as high sexual risk behaviours, increase in sexual partners, low usage of condoms among others. The effective transmission rate β is also an important indicative parameter in a population. Apart from the reproduction number $\mathfrak{R}_o$, it gives detailed insight

into the sexual behaviour of individuals in a population.

Figure 3.5 shows that the model bifurcates from the stable persistent state to the stable infection free state. The biological implication of this is that as more individuals are enrolled in treatment, the density of the infected population reduces since their viral load is significantly suppressed. This will eventually reduce the number of secondary infections caused by individuals from this population. This tends to suggest that enrolling more people into treatment together with high compliance to other intervention measures will significantly reduce the reproduction number. It suffice that individuals attitude towards HIV diagnosis must be encouraged. Their attitude towards treatment must also be improved. Continuos education on HIV treatment, sensitization, making ARTs affordable to infected HIV individuals must be enhanced to reduce the burden of HIV in Ghana. Also, health personnel's and other role players in Ghana needs to sustain and continue implementation of the pre-existing policies to enroll more infected individuals into ARTs. They need to also know the significant rate at which an HIV infected individual should commence treatment to reduce the burden of HIV in the Ghanaian population. We gave hypothetical values in this section to confirm the analytic solution.

Table 3.1: Parameter values and range obtained from the best fit, where units are yr^{-1}

Parameter	Range	Estimated values
Π	0.3	[46, 60]
Λ	-	1600000
ϵ	(0.1, 0.5)	0.5.
p	(0.059, 0.1)	0.1
ϕ_1	(0.05, 0.5)	0.5
ϕ_2	($2.1x10^{-5}$, $9.0x10^{-5}$)	$9.0x10^{-5}$
τ_1	(0.0998, 0.4)	0.4
τ_2	(0.1, 0.9)	0.5812
μ_0	(0.001, 0.0054)	0.0054
μ	0.016	[66]
η	(0.1, 0.5)	0.5
β	(0.3, 0.89)	0.890
ρ_1	(0.010, 0.03)	0.030
ρ_2	(0.008, 0.2)	0.02
ρ_3	(0.115, 0.3)	0.1150
ρ_4	(0.088, 0.2)	0.1211

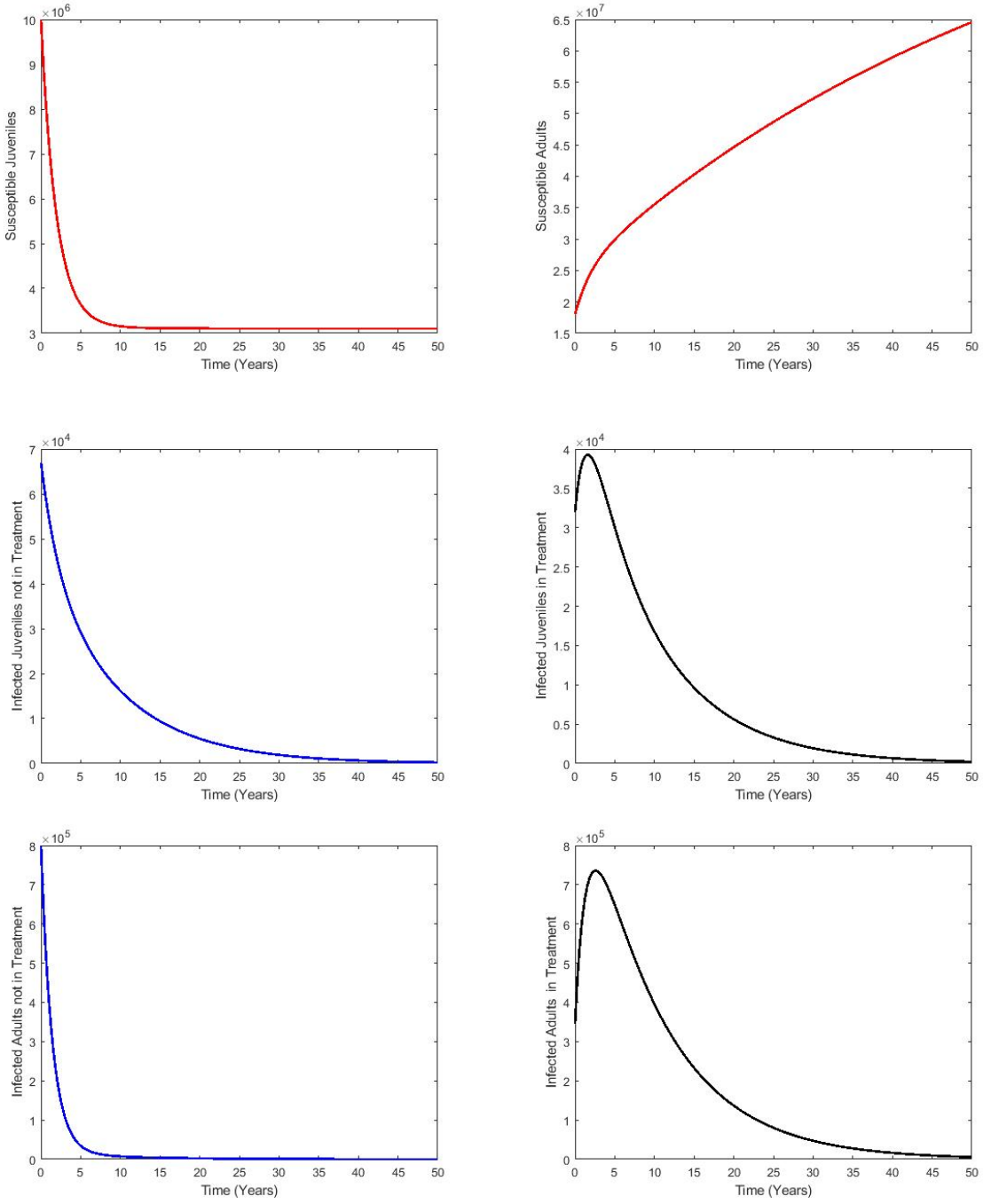

Figure 3.2: Shows the result of simulations for the given parameter values $\epsilon = 0.5$, $\phi_1 = 0.5$, $\phi_2 = 0.00009$, $\tau_1 = 0.4$, $\tau_2 = 0.5812, p = 0.1$, $\eta = 0.5$, $\beta = 0.02, \mu_0 = 00.54$, $\rho_1 = 0.03$, $\rho_2 = 0.02$, $\rho_3 = 0.1150$, $\rho_4 = 0.1211$. $SJ0 = 10000000$, $SA0 = 18000000$ for Ghana. $\mathfrak{R}_o = 0.0951$. The value of $\mathfrak{R}_o$ here indicate a stable infection-free state, thus, $\mathfrak{R}_o < 1$ for the given parameter values which is further confirm by the graphical representation.

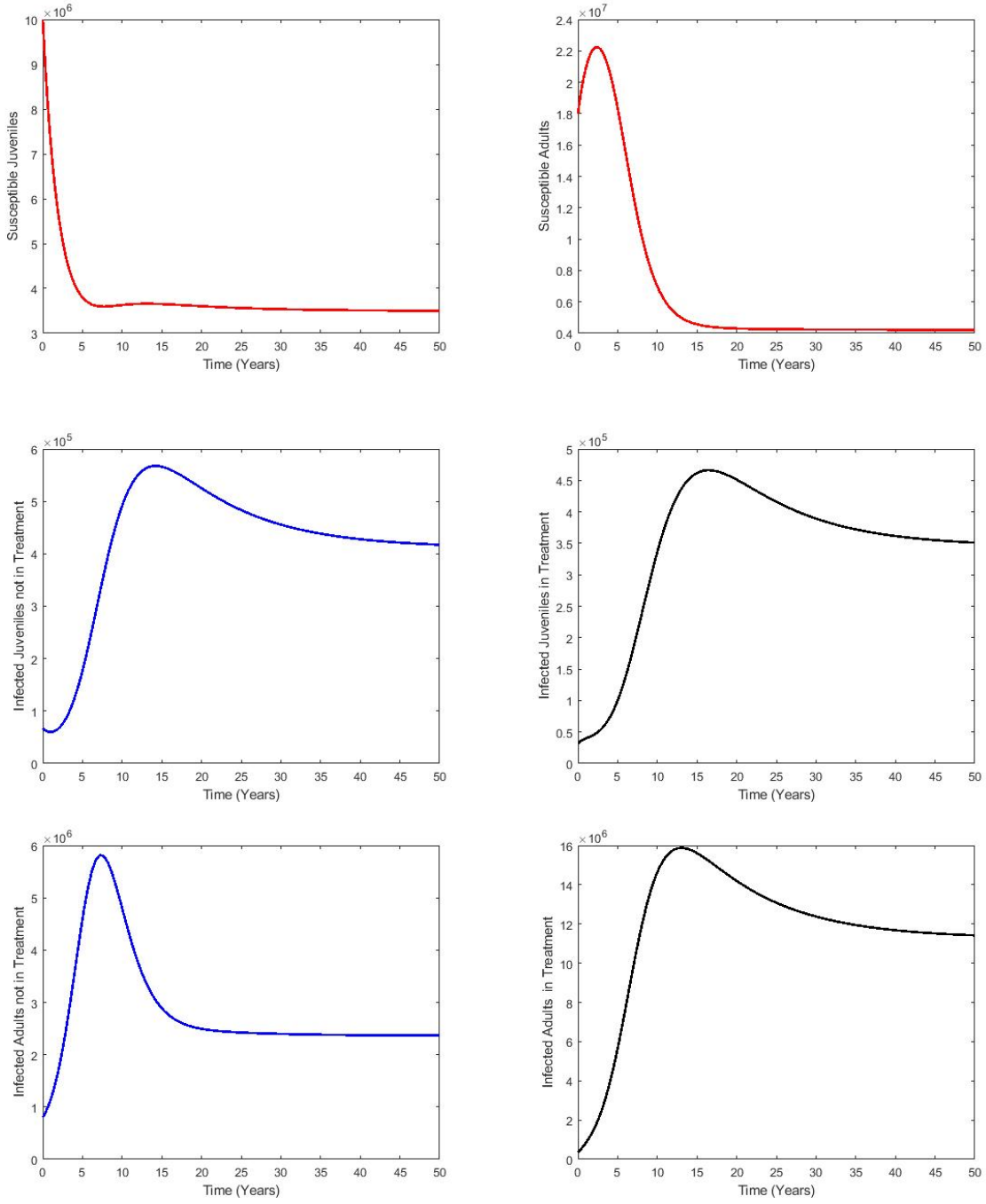

Figure 3.3: Shows the result of simulations for the given parameter values $\epsilon = 0.5$, $\phi_1 = 0.5$, $\phi_2 = 0.00009$, $\tau_1 = 0.4$, $\tau_2 = 0.5812, p = 0.1$, $\eta = 0.5$, $\beta = 0.89, \mu_0 = 00.54$, $\rho_1 = 0.03$, $\rho_2 = 0.02$, $\rho_3 = 0.1150$, $\rho_4 = 0.1211$. $SJ0 = 10000000$, $SA0 = 18000000$ for Ghana. $\Re_o = 4.2315$. The value of $\Re_o$ here depicts a persistent state, thus, $\Re_o > 1$ for given parameter values and is also confirm by the graphical representation.

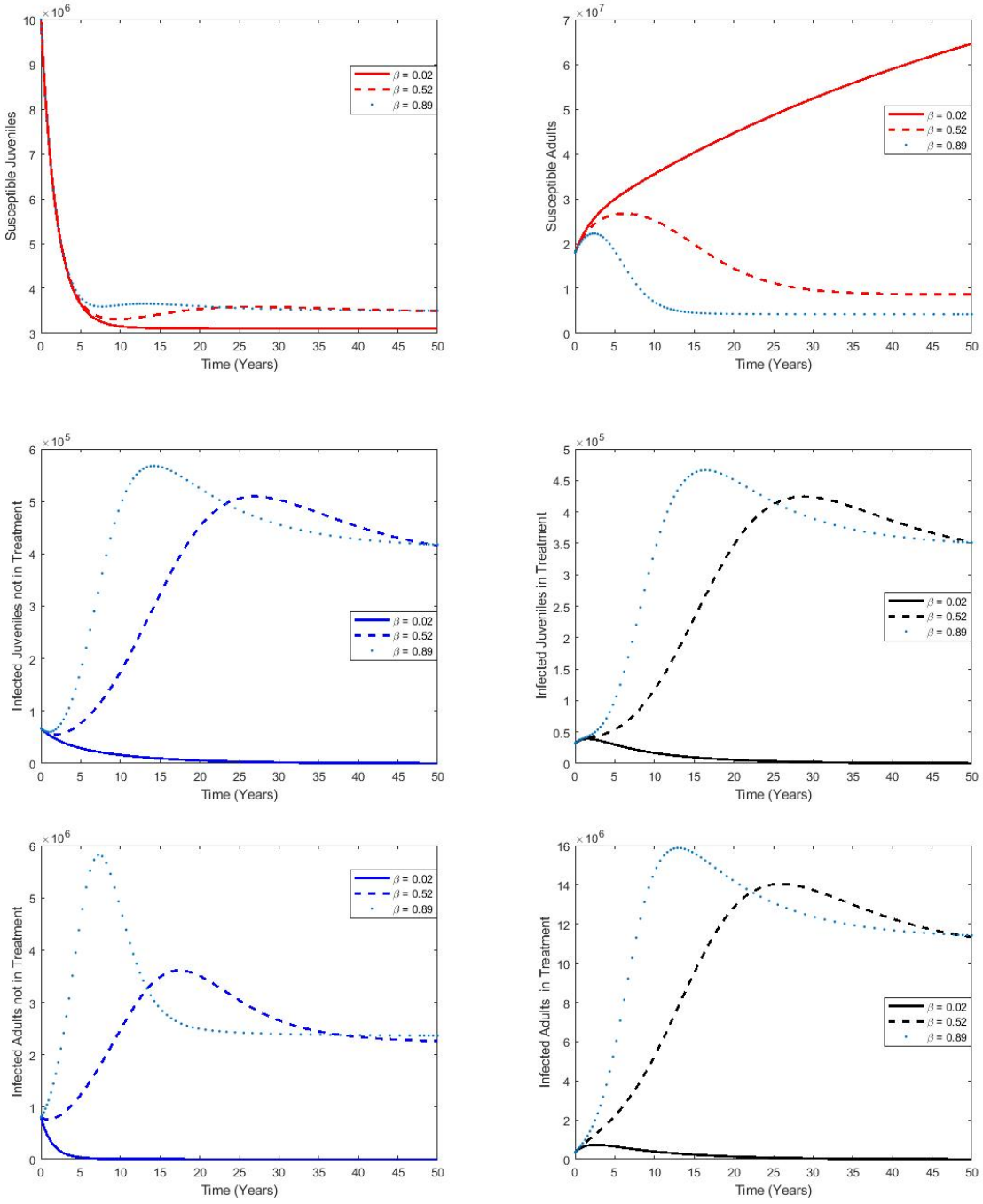

Figure 3.4: Shows the result of the dynamics of the model system (3.10) population variables from the stable infection-free state to the endemic state for different values of β (transmisson rate). The given parameter values are, $\epsilon = 0.5$, $\phi_1 = 0.5$, $\phi_2 = 0.00009$, $\tau_1 = 0.4$, $\tau_2 = 0.5812, p = 0.1$, $\eta = 0.5, \mu_0 = 0.0054$, $\rho_1 = 0.03$, $\rho_2 = 0.02$, $\rho_3 = 0.1150$, $\rho_4 = 0.1211$. Initial conditions $SJ0 = 10000000$, $SA0 = 18000000$ for Ghana. Results here shows the transition of the state variables from the infection-free state with $\mathfrak{R}_o < 1$ to the persistent state as β increases with $\mathfrak{R}_o > 1$ as confirmed by the graphical representation.

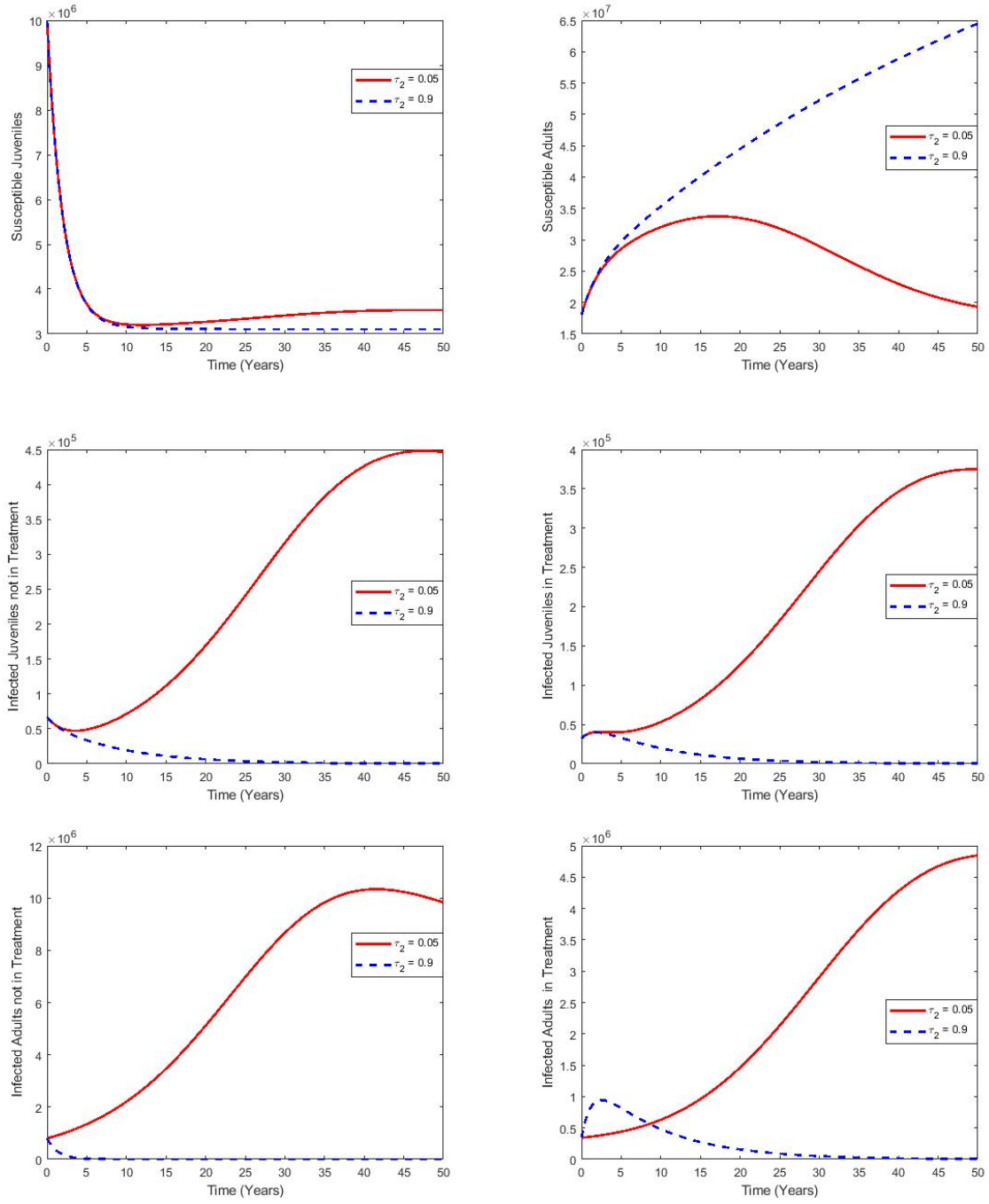

Figure 3.5: Shows the result of the dynamics of the model system (3.10) population variables from the stable persistent state to the infection-free state for different values of τ_2 (treatment rate). The given parameter values are, $\epsilon = 0.5$, $\phi_1 = 0.5$, $\phi_2 = 0.00009$, $\tau_1 = 0.4$, $\tau_2 = 0.5812, p = 0.1$, $\eta = 0.01$, $\beta = 0.3\mu_0 = 00.54$, $\rho_1 = 0.03$, $\rho_2 = 0.02$, $\rho_3 = 0.1150$, $\rho_4 = 0.1211$. Initial conditions $SJ0 = 10000000$, $SA0 = 18000000$ for Ghana. Also, results here shows the transition of the state variables from the persistent with $\Re_o > 1$ to the infection-free state with $\Re_o < 1$ as τ_2 is varied as confirmed by the graphical representation.

3.7 Sensitivity analysis

Sensitivity analysis is a method used to determine the response in the output of a mathematical model or a system as a result of changes in input parameters. In disease dynamics or dynamical system, the analysis is used for showing how epidemiological quantities like the basic reproduction number and prevalence of a disease respond to changes in parameter values.

3.7.1 Latin hypercube sampling

In this research, we examine the sensitivity of the reproduction number $\mathfrak{R}_o$ to the changes or variations in parameters. Latin hypercube sampling and partial rank correlation coefficients (PRCCs) was adopted together with 1000 simulations per run in Matlab. Latin hypercube sampling is a statistical sampling method that allows for an effective investigation of changes in parameters across simultaneous uncertainty ranges in each parameter (Blower and Dowlatabadi 1994). PRCCs illustrate the magnitude of the impact that each parameter has on the final outcome of the reproduction number $\mathfrak{R}_o$. Basically, the reproduction number $\mathfrak{R}_o$ increases when parameters having positive PRCCs increases whiles parameters having negative PRCCs decreases $\mathfrak{R}_o$ when they are increased.

We initially estimated the parameter values listed in the final column of Table 3.1 to determine the appropriate parameter ranges. Results from this indicates that τ_2 and β were the two parameters with the most significant impact on the output of the reproduction number $\mathfrak{R}_o$.

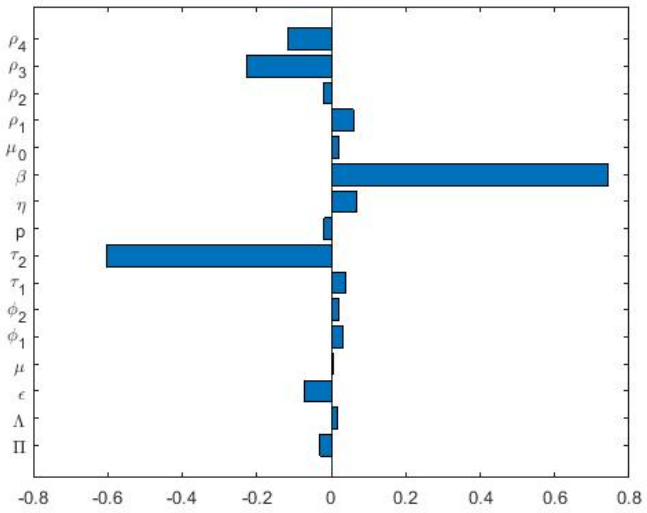

Figure 3.6: Partial Rank Correlation Coefficients (PRCCs) for the range of parameters from 3.1. It can be noted that the parameter with the highest potential to reduce the epidemics is τ_2. While β is the parameter with the highest potential to make the epidemic worse when it is maximized. Thus, the influence of τ_2 is critical in reducing HIV epidemics in a population.

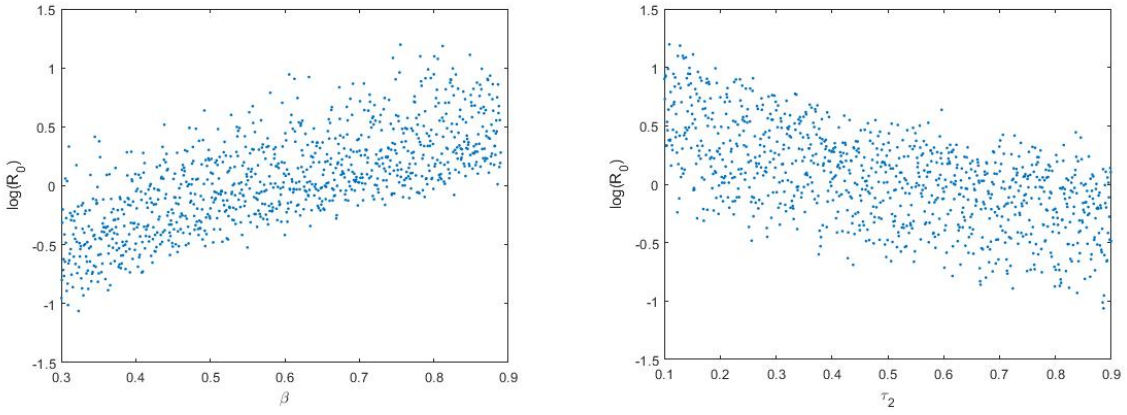

Figure 3.7: shows the scater plot of the sensitive parameters τ_2 and β

Results from Figure 3.7 shows the variation in $\mathfrak{R}_o$ with respect to the parameters τ_2 and β. A positive correlation exist between $\mathfrak{R}_o$ and β whiles a negative correlation exist between τ_2 and $\mathfrak{R}_o$ indicating that efforts must be made to increase compliance to significant treatment protocols already in place to enroll more people living with HIV/AIDS in Ghana into treatment to reduce the burden of the disease. This is not far fetched and can be achieved since about 90% of women are already enrolled on treatment [78]. This will aid in the total elimination of vertical transmission in Ghana.

3.8 Application to data from Ghana

The purpose of developing a mathematical model for an epidemic disease is for planning, management, prevention and control of emerging and re-emerging epidemics. It is very significant to government and stakeholders to develop and enhance their health policies with respect to epidemics. Data fitting to a mathematical model or a system is mostly used to test the robustness of a mathematical model or system. It also helps in forecasting or making projections of diseases or a studied quantity. In this section, the model system (3.10) is fitted to data obtained from Ghana from 2003-2016 on the total number of individuals enrolled in HIV/AIDS Antiretroviral therapy (ART). The original data set was multiplied by 1000 to get the estimated fit.

In 2016, HIV prevalence among pregnant women attending antenatal care in Ghana was 2.4%. Total number of pregnant women tested and counselled for HIV were (702 381); 18 116 (2.8%) were HIV positive and 9 680, thus, (53%) of the HIV positive were on ARTs to prevent mother-to-child-transmission (PMTCT). 20 497 adults and children were initiated on ARTs in 2016 (5 568 males and 14 929 females) in 245 sites across the country. Estimated population on ART coverage is, therefore, 35%. Total ART clients as at December 2016 were 100 665 consisting of 95 521 adults and 5 144 juveniles (National AIDS Commission program, NACP, 2016, annual report) [57].

Table 3.2 shows the data obtained from the Ghana Health Service on the num-

ber of children and adults enrolled in ART from 2003-2016.

Table 3.2: Data set for the number of people enrolled on ART in Ghana from 2003-2016, [58]

Year	**Children on ART**	**Adults on ART**	Total
2003	0	197	197
2004	27	1804	1831
2005	119	1913	2032
2006	122	3156	3278
2007	308	5783	6091
2008	450	9735	10185
2009	722	9409	10131
2010	894	12920	13814
2011	942	13441	14383
2012	684	13648	14332
2013	843	13456	14299
2014	1185	13809	14994
2015	1093	15875	16968
2016	1390	15107	16497

Our results in Figure 3.8 are indicative of a consistent increment of the total number of individuals who enrolled for treatment in Ghana each year. The estimated HIV prevalence can be seen in Figure 3.9 which shows, a gradual increase in prevalence from 2000 to 2015 and a decline in 2016. Likewise, projected HIV prevalence can be seen in Figure 3.10, which indicates, an increment of HIV prevalence from 2000 and a decline from 2016 towards 2020. The projected decline in prevalence may be attributed to better government policies put in place on HIV/AIDS management and control. This can be justified since Ghana has the lowest population based HIV Prevalence of 2.0% according to the Ghana Demographic Health Survey report (GDHS, 2014). There also exist many strategic plans in place by United Nations Programme on HIV and AIDS

(UNAIDS) to reduce the prevalence and the burden of the disease in countries by enrolling more people into treatment by 2020 [80].

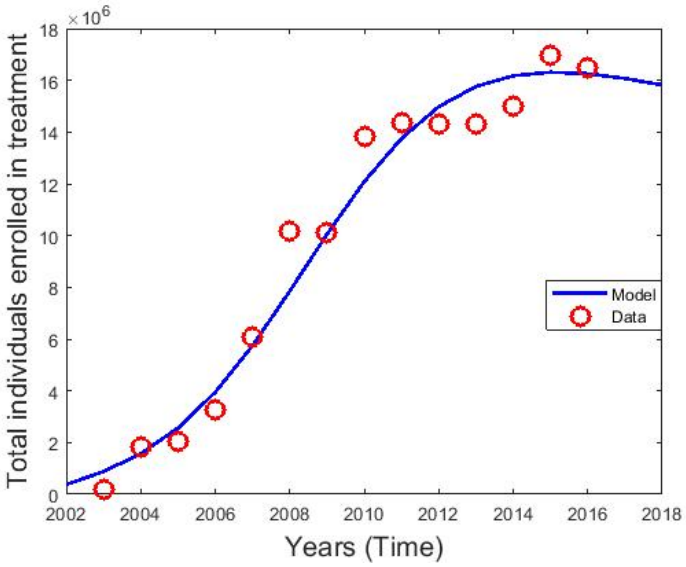

Figure 3.8: Model system (3.10) fitted to data for individuals enrolled in treatment for HIV/AIDS. The red circles indicate the actual data and the solid blue line indicates the model fit to the data.

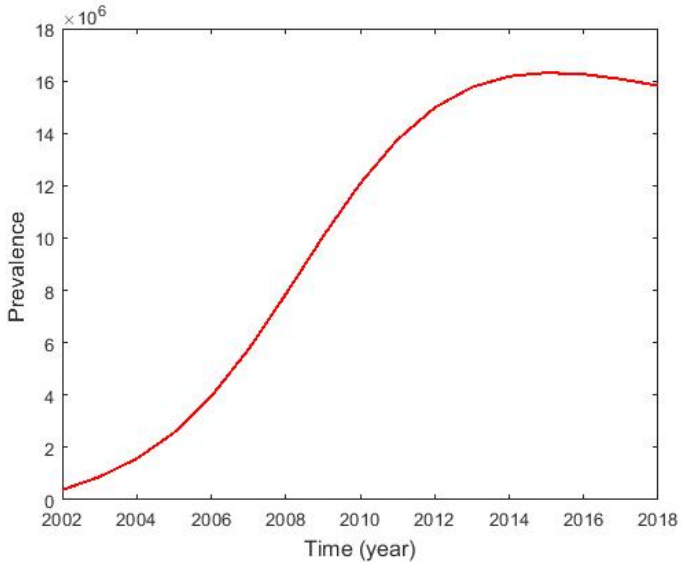

Figure 3.9: Total HIV prevalence in Ghana

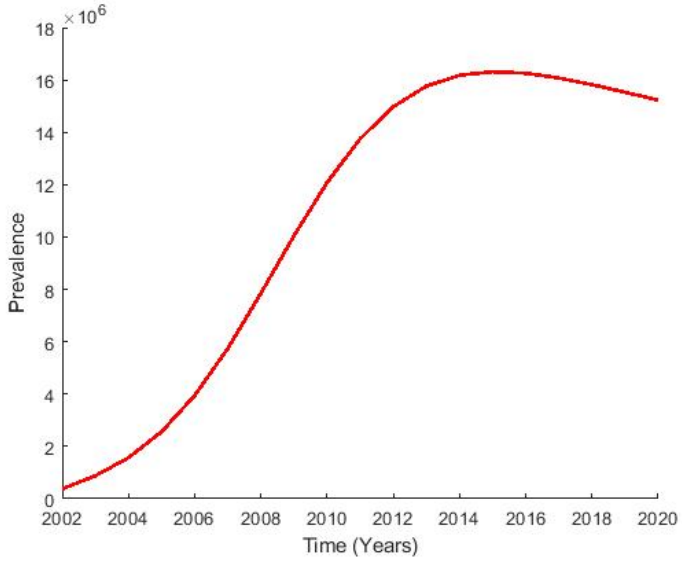

Figure 3.10: Projected Total HIV prevalence in Ghana

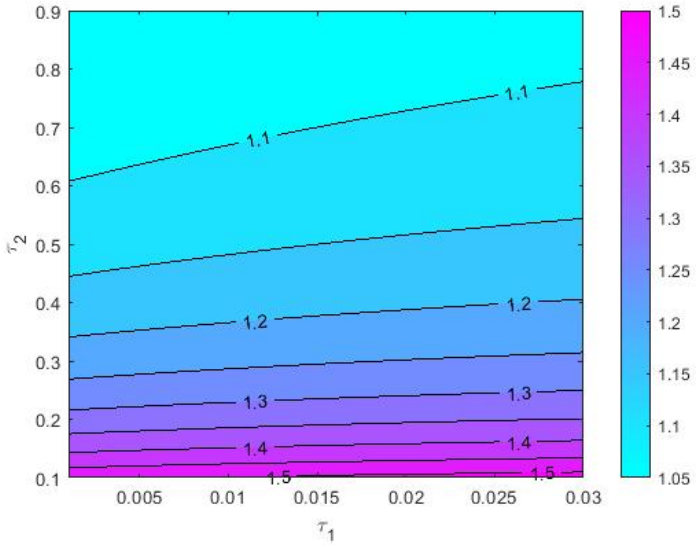

Figure 3.11: Contour plot of the basic reproduction number $\mathfrak{R}_o$ as a function of τ_1 and τ_2

We use the contour plots in Figure 3.11 to verify the relationship or correlation between selected pairs of parameters and the reproduction number $\mathfrak{R}_o$. In Figure 3.11, τ_2 which is the treatment rate of the adult population reduces $\mathfrak{R}_o$ as it increases whiles, τ_1 which is the treatment rate of the juvenile population does not have any significant effect on $\mathfrak{R}_o$. Therefore, biologically, treatment of the juvenile population does not have any meaningful impact on the reproduction number of HIV/AIDS.

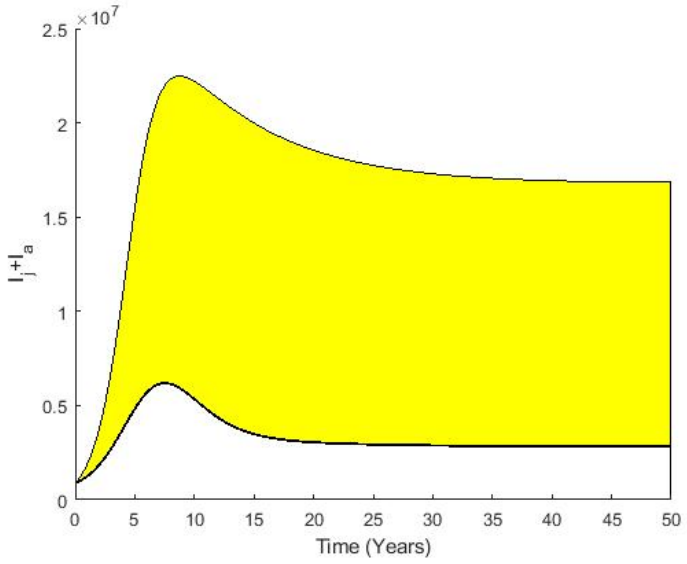

Figure 3.12: Shows the influence of both τ_1 and τ_2 on the infected population not under treatment

We investigated the impact of the treatment parameters τ_1 and τ_2 on the infected classes not under treatment in Figure 3.12. It is interesting to note how initiation of treatment affect the infected classes not in treatment. The yellow shaded area represent individuals that are newly enrolled into treatment through intervention programs. We note that when τ_1 and τ_2 are both zero, thus, no treatement protocol in place the infected class $I_J + T_J$ increases significantly. However, when τ_1 and τ_2 are given their estimated value, thus, existence of treatment protocol from Table 3.1, $I_J + T_J$ declines. This shows the significant impact treatment has on both infected juvenile and adult population not enrolled in treatment. It tends to suggest that compliance to already existing PMTCT and antiretroviral intervention programs must be increased to reduce the number of people infected by HIV.

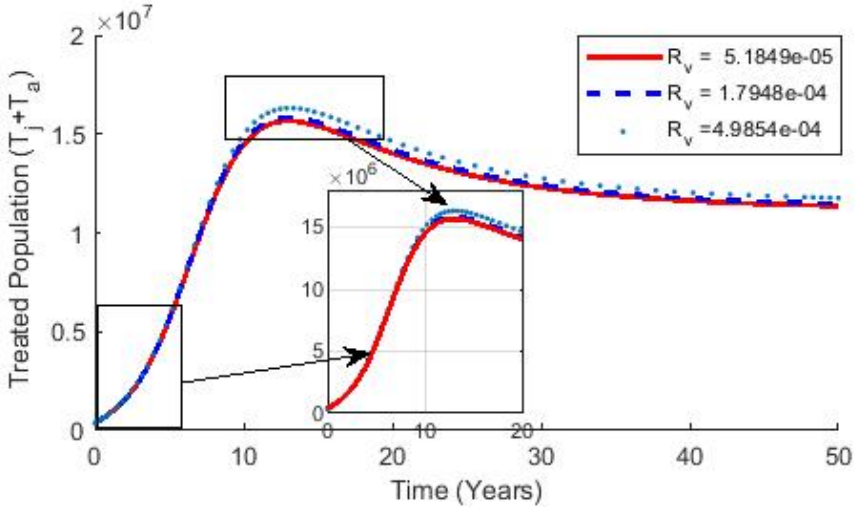

Figure 3.13: Shows the influence of reproduction number through vertical transmission R_v on the treatment class. That is, HIV epidemic in the presence of vertical transmission.

We also investigated the overall impact of vertical transmission on HIV transmission. From the model analysis, we already determined R_v to be $0 < R_v < 1$. We use the estimated parameters in Table 3.1 but we vary ϵ to be 0.052, 0.18, and 0.5. We note from the Figure 3.13 that as R_v increases, the treated populations also increases but with a very little increment. The smaller box in Figure 3.13 is a zoomed out plot, which shows no major change on the treated infected class when R_v increases. This means that even if R_v increases, the infected juveniles under treatment can still join the infected adults under treament population and still keep the disease under control. We can therefore find an $R_v* > R_v$ such that even if R_v* increases, the disease will still be kept under control among the juvenile population under treatment. Epidemiologically, this implies that without treatment, pregnant women have high risk of transmitting HIV to their babies. However, with treatment even if R_v increases, the disease can still be kept under control and less babies will be born with the disease. Vertical transmission therefore, is significant with respect to pregnant women and unborn babies. It is, however, not much significant to the sexual transmission of HIV/AIDS.

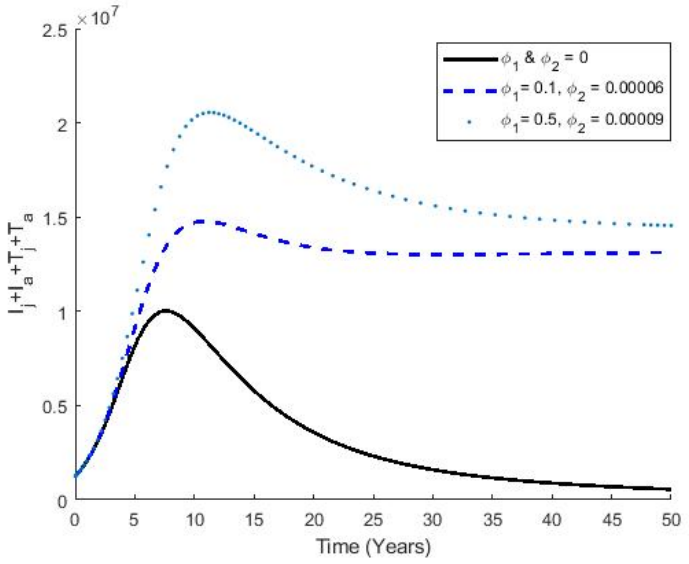

Figure 3.14: Shows the varying of the progression parameters, ϕ_1 and ϕ_2

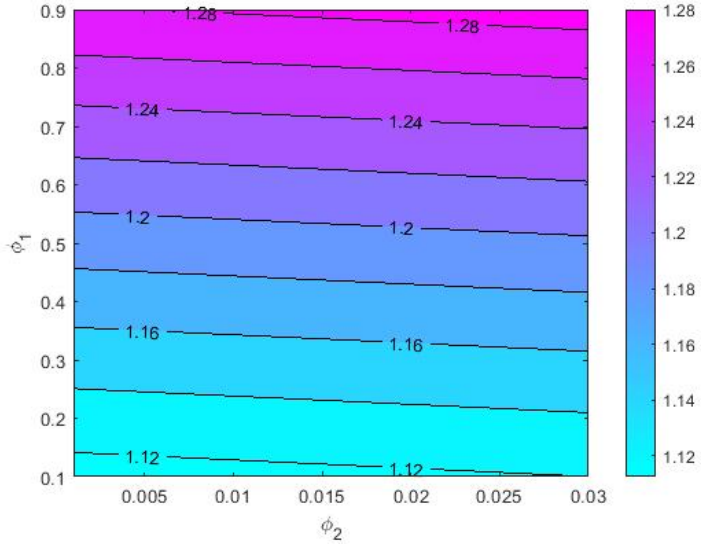

Figure 3.15: Shows the contour plot of ϕ_1 and ϕ_2

One of the objective was to evaluate the progression rates ϕ_1 and ϕ_2 in order to draw out conclusion on the HIV/AIDS epidemics. We note that in Figure 3.14, when the progression rates ϕ_1 and ϕ_2 are gradually increased from zero to

some rates, the infected classes either under treatment or not under treatment increases. However, in the contour plot shown in Figure 3.15, when ϕ_1 is increased, the reproduction number $\mathfrak{R}_o$ increases. In addition, increasing ϕ_2 also increases $\mathfrak{R}_o$, but, we can notice that with increment in these two progression rates, the basic reproduction number increases but not by a large margin. Analytic results for these two progression rates can also be obtained by carrying out sensitivity analysis on $\mathfrak{R}_o$ to determine how changes in these parameters affect $\mathfrak{R}_o$. We can therefore, conclude that the rates of progression from infected juveniles to infected adults though significant are not a major concern for health policy makers. Focus should be place more on other public health measures such as early and effective enrollment of infected mothers and juveniles into treatment, and education on number of sexual patners and risky sexual behaviours to control HIV/AIDS and eliminate MTCT of HIV.

3.9 Discussion and conclusion

We proposed and analyzed a deterministic non-linear ordinary differential equation model for HIV/AIDS in Ghana. This model included the juvenile and adult populations. Treatment of juveniles infected with HIV/AIDS via mother-to-child transmission (vertical) and treatment of adults were included in both juvenile and adult populations respectively. We studied the local stability of the infection free state for the model system (3.10). From the steady state analysis, we determined the reproduction number for the model system (3.10), which from the analysis of the model reproduction number was found to be an increasing function of the effective transmission rate β and a decreasing function of the treatment rate τ_2 if $\beta > R_2$ (the parameter which measures the average number of individuals that infectives in the treated adult population infect during their duration of infectiousness). We also found out that the basic reproduction number $\mathfrak{R}_o$ is an increasing function of R_v (the reproduction number due to the mother-to-child-transmission of HIV/AIDS).

Simulations were made to study the population dynamics at the disease-free

and the endemic equilibrium. Results suggested that when the reproduction number is less than one and given that treatment rate together with other parameters and initial conditions do not change, increasing β will ultimately increase $\mathfrak{R}_o$ and shift the population dymamics from the stable infection-free state to the persistent state. Increasing the treatment rate will on the other hand reduces $\mathfrak{R}_o$ and the population variables transition from the persistent state to a stable infection-free state giving the effective transmission rate is not very high and all other parameters and initial conditions do not change.

It was note that without treatment programs, HIV-positive mothers have a higher risk of transmitting HIV to their child through birth or after birth. However, in the presence of treatment protocols such as early diagnosis and enrollment of infected juveniles and mothers on ART or antiretroviral prophylaxis, the burden of HIV reduces significantly. This tends to suggest adherence to PMTCT programs needs to be intensified and sustained to achieve this reduction.

The model projected a decline in the prevalence of HIV in Ghana which was due to a decline in the transmission rate. The decline was observe from 2016 towards 2020 and gradually stablizing after 2020 given all intervention programs are kept in place and sustained, and also more infected HIV mothers and juveniles are enrolled through the intervention programs. This result is consistent with [44]. Furthermore, it was determined that the progresion rates of infected juveniles wherther on treatment or not significantly increase the total infected classes. This suggest that infected juveniles when they enter into early adulthood can have a significant impact on the reproduction number of HIV and the over-all total number of people infected.

Sensitivity analysis for parameters of the model system (3.10) was also considered. Latin hypercube sampling and partial rank correlation coefficients (PRCCs) demonstrated that the two parameters with the most significant impact on the reproduction number $\mathfrak{R}_o$ and the behaviour of the population variables are τ_2 and β, the treatment and effective transmission rate respectively. Again, from the partial rank correlation coefficients (PRCCs) plot in Figure 3.6, we can note that the progression rate to AIDS for both infected adults in treat-

ment and not in treatment, ρ_3 and rho_4 have a negative impact on $\mathfrak{R}_o$. This implies, that the HIV infected adult classes reduces as more people from these classes progress to AIDS. We also observed in Figure 3.11 that there is no significant correlation between the treatment rate of juveniles τ_1 and $\mathfrak{R}_o$, whiles increasing τ_2 reduces $\mathfrak{R}_o$ significantly. Epidemiologically, it means treatment of juveniles does not have any significant impact on the secondary infection of HIV/AIDS. Treatment of adults on the other hand does significantly.

The model system (3.10) was also fitted to data on individuals enrolled in treatment. The objective was to utilize the model parameters that give the best fit to obtain the prevalence curve in Figure 3.9 and to project future prevalence of HIV/AIDS as seen in Figure 3.10. The projection shows a decrease in HIV prevalence from 2016 to 2020. This suggest that, more individuals would be enrolled into treatment towards 2020 since, ARTs reduces the viral load of HIV patients, the effective transmission rate of HIV will decline, eventually reducing the reproduction number and HIV prevalence. It follows therefore, that even though the prevalence rate of HIV in Ghana is low, persistent efforts must be intensified. These efforts must be made by the health policy makers for continuous sustainability and compliance to treatment protocols against HIV/AIDS. The objective is to reduce the disease burden, to eliminate vertical transmission of the disease, and make the disease evade the Ghanaian population.

In conclusion, transmission rate and the rate at which adults and juveniles are enrolled into treatment significantly reduces the infected class and the reproduction number. Hence, the need to sustain and ensure high and continuous compliance to treatment programs. Progression rates of infected juveniles either in treatment or not increases both infected adult classes and the reproduction number as well. This tends to suggest higher progression rates of infected juveniles will increase the HIV epidemics in a population. The model also projected a fall in the prevalence rate of HIV in Ghana which is observed from 2016 towards 2020. It was also noted that vertical transmission of HIV/AIDS alone cannot lead to an epidemic. However, increment in vertical transmission without treatment can lead to high burden of the disease among juveniles. With treatment however, the disease burden among juveniles can still be kept under

control even if vertical transmission increases.

This work cannot be without limitations. We used estimates for some parameters due to unavailability of published data on those parameters. Consequently, we resorted to computational iterative method to provide the estimates of these parameters. The model could have been extended by the inclusion of some determinant factors significant to HIV epidemiology, such as variable infectivity, genetic variation, sex-structures, population density, mixing patterns, and time from infection to AIDS. These constraints raised above will be taken into account in future work to provide for a better model and a more realistic estimation of parameters.

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