Stochastic modeling of an HIV/AIDS epidemic with treatment

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KEYWORDS

HIV/AIDS epidemic model

Stochastic HIV/AIDS model

Global stability of disease-free and endemic equilibria

Basic reproduction number

Incidence rate

Stability in the mean

Asymptotic stability

Almost sure exponential stability

ABSTRACT

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The HIV/AIDS epidemic continues to be among the most devastating diseases in human history despite the new scientific advances and serious public health interventions. The greatest burden of HIV/AIDS is still in sub-Saharan Africa, and within this specific region, women are severely affected. Despite an increase in prevention interventions, including such as ARV treatment and pre-exposure prophylaxis (PrEP), behavioural change remains a key role in the transmission of HIV/AIDS. In this thesis, we investigate several related models for the population dynamics of HIV/AIDS epidemic model with treatment. We start off with a four compartmental HIV deterministic model with stages of HIV infection and with inflow of HIV infectives. Thereafter, we impose stochastic perturbations on the underlying HIV/AIDS deterministic model without inflow of infectives. For this version of HIV stochastic model, we prove global existence and positivity of solutions to the HIV/AIDS-perturbed model. Some useful properties such as boundedness property, stochastic permanence property and asymptotic stability have been derived. Under the

asymptotic stability, it is found that whenever the intensities of the noise are not too large, then the stochastic solution remains close to the underlying deterministic solution. Otherwise strong noise gives a divergence between stochastic and deterministic behaviours. We also investigate another type of stochastic HIV model with inflow of infectives and we study stability in the mean. In the absence of inflow of infectives, we introduce an analogue of the basic reproduction number which we link to a theorem on almost sure exponential stability in the case of a disease-free equilibrium. It is found that stochastic perturbation does not destabilize the disease-free equilibrium, i.e., whenever the analogue of the basic reproduction number is below unit, then the disease-free equilibrium is almost surely exponentially stable. Furthermore, we propose a new model for the transmission of HIV/AIDS including ART treatment and pre-exposure prophylaxis (PrEP). Our model can be used to test the effects of ART and of the uptake of PrEP in a given population, as we demonstrate through simulations. The model can also be used to estimate future projections of HIV prevalence. We prove global stability of the disease-free equilibrium. We also prove global stability of the endemic equilibrium for the most general case of the model, i.e., which allows for PrEP individuals to default. We include insightful simulations based on published South-African HIV trend from 2016. Finally, we also investigate other stochastic HIV/AIDS epidemic models such as: stochastic HIV model with saturated incidence rate and stochastic HIV model with the use of PrEP. The results obtained in both models were very meaningful, and we show insightful simulations in this regard.

DECLARATION

I declare that *Stochastic modeling of an HIV/AIDS epidemic with treatment* is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Mozart Umba Nsuami

Signed: .....

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Proverbs 2: 6

For the LORD gives wisdom; from his mouth come knowledge and understanding.

First and foremost, I am thankful to almighty God for that he always orders my steps in his word. And so no matter how hard life and challenges are, I can always stand tall and prevail.

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Last but not least, to my whole family, thank you for always believing in me and rooting for my success. God bless you abundantly.

DEDICATION

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List of Acronyms

a.s, almost surely

ART, Anti-retroviral Treatment

HIV, Human Immunodeficiency Virus

AIDS, Acquired Immune Deficiency Syndrome

UN, United Nations

WHO, World Health Organization

SDE, Stochastic Differential Equation

PrEP, Oral Pre-Exposure prophylaxis

CD4, Cluster of Differentiation 4

MTCT, Mother to Child Transmission

List of Notations

$\mathbb{P}$, a probability measure

$(\Omega, \mathcal{F}, \mathbb{P})$, Probability triple

$\mathbb{P}[X|Y]$, Conditional probability of X given Y

$\{\mathcal{F}_n\}_{n\geq 0}, \{\mathcal{F}_t\}_{t\geq 0}$, Filtration

$\mathbb{E}[X|\mathcal{F}]$, $\mathbb{E}[X_{n+1}|X_n]$, Conditional expectation

$\mathcal{L}^p([a,b];\mathbb{R}^d)$, the family of $\mathbb{R}^d$-valued $\mathcal{F}_t$-adapted processes $\{f(t)\}_{a\leq t\leq b}$ such that $\mathbb{E}\int_b^a |f(t)|^p dt < \infty$

$\mathcal{M}^p([a,b];\mathbb{R}^d)$, the family of processes $\{f(t)\}_{a\leq t\leq b}$ in $\mathcal{L}^p([a,b];\mathbb{R}^d)$ such that $\mathbb{E}\int_b^a |f(t)|^p dt < \infty$

W, Brownian motion or Wiener process

List of Tables

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List of Publications

Part of this thesis has been either submitted for publication or published in the form of the following research papers in international journals.

[1] M.U. Nsuami, P.J. Witbooi. Stochastic dynamics of an HIV/AIDS epidemic model with treatment. *Quaestiones Mathematicae*, (2018)1-17.

[2] M.U. Nsuami, P.J. Witbooi. A stochastic model for HIV epidemic with treatment and inflow of HIV infectives. *International Journal of Applied Mathematics*, Volume **31** No. **5** 2018, 545-568.

[3] M.U. Nsuami, P.J. Witbooi. A model of HIV/AIDS population dynamics including ARV treatment and pre-exposure prophylaxis. *Advances in Difference Equations* (2018) 2018:11 https://doi.org/10.1186/s13662-017-1458-x

[4] M.U. Nsuami, P.J. Witbooi. Exponential stability of a disease-free for an HIV epidemic model with the use of prophylaxis. (submitted for publication).

Contents

Chapter 1

General Introduction

1.1 HIV/AIDS background

Acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS) is a disease of the human immune system caused by human immunodeficiency virus (HIV). In the summer of 1981, clinicians in New York and California observed among young, previously healthy, homosexual men an unusual clustering of cases of rare diseases, notably *kaposi sarcoma* and opportunistic infections such as *Pneumocystis carinii pneumonia*, as well as cases of unexplained, persistent lymphadenopathy [30, 53]. It soon became evident that these individuals had a common immunological deficit in cell-mediated immunity, resulting predominantly from a significant diminution of circulating $CD4^+$ T cells [33, 62]. Acquired Immune Deficiency Syndrome (AIDS) occurs when an HIV-positive individual has such lowered immune levels that he/she falls prey to a variety of opportunistic infections. The rate of HIV infection and death due to AIDS first increased rapidly during the 1980s in the United States and in Western Europe. Since 1982 AIDS has developed into a global pandemic across the world.

There are two types of HIV virus: HIV1 which is most common in sub-Saharan Africa and throughout the world, and HIV2 which is most often found in West Central Africa,

parts of Europe and India. It is important though to notice that both produce the same patterns of illness. HIV2 causes a slower progression of disease than HIV1. HIV is the virus that causes AIDS. Not everyone who is infected with HIV has AIDS. Everyone with AIDS is infected with HIV. AIDS is the result of progression of HIV Infection. Anyone infected with HIV, although healthy, can still transmit the virus to another person. The HIV/AIDS pandemic consists of many separate epidemics. Each epidemic has its own distinct origin, in terms of geography and specific populations affected, and involve different types and frequencies of risk behaviours and practices, for example, unprotected sex with multiple partners or sharing of drug injection equipment. It has been observed many years ago that the virus cannot spread by means of a handshake, kiss, or a sneeze, nor by means of a mosquito bite. Sharing of food, drinking glasses or clothes will not transmit the virus. Thus the main means of transmission worldwide is human sexual intercourse in which bodily fluids like semen or blood are exchanged. This is the reason why the sexually active age group from 15 to 45 is most at risk. Also important in HIV transmission is the sharing of unclean needles, such as between injection drug users, and in rare instances, the virus is transmitted by means of accidental needle-sticks. Mother-to-child transmission (also called MTCT or vertical transmission) is common today, resulting in millions of pediatric HIV cases. The chances of a baby born to an HIV plus mother being infected are about 40 percent. Because mother-to child HIV transmission can be so easily prevented (or at least minimized) by an anti-retroviral drug at a low cost, infected infants are an especially painful problem for the world.

1.1.1 HIV/AIDS stages of infection

The process from HIV to AIDS may take several years and includes different stages, see for instance in [102]. The WHO system for adults sorts patients into one of four hierarchical clinical stages ranging from stage 1 (asymptomatic) to stage 4 (AIDS). Patients are assigned to a particular stage when they demonstrate at least one clinical condition in

that stage's criteria. Patients remain at a higher stage after they recover from the clinical condition which placed them in that stage. These stages are as follows.

1. Stage 1.

   Patients who are asymptomatic or have persistent generalized lymphadenopathy (lymphadenopathy of at least two sites [not including inguinal] for longer than 6 months) are categorized as being in stage 1, where they may remain for several years.

2. Stage 2.

   Even in early HIV infection, patients may demonstrate several clinical manifestations. Clinical findings included in stage 2 (mildly symptomatic stage) are unexplained weight loss of less than 10 percent of total body weight and recurrent respiratory infections (such as sinusitis, bronchitis, otitis media, and pharyngitis), as well as a range of dermatological conditions including herpes zoster flares, angular cheilitis, recurrent oral ulcerations, papular pruritic eruptions, seborrhoeic dermatitis, and fungal nail infections.

3. Stage 3.

   As disease progresses, additional clinical manifestations may appear. Those encompassed by the WHO clinical stage 3 (the moderately symptomatic stage) category are weight loss of greater than 10 percent of total body weight, prolonged (more than 1 month) unexplained diarrhea, pulmonary tuberculosis, and severe systemic bacterial infections including pneumonia, pyelonephritis, empyema, pyomyositis, meningitis, bone and joint infections, and bacteremia. Mucocutaneous conditions, including recurrent oral candidiasis, oral hairy leukoplakia, and acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis, may also occur at this stage.

4. Stage 4.

   The WHO clinical stage 4 (the severely symptomatic stage) designation includes all of the AIDS-defining illnesses. Clinical manifestations for stage 4 disease that allow presumptive diagnosis of AIDS to be made based on clinical findings alone are HIV wasting syndrome, *Pneumocystis pneumonia* (PCP), recurrent severe or radiological bacterial pneumonia, extrapulmonary tuberculosis, HIV encephalopathy, CNS toxoplasmosis, chronic (more than 1 month) or orolabial herpes simplex infection, esophageal candidiasis, and *Kaposi's sarcoma*. Other conditions that should arouse suspicion that a patient is in clinical stage include cytomegaloviral (CMV) infections (CMV retinitis or infection of organs other than the liver, spleen or lymph nodes), extrapulmonary cryptococcosis, disseminated endemic mycoses (e.g., coccidiomycosis, penicilliosis, histoplasmosis), cryptosporidiosis, isosporiasis, disseminated non-tuberculous mycobacteria infection, tracheal, bronchial or pulmonary candida infection, visceral herpes simplex infection, acquired HIV-associated rectal fistula, cerebral or B cell non-Hodgkin lymphoma, progressive multifocal leukoencephalopathy (PML), and HIV-associated cardiomyopathy or nephropathy. Presence of these conditions unaccompanied by the AIDS-defining illnesses, however, should prompt confirmatory testing.

1.1.2 HIV/AIDS in the history

In recent years, the HIV/AIDS epidemic has been spreading at an alarming rate, and the prevalence of HIV infection is still extremely high. It is reported that more than 35 million of people were living with HIV in 2012 compared to 36.5 million in 2016. It is reported in [44] that 2.5 million people were newly infected in 2012 compared to 1.8 million in 2016. There has been 1.5 million AIDS-related causes of death worldwide in 2013 compared to 1 million in 2016 (UNAIDS DATA 2017, [46]). The most significant advance in medical management of HIV infection includes two recommendations [110]. First, antiretroviral therapy (ART) should be initiated for everyone living with HIV at

any $CD4^+$ cell count. The HIV treatment reduces viral load to levels below the limits of detection of the most sensitive clinical assays, resulting in a significant reconstitution of the immune system [4]. The Global AIDS Update 2016 of the Joint United Nations Programme on HIV/AIDS, reports that the global coverage of ART therapy reached approximately 46% at the end of 2015. The gains in treatment are largely responsible for a 26% decline in AIDS-related deaths globally since 2010, from an estimated 1.5 million in 2010, to 1.1 million in 2015. Despite this significant achievement, globally there has been 1.8 million new infections reported in 2015 [45]. Second, the use of daily oral pre-exposure prophylaxis (PrEP) is recommended as a prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches. Substantial gaps remain in understanding the trade-offs between costs and benefits of choosing alternative HIV prevention strategies, such as the initiation of PrEP by high risk uninfected individuals [29]. Following WHO, making PrEP drugs available for safe, effective prevention outside the clinical trial setting is the current challenge. However, it is important to highlight and recall that PrEP is not for everyone: only people who are HIV-negative and at very high risk for HIV infection should take PrEP [111]. In 2015, the Medicines Control Council of South Africa issued a full regulatory approval of PrEP, and the country became the first in Sub-Saharan Africa to include PrEP in its national HIV programme. Globally, female sex workers (FSWs) are 13.5 times more likely to be living with HIV than women in the general population [50]. There are many countries with regulatory approval for PrEP. The European Medicines Agency has also granted market authorization for PrEP to be marketed across the European Union's 28 countries [25].

South Africa is a country homing the largest concentration of people living with HIV in the world. The first AIDS-related deaths in this country occurred in late December 1981 and January 1982 [79, 64]. The HIV epidemic was not an issue of major concern to the government and therefore received a very limited attention [87]. The prevalence of HIV/AIDS increased from 0.8% in 1990 to 4.3% in 1994, and almost 10% of the total population in 2014 [63]. The provision of ART in 2013 has reduced the prevalence of

HIV from an estimated 15% to 9% among adults not on ART. The annual incidence decreased from 2% to 0.9% and the AIDS related deaths from 0.9% to 0.3% *p.a.*, saving 1.5 million lives and US 727 million, see [104]. In April 2010, a large HIV counselling and testing campaign was launched in South Africa, a principle part of which was to scale up awareness of HIV [34, 42] and the result was positive. In [36], a model based on the case scenario of 90% annual HIV testing coverage in adults $15-49$ years old and four ART eligibility scenarios of $CD4^+$ count has been studied. The authors found that increasing the provision of ART to less than 350 cells $/mm^3$ may significantly reduce costs while reducing the HIV burden. In the paper [104] the authors use trend data for the prevalence of HIV among woman attending ante-natal clinics in South Africa and the reported coverage of ART. The authors found that a main reason why countries of Southern Africa have the highest rates of HIV in the world is because of the system of oscillating migrant labour historically.

1.1.3 HIV/AIDS Treatment

HIV treatment is actually deeply affecting the epidemic in countries where it has been brought to scale. Antiretroviral treatment is usually started once an individuals $CD4^+$ count (the number of T helper cells) drops to a low level, an indication that the immune system is deteriorating. Treatment can stop HIV from damaging the immune system, therefore, HIV-infected individuals on treatment usually remain clinically asymptomatic. Accelerating the scale up of antiretroviral therapy will drive progress across the broader AIDS response. It will reduce HIV-related illness and death, prevent people from acquiring HIV infection, address the needs of women and girls, reduce stigma and social exclusion and promote service integration.

In the rapidly developing countries most heavily affected by HIV, scaling up antiretroviral therapy preserves and strengthens the health and well-being of the adolescents and working-age adults on which future economic growth depends. Investing in HIV treatment

generates economic returns up to three times the investment, increasing productivity, preventing children from becoming orphaned and deferring the health care costs associated with advanced HIV-related illnesses [94, 81].

In South Africa, where HIV treatment coverage reached 83% in 2012 under WHOs 2010 treatment guidelines [94, 109, 103] (initiating treatment at a $CD4^+$ cell count of 350 cells/mm3), scaling up treatment is estimated to have reduced the number of people newly infected with HIV by 17-32% in 2011 [94, 23]. In KwaZulu-Natal, South Africa, life expectancy in 2011 was 11.3 years greater than in 2003, when HIV treatment in the province began to be scaled up [10]. In parts of KwaZulu-Natal where a substantial level of HIV treatment coverage $(30-40\%)$ had been achieved, the odds of acquiring HIV were 38% lower than in communities in which fewer than 10% of treatment-eligible individuals were receiving therapy [92].

However, in HIV-infected individuals not receiving treatment or on treatment that is not working, the immune system fails and symptoms develop. Initially many of the symptoms are mild, but as the immune system deteriorates the symptoms worsen. Symptomatic HIV infection is mainly caused by the emergence of certain opportunistic infections that the immune system would normally prevent. This stage of HIV infection is often characterised by multi-system disease and infections can occur in almost all body systems. Treatment for the specific infection is often carried out, but the underlying cause is the action of HIV as it erodes the immune system. Unless HIV itself can be slowed down the symptoms of immune suppression will continue to worsen.

1.2 Research questions, aims and objectives

The major objectives of this research are the construction and analysis of deterministic and stochastic models for the population dynamics of HIV/AIDS disease. We shall build a mathematical model or models for the numerical dynamics of the disease in a

population, that will be able to make future projections and to assess or plan for interventions towards curbing the disease. This work entails literature searching, pencil and paper mathematical investigation, and computer code writing and then running such code.

In this dissertation, we address the following matters:

1. Should HIV/AIDS be considered as a chronic manageable disease rather than a fatal one?

2. What is the impact of inflow of infectives on the epidemiology of HIV/AIDS?

3. What is the extent to which ARV treatment and pre-exposure prophylaxis (PrEP) significantly help to reduce the endemicity of the disease in a population?

4. What is the impact of the incidence rate on the force of infection?

5. Would the environmental perturbation be catastrophic on the system and prevent the policy makers to launch a certain intervention programme?

6. How can public health authorities optimally intervene on the epidemic?

1.3 Literature review

The dynamics between virus infections and the immune system involve many different components. In such cases, the principles governing the dynamics and the outcome of infection cannot be understood by verbal or graphical reasoning. Thus mathematical modeling in epidemiology has become a very powerful tool in analyzing the spread, and control of infectious diseases qualitatively and quantitatively. The research results help to predict and develop tendencies of the infectious disease, for determining the key factors of the disease spreading, and for seeking the optimum strategies for preventing and controlling the spread of infectious diseases [59]. In [39] the authors show that the implications of parents in perceptions of HIV counselling and testing are meaningful. Through the use

of semi-structured interviews, qualitative study explored perceptions of parents regarding the ethico-legal and social implications in the process of fighting against HIV/AIDS.

Cai et al. [14] investigate an HIV/AIDS epidemic model with two stages of infections. The authors study local and global stability of the equilibria of a deterministic HIV/AIDS model with treatment. Z. Osman et al. [75] extend the model of Cai et al. in [14] by introducing the infectives through vertical transmission at any time t. The authors prove global stability of the disease-free as well as the endemic equilibrium.

Research shows that access to treatment increases the expected available time for the transmission of HIV, but it is also shown that treatment without reduction of risky behaviour may even increase the proportions of infected individuals. Such cases have been studied in [14, 5]. In the paper by S. Blower [7], it is shown that incidence rates of HIV will decrease due to the fact that more HIV-positive individuals gain access to treatment, and hopefully the treated individuals would change their behaviour and the levels of risky behaviour do not increase.

Many papers, whether in deterministic modeling or stochastic modeling, have studied the effect of migrants on established populations. These papers study the stability of equilibrium states and /or control of the spread of the disease. In general, there are two types of stability analysis, local and global, widely used in the literature. Local stability is concerned with behaviour of the model solution near an equilibrium point, while global stability can describe solution behaviour in the whole domain. Examples of such contributions can be found in [43, 68, 82, 95]. In the paper [68] of R. Naresh et al., the authors analyze a mathematical model of the spread of HIV/AIDS in a population of varying size with immigration of infectives. On analyzing this situation, they found that the disease is always persistent if the direct immigration of infectives is allowed in the community. However, in the absence of inflow of infectives, the endemicity of the disease is found to be higher if pre-AIDS individuals also interact sexually, in comparison to the

case when they do not. The paper [82] of T. Roy et al. describes and studies the prevalence of risky behaviours and factors affecting sexual practices among rural-to-urban male migrant taxi drivers. Based on a survey, the authors' results demonstrate that rural-to-urban male migrants in the region under consideration significantly increase the spread of sexually transmitted infections and HIV because of their mobility, their high-risk sexual practices and their extensive sexual networks. In [95] the authors analyze a model of HIV/AIDS transmission with infective immigrants with time delay and treatment. The model incorporates some essential parameters of the HIV/AIDS transmission and enables the assessment of the effect of recruitment of infected immigrants into the community. They found that the direct inflow of infectives makes the disease more difficult to control.

PrEP can be cost-saving if delivered to individuals at increased risk of infection. The word prophylaxis means to prevent or control the spread of an infection or disease. PREP is a new HIV prevention method in which people who do not have HIV infection take a pill daily to reduce their risk of becoming infected. In particular, HIV models that account for the use of PrEP are featured in the papers [86, 66, 37]. In [86] for instance, a mathematical model for HIV/AIDS transmission using PrEP has been proposed, and then translated into a control problem where the objective was to determine the PrEP strategy that minimizes the number of individuals with pre-AIDS HIV-infection as well as the costs associated with PrEP. The paper by Mukandavire et al. [66] compares the impact of increasing condom use or HIV PrEP use among sex workers. The authors found that condom promotion interventions should remain the mainstay HIV prevention strategy for FSWs, with PrEP only being implemented once condom interventions have been maximised or to fill prevention gaps where condoms cannot be used. In [37], the authors develop a static model of HIV risk and compare HIV-risk estimates before and after the introduction of PrEP to determine the maximum tolerated reductions in condom use with regular partners and clients for HIV risk not to change. With a case study in South Africa for FSWs, it is found that PrEP is likely to be of benefit in reducing HIV risk, even if reductions in condom use do occur.

The models mentioned so far are deterministic and do not consider explicitly the stochasticities in or on the system. As a matter of fact, when modeling population dynamics, it is also important to consider environmental fluctuations due to the fact that parameters involved in epidemic models are not absolutely constant. They may fluctuate around some average values. In the real world, population dynamics is inevitably subjected to environmental noise, which is an important component for the population dynamics of HIV/AIDS. The large white noise may be a serious epidemic, which can be considered as the decisive factor responsible for the extinction of populations and human activities without control will affect the biological diffusion process which is likely to cause fatal consequences [118]. Based on these facts, the research towards stochastic population systems became very interesting and valuable. Stochastic models for the epidemic populations have been proposed or developed by many authors; see for instance [60, 19, 38, 28, 76, 52, 58, 93, 107, 78, 100]. Stochastic models involved in a certain ecological relationship are also featured in [74, 91].

In [58], the authors obtain sufficient criteria for the existence of periodic solutions to deterministic epidemic models with modified saturation incidence rates and their corresponding stochastic epidemic models with random perturbation. The authors also utilise stochastic Lyapunov functions to investigate the asymptotic behaviour of the solution. In [76], a stochastic mutualism model is proposed and investigated. The authors show that there is a unique solution to the model for any positive initial value. They also further show that the solution is stochastically bounded, uniformly continuous and globally attractive. Under some conditions, they show that the stochastic model is stochastically permanent and persistent in mean. One of the topics that has been studied quite extensively in sde models, is the stability of solutions, especially of the disease free equilibrium. There are various versions of stability, see e.g. in [60]. Now it is known that stochastic perturbations can stabilize a system. This is true also in epidemiological models. Although many papers have studied stability, very few of these have proofs of stability of the disease free equi-

librium beyond the condition $\mathcal{R}_0 < 1$. Here $\mathcal{R}_0$ denotes the basic reproduction number of the underlying deterministic model. Examples of stochastic perturbation improving stability of the disease-free equilibrium of an epidemic model of can be found in [38, 19].

In [78], the author investigates an SIR epidemic model with stochastic perturbations. Some qualitative properties such as stochastic boundedness and permanence are proved. X. X. Wang et al. [100] formulate and analyse a modified stochastic ratio-dependent Leslie-Gower predator-prey model. Thus by applying Itô formula and constructing Lyapunov functions, some qualitative properties as well such as the existence of global positive solutions, stochastic boundedness, and the global asymptotic stability are explored. Based on these results, they perform a series of numerical simulations and make a comparative analysis of the stability of the model system within deterministic and stochastic environments. In [52], an SIRS epidemic model with saturated incidence rate and disease-inflicted mortality is studied. The Global stability of the endemic equilibrium state is proved by constructing a Lyapunov function. The investigation of the authors stochastic model revealed that the stochastic stability of disease free equilibrium depends on the magnitude of the intensity of noise as well as the parameters involved within the model system. In [99] the authors extend the classical SIRS epidemic model incorporating media coverage from a deterministic framework to a stochastic differential equation (SDE) and focus on how environmental fluctuations of the contact coefficient affect the extinction of the disease. It is shown that the magnitude of environmental fluctuations will have an effective impact on the control and spread of infectious diseases.

Examples of stochastic models for HIV/AIDS can be found in [113, 26, 47]. In [26], the authors study a model of AIDS and condom use via the technique of parameter perturbation which is standard in stochastic population modeling. Their research indicates that introducing environmental noise into the deterministic model can have a stabilising effect. The paper by Yang et al. [113] investigates the dynamic behaviour of an HIV model with stochastic perturbation and the authors obtain the asymptotic behaviour results.

Kamina et al. [47] apply the multi-dimensional diffusion process to model early human immunodeficiency virus type-1 (HIV-1) population dynamics. The authors incorporate more of the randomness of the HIV-1 infection process to investigate the probability and the possibility of viral extinction in their model.

Many authors investigate asymptotic behaviour of stochastic systems around the equilibria of the underlying deterministic models and examples of those can be found in [28, 57, 116, 117, 51, 114].

1.4 Outline of the thesis

This thesis is structured as follows:

Chapter 1 provides a general introduction on HIV/AIDS epidemic, biological background on the disease in question. It also covers literature review on mathematical modeling of HIV/AIDS, deterministic and stochastic models.

Chapter 2 produces background preliminaries on epidemiological modeling; some theories of ordinary differential equations as well as stochastic differential equations.

In chapter 3 we start off first by presenting the relevant HIV/AIDS epidemic model with two infection stages and inflow of infectives. We perform stability analysis of both the disease-free and endemic equilibrium points.

In Chapter 4 we investigate stochastic dynamics of an HIV/AIDS epidemic model with treatment. We show different approaches of introducing randomness in the model. We prove existence of global positive solutions. Some useful properties such as boundedness, stochastic permanence and asymptotic behaviour around the equilibrium of the underly-

ing deterministic model are also studied.

In Chapter 5 we introduce a stochastic HIV/AIDS epidemic model with inflow of infectives. A Theorem on almost sure exponential stability is studied in the absence of inflow of infectives. Furthermore, we study stability in the mean.

In Chapter 6 we investigate a model describing the population dynamics of HIV/AIDS including treatment and pre-exposure prophylaxis (PrEP) in the context of South Africa.

In Chapter 7 we propose a stochastic model of HIV/AIDS epidemic with saturated incidence rate. Our aim is this chapter is to investigate both the impact of the stochastic perturbation as well as that of the incidence rate on the transmission HIV.

Chapter 8 is devoted to study exponential stability of a disease-free equilibrium for an HIV epidemic model with the use of prophylaxis.

In Chapter 9 we give some concluding remarks, including insightful and constructive ideas for future research.

Chapter 2

Preliminaries

2.1 Existence and uniqueness of solutions

We start off by presenting a general theorem about existence and uniqueness of solutions of the first order initial value problem and we shall refer to [27]. Consider an ordinary differential equation (ODE):

$$x'(t) = f(t, x(t)), \; x(t_0) = x_0, \tag{2.1}$$

where t_0 and x_0 are real numbers. Thus we shall show that if $f(t, x)$ and $\frac{\partial f}{\partial x}(t, x)$ are continuous in some region containing the point (t_0, x_0), then there is an interval (containing t_0) on which a unique solution of equation (2.1) exists.

Theorem 2.1.1. *([27]) Let $f(t, x)$ be continuous for all values t and x. Then the initial value problem is equivalent to the integral equation*

$$x(t) = x_0 + \int_{t_0}^{t} f(s, x(s))ds \tag{2.2}$$

in the sense that $x(t)$ is a solution of (2.1) *if and only if $x(t)$ is a solution of* (2.2).

Let D denote the rectangular region in the tx-plane defined by

$$D : a \leq t \leq b, c \leq x \leq d, \tag{2.3}$$

where $-\infty < a < b < +\infty$ and $-\infty < c < d < +\infty$. We say that the function $f(t,x)$ is Lipschitz continuous in x over D if there exists a constant k, $0 < k < \infty$, such that

$$|f(t,x_1) - f(t,x_2)| \leq k|x_1 - x_2| \tag{2.4}$$

whenever (t,x_1) and (t,x_2) belong to D. The constant k is called a *Lipschitz constant*. Clearly, every Lipschitz continuous function is continuous in x for each fixed t. However, *not every continuous function is Lipschitz continuous.*

Theorem 2.1.2. *[20] Let $f(t,x)$ and $\frac{\partial f}{\partial x}(t,x)$ be continuous on D. Then $f(t,x)$ is Lipschitz continuous in x over D.*

Definition 2.1.3. *([61, 73, 83]) Equilibrium and stability*
A point x^* is an equilibrium solution of (2.1) if $f(t,x^*) = 0$. We say an equilibrium point is

1. *locally stable, if for every $R > 0$ there exists $r > 0$, such that*

$$\|x(0) - x^*\| < r \ \Rightarrow \|x(t) - x^*\| < R, \ t \geq 0$$

2. *locally asymptotically stable, if locally stable and*

$$\|x(0) - x^*\| < r \ \Rightarrow \lim_{t\to\infty} x(t) = x^*$$

3. *globally asymptotically stable, asymptotically stable for all $x(0) \in \mathbb{R}^n$.*

Theorem 2.1.4. *Lyapunov Global Asymptotic Stability*
Let $\dot{x} = f(x)$ and $f(x^*) = 0$. If there exists a C^1 function $V : \mathbb{R}^n \to \mathbb{R}$ such that

1. *$V(x^*) = 0$*
2. *$V(x) > 0$, for all $x \neq x^*$*
3. *$\dot{V}(x) < 0$ for all $x \neq x^*$*

4. $V(x) \to \infty$ *as* $\|x\| \to \infty$

then x^* is a globally asymptotically stable equilibrium.

Definition 2.1.5. *Invariant Sets*
A set M *is called invariant if for the system*

$$\dot{x} = f(x),$$

$x(0) \in M$ *implies that* $x(t) \in M$ *for all* $t \geq 0$.

2.2 Compartment Modeling

A compartmental disease model is one for which the individuals in a population are classified into compartments depending on their status with regard to the infection under study and assumptions about the nature and time rate of transfer from one compartment to another. The standard susceptible-exposed-infectious-removed ($SEIR$) model divides the total population into four compartments: susceptible (S, previously unexposed to the pathogen), exposed (E, infected, but not yet infectious), infected (I, infected and infectious) and recovered (R, recovered from infection and acquired lifelong immunity) [3, 49, 1]. The infection process is represented in Figure 2.1. Children are born susceptible to the disease and enter the compartment S. A susceptible individual in compartment S is infected after effective contact with an infectious individual in compartment I and then enters the exposed compartment E. After the latent period ends, the individual enters the compartment I and becomes capable of transmitting the infection. When the infectious period ends, the individual enters the recovered class R and will never be infected again [49, 1]. In each compartment, individual death occurs at a constant rate, μ, which is equal to the birth rate. Death induced by the disease is not considered here. Therefore, the total population size in the model, N, remains unchanged. The SEIR model and its extension have been used to model many infectious diseases, for example, measles [2, 17], rubella [31, 13], influenza [35, 18] and SARS [56, 101], among others.

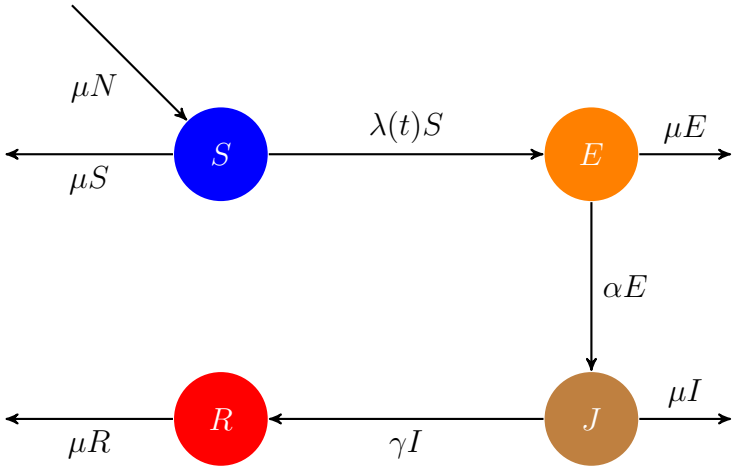


Figure 2.1: Structure of a susceptible-exposed-infectious-recovered (SEIR) model.

where the parameter α is the rate at which individuals in the exposed category become infectious per unit time, and its reciprocal is the average latent period; the parameter γ is the rate at which infectious individuals recover (become immune) per unit time, and its reciprocal is the average infectious period; and the parameter μ refers to the birth and death rates. The probability per unit of time at which the susceptible individuals of the population become infected is called force of infection which is represented by λ. The latter generally seen as a function of total number of infective individuals. The term incidence represents the number of individuals that become infected in any given period of time. It is often referred to as incidence rate, which is the incidence per unit time. Prevalence is defined as the proportion of the population that is infected.

2.2.1 HIV/AIDS compartment modeling

For the case of HIV/AIDS modeling, we can also refer in [6, 54, 14, 88]. In [6] for instance, a model for HIV/AIDS in four compartment is presented. The total sexually-active population at time t, is denoted by $N(t)$. This population $N(t)$ is divided into four mutually-exclusive compartments, namely susceptible class $S(t)$, the infected individuals who do not know that they are infected $I_1(t)$, the infected individuals who do know that

they are infected $I_2(t)$, and that of the AIDS populations $A(t)$. Hence the total population at time t, $N(t)$ can be written as $N(t) = S(t) + I_1(t) + I_2(t) + I_1(t)$. It is assumed that individuals are recruited at a constant rate π to the susceptible class $S(t)$. Susceptible individuals can be infected with HIV following contact with infected individuals at a rate λ, where $\lambda = \frac{\beta_1\lambda_1+\beta_2\lambda_2}{N}$, with β_1, β_2 are the transmission rates for HIV. The individuals in the I_2 class are more infectious than those in the I_1 class. Therefore we must have $\beta_1 < \beta_2$. Suppose that the individuals of the $I_1(t)$ class enter into the $I_2(t)$ class at a rate ω and into the AIDS class $A(t)$ at a rate δ_1. Again suppose that the individuals of the $I_2(t)$ class progress into the AIDS class at a rate $I_2(t)$. Let μ and d denote the natural mortality rate and disease induced death rate respectively.

In [88], the authors present a mathematical model for the transmission dynamics of HIV/AIDS epidemic with treatment by considering the three latent compartments for slow, medium and fast progresses of developing the AIDS. The model is developed by dividing the total population into six compartments, namely susceptible compartment S, slow latent compartment I_1, medium compartment I_2, fast latent compartment I_3, symptomatic stage J and a full-blown AIDS A group. Thus, the total number of population at time t is given by

$$N(t) = S(t) + I_1(t) + I_2(t) + I_3(t) + J(t) + A(t).$$

In the paper by Cai et al., [14], an HIV/AIDS epidemic treatment model is presented. To construct the model, the authors first divide the total population into four classes. The classes are: the class of susceptible individuals $S(t)$, the class of asymptomatic individuals $I(t)$, the class of symptomatic individuals $J(t)$ and the class of the population who have full-blown AIDS $A(t)$. The term μK is the recruitment rate into the population, μ being the birth rate which is assumed to coincide with the average mortality rate by natural causes. The disease-induced mortality rate is denoted by δ. The parameters β; βbdenote the probabilities of disease transmission per contact by an infective in the first and second stage respectively. For an individual, c is the average number of contacts with

others per unit time. By k_1 and k_2 we denote the transfer rates from the asymptomatic phase I to the symptomatic phase J and from the symptomatic phase to the A-class, respectively. The parameter α is the rate of transfer from the symptomatic phase J to the asymptomatic phase I due to treatment.

The structure of the model is given by the following diagram:

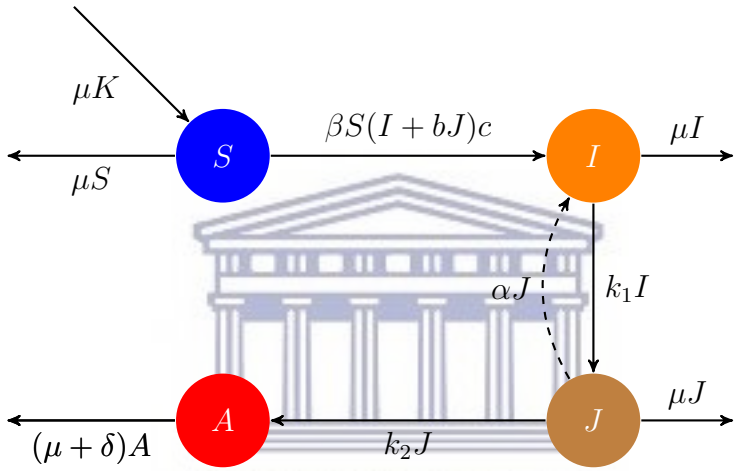


Figure 2.2: Flow diagram of an HIV/AIDS model

2.2.2 Basic Reproduction number $\mathcal{R}_0$

The basic reproduction number can be obtained by inspection in models with only one infective class. How ever if number of infective classes is two or more, then the technique due to Diekmann (1990) is more appropriate. The technique has also been studied by Van den Driessche and Watmough (2002) [11], Hyman et al. (2004) [41]. The technique is called the next generation method and defines $\mathcal{R}_0$ as the spectral radius of the next generator operator.

2.2.3 $\mathcal{R}_0$ using the next generation method

Let us assume that there are n compartments of which m are infected. We define the vector $x = (x_1, ..., x_n)^T$, where $x_i \geq 0$ denotes the number of proportion of individuals in the ith compartment. For simplicity we sort the compartments so that the first m compartments correspond to infected individuals.

Define X_s to be set of all disease free states, that is

$$X_s = \{x \geq 0 | x_i = 0, i = 1, 2, ...m\}.$$

Let $\mathcal{F}_i(x)$ be the rate of appearance of new infections in compartment i and let $\mathcal{V}_i(x) = V_i^-(x) - V_i^+(x)$, where V_i^+ is the rate of transfer of individuals into compartment i by all other means and V_i^- is the rate of transfer of indivuals out of the ith compartment.
The disease transmission model consists of nonnegative initial conditions together with the following system of equations:

$$\dot{x}_i = f_i(x) = \mathcal{F}_i(x) - \mathcal{V}_i(x) \tag{2.5}$$

Let us consider the following assumptions as in [11];

1. If $x \geq 0$, then $\mathcal{F}_i, \mathcal{V}_i^-, \mathcal{V}_i^+ \geq 0$ for $i = 1, 2, ..., n$.
   It is noted that in the case where the compartment is empty, then there can be no transfer of individuals out of the compartment by death, infection nor any other means.

2. If $x_i = 0$, then $\mathcal{V}_i^- = 0$. This simply means that nobody leaves the compartment. In particular if $x \in X_s$, then $\mathcal{V}_i^- = 0$ for $i = 1, 2, ..., m$.

3. If $\mathcal{F}_i = 0, i > m$. (m is the number of infectives classes)

4. If $x \in X_s$, then $\mathcal{F}_i = 0$, and $\mathcal{V}_i = 0$ for all $i = 1, 2, ..., m$.

5. If $\mathcal{F}(x)$ is set to zero, then all the eigenvalues of $Df(x_0)$ have negative real parts and $Df(x_0)$ is the derivative $\left[\frac{\partial f_1}{\partial x_j}\right]$ evaluated at the disease free equilibrium x_0.

Assuming that $\mathcal{F}_i$ and $\mathcal{V}_i$ meet the assumptions above, we can form the next generation matrix FV^{-1} from the matrices of partial derivatives of $\mathcal{F}_i$ and V_i. More specifically we have,

$$F = \left[\frac{\partial \mathcal{F}_i}{\partial x_j}(x_0)\right] \text{ and } V = \left[\frac{\partial \mathcal{V}_i}{\partial x_j}(x_0)\right]$$

where $i, j = 1, ..., m$ and x_0 is the disease free equilibrium.

The entries of FV^{-1} give the rate at which infected individuals in x_j produce new infections in x_i, multiplied by the average length of time an individual spends on a single visit to compartment j.

Definition 2.2.1. *The basic reproduction number is given by*

$$\mathcal{R}_0 = \rho(FV^{-1}) \tag{2.6}$$

where ρ denotes the spectral radius of the matrix FV^{-1}.

Thus, we call FV^{-1} the next generation matrix for the model and we shall set $\mathcal{R}_0$ as equal to the spectral radius FV^{-1}.

2.3 Stochastic Processes

Let $(\Omega, \mathcal{F}, \mathbb{P})$ be a probability space, see [60, pp9-11]. A filtration is an increasing family $\{\mathcal{F}_t\}_{t\geq 0}$ of increasing sub-σ-algebras of $\mathcal{F}$ (*i.e.* $\mathcal{F}_t \subset \mathcal{F}_s \subset \mathcal{F}$ for all $0 \leq t < s < \infty$). The filtration is said to be right continuous if $\mathcal{F}_t = \bigcap_{s>t} \mathcal{F}_s$ for all $t \geq 0$. When the probability space is complete, the filtration is said to satisfy the usual conditions if it is right continuous and $\mathcal{F}_0$ contains all P-null sets.

A family $\{X_t\}_{t\in I}$ of $\mathbb{R}^d$-valued random variables is called a stochastic process with parameter set (or index set) I and state space $\mathbb{R}^d$. The parameter set I is usually the halfline

$\mathbb{R}_+ = [0, \infty\}$, but it may also be an interval $[a, b]$, the nonegative integers or even subsets of $\mathbb{R}^d$. Note that for each fixed $t \in I$ we have a random variable

$$\Omega \ni \omega \to X_t(\omega) \in \mathbb{R}^d.$$

On the other hand, for each fixed $\omega \in \Omega$ we have a function

$$I \ni t \to X_t(\omega) \in \mathbb{R}^d$$

which is called a sample path of the process, and we shall write $X.(\omega)$ for the path.

Theorem 2.3.1. *([60]) If $\{X_t\}_{t\geq 0}$ is a progressively measurable process and τ is a stopping time, then $X_\tau I_{I<\infty}$ is $\mathcal{F}_\tau$-measurable. In particular, if τ is finite, then X_τ is $\{\mathcal{F}_\tau\}$-measurable.*

Theorem 2.3.2. *([60]) Let $\{M_t\}_{t\geq 0}$ be an $\mathbb{R}^d$-valued martingale with respect to $\{\mathcal{F}_t\}$, and let θ, ρ be two finite stopping times.*
Then

$$E(M_\theta | \mathcal{F}_\rho) = M_{\theta\wedge\rho} \ a.s.$$

In particular, if τ is a stopping time, then

$$E(M_{\tau\wedge t} | \mathcal{F}_s) = M_{\tau\wedge s} \text{ a.s.}$$

holds for all $0 \leq s < t < \infty$. That is, the stopped process $M^\tau = \{M_{\tau\wedge t}\}$ is still a martingale with respect to the same filtration $\{\mathcal{F}_t\}$.

2.4 Brownian Motions

Brownian motion is the name given to the irregular movement of pollen grains, suspended in the water, observed by the Scottish botanist Robert Brown in 1982. The motion was later explained by the random collisions with the molecules of water. To describe the motion mathematically it is natural to use the concept of a stochastic process $B_t(\omega)$, interpreted as the position of the pollen grain w at time t. Let us define Brownian motion mathematically in what follows, see for instance [60, p15]

Definition 2.4.1. *Let $(\Omega, \mathcal{F}, \mathbb{P})$ be a probability space with a filtration $\{\mathcal{F}_t\}_{t\geq 0}$. A (standard) one-dimensional Brownian motion is a real-valued continuous $\{\mathcal{F}_t\}$-adapted process $\{\mathcal{B}_t\}_{t\geq 0}$ with the following properties:*

- $B_0 = 0$ *a.s.;*
- *for $0 \leq s < t < \infty$, the increment $B_t - B_s$ is normally distributed with mean zero and variance $t - s$;*
- *for $0 \leq s < t < \infty$, the increment $B_t - B_s$ is independent of $\mathcal{F}_s$.*

2.5 Itô's Formula

Let $\{B_t\}_{t\geq 0}$ be a one-dimensional Brownian motion defined on the complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ adapted to the filtration $\{\mathcal{F}\}_{t\geq 0}$, see [60, p31]. Let $\mathcal{L}^1(\mathbb{R}_+; \mathbb{R}^d)$ denote the family of all $\mathbb{R}^d$-valued measurable $\{\mathcal{F}\}$-adapted processes $f = \{f(t)\}_{t\geq 0}$ such that

$$\int_0^T |f(t)|dt < \infty \quad \text{a.s. for every } T > 0.$$

Definition 2.5.1. *A one-dimensional Itô process is a continuous adapted process $x(t)$ on $t \geq 0$ of the form*

$$x(t) = x(0) + \int_0^t f(s)ds + \int_0^t g(s)dB_s,$$

where $f \in \mathcal{L}^1(\mathbb{R}_+; \mathbb{R})$ and $g \in \mathcal{L}^2(\mathbb{R}_+; \mathbb{R})$. We shall say that $x(t)$ has stochastic differential $dx(t)$ on $t \geq 0$ given by

$$dx(t) = f(t)dt + g(t)dB_t.$$

Let $C^{2,1}(\mathbb{R}^d \times \mathbb{R}_+; \mathbb{R})$ denote the family of all real-valued functions $V(x,t)$ defined on $\mathbb{R}^d \times \mathbb{R}_+$ such that they are continuously twice differentiable in x and once in t. If $V \in C^{2,1}(\mathbb{R}^d \times \mathbb{R}_+; \mathbb{R})$, we set

$$V_t = \frac{\partial V}{\partial t}, \quad V_x = \left(\frac{\partial V}{\partial x_1}, ..., \frac{\partial V}{\partial x_d}\right),$$

$$V_{xx} = \left(\frac{\partial^2 V}{\partial x_i \partial x_j}\right)_{d\times d} = \begin{pmatrix} \frac{\partial^2 V}{\partial x_1 \partial x_2} & \cdots & \frac{\partial^2 V}{\partial x_1 \partial x_d} \\ \vdots & & \vdots \\ \frac{\partial^2 V}{\partial x_1 \partial x_1} & \cdots & \frac{\partial^2 V}{\partial x_d \partial x_d} \end{pmatrix}$$

Clearly, when $V \in C^{2,1}(\mathbb{R}\times\mathbb{R}_+;\mathbb{R})$, we have $V_x = \frac{\partial V}{\partial x}$ and $V_{xx} = \frac{\partial^2 V}{\partial x^2}$.

Theorem 2.5.2. *([60])* (The one-dimensional Itô formula) *Let $x(t)$ be an Itô process on $t \geq 0$ with the stochastic differential*

$$dx(t) = f(t)dt + g(t)dB_t,$$

where $f \in \mathcal{L}^1(\mathbb{R}_+;\mathbb{R})$ and $g \in \mathcal{L}^2(\mathbb{R}_+;\mathbb{R})$. Let $V \in C^{2,1}(\mathbb{R}\times\mathbb{R}_+;\mathbb{R})$. Then $V(x(t),t)$ is again an Itô process with the stochastic differential given by

$$dV(x(t),t) = [V_t(x(t),t) + V_x(x(t),t)f(t) + \frac{1}{2}V_{xx}(x(t),t)g^2(t)]dt + V_x(x(t),t)g(t)dB_t \quad \text{a.s.}$$

Theorem 2.5.3. *([60])* (The multi-dimensional Itô formula) *Let $x(t)$ be a d-dimensional Itô process on $t \geq 0$ with the stochastic differential*

$$dx(t) = f(t)dt + g(t)dB(t),$$

where $f \in \mathcal{L}^1(\mathbb{R}_+;\mathbb{R}^d)$ and $g \in \mathcal{L}^2(\mathbb{R}_+;\mathbb{R}^{d\times m})$. Let $V \in C^{2,1}(\mathbb{R}^d\times\mathbb{R}_+;\mathbb{R})$. Then $V(x(t),t)$ is again an Itô process with the stochastic differential given by

$$\begin{aligned} dV(x(t),t) &= [V_t(x(t),t) + V_x(x(t),t)f(t) + \frac{1}{2}trace(g^T(t)V_{xx}(x(t),t)g(t))]dt \\ &\quad + V_x(x(t),t)g(t)dB(t) \quad \text{a.s} \end{aligned}$$

Let us now introduce formally a multiplication rule:
$dtdt = dB_i dt = 0, dB_i dB_i = dt, dB_i dB_j = 0$ if $i \neq j$,
Then, for example,

$$dx_i(t)dx_j(t) = \sum_{k=1}^{m} g_{ik}(t)g_{jk}(t)dt.$$

Example 2.5.4. *Let us consider a real-valued function of the form $g = g(S(t), I(t), J(t), A(t))$. In particular we note that $\frac{\partial g}{\partial t} = 0$. For convenience we write down the formula for the differential of g. Applying the multi-dimensional Itô formula we obtain*

$$
\begin{aligned}
dg &= \frac{\partial g}{\partial S}dS + \frac{\partial g}{\partial I}dI + \frac{\partial g}{\partial J}dJ + \frac{\partial g}{\partial A}dA + \frac{1}{2}\left[\frac{\partial^2 g}{\partial I^2}dSdS + \frac{\partial^2 g}{\partial I^2}dIdI + \frac{\partial^2 g}{\partial J^2}dJdJ \right.\\
&\left. + \frac{\partial^2 g}{\partial A^2}dAdA\right] + \left[\frac{\partial^2 g}{\partial S\partial I}dSdI + \frac{\partial^2 g}{\partial S\partial J}dSdJ + \frac{\partial^2 g}{\partial S\partial A}dSdA + \frac{\partial^2 g}{\partial I\partial J}dIdJ \right.\\
&\left. + \frac{\partial^2 g}{\partial I\partial A}dIdA + \frac{\partial^2 g}{\partial J\partial A}dJdA\right].
\end{aligned}
$$

2.6 Stochastic Differential equations

Consider the d-dimensional stochastic differential equation of Itô type, see [60, pp.48-51]

$$dx(t) = f(x(t), t)dt + g(x(t), t)dB(t) \quad on \quad t_0 \leq t \leq T \tag{2.7}$$

with initial value $x(t_0) = x_0$. By the definition of stochastic differential, this equation is equivalent to the following stochastic integral equation:

$$x(t) = x(0) + \int_{t_0}^{t} f(x(s), s)ds + \int_{t_0}^{t} g(x(s), s)dB(s) \quad on \quad t_0 \leq t \leq T. \tag{2.8}$$

2.7 Existence and Uniqueness of Solutions

Theorem 2.7.1. *Assume that there exist two positive constants $\bar{K}$ and K such that*
(i) (Lipschitz condition) for all $x, y \in \mathbb{R}^d$ and $t \in [t_0, T]$

$$|f(x,t) - f(y,t)|^2 \wedge |g(x,t) - g(y,t)|^2 \leq \bar{K}|x - y|^2; \tag{2.9}$$

(ii) (Linear growth condition) for all $(x,t) \in \mathbb{R}^d \times [t_0, T]$

$$|f(x,t)|^2 \wedge |g(x,t)|^2 \leq K(1 + |x|^2). \tag{2.10}$$

Then there exists a unique solution $x(t)$ to equation (2.7) and the solution belongs to $\mathcal{M}^2([t_0, T]; \mathbb{R}^d)$.

2.8 Stability of Stochastic Differential equations

Consider the d-dimensional stochastic differential equation, see for instance [60, pp.110-128]

$$dx(t) = f(x(t), t)dt + g(x(t), t)dB(t) \tag{2.11}$$

on $t \geq 0$ with initial value $X(0) = X_0$, the solution is denoted by $X(t, X_0)$. Assume that $f(t, 0) = g(t, 0) = 0$ for all $t \geq 0$, so the origin point is an equilibrium of (2.11).

Definition 2.8.1. *The equilibrium $X = 0$ of the system (2.11) is said to be:*

(i) Stable in probability if for all $\epsilon > 0$,

$$\lim_{X_0 \to 0} \mathbb{P}\left(\sup_{t \geq 0} |X(t, X_0)| \geq \epsilon\right) = 0; \tag{2.12}$$

(ii) asymptotically stable if it is stable in probability and moreover;

$$\lim_{X_0 \to 0} \mathbb{P}\left(\lim_{t \to \infty} X(t, X_0) = 0\right) = 1; \tag{2.13}$$

(iii) globally asymptotically stable if it is stable in probability and moreover, for all $X_0 \in \mathbb{R}^n$

$$\mathbb{P}\left(\lim_{t \to \infty} X(t, X_0) = 0\right) = 1; \tag{2.14}$$

(iv) almost surely exponentially stable if for all $X_0 \in \mathbb{R}^n$,

$$\lim_{t \to \infty} \sup \frac{1}{t} \ln |X(t, X_0)| < 0 \ a.s.; \tag{2.15}$$

(v) pth moment exponentially stable if there is a pair of positive constants C_1 and C_2 such that for all $X_0 \in \mathbb{R}^n$,

$$\mathbb{E}\left(|X(t, X_0|^p\right) \leq C_1 |X_0|^p e^{-C_2 t} \quad \text{on} \quad t \geq 0. \tag{2.16}$$

Let us denote by $\mathcal{L}$ the differential operator associated to (2.11), defined for a function $V(t, x) \in C^{1,2}(\mathbb{R} \times \mathbb{R}^n)$ by

$$\mathcal{L}V = \frac{\partial V}{\partial t} + f^T \frac{\partial V}{\partial x} + \frac{1}{2} Tr\left[g^T \frac{\partial^2 V}{\partial x^2} g\right].$$

Chapter 3

Stability of an HIV/AIDS epidemic model with treatment and inflow of infectives

3.1 Introduction

We investigate an HIV/AIDS epidemic model with treatment similar to that in [14]. The model allows for two stages of infection namely the asymptomatic phase and the symptomatic phase. The ARV treatment helps the symptomatic individuals to move back to asymptomatic phase. Thus, we only consider two stages according to clinic stages, i.e., the asymptomatic phase I and the symptomatic phase J. In this chapter and throughout, we find it convenient to replace $\beta S(I + bJ)c$ in [14] by $S(\beta_1 I + \beta_2 J)c$. We also introduce inflow of infectives Q_1 and Q_2 in the model as in the diagram below:

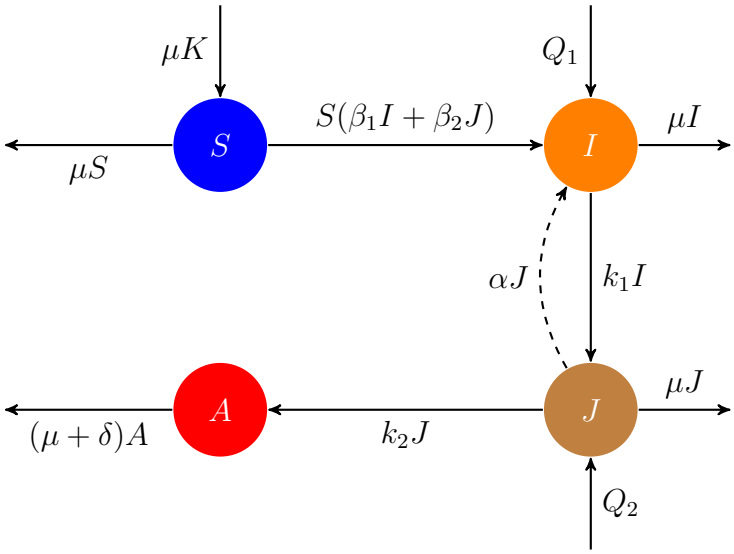


Figure 3.1: Flow diagram of HIV/AIDS model with inflow of infectives

We now give the description of parameters.

- μ Birth and mortality rates by natural causes,
- K Size of the total population,
- c An individual average number of sexual contacts with others per unit time,
- β_1 Probability of disease transmission in the asymptomatic phase,
- β_2 Probability of disease transmission in the symptomatic phase,
- k_1 Progression rate from I to J,
- k_2 Progression rate from the symptomatic phase J to A,
- α Rate of transfer from J to I due to ARV treatment,
- δ Disease induced mortality rate.

Our model is then constructed by considering the appropriate in-flow and out-flow rates of each compartment as in figure (3.1) and parameters in the list above.

$$\begin{aligned}
\frac{dS}{dt} &= \mu k - S\lambda - \mu S, \\
\frac{dI}{dt} &= Q_1 + S\lambda - (\mu + k_1)I + \alpha J, \\
\frac{dJ}{dt} &= Q_2 + k_1 I - (\mu + k_2 + \alpha)J, \\
\frac{dA}{dt} &= k_2 J - (\mu + \delta)A. \qquad (3.1)
\end{aligned}$$

where

$$\lambda = c(\beta_1 I + \beta_2 J)$$

and

with $S(0) = S_0 > 0$, $I(0) = I_0 \geq 0$, $J(0) = J_0 \geq 0$, $A(0) = A_0 \geq 0$

In the absence of Q_1 and Q_2, then the model system (3.1) permits two equilibria; the disease-free equilibrium $E_0 = (K, 0, 0, 0)$ and the equilibrium point $E^* = (S^*, I^*, J^*, A^*)$. The coordinates of the equilibrium point will be calculated at a later stage.

For calculating the basic reproduction number $\mathcal{R}_0$ we take $Q_1 = Q_2 = 0$. Using the next generation matrix we re-arrange the equations so that the infective classes come first, we obtain

$$\begin{aligned}
\frac{dI}{dt} &= S\lambda - (\mu + k_1)I + \alpha J, \\
\frac{dJ}{dt} &= k_1 I - (\mu + k_2 + \alpha)J, \\
\frac{dS}{dt} &= \mu K - S\lambda - \mu S. \qquad (3.2)
\end{aligned}$$

We eliminate that last compartment since it does not appear in any other compartment and we write (3.2) by

$$x^{'} = F(x) - V(x)$$

which can also be expressed by

$$x_i^{'} = F_i - V_i \quad \text{or} \quad x_i^{'} = F_i - (V_i^{-} - V_i^{+})$$

where F and V are the $m \times n$ matrices given by

$$F = \left(\frac{\partial F_i(x_0)}{\partial x_j} \right), \qquad V = \left(\frac{\partial V_i(x_0)}{\partial x_j} \right).$$

Then from our system we have

$$F = \begin{pmatrix} \frac{\partial F_i}{\partial I} & \frac{\partial F_i}{\partial J} \\ 0 & 0 \end{pmatrix} = \begin{pmatrix} \beta_1 Sc & \beta_2 Sc \\ 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \frac{\partial V}{\partial I} & \frac{\partial V}{\partial J} \\ \frac{\partial V}{\partial I} & \frac{\partial V}{\partial J} \end{pmatrix} = \begin{pmatrix} \mu + k_1 & -\alpha \\ -k_1 & (\mu + k_2 + \alpha) \end{pmatrix}$$

The derivatives of F and V at $E_0(0, 0, K)$ are given by

$$F = \begin{pmatrix} \beta_1 cK & \beta_2 cK \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} (\mu + k_1) & -\alpha \\ -k_1 & (\mu + k_2 + \alpha) \end{pmatrix}$$

The inverse of V is given by

$$V^{-1} = \frac{1}{(\mu+k_1)(\mu+k_2)+\mu\alpha} \begin{pmatrix} (\mu + k_2 + \alpha) & k_1 \\ \alpha & (\mu + k_1) \end{pmatrix}$$

and a calculation of FV^{-1} gives the basic reproductive number of the model as

$$\rho(FV^{-1}) = \mathcal{R}_0 = \frac{cK\left((\mu + k_2 + \alpha)\beta_1 + \beta_2 k_1\right)}{((\mu + k_1)(\mu + k_2) + \alpha\mu)}. \tag{3.3}$$

3.1.1 Existence of the endemic equilibrium

We first compute the coordinates of the endemic equilibrium E^* by

$$\begin{aligned}
S^* &= \frac{\mu K}{\lambda+\mu},\\
I^* &= \frac{\alpha(\lambda+\mu)Q_2+(\alpha+\mu+k_2)(k\lambda\mu+(\lambda+\mu)Q_1)}{[(\mu+k_1)(\mu+k_2)+\alpha\mu](\lambda+\mu)},\\
J^* &= \frac{1}{(\alpha+\mu+k_2)}\left[Q_2+k_1\left(\frac{\alpha(\lambda+\mu)Q_2+(\alpha+\mu+k_2)(k\lambda\mu+(\lambda+\mu)Q_1)}{[(\mu+k_1)(\mu+k_2)+\alpha\mu](\lambda+\mu)}\right)\right],\\
A^* &= \frac{k_2}{(\mu+\delta)(\alpha+\mu+k_2)}\left[Q_2+k_1\left(\frac{\alpha(\lambda+\mu)Q_2+(\alpha+\mu+k_2)(k\lambda\mu+(\lambda+\mu)Q_1)}{[(\mu+k_1)(\mu+k_2)+\alpha\mu](\lambda+\mu)}\right)\right],
\end{aligned}$$

We now prove existence of the endemic equilibrium by considering λ as defined in the model system (3.1). At the same time, λ is a root of the following polynomial

$$Z_1\lambda^2+Z_2\lambda+Z_3=0; \tag{3.4}$$

where

$$\begin{aligned}
Z_1 &= \mu(\alpha+k_2+\mu)+k_1(k_2+\mu)\\
Z_2 &= c\beta_1((-\alpha-k_2-\mu)(\mu K+Q_1)-\alpha Q_2)+k_1(\mu(\mu+k_2)-c\beta_2(\mu K+Q_1+Q_2))\\
&\quad +\mu(\mu(\alpha+k_2)-c\beta_2 Q_2)\\
Z_3 &= -\mu(c\beta_1(Q_1(\alpha+k_2+\mu)+\alpha Q_2)+c\beta_2(k_1(Q_1+Q_2)+\mu Q_2)).
\end{aligned}$$

For the case $Q_1=Q_2=0$, the quadratic equation admits a root $\lambda_0=0$ which corresponds to the disease-free equilibrium and another root

$$\lambda_1=\frac{\mu(c\beta_1K(\alpha+k_2+\mu)-k_1(-c\beta_2K+k_2+\mu)+\mu(\alpha+k_2+\mu))}{\alpha\mu+k_1\mu+k_2\mu+k_1k_2+\mu^2}$$

which is positive if and only if $-Z_2>0$. It is also noted that a negative value of λ will result in a point E_1 which is non-feasible. Thus, if $Q_1,Q_2>0$ as $-Z_2=h>0$ the quadratic equation admits one positive and one negative root. The negative root is not meaningful biologically, and so we only consider the positive root given by

$$\lambda^* = \frac{-Z_2 + \sqrt{Z_2^2 - 4Z_1Z_3}}{2Z_1}.$$

We note that $h > 0$ if and only if $\mathcal{R}_0 > 1$, and $h < 0$ if and only if $\mathcal{R}_0 < 1$. We observe that

$$\lim_{Q_1,Q_2\to 0} \lambda^* = \frac{h + |h|}{2Z_1} = \begin{cases} 0, & h < 0, \\ \frac{h}{Z_1}, & h > 0. \end{cases}$$

In particular it is noticed that as Q_1, Q_2 get closer to zero, the model has threshold $\mathcal{R}_0 = 1$. Therefore, for $Q_1, Q_2 > 0$, the disease remains endemic, so the system (3.1) has one endemic equilibrium point and the disease will remain in the population. In this case the system (3.1) would not exhibit a disease-free equilibrium.

3.1.2 Feasible solutions

Thus, we shall study system (3.1) in the following feasible region:

$$\Delta = \left\{ x \in \mathbb{R}^4 | x_1 > 0, x_2 > 0, x_3 > 0, x_4 > 0, x_1 + x_2 + x_3 + x_4 < k \right\}. \tag{3.5}$$

which can be shown to be positively invariant with respect to (3.1).

3.1.3 Global stability of the disease-free equilibrium

We now prove by means of Lyapunov function that for $\mathcal{R}_0 < 1$ the disease-free equilibrium $E_0(K, 0, 0, 0)$ is globally asymptotically stable if $Q_1 = Q_2 = 0$.

Let us first define the numbers π, ξ_0, ξ_1, ξ_2 and ξ_3

$$\begin{aligned}\pi &= (\mu+k_1)(\mu+k_2)+\alpha\mu,\\ \xi_1 &= \beta_1(\mu+k_2+\alpha)+\beta_2 k_1,\\ \xi_2 &= \beta_1\alpha+\beta_2(\mu+k_1).\end{aligned} \tag{3.6}$$

The values of ξ_0 and ξ_3 will be displayed at later stage, meanwhile they are declared to be positives.

Theorem 3.1.1. *For the case $Q_1 = Q_2 = 0$, then the disease-free equilibrium E_0 of system* (3.1) *is globally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. Consider the numbers as displayed (3.6).
Assuming that $\mathcal{R}_0 < 1$, it is possible to find positive numbers ξ_0 and ξ_3 sufficiently small such as to have the following inequality:

$$\xi_0 c\beta_1 K + \pi\beta_1(\mathcal{R}_0-1) < 0,\ \xi_0 c\beta_2 K + \xi_3 k_2 + \pi\beta_2(\mathcal{R}_0-1) < 0.$$

Define the following function

$$V_1(S(t),I(t),J(t),A(t)) = \xi_0(K-S(t)) + \xi_1 I(t) + \xi_2 J(t) + \xi_3 A(t).$$

Differentiating $V_1(t)$, we have

$$\begin{aligned}\dot{V}_1(t) &= -\xi_0\dot{S}(t) + \xi_1\left[c(\beta_1 I+\beta_2 J)S - (\mu+k_1)I + \alpha J\right] + \xi_2\left[k_1 I - (\mu+k_2+\alpha)J\right] + \xi_3\dot{A}(t)\\ &\le -\xi_0\dot{S}(t) + \pi(\mathcal{R}_0-1)(\beta_1 I+\beta_2 J) + \xi_3\dot{A}(t)\\ &= -\xi_0(\mu(K-S) - cK(\beta_1 I+\beta_2 J)) + \pi(\mathcal{R}_0-1)(\beta_1 I+\beta_2 J) + \xi_3(k_2 J - (\mu+\delta)A)\\ &= -\xi_0\mu(K-S) + I[\xi_0 c\beta_1 K + \pi\beta_1(\mathcal{R}_0-1)] + J[\xi_0 c\beta_2 K + \xi_3 k_2 + \pi\beta_2(\mathcal{R}_0-1)]\\ &\quad -\xi_3(\mu+\delta)A.\end{aligned} \tag{3.7}$$

We note that V_1 is positive-definite and $\dot{V}_1$ is negative-definite. Therefore the function V_1 is a Lyapunov function for system (3.1) without inflow of infectives. By the Lyapunov

asymptotic stability theorem, the disease-free equilibrium E_0 is globally asymptotically stable. This completes the proof.

□

3.1.4 Global stability of the endemic equilibrium

We shall now prove global stability of the endemic equilibrium.

Theorem 3.1.2. *The endemic equilibrium E^* of system (3.1) is globally asymptotically stable for $\mathcal{R}_0 > 1$.*

Proof. Setting $r = (S, I, J) \in \Omega \subset \mathbb{R}^4$, we can now construct a Lyapunov function of the form

$$\begin{aligned} V_2 = V_2(r) &= \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + C_1 \left(I - I^* - I^* \ln \frac{I}{I^*}\right) \\ &+ C_2 \left(J - J^* - J^* \ln \frac{J}{J^*}\right) \end{aligned} \tag{3.8}$$

where $r^* = E^* = (S^*, I^*, J^*)$ and $C_i > 0$ is a constant. Thus, $V_2(r) \geq 0$ for $r \in \text{Int } \Delta$, and $V_2(r) = 0 \iff r = r^*$.

By equating each equation in system (3.1) to zero, the equilibrium equations as follows are useful:

$$\begin{aligned} \mu K &= S^*(\beta_1 I^* + \beta_2 J^*)c + \mu S^*, \\ (\mu + k_2 + \alpha) &= \frac{Q_2}{J^*} + k_1 \frac{I^*}{J^*}, \\ (\mu + k_1) &= \frac{Q_1}{I^*} + \frac{S^*(\beta_1 I^* + \beta_2 J^*)c}{I^*} + \alpha \frac{J^*}{I^*}. \end{aligned} \tag{3.9}$$

The time derivative of V_2 is

$$\begin{aligned}\dot{V}_2 &= \dot{S}\left(1-\frac{S^*}{S}\right)+C_1\dot{I}\left(1-\frac{I^*}{I}\right)\\ &+ C_2\dot{J}\left(1-\frac{J^*}{J}\right).\end{aligned} \tag{3.10}$$

We substitute (3.9) into (3.10)

$$\begin{aligned}\dot{V}_2 &= \left(1-\frac{S^*}{S}\right)(-cS(\beta_1 I+\beta_2 J)-\mu S+cS^*(\beta_1 I^*+\beta_2 J^*)+\mu S^*)\\ &+C_1\left(1-\frac{I^*}{I}\right)(Q_1+S(\beta_1 I+\beta_2 J)c+\alpha J\\ &-\frac{(Q_1+\beta_1 S^* cI^*+\beta_2 S^* cJ^*+\alpha J^*)I}{I^*}\Bigg)\\ &+C_2\left(1-\frac{J^*}{J}\right)\left(Q_2+k_1 I-\left(\frac{Q_2}{J^*}+k_1\frac{I^*}{J^*}\right)\right).\end{aligned} \tag{3.11}$$

Expanding and grouping some terms we have

$$\begin{aligned}\dot{V}_2 &= \mu S^*\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right)+\left(1-\frac{S^*}{S}\right)c\beta_1(I^*S^*-IS)\\ &+\left(1-\frac{S^*}{S}\right)c\beta_1(J^*S^*-JS)+C_1\left(1-\frac{I^*}{I}\right)\left(Q_1-Q_1\frac{I}{I^*}\right)\\ &+C_1\left(1-\frac{I^*}{I}\right)\beta_1 c\left(IS-I^*S^*\frac{I}{I^*}\right)\\ &+C_1\left(1-\frac{I^*}{I}\right)\beta_2 c\left(JS-J^*S^*\frac{I}{I^*}\right)+C_1\alpha\left(1-\frac{I^*}{I}\right)\left(J-J^*\frac{I}{I^*}\right)\\ &+C_2k_1\left(1-\frac{J^*}{J}\right)\left(I-I^*\frac{J}{J^*}\right)+C_2\left(1-\frac{J^*}{J}\right)\left(Q_2-Q_2\frac{J}{J^*}\right).\end{aligned} \tag{3.12}$$

Let

$$\frac{S}{S^*}=x,\frac{I}{I^*}=y,\frac{J}{J^*}=z.$$

Then (3.12) becomes

$$\begin{aligned}\dot{V}_2 &= \mu S^*\left(2-\frac{1}{x}-x\right)+c\beta_1 I^*S^*\left(1-xy-\frac{1}{x}+y\right)\\ &\quad +c\beta_2 J^*S^*\left(1-xz-\frac{1}{x}+z\right)+C_1\left(2-\frac{1}{y}-y\right)Q_1\\ &\quad +C_1\beta_1 cS^*I^*(xy-y-x+1)+C_1\beta_2 cS^*J^*\left(xz-\frac{xz}{y}-y+1\right)\\ &\quad +C_1\alpha J^*\left(z-y-\frac{z}{y}+1\right)+C_2k_1I^*\left(y-z-\frac{y}{z}+1\right)\\ &\quad +C_2\left(2-\frac{1}{z}-z\right)Q_2. \end{aligned} \tag{3.13}$$

Expanding further we have

$$\begin{aligned}\dot{V}_2 &= \mu S^*\left(2-\frac{1}{x}-x\right)+C_1\left(2-\frac{1}{y}-y\right)Q_1+c\beta_1 I^*S^*-c\beta I^*S^*xy-c\beta I^*S^*\frac{1}{x}\\ &\quad +c\beta_1 I^*S^*y+c\beta_2 J^*S^*-c\beta_2 J^*S^*xz-c\beta_2 J^*S^*\frac{1}{x}+c\beta_2 J^*S^*z\\ &\quad +C_1\beta_1 cS^*I^*xy-C_1\beta_1 cS^*I^*y-C_1\beta_1 cS^*I^*x+C_1\beta_1 cS^*I^*+C_1\beta_2 cS^*J^*xz\\ &\quad -C_1\beta_2 cS^*J^*\frac{xz}{y}-C_1\beta_2 cS^*J^*y+C_1\beta_2 cS^*J^*\\ &\quad +C_1\alpha J^*z-C_1\alpha J^*y-C_1\alpha J^*\frac{z}{y}+C_1\alpha J^*+C_2k_1I^*y-C_2k_1I^*z\\ &\quad -C_2k_1I^*\frac{y}{z}+C_2k_1I^*. \end{aligned} \tag{3.14}$$

Grouping some terms like xy, xz, y and z, then we have

$$\begin{aligned}\dot{V}_2 &= \mu S^*\left(2-\frac{1}{x}-x\right)+C_1\left(2-\frac{1}{y}-y\right)Q_1+c\beta_1 I^*S^*xy(C_1-1)+c\beta_2 J^*S^*xz(C_1-1)\\ &\quad +y(c\beta_1 S^*I^*-C_1c\beta_1 S^*I^*-C_1c\beta_2 S^*J^*-C_1\alpha J^*+C_2k_1I^*)\\ &\quad +z(c\beta_2 S^*J^*+C_1\alpha J^*-C_2k_1I^*)+c\beta_1 I^*S^*-c\beta_1 I^*S^*\frac{1}{x}\\ &\quad +c\beta_2 J^*S^*-c\beta_2 J^*S^*\frac{1}{x}+C_1\beta_1 cS^*I^*-C_1\beta_2 cS^*J^*\frac{xz}{y}+C_1\beta_2 cS^*J^*\\ &\quad -C_1\alpha J^*\frac{z}{y}+C_1\alpha J^*-C_2k_1I^*\frac{y}{z}+C_2k_1I^*-C_1\beta_1 cS^*I^*x \end{aligned} \tag{3.15}$$

We choose the coefficients of xy, xz, y and z which are equal to zero; that is,

$$(C_1 - 1) = 0,$$

$$c\beta_1 S^* I^* - C_1 c\beta_1 S^* I^* - C_1 c\beta_2 S^* J^* - C_1 \alpha J^* + C_2 k_1 I^* = 0,$$

$$c\beta_2 S^* J^* + C_1 \alpha J^* - C_2 k_1 I^* = 0.$$

Thus we have

$$C_1 = 1,\ C_2 = \frac{c\beta_2 S^* J^* + \alpha J^*}{k_1 I^*}.$$

Equation (3.15) is reduced to the following.

$$\begin{aligned}
\dot{V}_2 &= \mu S^* \left(2 - \frac{1}{x} - x\right) + C_1 \left(2 - \frac{1}{y} - y\right) Q_1 + c\beta_1 S^* I^* \left(2 - \frac{1}{x} - x\right) \\
&+ c\beta_2 S^* J^* \left(2 - \frac{1}{x} - \frac{xz}{y}\right) - \frac{z}{y}\alpha J^* + \alpha J^* - \frac{y}{z} C_2 k_1 I^* \\
&+ C_2 k_1 I^* + C_2 \left(2 - \frac{1}{z} - z\right) Q_2. \qquad (3.16)
\end{aligned}$$

By substituting C_1, C_2 in (3.16) it follows that

$$\begin{aligned}
\dot{V}_2 &= S^*(\mu + c\beta_1 I^*) \left(2 - \frac{1}{x} - x\right) + \left(2 - \frac{1}{y} - y\right) Q_1 + c\beta_2 S^* J^* \left(3 - \frac{1}{x} - \frac{xz}{y} - \frac{y}{z}\right) \\
&+ \alpha J^* \left(2 - \frac{z}{y} - \frac{y}{z}\right) + C_2 \left(2 - \frac{1}{z} - z\right) Q_2. \qquad (3.17)
\end{aligned}$$

Note that since the arithmetical mean is greater than or equal to the geometric mean, that is

$$(a_1 + a_2 + ... + a_n)/n \geq \sqrt[n]{a_1 a_2 ... a_n} \ \text{ for } a_i \geq 0, i = 1, .., n,$$

then it follows that $(2 - x - 1/x) \leq 0$ for $x > 0$ and $(2 - x - 1/x) = 0$ if and only if $x = 1$; $(2 - y - 1/y) \leq 0$ for $y > 0$ and $(2 - y - 1/y) = 0$ if and only if $y = 1$; $(2 - z - 1/z) \leq 0$ for $z > 0$ and $(2 - z - 1/z) = 0$ if and only if $z = 1$; $\left(2 - \frac{z}{y} - \frac{y}{z}\right) \leq 0$ for $y, z > 0$ and $\left(2 - \frac{z}{y} - \frac{y}{z}\right) = 0$ if and only if $y = z$; $\left(3 - \frac{1}{x} - \frac{xz}{y} - \frac{y}{z}\right) \leq 0$ for $x > 0$, $y > 0$, and $z > 0$

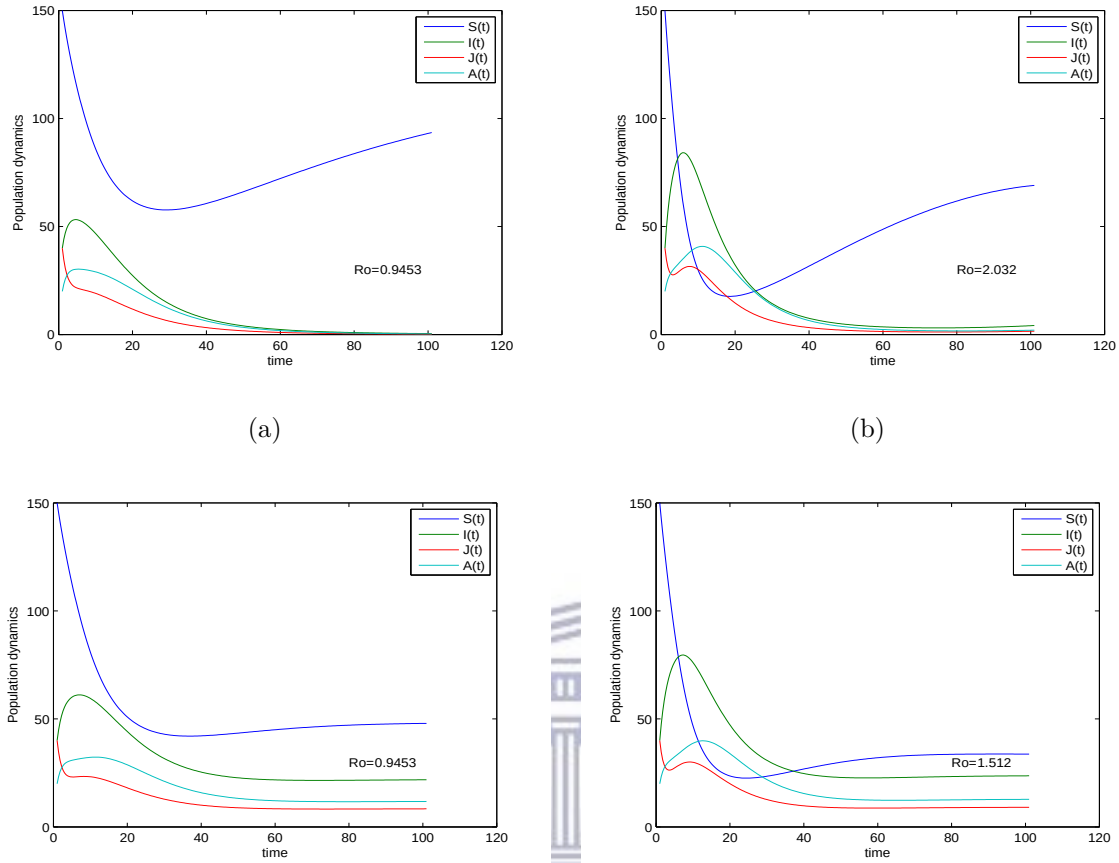
and $\left(3-\frac{1}{x}-\frac{xz}{y}-\frac{y}{z}\right)=0$ if and only if $x=y=z=1$. Therefore, it is easy to see that $\dot{V}_2 \leq 0$. Furthermore, $\dot{V}_2=0$ if and only if $x=y=z=1$. The maximum invariant set of system (3.1) on the set $\{(x,y,z):\dot{V}=0\}$ is the singleton $(1,1,1)$. Thus, for system (3.1), the endemic equilibrium E^* is globally asymptotically stable if $\mathcal{R}_0>1$ by the Lasalle invariance principle. □

3.2 Numerical simulations and concluding remarks

We present some numerical simulations in the general context to investigate the dynamics of the model system with and without the inflow of infectives. For some numerical simulations in the context of the South African HIV historical data, we let the reader refer to chapters 5, 6, 7 and 8. The parameter values of the model are given in the table below.

Table 3.1: Estimating parameters for model system 3.1

Parameter	Estimated values	Ref
μ	0.017	[7]
μ_0	0.017	[7]
α	0.21	[7]
k_1	0.3	Estimated
k_2	0.3	Estimated
c	3	[7]
δ	0.21	Estimated



(a) (b)

(c) (d)

Figure 3.2: The population dynamics with and without inflow

In Figure 3.2, we show the population dynamics of HIV/AIDS with and without positive flow of infectives. It can be seen that whenever there is positive inflow of infectives, then the model system (3.1) does not permit a disease-free equilibrium even when $\mathcal{R}_0 < 1$, see for example in Figure 3.2 (c). In Figure 3.2 (b) and (d), we show that the presence of the inflow of infectives makes the disease to stabilize more at the endemic level. The basic reproduction number in (d) is less than in (b), but the graph in Figure (d) is more endemic than in Figure (b).

Chapter 4

Stochastic dynamics of an HIV/AIDS epidemic model with treatment[1]

4.1 Introduction

In this chapter, we investigate a stochastic HIV/AIDS epidemic model with treatment. The model allows for two stages of infection namely the asymptomatic phase and the symptomatic phase. We prove existence of global positive solutions. We show that the solutions are stochastically ultimately bounded and stochastically permanent. We also study asymptotic behaviour of the solution to the stochastic model around the disease-free equilibrium of the underlying deterministic model. Our theoretical results are illustrated by way of numerical simulations.

Examples of stochastic models for HIV/AIDS can be found in [113, 26, 47]. In [26], the authors study a model of AIDS and condom use via the technique of parameter perturba-

[1]A modified version of this chapter was published as:
M.U. Nsuami, P.J. Witbooi. Stochastic dynamics of an HIV/AIDS epidemic model with treatment. *Quaestiones Mathematicae*, (2018) 1-17.

tion which is standard in stochastic population modeling. Their research indicates that introducing environmental noise into the deterministic model can have a stabilising effect. The paper by Yang et al. [113] investigates the dynamic behaviour of an HIV model with stochastic perturbation and the authors obtain the asymptotic behaviour results. Kamina et al. [47] models the population dynamics of the human immunodeficiency virus type-1 (HIV-1) population dynamics with the use of diffusion processes. The authors incorporate more of the randomness of the HIV-1 infection process to investigate the probability and the possibility of viral extinction in their model.

The chapter is structured as follows. In Section 4.2 we give some preliminaries. In Section 4.3 we present the model and we show the existence of global solutions. In Section 4.4 we study the ultimate boundedness and stochastic permanence properties. Section 4.5 studies asymptotic behaviour around the disease-free equilibrium of the underlying deterministic model. Section 4.6 gives a numerical illustrations and Section 4.7 provides some concluding remarks.

4.2 Preliminaries

Let us denote by $\mathbb{R}^n_+$ (resp. $\mathbb{R}^n_{++}$) the set of points in $\mathbb{R}^n$ having only non-negative (resp. strictly positive) coordinates.

Throughout this paper we assume a complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ with a filtration, $\{\mathcal{F}_t\}_{t\geq 0}$, that is right continuous and with $\mathcal{F}_0$ containing all the subsets having measure zero.

Consider an equation of the form (4.1) below, for an k-dimensional Brownian motion $B(t)$ on Ω.

$$dx(t) = f(t,x)dt + g(t,x)dB(t) \tag{4.1}$$

A solution with initial value $x(0) = x_0$ is denoted by $x(t, x_0)$. Assume that $f(t, 0) = g(t, 0) = 0$ for all $t \geq 0$, so the origin point is an equilibrium of (4.1).

For a stochastic process $x(t)$ which is a function of $B(t)$, when we wish to single out a specific Brownian path ω, we shall write $x(t, \omega)$.

By $\mathcal{L}$ we denote the infinitesimal generator of an equation of the form (4.1), see [72] of Øksendal, defined for a function $V(t, x) \in C^{1,2}(\mathbb{R}_+ \times \mathbb{R}^k)$.

Definition 4.2.1. *(see [51, 115]) A solution $x(t)$ of the system (4.1) is said to be stochastically ultimately bounded if for any $\epsilon \in (0, 1)$, there is a positive constant $\varphi = \varphi(\epsilon)$, such that for any positive initial value $x(0)$,*

$$\limsup_{t\to\infty} \mathbb{P}\{|x(t)| > \varphi\} \leq \epsilon.$$

Definition 4.2.2. *(see [77]) A solution $x(t)$ of system (4.1) is said to be stochastically permanent if for any $\epsilon \in (0, 1)$, there exists a pair of positive constants $\varphi = \varphi(\epsilon)$ and $\xi = \xi(\epsilon)$, such that for any positive initial value $x(0)$, the following condition holds:*

$$\liminf_{t\to\infty} \mathbb{P}\{|x(t)| \leq \varphi\} \geq 1 - \epsilon, \quad \text{and} \quad \liminf_{t\to\infty} \mathbb{P}\{|x(t)| \geq \xi\} \geq 1 - \epsilon.$$

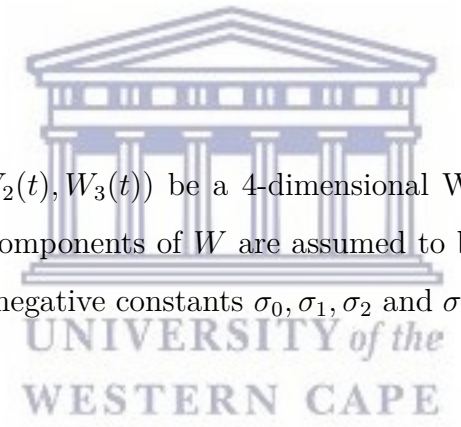
Remark 4.2.3. *The following inequality will be useful in Sections 4 and 5.*
Given any finite sequence of real numbers $u_1, u_2, \ldots, u_n$, then

$$(\sum_{i=1}^{n} u_i)^2 \leq n(\sum_{i=1}^{n} u_i^2). \tag{4.2}$$

4.3 The model and global solutions

In the underlying deterministic model, we assume a total population which at any time t is subdivided into four classes. The classes are: the class of susceptible individuals

$S(t)$, the class of asymptomatic individuals $I(t)$, the class of symptomatic individuals $J(t)$ and the class of the population who have full-blown AIDS $A(t)$. The term μK is the recruitment rate into the population, μ being the birth rate which is assumed to coincide with the average mortality rate by natural causes. The disease-induced mortality rate is denoted by δ. The parameters β_1, β_2 denote the probabilities of disease transmission per contact by an infective in the first and second stage respectively. For an individual, c is the average number of contacts with others per unit time. By k_1 and k_2 we denote the transfer rates from the asymptomatic phase I to the symptomatic phase J and from the symptomatic phase to the A-class, respectively. The parameter α is the rate of transfer from the symptomatic phase J to the asymptomatic phase I due to treatment.



Let $W(t) = (W_0(t), W_1(t), W_2(t), W_3(t))$ be a 4-dimensional Wiener process defined on this probability space. The components of W are assumed to be mutually independent. In the model below, the non-negative constants $\sigma_0, \sigma_1, \sigma_2$ and σ_3 denote the intensities of the stochastic perturbations.

In the literature, it is showed that there are different possible approaches to introduce random effects in the epidemic models affected by environmental white noise from biological significance and mathematical perspective. Here, we mainly mention three approaches to the model (3.1) as an example. For the first model, we assume that white noise type stochastic perturbations are directly proportional to S, I, J, A influenced on the dS, dI, dJ and dA in the model (3.1) with or without the positive inflow of infected individuals. The model takes the following form.

$$
\begin{aligned}
dS &= [\mu K - c(\beta_1 I + \beta_2 J)S - \mu S]\,dt + \sigma_0 S dW_0(t),\\
dI &= [c(\beta_1 I + \beta_2 J)S - (\mu + k_1)I + \alpha J]\,dt + \sigma_1 I dW_1(t),\\
dJ &= [k_1 I - (\mu + k_2 + \alpha)J]\,dt + \sigma_2 J dW_2(t),\\
dA &= [k_2 J - (\mu + \delta)A]\,dt + \sigma_3 A dW_3(t). \qquad (4.3)
\end{aligned}
$$

The second one, because system (3.1) has a positive equilibrium $E^* = (S^*, I^*, J^*, A^*)$ under $\mathcal{R}_0 > 1$, we can introduce stochastic perturbations which are linked to $S(t), I(t), J(t), A(t)$ from values of S^*, I^*, J^*, A^*, respectively. In detail, that is,

$$
\begin{aligned}
dS &= [\mu K - c(\beta_1 I + \beta_2 J)S - \mu S]\,dt + \sigma_0 (S - S^*) dW_0(t),\\
dI &= [c(\beta_1 I + \beta_2 J)S - (\mu + k_1)I + \alpha J]\,dt + \sigma_1 (I - I^*) dW_1(t),\\
dJ &= [k_1 I - (\mu + k_2 + \alpha)J]\,dt + \sigma_2 (J - J^*) dW_2(t),\\
dA &= [k_2 J - (\mu + \delta)A]\,dt + \sigma_3 (A - A^*) dW_3(t). \qquad (4.4)
\end{aligned}
$$

As a third approach, one can add randomly fluctuation affecting directly the deterministic model. Suppose that infection rate β_1 and β_2 are stochastically perturbed with $\beta_1 \to \beta_1 + \sigma_0 \dot{B}(t)$, $\beta_2 \to \beta_2 + \sigma_0 \dot{B}(t)$, namely

$$
\begin{aligned}
dS &= [\mu K - c(\beta_1 I + \beta_2 J)S - \mu S]\,dt - \sigma_0 c\beta_1 I S dW_0(t) - \sigma_1 c\beta_2 J S dW_0(t),\\
dI &= [c(\beta_1 I + \beta_2 J)S - (\mu + k_1)I + \alpha J]\,dt - \sigma_0 c\beta_1 I S dW_0(t) - \sigma_1 c\beta_2 J S dW_0(t),\\
dJ &= [k_1 I - (\mu + k_2 + \alpha)J]\,dt\\
dA &= [k_2 J - (\mu + \delta)A]\,dt \qquad (4.5)
\end{aligned}
$$

Let us consider the model (4.3).

In the special case when $\sigma_0 = 0$, the model system (4.3) permits a disease-free equilibrium $E_0 = (K, 0, 0, 0)$. The basic reproduction number of the underlying deterministic model

is very similar to the one in [14] and is computed as

$$\mathcal{R}_0 = \frac{cK[\beta_1(\mu + k_2 + \alpha) + \beta_2 k_1]}{(\mu + k_1)(\mu + k_2) + \alpha\mu}.$$

We use the notation:

$$X(t) = (S(t), I(t), J(t), A(t)).$$

In what follows we show that solutions of (4.3) exist globally and are positive (a.s), see for instance [77, 115].

Theorem 4.3.1. *For model* (4.3) *and any initial value* $(S(0), I(0), J(0), A(0)) \in \mathbb{R}^4_{++}$, *there is a unique solution* $(S(t), I(t), J(t), A(t))$ *on* $t \geq 0$ *which remains in* $\mathbb{R}^4_{++}$ *with probability one.*

Proof. Note that the coefficients of the system (4.3) are locally Lipschitz continuous. Thus there exists a unique local solution on $t \in [0, \tau_e)$, where τ_e is the explosion time. We need to show that this solution is global almost surely (a.s) ; that is, $\tau_e = \infty$ a.s.

Let $m_0 > 0$ be sufficiently large so that $S(0), I(0), J(0)$, and $A(0)$ sits within the interval $[1/m_0, m_0]$. For each integer $m \geq m_0$, define a sequence of stopping times by

$$\begin{aligned}\tau_m \;=\; & \inf\Big\{t \in [0, \tau_e) :\; S(t) \notin \left(\frac{1}{m}, m\right) \text{ or } I(t) \notin \left(\frac{1}{m}, m\right) \text{ or } J(t) \notin \left(\frac{1}{m}, m\right) \\ & \text{or } A(t) \notin \left(\frac{1}{m}, m\right)\Big\}\end{aligned}$$

where we set $\inf\emptyset = \infty$. Now since the sequence (τ_m) is non-decreasing, the following limit exists:

$$\tau_\infty = \lim_{m \to \infty} \tau_m,$$

and $\tau_\infty \leq \tau_e$ (a.s.). Now we need to show $\tau_\infty = \infty$ a.s. If this statement is violated, then there exist $T > 0$ and $\epsilon \in (0, 1)$ such that

$$\mathbb{P}\{\tau_\infty \leq T\} > \epsilon. \tag{4.6}$$

Thus, there is an integer $m_1 \geq m_0$ such that

$$\mathbb{P}\{\tau_m \leq T\} \geq \epsilon \quad \forall m \geq m_1. \tag{4.7}$$

Choose $a_0 > 0$ sufficiently small in order to have $a_0 c\beta_1 < \mu$ and $a_0 c\beta_2 < \mu$. Consider the function V_1 defined by

$$\begin{aligned} V_1(S,I,J,A) &= \Big(S - a_0 - a_0 \ln \frac{S}{a_0}\Big) + \Big(I - 1 - \ln I\Big) + \Big(J - 1 - \ln J\Big) \\ &\quad + \Big(A - 1 - \ln A\Big). \end{aligned}$$

Note that each of the four bracketed terms are non-negative while $(S(t), I(t), J(t), A(t)) \in \mathbb{R}^4_{++}$. By applying Itô's formula we have,

$$\begin{aligned} dV_1(S,I,J,A) &= \mathcal{L}V_1 dt + (S - a_0)\sigma_0 dW_0(t) + (I-1)\sigma_1 dW_1(t) \\ &\quad + (J-1)\sigma_2 dW_2(t) + (A-1)\sigma_3 dW_3(t), \end{aligned} \tag{4.8}$$

where

$$\begin{aligned} \mathcal{L}V_1 &= \Big[\Big(1 - \frac{a_0}{S}\Big)\Big(\mu K - c(\beta_1 I + \beta_2 J)S - \mu S\Big)\Big] + \Big[\Big(1 - \frac{1}{I}\Big)\Big(c(\beta_1 I + \beta_2 J)S \\ &\quad -(\mu + k_1)I + \alpha J)\Big)\Big] + \Big[\Big(1 - \frac{1}{J}\Big)\Big(k_1 I - (\mu + k_2 + \alpha)J\Big)\Big] \\ &\quad + \Big[\Big(1 - \frac{1}{A}\Big)\Big(k_2 J - (\mu + \delta)A\Big)\Big] + \frac{1}{2}(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2) \\ &\leq \mu K - \mu(I + J) + a_0 c(\beta_1 I + \beta_2 J) + \mu(3 + a_0) + k_1 + k_2 + \alpha + \delta \\ &\quad + \frac{1}{2}\left(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2\right). \end{aligned}$$

Note that by the choice of a_0 we have:

$$a_0c\beta_1 I - \mu I = I\left(a_0c\beta_1 - \mu\right) < 0 \quad \text{and} \quad a_0c\beta_2 J - \mu J = J\left(a_0c\beta_2 - \mu\right) < 0.$$

Therefore

$$\mathcal{L}V_1 \leq C,$$

where $C = \mu K + \mu(3 + a_0) + k_1 + k_2 + \alpha + \delta + \frac{1}{2}\left(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2\right)$ is a constant.

Integrating both sides of (4.8) from 0 to $\tau_m \wedge T$ yields

$$\int_0^{\tau_m \wedge T} dV_1(S(s), I(s), J(s), A(s)) \;\leq\; \int_0^{\tau_m \wedge T} C ds + H(\tau_m \wedge T),$$

where

$$\begin{aligned} H(s) \;&=\; \int_0^s (S(u) - a_0)\sigma_0 dW_0(u) + \int_0^s (I(u) - 1)\sigma_1 dW_1(u) + \int_0^s (J(u) - 1)\sigma_2 dW_2(u) \\ &\quad + \int_0^s (A(u) - 1)\sigma_3 dW_3(u). \end{aligned}$$

Note that $H(s)$ is a mean zero martingale process. Thus by taking expectations we have

$$\mathbb{E}\Big[V_1(S(\tau_m \wedge T), I(\tau_m \wedge T), I(\tau_m \wedge T), J(\tau_m \wedge T))\Big]$$

$$\leq V_1(S(0), I(0), J(0), A(0)) + CT.$$

Set $\Omega_m = \{\tau_m \leq T\}$ for $m \geq m_1$. From equation (4.7), we have that $\mathbb{P}(\Omega_m) \geq \epsilon$ for each $m > m_1$. For every $\nu \in \Omega_m$, we have

$$\{S(\tau_m, \nu), I(\tau_m, \nu), J(\tau_m, \nu), A(\tau_m, \nu)\} \bigcap \{m,\ 1/m\} \neq \emptyset.$$

Consequently, for every $\nu \in \Omega_m$

$$V_1(S(\tau_m \wedge T), I(\tau_m \wedge T), J(\tau_m \wedge T), A(\tau_m \wedge T)) \geq D_m$$

where

$$D_m = \min_{u\in\{1,a_0\}} \left\{ m - u - u\ln\frac{m}{u}, \frac{1}{m} - u - u\ln\frac{1}{um} \right\} > 0.$$

Then we obtain

$$\begin{aligned} & V_1(S(0), I(0), J(0), A(0)) + CT \\ & \quad \geq \mathbb{E}\Big[(1_{\Omega_m} V_1(S(\tau_m \wedge T), I(\tau_m \wedge T), J(\tau_m \wedge T), A(\tau_m \wedge T))\Big] \\ & \quad \geq \epsilon D_m, \end{aligned}$$

where 1_{Ω_m} is the indicator function of Ω_m. Letting $m \to \infty$ leads to the contradiction $\infty = V_1(S(0), I(0), J(0), A(0)) + CT < \infty$. Therefore, the solution of model (4.3) is positive and will not explode in finite time, with probability one. This completes the proof. □

The solution $X(t)$ of model system (4.3) is stochastically ultimately bounded and stochastically permanent.

4.4 Ultimate boundedness and permanence

The solutions to system (4.3) are expected to exhibit some further properties, other than positivity. In this section we investigate for stochastically ultimate boundedness and stochastic permanence.

Theorem 4.4.1. *For any initial value $X(0)$ in $\mathbb{R}^4_{++}$, system (4.3) is stochastically ultimately bounded.*

Proof. Let $m_0 > 0$ be sufficiently large such that every coordinate of $X(0)$ is contained within the interval $(\frac{1}{m_0}, m_0)$. For each integer $k \geq m_0$, define the stopping time

$$\begin{aligned}\tau_k &= \inf\left\{t \geq 0 : S(t) \notin \left(\frac{1}{k}, k\right) \text{ or } I(t) \notin \left(\frac{1}{k}, k\right) \text{ or } J(t) \notin \left(\frac{1}{k}, k\right)\right. \\ &\quad \left. \text{or } A(t) \notin \left(\frac{1}{k}, k\right)\right\}. \end{aligned} \tag{4.9}$$

By Theorem 4.3.1, $\tau_k \to \infty$ almost surely as $k \to \infty$. We have

$$\begin{aligned} dN &= d(S + I + J + A) \\ &= (\mu K - \mu N - \delta A)dt + \sigma_0 S dW_0(t) + \sigma_1 I dW_1(t) \\ &\quad + \sigma_2 J dW_2(t) + \sigma_3 A dW_3(t). \end{aligned}$$

Applying Itô's formula to $e^{\mu t}N$ gives

$$\begin{aligned} de^{\mu t}N &= \mu e^{\mu t} N dt + e^{\mu t} dN \\ &= (\mu e^{\mu t} K - e^{\mu t}\delta A)dt + \sigma_0 e^{\mu t} S dW_0(t) + \sigma_1 e^{\mu t} I dW_1(t) \\ &\quad + \sigma_2 e^{\mu t} J dW_2(t) + \sigma_3 e^{\mu t} A dW_3(t). \\ &\leq \mu e^{\mu t} K dt + \sigma_0 e^{\mu t} S dW_0(t) + \sigma_1 e^{\mu t} I dW_1(t) \\ &\quad + \sigma_2 e^{\mu t} J dW_2(t) + \sigma_3 e^{\mu t} A dW_3(t) \end{aligned} \tag{4.10}$$

By integrating this inequality and then taking expectations on both sides of (4.10), one can see that

$$\mathbb{E}\Big[e^{\mu(t\wedge\tau_k)}N(t\wedge\tau_k)\Big] - N(0) \leq \mathbb{E}\left[\int_0^{t\wedge\tau_k} \mu e^{\mu s} K ds\right] \leq K(e^{\mu t} - 1).$$

Letting $k \to \infty$ we obtain the inequality

$$e^{\mu t}\mathbb{E}[N(t)] - N(0) \leq K(e^{\mu t} - 1).$$

Consequently,

$$\limsup_{t\to\infty} \mathbb{E}[N(t)] \leq K.$$

Note that $|X| = \sqrt{S^2 + I^2 + J^2 + A^2} \leq N$, and therefore

$$\limsup_{t\to\infty} \mathbb{E}[|X(t)|] \leq K.$$

Now for any given $\epsilon > 0$, let us write $\varphi = K/\epsilon$. We complete the proof by using Markov's inequality, obtaining

$$\limsup_{t\to\infty} \mathbb{P}\{|X(t)| > \varphi\} \leq \limsup_{t\to\infty} \frac{\mathbb{E}[|X(t)|]}{\varphi} \leq \frac{K}{\varphi} = \epsilon.$$

□

The property of permanence is quite a significant property since it refers to the long term boundedness of $|X(t)|$ as well as boundedness away from zero in the long term.

Lemma 4.4.2. *Assume that there exist positive constants ρ and h satisfying:*

$$\frac{h}{\rho} + \mu + \delta + \frac{\rho+1}{2}\max\{\sigma_0^2, \sigma_1^2, \sigma_2^2, \sigma_3^2\} < \mu K. \tag{4.11}$$

For any initial value $X(0) \in \mathbb{R}^4_{++}$, the solution $X(t)$ satisfies the inequality

$$\limsup_{t\to\infty} \mathbb{E}\left[\frac{1}{|X(t)|^\rho}\right] \leq 2^\rho H,$$

where

$$H = \left(\frac{C_2^2}{4hC_1} + 1\right)\max\left\{1, (1 + v^{\#})^{\rho-2}\right\},$$

$$v^{\#} = \frac{C_2 + \sqrt{C_2^2 + 4C_1 h}}{2C_1}$$

and

$$\begin{aligned} C_1 &= \rho\left(\mu K - \mu - \delta - \frac{\rho+1}{2}\max\{\sigma_0^2, \sigma_1^2, \sigma_2^2, \sigma_3^2\}\right) - h, \\ C_2 &= \rho\left(\mu + \delta + \max\{\sigma_0^2, \sigma_1^2, \sigma_2^2, \sigma_3^2\}\right) + 2h. \end{aligned} \tag{4.12}$$

Proof. Let us assume existence of ρ and h to satisfy condition (4.11). Now we define the function $V_2(S,I,J,A) = (S+I+J+A)^{-1}$ for $X(t) \in \mathbb{R}^4_{++}$. Applying the Itô formula, we have

$$\mathcal{L}[(1+V_2)^\rho] \;=\; \rho(1+V_2)^{\rho-2}\Gamma,$$

where

$$\begin{aligned}\Gamma \;=\; & \left[\frac{1}{2}(\rho-1)V_2^4 + (1+V_2)V_2^3\right](\sigma_0^2S^2+\sigma_1^2I^2+\sigma_2^2J^2+\sigma_3^2A^2)\\ & -(1+V_2)V_2^2\left(\mu K-\mu N-\delta A\right).\end{aligned}$$

Note that

$$\frac{1}{2}(\rho-1)V_2^4 + (1+V_2)V_2^3 = \frac{1}{2}(\rho+1)V_2^4 + V_2^3.$$

Using the identity $V_2N = 1$ together with the inequalities $V_2A < 1$ and

$$V_2^2\left(\sigma_0^2S^2+\sigma_1^2I^2+\sigma_2^2J^2+\sigma_3^2A^2\right) < \max\left\{\sigma_0^2,\sigma_1^2,\sigma_2^2,\sigma_3^2\right\},$$

we obtain an inequality as follows

$$\begin{aligned}\Gamma \;\leq\; & \left[\frac{1}{2}(\rho+1)V_2^2\max\left\{\sigma_0^2,\sigma_1^2,\sigma_2^2,\sigma_3^2\right\} + V_2\max\left\{\sigma_0^2,\sigma_1^2,\sigma_2^2,\sigma_3^2\right\}\right]\\ & -V_2^2(\mu K-\mu-\delta)+V_2(\mu+\delta)-V_2^3\mu K\ .\end{aligned}$$

On the right hand side of the latter inequality, we drop the negative term $-V_2^3\mu K$ and we reshuffle terms to obtain

$$\begin{aligned}\Gamma \;\leq\; & -V_2^2\Big(\mu K-(\mu+\delta)-\frac{\rho+1}{2}\max\left\{\sigma_0^2,\sigma_1^2,\sigma_2^2,\sigma_3^2\right\}\Big)\\ & +V_2\left(\mu+\delta+\max\{\sigma_0^2,\sigma_1^2,\sigma_2^2,\sigma_3^2\}\right)\ .\end{aligned}$$

In fact we can now express Γ in the inequality below, with C_1 and C_2 are as defined in (4.12):

$$\Gamma \leq -V_2^2\Big(\frac{C_1+h}{\rho}\Big)+V_2\Big(\frac{C_2-2h}{\rho}\Big).$$

Again by the Itô formula we have

$$\begin{aligned}\mathcal{L}[e^{ht}(1+V_2)^{\rho}] &= he^{ht}(1+V_2)^{\rho} + e^{ht}\mathcal{L}(1+V_2)^{\rho} \\ &= e^{ht}(1+V_2)^{\rho-2}(h(1+V_2)^2 + \rho\Gamma) \\ &\leq e^{ht}(1+V_2)^{\rho-2}(-C_1V_2^2 + C_2V_2 + h)\ .\end{aligned}$$

Recall that $v^{\#} = (C_2 + \sqrt{C_2^2 + 4C_1h})/(2C_1)$. If $V_2 > v^{\#}$, then $\mathcal{L}(e^{ht}(1+V_2)^{\rho}) \leq 0$. Now note that $e^{ht}(1+V_2)^{\rho-2}$ is positive. So in order to find an upper bound for the right hand side of the inequality above, it suffices to maximize the factors separately. We continue on this to find that

$$-C_1V_2^2 + C_2V_2 + h \leq \frac{C_2^2}{4C_1} + h,$$

and over $0 < V_2 \leq v^{\#}$ we get

$$(1+V_2)^{\rho-2} \leq \max\{1, (1+v^{\#})^{\rho-2}\}.$$

Therefore,

$$\mathcal{L}(e^{ht}(1+V_2)^{\rho}) \leq e^{ht}\Big(\max\{1, (1+v^{\#})^{\rho-2}\}\Big)\Big(\frac{C_2^2}{4C_1} + h\Big) = e^{ht}hH.$$

Thus it can be deduced that

$$\mathbb{E}\Big[e^{ht}(1+V_2(t))^{\rho}\Big] \leq e^{ht}(1+V_2(0))^{\rho} + hH\frac{e^{ht}}{h}.$$

Therefore

$$\limsup_{t\to\infty} \mathbb{E}\Big[V_2(t)^{\rho}\Big] \leq \limsup_{t\to\infty} \mathbb{E}\Big[(1+V_2(t))^{\rho}\Big] \leq H.$$

For $(S, I, J, A) \in \mathbb{R}^4_{++}$, from the inequality (4.2) it follows that

$$S + I + J + A \leq \sqrt{4(S^2 + I^2 + J^2 + A^2)}.$$

Consequently, for any $\rho > 0$,

$$(S + I + J + A)^{\rho} \leq 2^{\rho}(S^2 + I^2 + J^2 + A^2)^{\frac{\rho}{2}} = 2^{\rho} |X|^{\rho}.$$

Taking reciprocals the latter inequality yields

$$\frac{1}{|X|^{\rho}} \leq \frac{2^{\rho}}{(S + I + J + A)^{\rho}}.$$

Therefore we can conclude that

$$\limsup_{t\to\infty} \mathbb{E}\left[\frac{1}{|X(t)|^{\rho}}\right] \leq 2^{\rho} \limsup_{t\to\infty} \mathbb{E}[(V_2(t))^{\rho}] \leq 2^{\rho} H,$$

which completes the proof. □

We can now prove the stochastic permanence.

Theorem 4.4.3. *If* $\max\{\sigma_0^2, \sigma_1^2, \sigma_2^2, \sigma_3^2\} < 2(\mu K - (\mu + \delta))$, *then the solution of the model (4.3) is stochastically permanent.*

Proof. By Theorem 4.4.1, we have $\mathbb{P}\{|X(t)| > \varphi\} \leq \epsilon$. This implies

$$\mathbb{P}\{|X(t)| \leq \varphi\} \geq 1 - \epsilon,$$

from which it follows that

$$\liminf_{t\to\infty} \mathbb{P}\{|X(t)| \leq \varphi\} \geq 1 - \epsilon.$$

The assumption $\max\{\sigma_0^2, \sigma_1^2, \sigma_2^2, \sigma_3^2\} < 2(\mu K - (\mu + \delta))$ implies that there exists $\rho > 0$ such that

$$\mu + \delta + \frac{\rho + 1}{2} \max\{\sigma_0^2, \sigma_1^2, \sigma_2^2, \sigma_3^2\} < \mu K$$

and given the latter inequality, there exists $h > 0$ such that

$$\frac{h}{\rho}+\mu+\delta+\frac{\rho+1}{2}\max\{\sigma_0^2,\sigma_1^2,\sigma_2^2,\sigma_3^2\}<\mu K.$$

Therefore Lemma 4.4.2 applies, and so it follows that for H as in Lemma 4.4.2:

$$\limsup_{t\to\infty}\mathbb{E}\left[\frac{1}{|X(t)|^\rho}\right]\leq 2^\rho H.$$

Now, for any $\epsilon>0$, let $\xi=\frac{1}{2}\left(\frac{\epsilon}{H}\right)^{\frac{1}{\rho}}$. Then

$$\begin{aligned}\mathbb{P}\{|X(t)|<\xi\} &= \mathbb{P}\left\{\frac{1}{|X(t)|}>\frac{1}{\xi}\right\}=\mathbb{P}\left\{\frac{\xi}{|X(t)|}>1\right\}\\ &= \mathbb{P}\left\{\left(\frac{\xi}{|X(t)|}\right)^\rho>1\right\}\leq\xi^\rho\mathbb{E}\left[\frac{1}{|X(t)|^\rho}\right]\end{aligned}$$

Hence,

$$\limsup_{t\to\infty}\mathbb{P}\{|X(t)|<\xi\}\leq\xi^\rho(2^\rho H)=\epsilon,$$

from which it follows that

$$\liminf_{t\to\infty}\mathbb{P}\{|X(t)|\geq\xi\}\geq 1-\epsilon.$$

The proof is complete. □

4.5 Asymptotic behaviour around the disease-free equilibrium of the underlying deterministic model

In the deterministic models, the biological significance of the asymptotic stability of the disease-free equilibrium state is that the disease will go extinct, while the stability of the endemic equilibrium state means that the disease will persist in a given population. However, it can be seen that the model system (4.3) has no equilibrium states and that is why we study the asymptotic behaviour around the equilibrium of the underlying deterministic system.

Before stating the main theorem of this section, let us first define the following numbers:

$$\begin{aligned}
\pi &= (\mu+k_1)(\mu+k_2)+\alpha\mu,\ b_4=\beta_2\pi\frac{(1-\mathcal{R}_0)}{k_2},\\
b_5 &= \beta_1\pi\frac{(1-\mathcal{R}_0)}{2k_1},\quad b_1=\frac{b_2}{2K},\quad b_2=\beta_1(\mu+k_2+\alpha)+\beta_2k_1,\\
b_3 &= \beta_2(\mu+k_1)+\beta_1\alpha+b_5. \qquad (4.13)
\end{aligned}$$

Theorem 4.5.1. *Suppose that the following conditions are satisfied:*

$$\mathcal{R}_0<1,\ \sigma_0^2<\mu.$$

Then for any given initial value $(S(0),I(0),J(0),A(0))\in\mathbb{R}^4_{++}$*, the solution of the model (3.1) has the property:*

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t\Big[(S(\tau)-K)^2+I(\tau)+J(\tau)+A(\tau)\Big]d\tau\le 2b_1\sigma_0^2\frac{K^2}{\theta},$$

where

$$\theta=\min\left\{2(\mu-\sigma_0^2),\pi\frac{(1-\mathcal{R}_0)}{2}\beta_1,b_4(\mu+\delta),b_5(\mu+k_2+\alpha)\right\}.$$

Proof. Set $Q=S-K$. Then the system 4.3 can be written as

$$\begin{aligned}
dQ &= [-\mu Q-c(\beta_1I+\beta_2J)(K+Q)]\,dt+\sigma_0(K+Q)dW_0(t)\\
dI &= [c(\beta_1I+\beta_2J)(K+Q)-(\mu+k_1)I+\alpha J]\,dt+\sigma_1IdW_1(t),\\
dJ &= [k_1I-(\mu+k_2+\alpha)J]\,dt+\sigma_2JdW_2(t),\\
dA &= [k_2J-(\mu+\delta)A]\,dt+\sigma_3AdW_3(t).
\end{aligned}$$

For the numbers b_i as in display (4.13) above, consider the following positive-definite function:

$$V_3(Q,I,J,A)=b_1Q^2+b_2I+b_3J+b_4A.$$

Then

$$\int_0^t dV_3(Q,I,J,A) = \int_0^t \mathcal{L}V_3(Q,I,J,A)du + M_t$$

where

$$\begin{aligned} M_t &= \int_0^t 2b_1Q\sigma_0(K+Q)dW_0(u) + \int_0^t b_2\sigma_1 I dW_1(u) \\ &\quad + \int_0^t b_3\sigma_2 J dW_2(u) + \int_0^t b_4\sigma_3 A dW_3(u) \end{aligned}$$

and

$$\begin{aligned} \mathcal{L}V_3(Q,I,J,A) &= 2b_1Q[-\mu Q - c(\beta_1 I + \beta_2 J)(K+Q)] + b_1[\sigma_0^2(K+Q)^2] \\ &\quad + b_2[c(\beta_1 I + \beta_2 J)(K+Q) - (\mu + k_1)I + \alpha J] \\ &\quad + b_3[k_1 I - (\mu + k_2 + \alpha)J] + b_4[k_2 J - (\mu+\delta)A]. \end{aligned}$$

We simplify and reorganize the terms to get

$$\mathcal{L}V_3 = -2b_1\mu Q^2 + b_1[\sigma_0^2(K+Q)^2] + Y_1 + Y_2 - b_4(\mu+\delta)A \tag{4.14}$$

where Y_1 and Y_2 are given by:

$$\begin{aligned} Y_1 &= -2b_1c(\beta_1 I + \beta_2 J)Q(K+Q) + b_2c(\beta_1 I + \beta_2 J)(K+Q) \\ Y_2 &= b_2[-(\mu+k_1)I + \alpha J] + b_3[k_1 I - (\mu + k_2 + \alpha)J] + b_4 k_2 J. \end{aligned}$$

Following the inequality (4.2), regarding the second term in equation (4.14) we get

$$b_1\sigma_0^2[K+Q]^2 \leq 2b_1\sigma_0^2(K^2+Q^2).$$

The term Y_1 can be expanded as

$$Y_1 = -2b_1c(\beta_1 I + \beta_2 J)Q^2 + c(\beta_1 I + \beta_2 J)Q(b_2 - 2Kb_1) + b_2c(\beta_1 I + \beta_2 J)K.$$

Noting that $b_2 = 2Kb_1$, we obtain the inequality

$$Y_1 \leq b_2 c(\beta_1 I + \beta_2 J)K.$$

A routine calculation reveals that

$$b_2 c(\beta_1 I + \beta_2 J)K + Y_2 = \pi\frac{(\mathcal{R}_0 - 1)}{2}\beta_1 I - b_5(\mu + k_2 + \alpha)J.$$

Thus we obtain the following inequality:

$$\begin{aligned}\mathcal{L}V_3 \;\leq\; & -2b_1(\mu - \sigma_0^2)Q^2 + \pi\frac{(\mathcal{R}_0 - 1)}{2}\beta_1 I - b_4(\mu + \delta)A \\ & -b_5(\mu + k_2 + \alpha)J + 2b_1\sigma_0^2 K^2.\end{aligned}$$

Therefore

$$\begin{aligned}\int_0^t dV_3 \;\leq\; & \int_0^t \Big[-2b_1(\mu - \sigma_0^2)Q^2 - \pi\frac{(1 - \mathcal{R}_0)}{2}\beta_1 I \\ & -b_5(\mu + k_2 + \alpha)J - b_4(\mu + \delta)A + 2b_1\sigma_0^2 K^2\Big]du + M_t.\end{aligned}$$

We take expectation and note that $\mathbb{E}[M_t] = 0$. Thus we obtain

$$\begin{aligned}0 \;\leq\; & \mathbb{E}\Big[V_3(Q(t), I(t), J(t), A(t))\Big] \\ \leq\; & \mathbb{E}\Big[V_3(Q(0), I(0), J(0), A(0))\Big] + \mathbb{E}\Big[\int_0^t \Big\{ -2b_1(\mu - \sigma_0^2)(Q(u))^2 - \pi\frac{(1 - \mathcal{R}_0)}{2}\beta_1 I(u) \\ & -b_5(\mu + k_2 + \alpha)J(u) - b_4(\mu + \delta)A(u) + 2b_1\sigma_0^2 K^2\Big\}du\Big]\end{aligned}$$

which gives

$$\mathbb{E}\Big[\int_0^t \Big\{2b_1(\mu - \sigma_0^2)(Q(u))^2 + \pi\frac{(1 - \mathcal{R}_0)}{2}\beta_1 I(u) + b_5(\mu + k_2 + \alpha)J(u) + b_4(\mu + \delta)A(u)\Big\}du\Big]$$

$$\leq \mathbb{E}[V_3(Q(0), I(0), J(0), A(0))] + 2b_1\sigma_0^2 K^2 t.$$

Therefore,

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\Big[\int_0^t \Big\{2b_1(\mu - \sigma_0^2)(Q(u))^2 + \pi\frac{(1 - \mathcal{R}_0)}{2}\beta_1 I(u) + b_5(\mu + k_2 + \alpha)J(u) + b_4(\mu + \delta)A(u)\Big\}du\Big]$$

$\leq 2b_1\sigma_0^2K^2$.

We take θ as in the formulation of the theorem, and then it follows that:

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\Big[\int_0^t\Big\{(S(\tau)-K)^2+I(\tau)+J(\tau)+A(\tau)\Big\}d\tau\Big]\leq 2b_1\sigma_0^2\frac{K^2}{\theta}.$$

The proof is complete.

□

Remark 4.5.2. *Theorem 4.5.1 asserts that under the given conditions if the stochastic perturbations are small, then in the long term the sample paths of a solution of the stochastic system (4.3) will tend to stay within a certain neighbourhood of the disease-free equilibrium of the deterministic model.*

4.6 Simulations

We present some numerical simulations in order to illustrate the analytical results of stochastic model (4.3). Regarding the parameters we note the following. The parameters have been chosen so as to be applicable to Southern Africa, mostly taken from [9]. We expect to see a value of β_2 significantly bigger than β_1, since the more advanced the infection has become, the probability of disease transmission in the symptomatic phase exceeds that of the asymptomatic phase. In [40], the parameter c is assigned values ranging from 1 to 2 for the average number of sexual partners per given time. In our case we take $c = 3$ in order to avoid addressing a problem that is simpler than the actual one. The value of K is the size of the population and does not have an effect on the relative sizes of the different classes. Consequently we regard K as *nominal*. In order to illustrate the results, we vary the values of β_1 and β_2. The parameter values of the model are given in the table below.

Table 4.1: Description of parameters and their values for model system 3.1

Parameters	Value	Source
μ	0.02	[9]
α	0.33	[9]
k_1	0.125	[41]
k_2	0.1	[9]
c	3	cf. [40]
δ	0.333	[9]
K	6.5	Nominal

with the initial conditions: $S_0 = 4.5,\ I_0 = 1,\ J_0 = 0.6,\ A_0 = 0.4$. In each graph we show four trajectories, the S-class and the J=class of the stochastic model (one sample path) and of the underlying deterministic model.

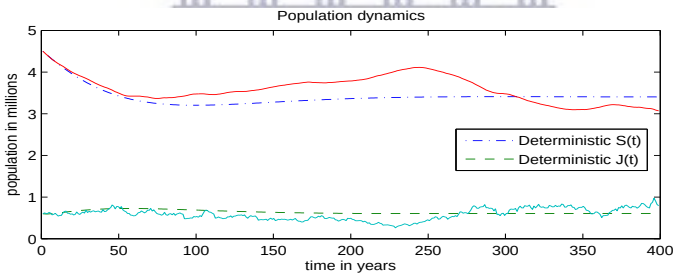


Figure 4.1: A case with $\mathcal{R}_0 > 1$ and $\mathcal{R}_0 = 2.938838313$

Chosen Values:

$\beta_1 = 0.002; \beta_2 = 0.005; \sigma_0 = 0.001; \sigma_1 = 0.05; \sigma_2 = 0.05; \sigma_3 = 0.05; \mathcal{R}_0 = 2.938838313.$

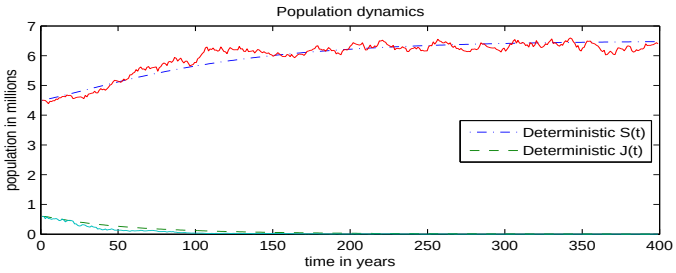


Figure 4.2: Theorem 4.5.1 guarantees stability in the mean.

Chosen Values:

$\beta_1 = 0.00067; \beta_2 = 0.001675; \sigma_0 = 0.01; \sigma_1 = 0.1; \sigma_2 = 0.1; \sigma_3 = 0.1; \mathcal{R}_0 = 0.9845108347.$

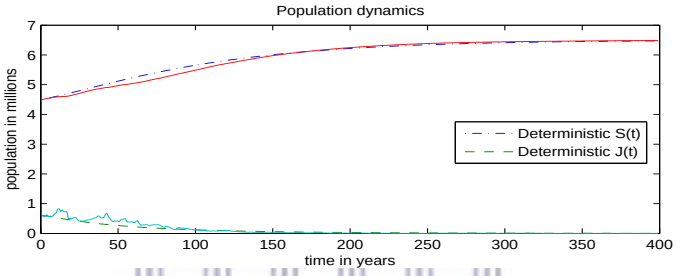


Figure 4.3: A case with $\mathcal{R}_0 = 1.043287601$ and $\sigma_0 = 0$.

Chosen Values:

$\beta_1 = 0.00071; \beta_2 = 0.001775; \sigma_0 = 0; \sigma_1 = 0.05; \sigma_2 = 0.05; \sigma_3 = 0.05; \mathcal{R}_0 = 1.043287601.$

In Fig. 4.1 we have $\mathcal{R}_0 = 2.938838313 > 1$, i.e., the basic reproduction number happens to be higher than unity, while $\sigma_0^2 < \mu$. The requirements of Theorem 4.5.1 are therefore not satisfied, and there does not seem to be convergence. In Figure 4.2 the basic reproduction number $\mathcal{R}_0$ is found to be less than one and the requirements of Theorem 4.5.1 are fulfilled. It can be seen that the stochastic solution remains close to the disease-free equilibrium of the underlying deterministic solution. In Fig. 4.3 we increase the value of β_1 and β_2, and we let $\sigma_0 = 0$. In this case the requirements of Theorem 4.5.1 are not satisfied but the stochastic solution remains close to the underlying deterministic solution. It may be that the condition $\sigma_0 = 0$ permits a stability theorem stronger than Theorem 4.5.1, (cf. [107]). We also noticed that in most of the simulations (not presented here), when the intensities of the noise are not too large, then the stochastic solution remains close to the

underlying deterministic solution. Otherwise strong noise may cause divergence between stochastic and deterministic behaviours.

4.7 Concluding remarks

Explicit inclusion of stochasticity into epidemiological models by way of Brownian motion provides further insight into the problem since randomness does feature in real life. In this chapter, for a treatment model of HIV/AIDS with stochastic perturbations, we have shown that there are solutions that are feasible (almost surely) in every sense that we have explored. We also investigated the asymptotic behaviour of the solutions with respect to the disease-free equilibrium of the underlying deterministic model 4.3. It is important that even when we would opt to work with the underlying deterministic model, then there is the assurance that minor random noise will not be catastrophical. There are even indications that noise on the system may enhance the extinction of the disease. Both models 4.4 and 4.5 need further investigations meanwhile a model similar to model 4.5 has been studied in Chapter 7.

Chapter 5

A stochastic model for HIV epidemic with treatment and inflow of HIV infectives[1]

5.1 Introduction

In this chapter, we introduce inflow of infectives on the stochastic compartmental model of Chapter 4. We present a theorem on almost sure exponential stability of the disease-free equilibrium. We also study the long term behaviour of the solutions to the stochastic model around the endemic equilibrium of the underlying deterministic model. Our theoretical results are illustrated by simulations with parameters applicable to South Africa.

The dynamics of HIV/AIDS in the context of Southern Africa present serious challenges due to its complexities and therefore requires interventions. Mathematical modeling in epidemiology has been utilized to assess the impact of the disease on the population, to identify key disease drivers and to make future projections. Parameters involved in epi-

[1]A modified version of this chapter was published as:
M.U. Nsuami, P.J. Witbooi. A STOCHASTIC MODEL FOR HIV EPIDEMIC WITH TREATMENT AND INFLOW OF INFECTIVES. *International Journal of Applied Mathematics*, **31(5)**, (2018) 545-568.

demic models may not be absolutely constant, due to inhomogeneities and environmental perturbations. Many authors investigate asymptotic behaviour of stochastic systems around the equilibria of the underlying deterministic models and examples of those can be found in [28, 51, 57, 114, 117]. In the papers by [26] Dalal et al. (HIV), [38] Gray et al. (SIS), [16] Chen et al. (SIR), and [105, 106] Witbooi (SEIR), it is proved that stochastic perturbation actually enhances stability of the disease-free equilibrium for the specific models. In this chapter we make another contribution in this regard.

We introduce the inflow of infectives on a deterministic compartmental model, and thereafter we impose the stochastic perturbation in such a manner that the total population size itself is perturbed by white noise. We study the long term behaviour of the *sde* model. We prove a result on almost sure exponential stability of the *dfe*, in the absence of inflow of infectives and with no perturbations on the class of susceptibles. We introduce an analogue of the basic reproduction number and we link it to almost sure exponential stability of the *dfe*. Here we note that for an *sde* system the concept of almost sure exponential stability is very similar to global asymptotic stability when working with ordinary differential equations. For the case of inflow of infectives we investigate for a type of stability in mean.

The remainder of this chapter is set up as follows. In Section 5.2 we give some preliminaries. In Section 5.3 we present the model and we study the existence of global positive solutions. Section 5.4 covers a theorem on almost sure exponential stability of the disease-free equilibrium. We present numerical simulations to illustrate the results. Section 5.5 deals with asymptotic behaviour of the solutions to the stochastic model around the endemic equilibrium of the underlying deterministic model. Again we provide numerical simulations to illustrate our theoretical results. In Section 5.6 we continue to discuss the long time behaviour of the stochastic system. In Section 5.7 we present some concluding remarks.

5.2 Preliminaries

Let us denote by $\mathbb{R}^n_+$ (resp. $\mathbb{R}^n_{++}$) the set of points in $\mathbb{R}^n$ having only non-negative (resp. strictly positive) coordinates.

The following observation which we quote from [108] is useful when dealing with exponential stability.

Lemma 5.2.1. *For $k \in \mathbb{N}$, let $X(t) = (X_1(t), X_2(t), \ ..., X_k(t))$ be a bounded $\mathbb{R}^k$-valued function and let $(t_{0,n})$ be any increasing unbounded sequence of positive real numbers. Then there is a family of sequences $(t_{l,n})$ such that for each $l \in \{1, 2, \ ..., k\}$, $(t_{l,n})$ is a subsequence of $(t_{l-1,n})$ and the sequence $X_l(t_{l,n})$ converges to the largest limit point of the sequence $X_l(t_{l-1,n})$.*

5.3 Stochastic HIV Model

Let $W(t) = (W_0(t), W_1(t), W_2(t), W_3(t))$ be a 4-dimensional Wiener process defined on this probability space. The components of W are assumed to be mutually independent. The non-negative constants $\sigma_0, \sigma_1, \sigma_2$ and σ_3 denote the intensities of the stochastic perturbations.

The parameters Q_1, Q_2 denote the inflow of infectives into the asymptomatic class and into the symptomatic class respectively. Based on the above assumptions, we then present the following stochastic model:

$$
\begin{aligned}
dS &= [\mu K - c(\beta_1 I + \beta_2 J)S - \mu S]\,dt + \sigma_0 S dW_0(t),\\
dI &= [Q_1 + c(\beta_1 I + \beta_2 J)S - (\mu + k_1)I + \alpha J]\,dt + \sigma_1 I dW_1(t),\\
dJ &= [Q_2 + k_1 I - (\mu + k_2 + \alpha)J]\,dt + \sigma_2 J dW_2(t),\\
dA &= [k_2 J - (\mu + \delta)A]\,dt + \sigma_3 A dW_3(t). \qquad (5.1)
\end{aligned}
$$

In what follows we show that solutions of (5.1) exist globally and are positive.

Let

$$\mathbb{R}^n_{++} = \{x \in \mathbb{R}^n | x_i > 0 \text{ for all } i = 1, 2, .., n\}. \qquad (5.2)$$

Theorem 5.3.1. *For model* (5.1) *and any initial value* $(S(0), I(0), J(0), A(0)) \in \mathbb{R}^4_{++}$, *there is a unique solution* $(S(t), I(t), J(t), A(t))$ *on* $t \geq 0$ *which remains in* $\mathbb{R}^4_{++}$ *with probability one.*

Proof. Consider the function V_1 below as defined in the proof of Theorem 4.3.1.

$$
\begin{aligned}
V_1(S, I, J, A) = \Big(S - a_0 - a_0 \ln \frac{S}{a_0}\Big) + \Big(I - 1 - \ln I\Big) + \Big(J - 1 - \ln J\Big)\\
+\Big(A - 1 - \ln A\Big).
\end{aligned}
$$

By applying Itô's formula we have,

$$
\begin{aligned}
dV_1(S, I, J, A) &= \mathcal{L}V_1 dt + (S - a_0)\sigma_0 dW_0(t) + (I - 1)\sigma_1 dW_1(t)\\
&\quad +(J - 1)\sigma_2 dW_2(t) + (A - 1)\sigma_3 dW_3(t), \qquad (5.3)
\end{aligned}
$$

where

$$
\begin{aligned}
\mathcal{L}V_1 &= \Big[\Big(1-\frac{a_0}{S}\Big)\big(\mu K - c(\beta_1 I+\beta_2 J)S - \mu S\big)\Big] + \Big[\Big(1-\frac{1}{I}\Big)\big(Q_1 + c(\beta_1 I+\beta_2 J)S \\
&\quad -(\mu+k_1)I + \alpha J\big)\Big] + \Big[(1-\frac{1}{J})(Q_2 + k_1 I - (\mu+k_2+\alpha)J)\Big] \\
&\quad +\Big[(1-\frac{1}{A})(k_2 J - (\mu+\delta)A)\Big] + \frac{1}{2}(a_0\sigma_0^2+\sigma_1^2+\sigma_2^2+\sigma_3^2) \\
&\leq \mu K - \mu(I+J) + a_0 c(\beta_1 I+\beta_2 J) + \mu(3+a_0) + k_1 + k_2 + \alpha + \delta \\
&\quad +Q_1 + Q_2 + \frac{1}{2}\big(a_0\sigma_0^2+\sigma_1^2+\sigma_2^2+\sigma_3^2\big).
\end{aligned}
$$

We choose a_0 sufficiently small such that:

$$a_0 c\beta_1 I - \mu I = I\,(a_0 c\beta_1 - \mu) < 0 \text{ and } a_0 c\beta_2 J - \mu J = J\,(a_0 c\beta_2 - \mu) < 0.$$

Therefore

$$\mathcal{L}V_1 \leq C,$$

where $C = \mu K + \mu(3+a_0) + k_1 + k_2 + \alpha + \delta + Q_1 + Q_2 + \frac{1}{2}\,(a_0\sigma_0^2 + \sigma_1^2 + \sigma_2^2 + \sigma_3^2)$ is a constant.

The rest of the proof comes readily as in the proof of Theorem 4.3.1. Therefore, the solution of model (5.1) is positive and will not explode in finite time, with probability one. This completes the proof. □

5.4 Almost sure exponential stability

We investigate the behaviour of the model system (5.1) under small perturbations, with $\sigma_0 = 0$, and $Q_1 = Q_2 = 0$. Note that we adopt condition $\sigma_0 = 0$ and $Q_1 = Q_2 = 0$ for two reasons: (1) This is the only condition to obtain a disease-free equilibrium in the case of a deterministic system by the definition. (2) Convergence of S becomes smooth graphically and not too complicated. Under these two conditions then, the disease-free equilibrium $E_0 = (K, 0, 0, 0)$ exists. The basic reproduction number of the underlying deterministic model is computed by

$$\mathcal{R}_0 = \frac{cK[\beta_1(\mu + k_2 + \alpha) + \beta_2 k_1]}{(\mu + k_1)(\mu + k_2) + \alpha\mu}.$$

The following subset Φ of sample paths will be of interest.

$$\Phi = \left\{\omega \in \Omega | \, (S(t,\omega), I(t,\omega), J(t,\omega), A(t,\omega) \in \mathbb{R}^4_{++} \text{ for all } t \geq 0\right\}.$$

From Theorem 5.3.1 it follows that $\mathbb{P}(\Omega \backslash \Phi) = 0$. In the remainder of this section we assume that sample paths are restricted to Φ.

Proposition 5.4.1. *If $(S(0), I(0), J(0), A(0)) \in \mathbb{R}^4_{++}$, then almost surely, $S(t) \leq K$ for all $t > 0$.*

Proof. Given any path (in Φ), then

$$\frac{d(S-K)}{dt} = -\mu(S-K) - c(\beta_1 I + \beta_2 J)S \leq -\mu(S-K). \tag{5.4}$$

Therefore $S(0) < K$ implies that $S(t) < K$ for all $t > 0$. □

The following numbers will play a key role in our study of exponential stability. Let $\xi_0, \xi_1, \xi_2, \xi_3$ and ξ_4 be non-negative numbers, chosen as follows.

$$\xi_1 = \beta_1(\mu + k_2 + \alpha) + \beta_2 k_1,$$

$$\xi_2 = \beta_1\alpha + \beta_2(\mu + k_1),$$

$$\xi_4 = (\mu + k_1)(\mu + k_2) + \mu\alpha.$$

The numbers ξ_0 and ξ_3 will be chosen later. For now we just bear in mind that they are both non-negative.

We continue by preparing notation and concepts for our theorem on almost sure exponential stability. Recall that we work with sample paths in Φ. This implies in particular that if $Z(t)$ is defined as below, then $Z(t) > 0$ for all $t \geq 0$. Thus we define

$$Z(t) = \xi_0(K - S(t)) + \xi_1 I(t) + \xi_2 J(t) + \xi_3 A(t) \tag{5.5}$$

and let

$$V_2(t) = \ln Z(t).$$

For a stochastic process $x(t)$ we write

$$\langle x \rangle_t = \frac{1}{t}\int_0^t x(s)ds.$$

In the following we build a proposition according to definition 2.8.1.

Proposition 5.4.2. *The disease-free equilibrium of System (5.1) is almost surely exponentially stable if*

$$\limsup_{t\to\infty} \langle \mathcal{L}V_2(X) \rangle_t < 0 \quad \text{(a.s.)}.$$

Proof. We start off by noting that

$$V_2(X(t)) = V_2(X(0)) + \int_0^t \mathcal{L}V_2(X(u))du + M_t,$$

where

$$\begin{aligned} M_t &= \int_0^t \left(-\xi_0\sigma_0 \frac{S(u)}{z(X(u))} dW_0(u) + \xi_1\sigma_1 \frac{I(u)}{z(X(u))} dW_1(u) + \xi_2\sigma_2 \frac{J(u)}{z(X(u))} dW_2(u) \right. \\ &\quad \left. + \xi_3\sigma_3 \frac{A(u)}{z(X(u))} dW_3(u) \right) \end{aligned}$$

The strong law of large numbers for local martingales, see [60, p12] for instance, implies that

$$\lim_{t\to\infty}\frac{1}{t}M_t = 0 \text{ (a.s.)}.$$

Also, we observe that

$$\lim_{t\to\infty}\frac{1}{t}V_2(X(0)) = 0.$$

Therefore

$$\limsup_{t\to\infty}\frac{1}{t}V_2(X(t)) = \limsup_{t\to\infty}\frac{1}{t}\int_0^t \mathcal{L}V_2(X(u))du = \limsup_{t\to\infty}\langle \mathcal{L}V_2(X)\rangle_t \quad \text{(a.s.)}.$$

This completes the proof. □

We now calculate $\mathcal{L}V_2$.

$$\begin{aligned}\mathcal{L}V_2 &= -\frac{\xi_0}{Z}\left[\mu K - c(\beta_1 I + \beta_2 J)S - \mu S\right] + \frac{\xi_1}{Z}\left[c(\beta_1 I + \beta_2 J)S - (\mu + k_1)I + \alpha J\right] \\ &+ \frac{\xi_2}{Z}\left[k_1 I - (\mu + k_2 + \alpha)J\right] + \frac{\xi_3}{Z}\left[k_2 J - (\mu + \delta)A\right] \\ &- \frac{1}{2}\left[\left(\frac{\xi_1\sigma_1 I}{Z}\right)^2 + \left(\frac{\xi_2\sigma_2 J}{Z}\right)^2 + \left(\frac{\xi_3\sigma_3 A}{Z}\right)^2\right].\end{aligned}$$

By Lemma 5.2.1 we can find, for every sample path w, a sequence t_n which is increasing and unbounded, such that

$$\limsup_{t\to\infty}\mathcal{L}\langle V_2(w)\rangle_t = \lim_{n\to\infty}\mathcal{L}\langle V_2(w)\rangle_{t_n},$$

and for which we can define the following limits:

$$s = \lim_{n\to\infty}\langle S\rangle_{t_n}, \quad i = \lim_{n\to\infty}\left\langle\frac{I}{Z}\right\rangle_{t_n}, \quad j = \lim_{n\to\infty}\left\langle\frac{J}{Z}\right\rangle_{t_n}, \quad a = \lim_{n\to\infty}\left\langle\frac{A}{Z}\right\rangle_{t_n},$$

and

$$q = \lim_{n\to\infty} \left\langle \frac{K-S}{Z} \right\rangle_{t_n}.$$

In particular we note that $\xi_0 q + \xi_1 i + \xi_2 j + \xi_3 a = 1$ and $\xi_0 q, \xi_1 i, \xi_2 j, \xi_3 a \in [0,1]$.

We define $F(\xi)$ as:

$$F(\xi) = F(\xi_0, \xi_1, \xi_2, \xi_3) = \limsup_{t\to\infty} \langle \mathcal{L}V_2 \rangle_t. \tag{5.6}$$

Then $F(\xi)$ takes the form:

$$\begin{aligned} F(\xi) &= \xi_0 \left[-\mu q + c(\beta_1 i + \beta_2 j)s\right] + \xi_1 \left[c(\beta_1 i + \beta_2 j)s - (\mu + k_1)i + \alpha j\right] \\ &\quad + \xi_2 \left[k_1 i - (\mu + k_2 + \alpha)j\right] + \xi_3 \left[k_2 j - (\mu + d)a\right] \\ &\quad - \frac{1}{2}\left[(\xi_1\sigma_1 i)^2 + (\xi_2\sigma_2 j)^2 + (\xi_3\sigma_3 a)^2\right]. \end{aligned} \tag{5.7}$$

An invariant $\mathcal{R}_\sigma$ of the model (5.1).

Let us define a function $h : [0,1] \to \mathbb{R}$ as follows:

$$h(u) = \frac{\xi_1\xi_2}{2} \frac{(\sigma_1 u)^2 + \sigma_2^2(1-u)^2}{\beta_1\xi_2 u + \beta_2\xi_1(1-u)}. \tag{5.8}$$

Then h is continuous and positive. Therefore h has a minimum, which we shall denote by h_*. Note that $h_* > 0$. In the final theorem we use the following number $\mathcal{R}_\sigma$, which we define to be:

$$\mathcal{R}_\sigma = \frac{cK[\beta_1(\mu + k_2 + \alpha) + \beta_2 k_1]}{(\mu + k_1)(\mu + k_2) + \alpha\mu + h_*}. \tag{5.9}$$

Theorem 5.4.3. *If $\mathcal{R}_\sigma < 1$, then restricted to the subset Φ, I and J almost surely converge exponentially to 0.*

Proof. For $\xi_1,\ \xi_2$ and ξ_4 as above (and for $\xi_0 = \xi_3 = 0$), we define $Z_0 = \xi_1 I + \xi_2 J$ and $V_0 = \ln Z_0$. It suffices to prove that $\limsup_{t\to\infty}\langle \mathcal{L}V_0\rangle_t < 0$. Also, we let $F_0 = F(0, \xi_1, \xi_2, 0)$. We need to prove that $F_0 < 0$.

From (5.7) it follows that

$$F_0 \leq \xi_1 \left[c(\beta_1 i + \beta_2 j)s - (\mu + k_1)i + \alpha j\right] + \xi_2 \left[k_1 i - (\mu + k_2 + \alpha)j\right] - \frac{1}{2}\left[(\xi_1\sigma_1 i)^2 + (\xi_2\sigma_2 j)^2\right].$$

This can further be simplified to yield

$$F_0 \leq \xi_1 cK(\beta_1 i + \beta_2 j) - \xi_4(\beta_1 i + \beta_2 j) - \frac{1}{2}\left[(\xi_1\sigma_1 i)^2 + (\xi_2\sigma_2 j)^2\right]. \tag{5.10}$$

Now we note that

$$(\xi_1\sigma_1 i)^2 + (\xi_2\sigma_2 j)^2 = \frac{(\xi_1\sigma_1 i)^2 + (\xi_2\sigma_2 j)^2}{\beta_1 i + \beta_2 j}(\beta_1 i + \beta_2 j),$$

and since $\xi_2 j = 1 - \xi_1 i$, we have

$$F_0 \leq cK\xi_1(\beta_1 i + \beta_2 j) - \xi_4(\beta_1 i + \beta_2 j) - h(\xi_1 i)(\beta_1 i + \beta_2 j).$$

This leads to the inequality below:

$$F_0 \leq cK\xi_1(\beta_1 i + \beta_2 j) - \xi_4(\beta_1 i + \beta_2 j) - h_*(\beta_1 i + \beta_2 j) = \xi_4(\mathcal{R}_\sigma - 1)(\beta_1 i + \beta_2 j) < 0.$$

This completes the proof.

□

We now prove the main theorem.

Theorem 5.4.4. *If $\mathcal{R}_\sigma < 1$, then the disease-free equilibrium is almost surely exponentially stable.*

Proof. The proof is by contradiction. From Theorem 5.4.3 we know that $\lim_{t\to\infty} I(t) = 0$ (a.s) and $\lim_{t\to\infty} J(t) = 0$ (a.s). Let us now suppose, contrary to the claim of this theorem, that for some subset Θ of Φ with $\mathbb{P}(\Theta) > 0$, on Θ we have:

$$\lim_{t\to\infty}[(K - S(t)) + A(t)] \neq 0. \tag{5.11}$$

Now let Z be as in (5.5) and $F(\xi)$ as in (5.7). In particular we choose $\xi_0 = \xi_1 = \xi_2 = \xi_3 = \xi_4 = 1$. Then in view of (5.11) and by the definition of i and j, on Θ we have $i = 0$ (a.s) and $j = 0$ (a.s). Thus, from (5.7) it follows that

$$F(\xi) \leq -\mu q - (\mu + \delta)a - \frac{1}{2}(\sigma_3 a)^2 \ \text{ (a.s)}.$$

Therefore, $F < 0$ (a.s). Then by Proposition 5.4.2 it follows that on Θ, we have that $\lim_{t\to\infty}(K - S(t)) = 0$ (a.s) and $\lim_{t\to\infty} A(t) = 0$ (a.s). This is a contradiction, and it completes the proof. □

5.5 A case study of HIV/AIDS in South Africa.

The parameters such as c, α, k_1, k_2 found in [9, 41, 40] are applicable to Southern African. We also assign nominal values to certain parameters. In [40] for instance, the average number of sexual partners per given time denoted by c has been assigned values ranging from 1 to 2 for a specific case. In our case we take $c = 3$ in order to avoid addressing a problem that is simpler than the actual one. We expect the following inequality holds $\beta_1 < \beta_2$, knowing that the probability of disease transmission in the symptomatic phase far exceeds that of the asymptomatic phase. In the year 2016, the life expectancy in South Africa was estimated at 62.4 years, see for instance in [90]. The mortality rate μ is simply the inverse of the life expectancy given by $\frac{1}{62.4}\ yr^{-1}$. The disease induced mortality rate δ is found in [90]. The parameter K is the size of the population and does not

complicate our task. We estimate values for the inflow of infectives Q_1 and Q_2 since they are not easily obtainable. The parameter values of the model are given in the table below.

Table 5.1: Epidemiological data used to estimate initial values for model (5.1)

Parameters	Value	Source
α	0.33	[9]
k_1	0.125	[41]
k_2	0.1	[9]
c	3	cf. [40]
μ	$\frac{1}{62.5}$	[90]
δ	0.279	[90]

Regarding the initial conditions, we start off by 2016 in order to do our projection. According to the South African 2016 mid-year population estimate [90], the total population which we denote by $N(t_{16}) = S(t_{16}) + I(t_{16}) + J(t_{16}) + A(t_{16})$, and where t_{16} is the time on 25 August 2016 was 55.91 million. An estimated 7.03 million of the total population were infected with HIV/AIDS in 2016. This means that the classes of $I(t_{16})$, $J(t_{16})$ and $A(t_{16})$ add up to 7.03 million. We shall then use the parameters listed in Table 1 to find a suitable equilibrium point to split the numbers between the classes of $I(t_{16})$, $J(t_{16})$ and $A(t_{16})$. We keep vary the value of β_1 and β_2 in order to vary the value of the basic reproduction number.

Let us denote the force of infection by

$$\lambda = c(\beta_1 I + \beta_2 J).$$

We note that with inflow of infectives, we find the following equilibrium values for I and J:

$$I = \frac{\alpha\ (\lambda+\mu)\ Q_2 + (\alpha+\mu+k_2)\,(K\lambda\,\mu + (\lambda+\mu)\ Q_1)}{(\lambda+\mu)\ ((\mu+k_1)\ (\mu+k_2) + \alpha\mu)}$$

and

$$J = \frac{1}{(\alpha+\mu+k_2)}\left[Q_2 + k_1\left(\frac{\alpha\ (\lambda+\mu)\ Q_2 + (\alpha+\mu+k_2)\,(K\lambda\,\mu + (\lambda+\mu)\ Q_1)}{(\lambda+\mu)\ ((\mu+k_1)\ (\mu+k_2) + \alpha\mu)}\right)\right]$$

This consideration leads us to assign initial values to I_0 and J_0, and thus our initial state is taken as:

$$S_0 = 48.88, I_0 = 5.22, J_0 = 1.46, A_0 = 0.344.$$

We present some simulations in order to illustrate the analytical results of stochastic model (5.1) and the underlying deterministic system. For simplicity we use one common value for σ_1, σ_2 and σ_3 (call it σ) while $\sigma_0 = 0$. In each graph we show trajectories of $J(t)$ for the stochastic model and of $J(t)$ for the underlying deterministic model with respect to time in years.

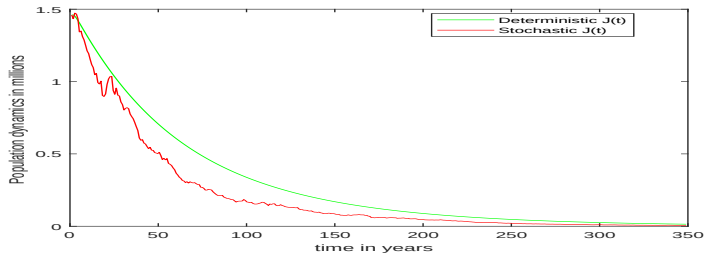


Figure 5.1: A case of $\mathcal{R}_\sigma < 0$, Theorem 5.4.3 guarantees stability.
Chosen values: $\beta_1 = 0.000176, \beta_2 = 0.00037$, $u = 0.9$, $\sigma = 0.03$. Calculated values: $\mathcal{R}_0 = 0.967734$, $\mathcal{R}_\sigma = 0.9557$, $h = 0.000272349$.

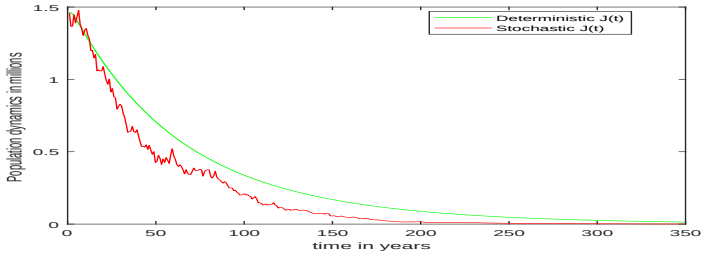


Figure 5.2: Improving stability in the case $\mathcal{R}_\sigma < 0$ and $\sigma = 0.05$.
Chosen values: $\beta_1 = 0.000176, \beta_2 = 0.00037$, $u = 0.9$, $\sigma = 0.05$. Calculated values: $\mathcal{R}_0 = 0.967734$, $\mathcal{R}_\sigma = 0.9350$, $h = 0.000756524$.

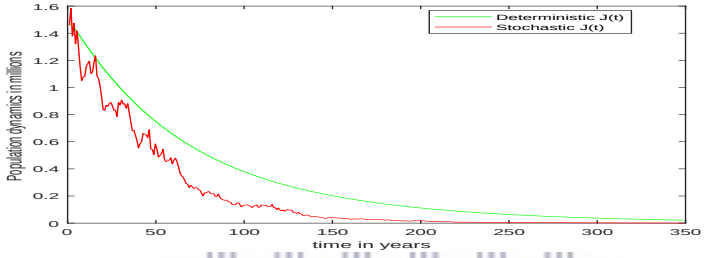


Figure 5.3: Stability obtained beyond $\mathcal{R}_0 < 1$ while $\mathcal{R}_\sigma < 1$.
Chosen values: $\beta_1 = 0.000186$, $\beta_2 = 0.00039$, $u = 0.9$, $\sigma = 0.06$. Calculated values: $\mathcal{R}_0 = 1.022$, $\mathcal{R}_\sigma = 0.9702$, $h = 0.00108939$.

In Figs. 5.1 and 5.2 we use $\beta_1 = 0.000176$ and $\beta_2 = 0.00037$, but with different values of σ. In both cases $\mathcal{R}_\sigma$ is found to be less than 1. In these cases Theorem 5.4.3 assures us that the disease-free equilibrium is almost surely exponentially stable. Indeed the graph shows that over time, the state of the system converges to disease-free equilibrium. It is also noticed that the convergence to the disease-free equilibrium is faster in Fig. 5.2 than in Fig. 5.1, in line with a lower value of $\mathcal{R}_\sigma$. In this case, we have expected the convergence to be faster for a smaller value of $\mathcal{R}_\sigma$. Fig. 5.3 shows that for small values of the perturbation parameter there is convergence to disease-free equilibrium for a bigger range of values of the basic reproduction number of the underlying deterministic model.

5.6 Asymptotic behaviour around endemic equilibrium of the underlying deterministic model

For $\sigma_0 \neq 0$ the model system (5.1) has no endemic equilibrium, but we can investigate the asymptotic behaviour around the endemic equilibrium of the underlying deterministic model system.

Before stating the main theorem, let us first define these positive numbers:

$$B_1 = 1 + \frac{2\mu + k_2}{\alpha},\ B_2 = \mu + \frac{(\mu + k_1)(2\mu + k_2)}{\alpha},$$
$$B_3 = 2\mu + \frac{(\mu + k_1)(2\mu + k_2)}{\alpha} + \frac{\mu(2\mu + k_2)}{\alpha},\ B_4 = \frac{2B_3}{c\beta_1} \tag{5.12}$$

Theorem 5.6.1. *Let $(S(t), I(t), J(t), A(t))$ be the solution of system (5.1) with any initial value $(S(0), I(0), J(0), A(0)) \in \mathbb{R}^4_{++}$. Let $E^* = (S^*, I^*, J^*, A^*)$ be an endemic equilibrium point of the underlying deterministic model. If $\mathcal{R}_0 > 1$, and the following condition is satisfied:*

$$2(\mu + \delta) - k_2 > 0,$$

then the solution of model (5.1) has the property:

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t \left[(S(\tau) - S^*)^2 + (I(\tau) - I^*)^2 + (J(\tau) - J^*)^2 + (A(\tau) - A^*)^2\right] d\tau \leq \frac{B_0}{\theta},$$

where

$$\theta = 2\min\left\{\mu B_1, B_2, \mu, 2(\mu + \delta) - k_2\right\},$$

and

$$B_0 = K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2) + \frac{1}{2}B_4\left(S^*\sigma_0^2 + 2I^*\sigma_1^2 + A_2 J^*\sigma_2^2\right).$$

Proof. We note that at the nontrivial equilibrium point $E^* = (S^*, I^*, J^*, A^*)$ we have,

$$\begin{aligned} \mu K + Q_1 + Q_2 &= \mu S^* + \mu I^* + (\mu + k_2) J^* \\ \mu K + Q_2 &= \mu S^* + (\mu + k_1) I^* - \alpha J^* \\ (\mu + \delta) &= k_2 \frac{J^*}{A^*}. \end{aligned} \tag{5.13}$$

Consider the following function

$$V_3(S, I, J, A) = V_4 + V_5 + V_6 + V_7$$

where

$$V_4 = [(S - S^*) + (I - I^*) + (J - J^*)]^2,$$

$$V_5 = \frac{(2\mu + k_2)}{\alpha}[(S - S^*) + (I - I^*)]^2, \; V_6 = 2(A - A^*)^2,$$

$$V_7 = B_4 \left(S - S^* - S^* \ln \frac{S}{S^*} \right) + 2B_4 \left(I - I^* - I^* \ln \frac{I}{I^*} \right) + A_2 B_4 \left(J - J^* - J^* \ln \frac{J}{J^*} \right)$$

with

$$A_2 = \frac{2\alpha J^* + c\beta_2 J^* S^*}{k_1 I^*} \; .$$

Then

$$\begin{aligned} \int_0^t dV_3(S, I, J, A) &= \int_0^t \mathcal{L} V_3 du + R_t \\ &= \int_0^t [\mathcal{L} V_4 + \mathcal{L} V_5 + \mathcal{L} V_6 + \mathcal{L} V_7] du + R_t \end{aligned}$$

where

$$
\begin{aligned}
R_t &= \int_0^t 2[(S-S^*)+(I-I^*)+(J-J^*)](\sigma_0 S dW_0(u)+\sigma_1 I dW_1(u)+\sigma_2 J dW_2(u)) \\
&+\int_0^t 2\frac{(2\mu+k_2)}{\alpha}[(S-S^*)+(I-I^*)](\sigma_0 S dW_0(u)+\sigma_1 I dW_1(u)) \\
&+\int_0^t 4(A-A^*)\sigma_3 dW_3(u)+\int_0^t B_4(S-S^*)\sigma_0 dW_0(u)+\int_0^t 2B_4(I-I^*)\sigma_1 dW_1(u) \\
&+\int_0^t A_2 B_4(J-J^*)\sigma_2 dW_2(u).
\end{aligned}
$$

We expand the $\mathcal{L}V_i$ terms as follows

$$
\begin{aligned}
\mathcal{L}V_4 &= 2[(S-S^*)+(I-I^*)+(J-J^*)][-\mu(S-S^*)-\mu(I-I^*)-(\mu+k_2)(J-J^*)] \\
&+(\sigma_0^2 S^2+\sigma_1^2 I^2+\sigma_2^2 J^2), \\
\mathcal{L}V_5 &= 2\frac{(2\mu+k_2)}{\alpha}[(S-S^*)+(I-I^*)][-\mu(S-S^*)-(\mu+k_1)(I-I^*)+\alpha(J-J^*)], \\
&+\frac{(2\mu+k_2)}{\alpha}(\sigma_0^2 S^2+\sigma_1^2 I^2),
\end{aligned}
$$

$$
\begin{aligned}
\mathcal{L}V_6 &= 4(A-A^*)[k_2(J-J^*)-(\mu+\delta)(A-A^*)]+2\sigma_3^2 A^2, \\
\mathcal{L}V_7 &= \mu S^* B_4\left(2-\frac{S}{S^*}-\frac{S^*}{S}\right)-B_4\left(1-\frac{S^*}{S}\right)c\beta_1(IS-I^*S^*)+2B_4\left(2-\frac{I}{I^*}-\frac{I^*}{I}\right)Q_1 \\
&-B_4\left(1-\frac{S^*}{S}\right)c\beta_2(JS-J^*S^*)+2B_4 c\beta_1\left(I-I^*\right)\left(S-S^*\right) \\
&+2B_4\left(1-\frac{I^*}{I}\right)c\beta_2\left(JS-J^*S^*\frac{I}{I^*}\right)+2B_4\alpha\left(1-\frac{I^*}{I}\right)\left(J-J^*\frac{I}{I^*}\right) \\
&+A_2B_4\left(1-\frac{J^*}{J}\right)\left(k_1 I-k_1 I^*\frac{J}{J^*}\right)+A_2B_4\left(2-\frac{J}{J^*}-\frac{J^*}{J}\right)Q_2 \\
&+\frac{1}{2}B_4\left(S^*\sigma_0^2+2I^*\sigma_1^2+A_2J^*\sigma_2^2\right).
\end{aligned}
$$

Let us compute $\mathcal{L}V_4, \mathcal{L}V_5$ and $\mathcal{L}V_6$ in detail.

$$
\begin{aligned}
\mathcal{L}V_4 &= -2\mu(S-S^*)^2 - 4\mu(S-S^*)(I-I^*) - 2(2\mu+k_2)(S-S^*)(J-J^*) \\
&\quad -2(2\mu+k_2)(I-I^*)(J-J^*) - 2\mu(I-I^*)^2 - 2(\mu+k_2)(J-J^*)^2 \\
&\quad +(\sigma_0^2 S^2 + \sigma_1^2 I^2 + \sigma_2^2 J^2) \\
\mathcal{L}V_5 &= -2\mu\frac{(2\mu+k_2)}{\alpha}(S-S^*)^2 - 2\frac{(\mu+k_1)(2\mu+k_2)}{\alpha}(I-I^*)^2 \\
&\quad -2\left(\frac{(\mu+k_1)(2\mu+k_2)}{\alpha} + \mu\frac{(2\mu+k_2)}{\alpha}\right)(S-S^*)(I-I^*) \\
&\quad +2(2\mu+k_2)(S-S^*)(J-J^*) + 2(2\mu+k_2)(I-I^*)(J-J^*) \\
&\quad +\frac{(2\mu+k_2)}{\alpha}(\sigma_0^2 S^2 + \sigma_1^2 I^2) \\
\mathcal{L}V_6 &= 4k_2(A-A^*)(J-J^*) - 4(\mu+\delta)(A-A^*)^2 + 2\sigma_3^2 A^2.
\end{aligned}
$$

Thus we have,

$$
\begin{aligned}
\mathcal{L}V_3 &= -2\mu B_1(S-S^*)^2 - 2B_2(I-I^*)^2 - 2(\mu+k_2)(J-J^*)^2 \\
&\quad -2B_3(S-S^*)(I-I^*) + 4k_2(A-A^*)(J-J^*) - 4(\mu+\delta)(A-A^*)^2 \\
&\quad +\sigma_0^2 S^2 B_1 + \sigma_1^2 I^2 B_1 + \sigma_2^2 J^2 + 2\sigma_3^2 A^2 + \mathcal{L}V_7 \qquad (5.14)
\end{aligned}
$$

where B_1, B_2 and B_3 are as in (5.12).

Following the inequality (4.2) in remark 4.2.3, regarding the second term in line two for equation (5.14) we get

$$2(A-A^*)(J-J^*) \leq (A-A^*)^2 + (J-J^*)^2.$$

Now from (5.14) we obtain the inequality:

$$
\begin{aligned}
\mathcal{L}V_3 &\leq -2\mu B_1\left(S-S^*\right)^2 - 2B_2\left(I-I^*\right)^2 - 2\mu\left(J-J^*\right)^2 \\
&\quad -2(2(\mu+\delta)-k_2)\left(A-A^*\right)^2 + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2) \\
&\quad -2B_3(S-S^*)(I-I^*) + \mathcal{L}V_7 \\
&\leq \Lambda, \qquad (5.15)
\end{aligned}
$$

where

$$\Lambda = \mathcal{L}V_7 - 2B_3(S - S^*)(I - I^*) + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2).$$

Then

$$\begin{aligned}
\Lambda &= \mu S^* B_4 \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) - B_4 \left(1 - \frac{S^*}{S}\right) c\beta_1 (IS - I^* S^*) + 2B_4 \left(2 - \frac{I}{I^*} - \frac{I^*}{I}\right) Q_1 \\
&\quad - B_4 \left(1 - \frac{S^*}{S}\right) c\beta_2 (JS - J^* S^*) + 2B_3 (I - I^*)(S - S^*) \\
&\quad + 2B_4 \left(1 - \frac{I^*}{I}\right) c\beta_2 \left(JS - J^* S^* \frac{I}{I^*}\right) + 2B_4 \alpha \left(1 - \frac{I^*}{I}\right) \left(J - J^* \frac{I}{I^*}\right) \\
&\quad + A_2 B_4 \left(1 - \frac{J^*}{J}\right) \left(k_1 I - k_1 I^* \frac{J}{J^*}\right) + A_2 B_4 \left(2 - \frac{J}{J^*} - \frac{J^*}{J}\right) Q_2 \\
&\quad + \frac{1}{2} B_4 \left(S^* \sigma_0^2 + 2I^* \sigma_1^2 + A_2 J^* \sigma_2^2\right) + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2).
\end{aligned}$$

Letting $\frac{S}{S^*} = x$, $\frac{I}{I^*} = y$, $\frac{A}{A^*} = z$, it follows that

$$\begin{aligned}
\Lambda &= S^*(B_4\mu + 2B_3 I^*) \left(2 - \frac{1}{x} - x\right) + 2B_4 \alpha J^* \left(2 - \frac{z}{y} - \frac{y}{z}\right) \\
&\quad + B_4 S c\beta_2 J^* \left(3 - \frac{xz}{y} - \frac{1}{x} - \frac{y}{z}\right) + 2B_4 \left(2 - \frac{1}{y} - y\right) Q_1 \\
&\quad + \frac{1}{2} B_4 \left(S^* \sigma_0^2 + 2I^* \sigma_1^2 + A_2 J^* \sigma_2^2\right) + A_2 B_4 \left(2 - \frac{1}{z} - z\right) Q_2 \\
&\quad + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2).
\end{aligned}$$

Note that since the arithmetic mean is greater than or equal to the geometric mean, it follows that

$$\frac{1}{y} + y \geq 2, \ \frac{1}{x} + x \geq 2, \ \frac{z}{y} + \frac{y}{z} \geq 2, \ \frac{1}{x} + \frac{xz}{y} + \frac{y}{z} \geq 3.$$

We now have

$$\Lambda \leq \frac{1}{2} B_4 \left(S^* \sigma_0^2 + 2I^* \sigma_1^2 + A_2 J^* \sigma_2^2\right) + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2). \tag{5.16}$$

Substituting (5.16) into (5.15), it follows that

$$\begin{aligned}\mathcal{L}V_3 \leq\ & -2\mu B_1 (S-S^*)^2 - 2B_2 (I-I^*)^2 - 2\mu (J-J^*)^2 \\ & -2(2(\mu+\delta)-k_2)(A-A^*)^2 + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2) \\ & +\frac{1}{2}B_4\left(S^*\sigma_0^2 + 2I^*\sigma_1^2 + A_2 J^*\sigma_2^2\right).\end{aligned}$$

Hence

$$\begin{aligned}\int_0^t dV_3 \leq\ & \int_0^t [-2\mu B_1 (S-S^*)^2 - 2B_2 (I-I^*)^2 - 2\mu (J-J^*)^2 \\ & -2(2(\mu+\delta)-k_2)(A-A^*)^2 + K^2(\sigma_0^2 B_1 + \sigma_1^2 B_1 + \sigma_2^2 + 2\sigma_3^2) \\ & +\frac{1}{2}B_4(S^*\sigma_0^2 + 2I^*\sigma_1^2 + A_2 J^*\sigma_2^2)]du + R_t.\end{aligned}$$

We take expectation and note that $\mathbb{E}[R_t] = 0$. Thus we obtain

$$\begin{aligned}0 \leq\ & \mathbb{E}[V_3(S(t), I(t), J(t), A(t))] \leq \mathbb{E}[V_3(S(0), I(0), J(0), A(0))] \\ & +\mathbb{E}\int_0^t [-2\mu B_1 (S-S^*)^2 - 2B_2 (I-I^*)^2 - 2\mu (J-J^*)^2 \\ & -2(2(\mu+\delta)-k_2)(A-A^*)^2 + B_0]du, \end{aligned} \tag{5.17}$$

which gives

$$\begin{aligned}& \mathbb{E}\int_0^t \left[2\mu B_1 (S(u)-S^*)^2 + 2B_2 (I(u)-I^*)^2 + 2\mu (J(u)-J^*)^2\right. \\ & \left.+2(2(\mu+\delta)-k_2)(A(u)-A^*)^2\right] du \\ & \leq \mathbb{E}[V_3(S(0), I(0), J(0), A(0))] + B_0 t.\end{aligned}$$

Therefore,

$$\begin{aligned}& \limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t \left[2\mu B_1 (S(u)-S^*)^2 + 2B_2 (I(u)-I^*)^2 + 2\mu (J(u)-J^*)^2\right. \\ & \left.+2(2(\mu+\delta)-k_2)(A(u)-A^*)^2\right] du \leq B_0.\end{aligned}$$

We take θ as in the formulation of Theorem 5.6.1, and then it follows that:

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t \left[(S(\tau)-S^*)^2+(I(\tau)-I^*)^2+(J(\tau)-J^*)^2+(A(\tau)-A^*)^2\right] d\tau \leq \frac{B_0}{\theta},$$

This completes the proof. □

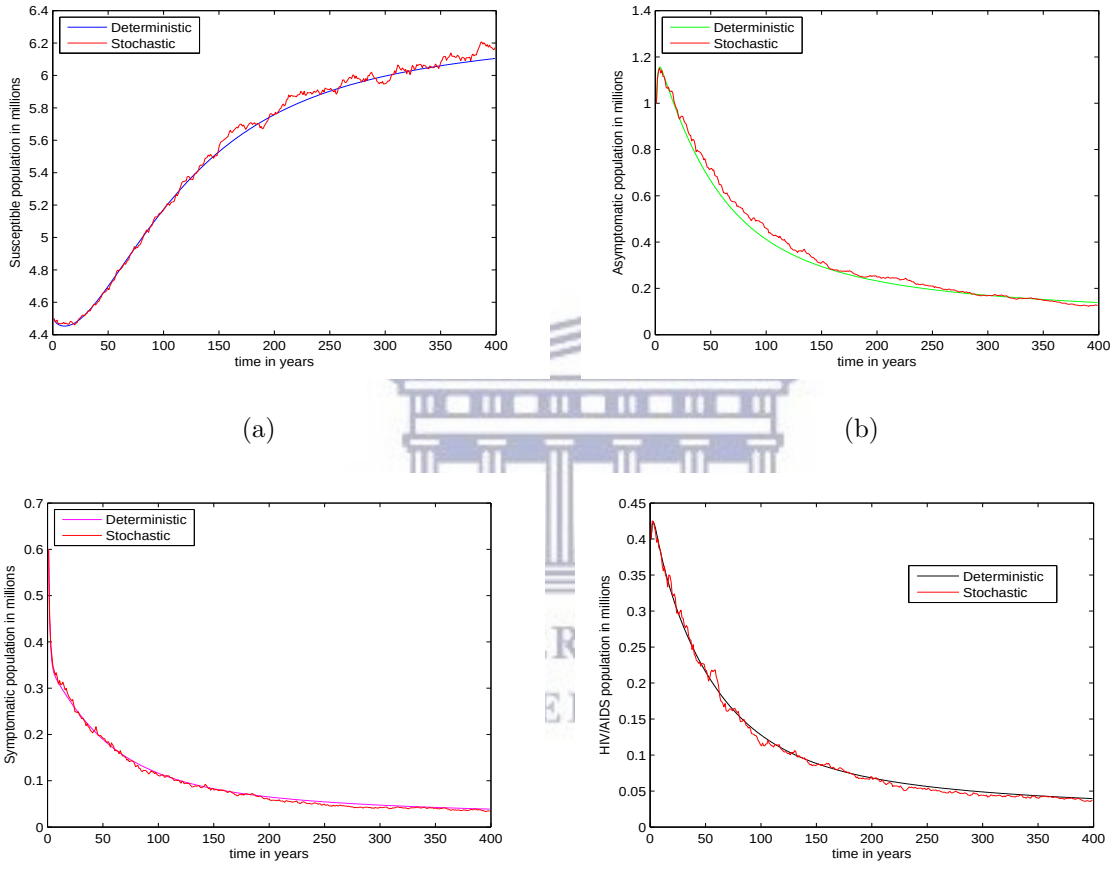
Remark 5.6.2. *Theorem 5.6.1 states that for small values of the perturbation parameters the solutions of the stochastic system (5.1) will eventually stay very close to the endemic equilibrium of the underlying deterministic model.*

We present numerical simulations in the general case as well as in the case the South-African historical HIV data with parameter values given in Table 5.2.

Table 5.2: Parameters estimates for the simulation of model system 5.1 in the general context.

Parameters	Value	Source
μ	0.02	[8]
α	0.33	[8]
k_1	0.125	[41]
k_2	0.1	[8]
c	3	Estimate
δ	0.333	[8]
b	2.5	Estimate
K	6.5	Nominal

with the initial conditions: $S_0 = 4.5,\ I_0 = 1,\ J_0 = 0.6,\ A_0 = 0.4$. In each graph we show two trajectories of the stochastic model (one sample path) and of the underlying deterministic model.



(a) (b)

(c) (d)

Figure 5.4: $\beta = 0.00165$, $Q_1 = Q_2 = 0$, $\sigma_0 = 0.002$, $\sigma_1 = 0.01$, $\sigma_2 = 0.02$, $\sigma_3 = 0.02$, $\mathcal{R}_0 = 1.022$,$B_1 = 1.42, B_2 = 0.0815$

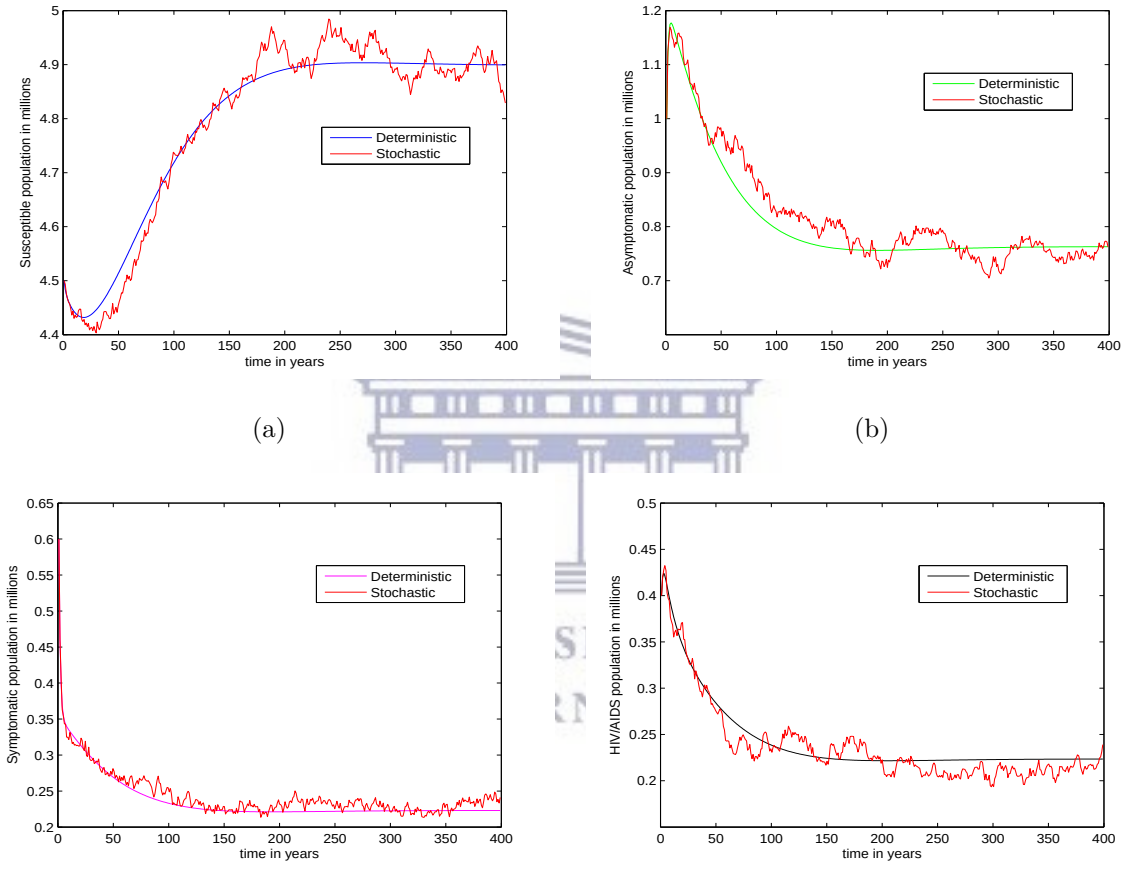


Figure 5.5: $\beta = 0.00165$, $Q_1 = Q_2 = 0.005$, $\sigma_0 = 0.002$, $\sigma_1 = 0.01$, $\sigma_2 = 0.02$, $\sigma_3 = 0.02$, $\mathcal{R}_0 = 1.022$, $B_1 = 1.42, B_2 = 0.0815$

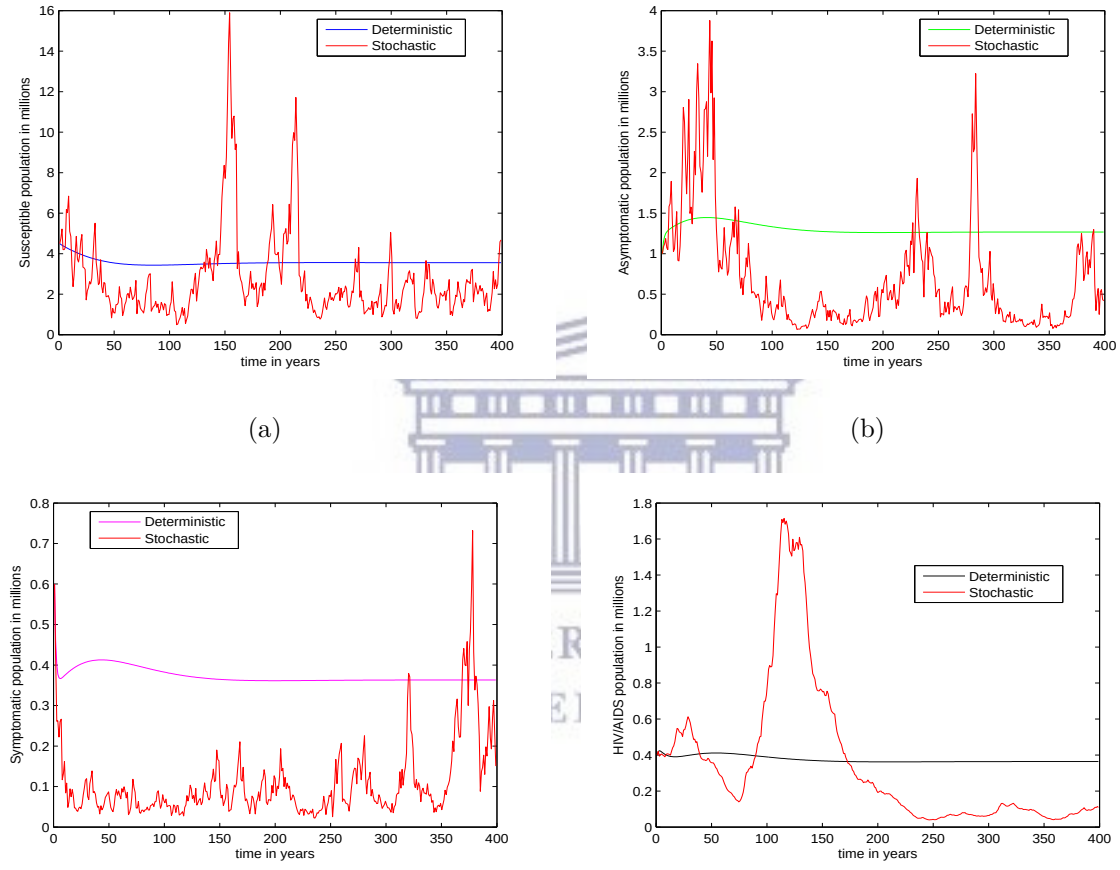
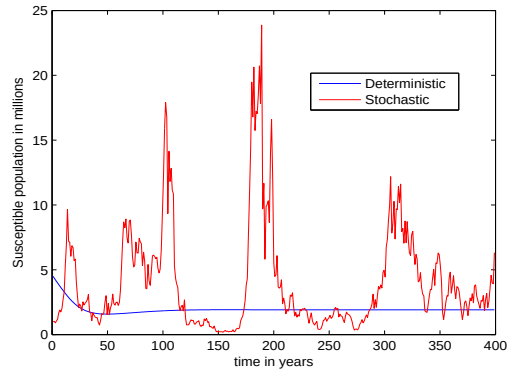
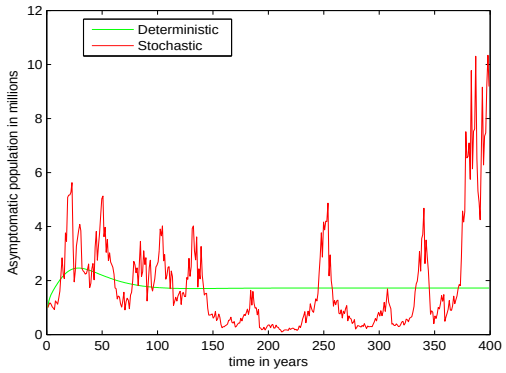


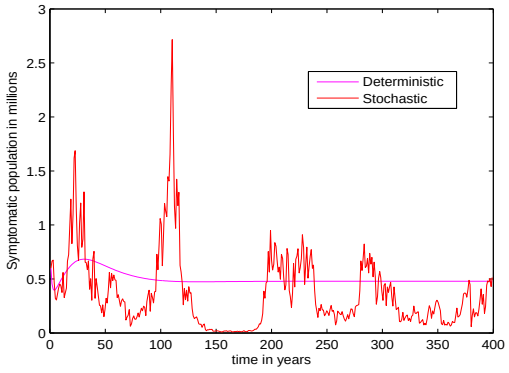
Figure 5.6: $\beta = 0.00254$, $Q_1 = Q_2 = 0.005$, $\sigma_0 = 0.25$, $\sigma_1 = 0.28$, $\sigma_2 = 0.22$, $\sigma_3 = 0.02$, $\mathcal{R}_0 = 1.574$, $B_1 = 1.42, B_2 = 0.0815$



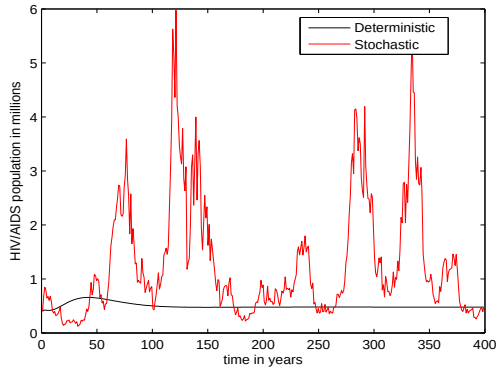
(a)



(b)



(c)



(d)

Figure 5.7: $\beta = 0.00550$, $Q_1 = Q_2 = 0$, $\sigma_0 = 0.25$, $\sigma_1 = 0.25$, $\sigma_2 = 0.25$, $\sigma_3 = 0.2$, $\mathcal{R}_0 = 3.407$, $B_1 = 1.42, B_2 = 0.0815$.

In the special case, the initial state is taken as:

$$S_0 = 48.88; I_0 = 5.22; J_0 = 1.46; A_0 = 0.344.$$

We present numerical simulations in order to illustrate the results of Theorem 5.5.1 with parameter values given in Table 1.

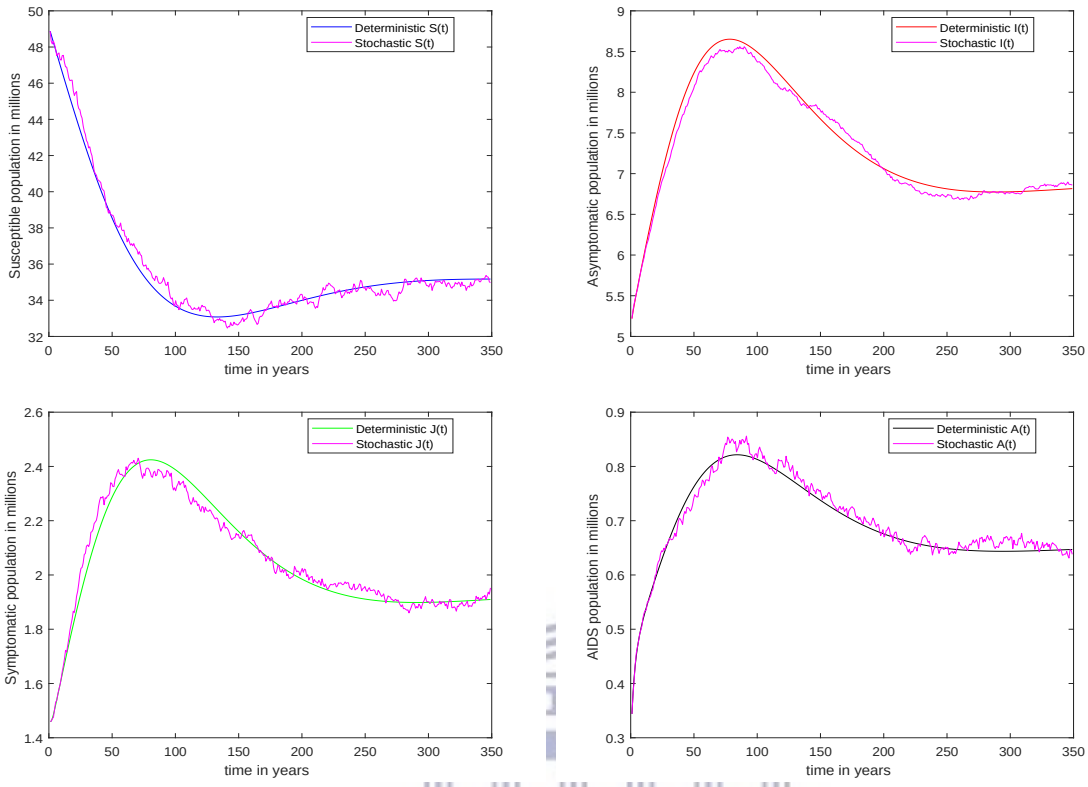


Figure 5.8: The dynamics of model system (5.1) without the inflow of infectives: Chosen values: $\beta_1 = 0.0002904, \beta_2 = 0.00061, Q_1 = Q_2 = 0, \sigma_0 = 0.005, \sigma_1 = 0.004, \sigma_2 = 0.009, \sigma_3 = 0.01$. Calculated value: $\mathcal{R}_0 = 1.595, \lambda = 0.009527, S^* = 35.04, I^* = 6.88, J^* = 1.92, A^* = 0.65$.

In Fig. 5.8 the basic reproduction number $\mathcal{R}_0$ is bigger than one and the stochastic solutions remain close to the endemic solutions of the underlying deterministic model. We observe a similar pattern in these graphs. In Fig. 5.9 all the parameters and their values have remained unchanged, except that the inflow of infectives Q_1, Q_2 now are taken as positive. In the case of the underlying deterministic model, the inflow of infectives lead to increasing the values of the force of infection λ, I, J and A while decreasing the value of S. In the stochastic case, the fluctuation in each graph is higher than the fluctuations in

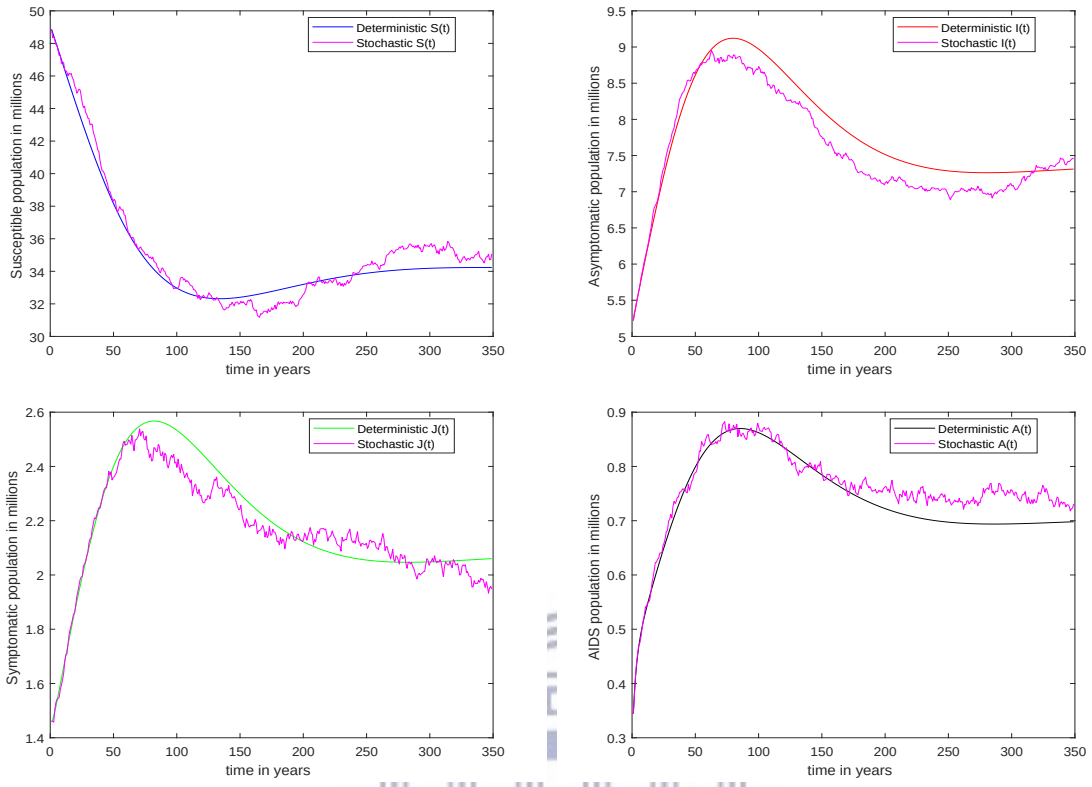


Figure 5.9: The dynamics of model system (5.1) with inflow of infectives:

Chosen values: $\beta_1 = 0.0002904, \beta_2 = 0.00061, Q_1 = Q_2 = 0.005, \sigma_0 = 0.005, \sigma_1 = 0.004, \sigma_2 = 0.009, \sigma_3 = 0.01$. Calculated value: $\mathcal{R}_0 = 1.595, \lambda = 0.01022, S^* = 34.12, I^* = 7.37, J^* = 2.077, A^* = 0.70$.

Fig. 5.8 due to the inflow of infectives. In Fig. 5.10, for $Q_1 = Q_2 = 0.005$, we increase the values of stochastic perturbations. In this case, strong perturbation has led to a strong divergence and we do not expect the stochastic solutions to be close to the endemic solutions of the underlying deterministic system.

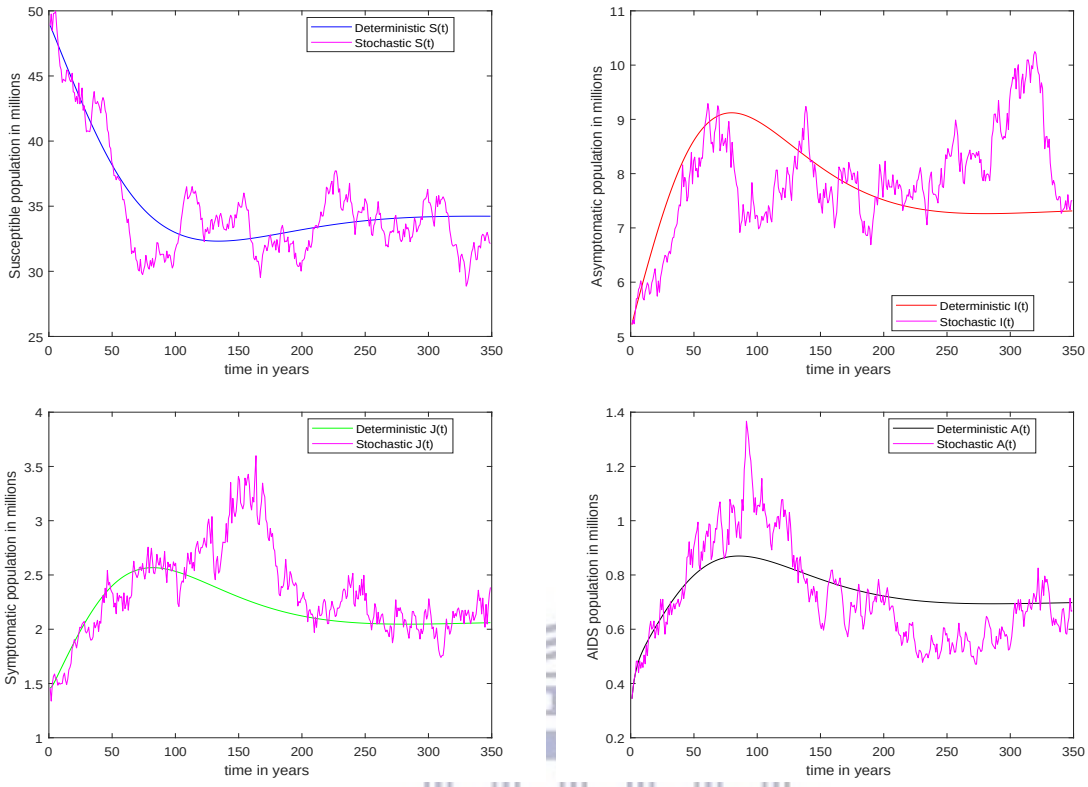


Figure 5.10: The dynamics of model system (5.1) with big stochastic perturbations: Chosen values: $\beta_1 = 0.0002904, \beta_2 = 0.00061$, $Q_1 = Q_2 = 0.005$, $\sigma_0 = 0.04$, $\sigma_1 = 0.03$, $\sigma_2 = 0.06$, $\sigma_3 = 0.06$. Calculated value: $\mathcal{R}_0 = 1.595, \lambda = 0.01022, S^* = 34.12, I^* = 7.37, J^* = 2.077, A^* = 0.70$.

5.7 Concluding remarks

We have presented an *sde* model of HIV, which we showed to have well-behaved solutions. In the special case that we have no inflow of infected individuals into the system and $\sigma_0 = 0$, Theorem 5.4.3 describes convergence to disease-free equilibrium. In particular, the theorem asserts that for sufficiently small values of the perturbation parameter, stability of the disease-free equilibrium is obtained for a bigger range of values of the

basic reproduction number $\mathcal{R}_0$ of the deterministic model, i.e., beyond the range $\mathcal{R}_0 < 1$. This is sufficiently significant that it can be observed in simulations. The almost sure exponential stability is a fairly strong type of stability, it being a stochastic version of global asymptotic stability. For the public health authorities it is comforting to know that the presence of minor stochasticity on their model will not be a hindrance if eradication strategies should be launched. However, although South Africa has more people infected with HIV, the country has kept many HIV infected people alive, due to it being among countries having the largest ART programmes in the world. The ART treatment has improved the lives of many individuals with HIV in the world and particularly in South Africa, but it is known that treatment without behavioural change may even lead to high prevalence of AIDS. With respect to the general model, we have been able to describe the long-term behaviour of solutions in comparison with that of the deterministic model, in Theorem 5.6.1. The theorem asserts that asymptotically the stochastic solutions stay within a certain bound from the (non-trivial) equilibrium point of the underlying deterministic model. This is very well observed in simulations. Further it is also investigated that the positive flow of infectives could affect the stability and also lead the dynamics of the model system from stable to the unstable situation. Our *sde* model has revealed some new phenomena and is useful when planning intervention strategies.

Chapter 6

A model of HIV/AIDS population dynamics including ARV treatment and pre-exposure prophylaxis[1]

6.1 Introduction

We investigate a deterministic compartmental model for HIV/AIDS epidemic model including ARV treatment and the use of oral prophylaxis. Antiretroviral treatment (ART) and oral pre-exposure prophylaxis (PrEP) have recently been used efficiently in management of HIV infection. Pre-exposure prophylaxis consists in the use of an antiretroviral medication to prevent the acquisition of HIV infection by uninfected individuals. We propose a new model for the transmission of HIV/AIDS including ART and PrEP. Our model can be used to test the effects of ART and of the uptake of PrEP in a given population, as we demonstrate through simulations. The model can also be used to estimate future projections of HIV prevalence. We prove global stability of the disease-free equilibrium. We also prove global stability of the endemic equilibrium for the most general case of the

[1]A modified version of this chapter was published as:

M.U. Nsuami, P.J. Witbooi. A model of HIV/AIDS population dynamics including ARV treatment and pre-exposure prophylaxis. *Advances in Difference Equations*, **2018(1)**, (2018) 11.

model, i.e., which allows for PrEP individuals to default. We include insightful simulations based on recently published South-African data.

The aim of this chapter is to demonstrate the extent to which PrEP can possibly reduce the prevalence of the HIV in a large population such as South Africa, in the presence of treatment. We introduce a model with two stages of infection and we assume that susceptible individuals have access to PrEP to prevent themselves from HIV. Such individuals become exposed to HIV once they stop taking oral PrEP. The model allows for individuals in the asymptomatic phase to move back to the asymptomatic phase after successful treatment.

The remainder of this chapter is set up as follows. In Section 6.2 we present the model. We calculate the basic reproduction number and prove existence of positive solutions. Section 6.3 covers both global stability of the disease-free and endemic equilibrium. In Section 6.4 we provide numerical simulations to illustrate our theoretical results and the utility of the model. In Section 6.5 we offer some concluding remarks.

6.2 The model

6.2.1 Model description

We consider a population with homogeneous mixing of individuals, of size $N(t)$ at time t. The total size $N(t)$ is assumed to be sufficiently large in order to approximate the population as a continuum of points. These are general assumptions for modeling with ordinary differential equations, see for instance [3] of Anderson and May. For this model, the population is subdivided into the classes of susceptibles $S(t)$, the asymptomatic phase $I_1(t)$ of HIV, the symptomatic phase $I_2(t)$, the AIDS patients $A(t)$ and the individuals under PrEP $E(t)$, so that

$$N(t) = S(t) + I_1(t) + I_2(t) + A(t) + E(t).$$

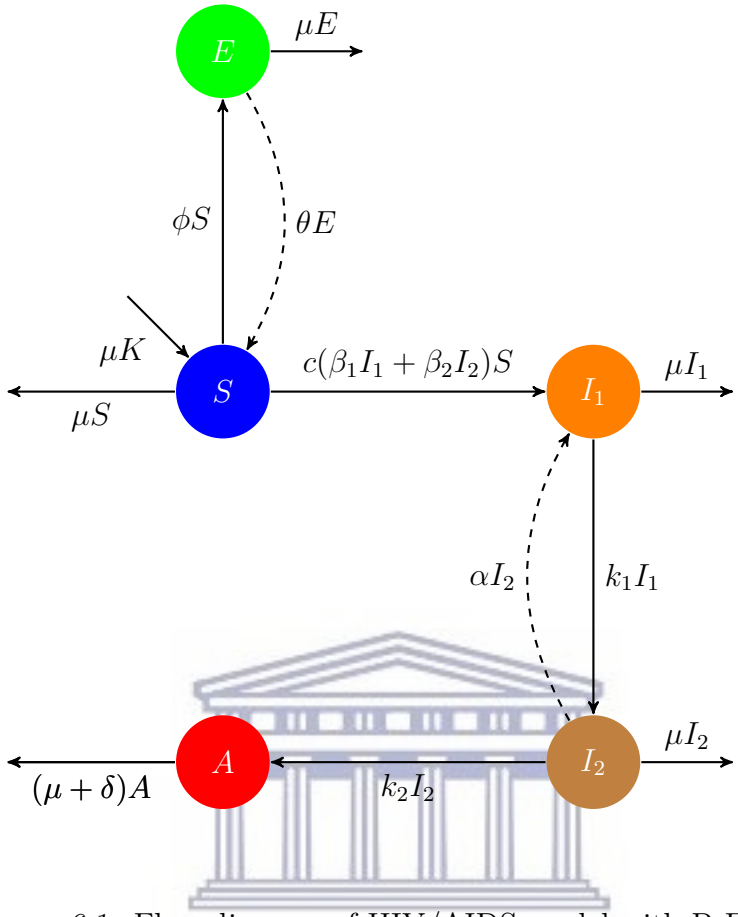


Figure 6.1: Flow diagram of HIV/AIDS model with PrEP

Our model is then constructed by considering the appropriate in-flow and out-flow rates of as in the diagram above

$$\begin{aligned}
\frac{dS}{dt} &= \mu K - c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + \phi)S + \theta E, \\
\frac{dI_1}{dt} &= c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2, \\
\frac{dI_2}{dt} &= k_1 I_1 - (\mu + k_2 + \alpha)I_2, \\
\frac{dA}{dt} &= k_2 I_2 - (\mu + \delta)A, \\
\frac{dE}{dt} &= \phi S - (\mu + \theta)E \ ; \qquad (6.1)
\end{aligned}$$

$$S(0) = S_0 > 0,\ I_1(0) = I_{1,0} > 0,\ I_2(0) = I_{2,0} > 0,\ A(0) = A_0 > 0,\ E(0) = E_0 > 0.$$

The functions $S(t), I_1(t), I_2(t), A(t)$ and $E(t)$ are assumed to be continuous. We introduce the following parameters that appear in the model equations:

μ	Birth and mortality rates by natural causes,
K	The size of the total population when disease-free,
c	The average number of sexual contacts of one individual with others, per unit time,
β_1	The probability of disease transmission in the asymptomatic phase,
β_2	The probability of disease transmission in the symptomatic phase,
ϕ	The proportion of susceptible individuals under PrEP,
θ	The proportion of susceptible individuals who default PrEP,
k_1	Progression rate from I_1 to I_2,
k_2	Progression rate from the symptomatic phase I_2 to A,
α	The rate of transfer from I_2 to I_1 due to ARV treatment,
δ	Disease induced mortality rate.

The model system (6.1) permits a disease-free equilibrium $\Sigma_0 = \left(\frac{(\mu+\theta)K}{(\mu+\phi+\theta)}, 0, 0, 0, \frac{\phi K}{(\mu+\phi+\theta)}\right)$ and an endemic equilibrium $\Sigma_* = (S^*, I_1^*, I_2^*, A^*, E^*)$ with the coordinates

$$\begin{aligned}
S^* &= \frac{\mu K(\mu+\theta)}{(\mu+\theta)(\lambda+\mu)+\mu\phi}, \\
I_1^* &= \frac{\lambda(\mu+k_2+\alpha)\mu K(\mu+\theta)}{[(\mu+k_2)(\mu+k_1)+\mu\alpha][(\mu+\theta)(\lambda+\mu)+\mu\phi]} \\
I_2^* &= \frac{k_1\lambda\mu K(\mu+\theta)}{[(\mu+k_2)(\mu+k_1)+\mu\alpha][(\mu+\theta)(\lambda+\mu)+\mu\phi]} \\
A^* &= \frac{k_1k_2\lambda\mu K(\mu+\theta)}{[(\mu+k_2)(\mu+k_1)+\mu\alpha][(\mu+\theta)(\lambda+\mu)+\mu\phi]} \\
E^* &= \frac{\mu K\phi}{(\mu+\theta)(\lambda+\mu)+\mu\phi}.
\end{aligned}$$

where

$$\lambda = c(\beta_1 I_1^* + \beta_2 I_2^*).$$

Following the method expounded in [98] the basic reproduction number of the model is calculated as

$$\mathcal{R}_0 = \frac{c(\mu+\theta)K(\beta_1(\mu+k_2+\alpha)+\beta_2 k_1)}{(\mu+\phi+\theta)((\mu+k_1)(\mu+k_2)+\alpha\mu)}.$$

6.2.2 Feasible solutions

Let us introduce the set Ω,

$$\Omega = \left\{x \in \mathbb{R}^5 |\ x_i > 0,\ i = 1,2,3,4,5 \text{ and } x_1+x_2+x_3+x_4+x_5 < K\right\}.$$

Theorem 6.2.1. *Assume that $X(t)$ is a solution of the system (6.1) with $X(0) \in \Omega$. Then $X(t) \in \Omega$ for all $t > 0$.*

Proof. The proof is by contradiction. Let $X(t)$ be a solution of the system (6.1) where $X(0) \in \Omega$. Suppose to the contrary that there exists a $t_0 > 0$ such that $X(t_0) \notin \Omega$. Let $T = \inf\{t > 0 : X(t) \notin \Omega\}$. Since Ω is an open set due to continuity of $X(t)$, T is strictly positive.

Choose $a_0 > 0$ sufficiently small in order to have $a_0 c\beta_1 < \mu$ and $a_0 c\beta_2 < \mu$. Consider the function V_1 defined by

$$V_1(t) = \Big(S - a_0 \ln \frac{S}{a_0}\Big) + \Big(I_1 - \ln I_1\Big) + \Big(I_2 - \ln I_2\Big) + \Big(A - \ln A\Big) + \Big(E - \ln E\Big) \tag{6.2}$$

Note that for every $T < t$, each of the five bracketed terms on the right hand side of equation (6.2) are positive while $(S, I_1, I_2, A, E) \in \Omega$.

Now we find an upper bound for the set

$$G = \{V_1(t) : 0 < t < T\}.$$

We note that for any $0 < t < T$,

$$\begin{aligned}
\dot{V}_1(t) &= \Big[\Big(1 - \frac{a_0}{S}\Big)\Big(\mu K - c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + \phi)S + \theta E\Big)\Big] + \Big[\Big(1 - \frac{1}{I_1}\Big)\Big(c(\beta_1 I_1 + \beta_2 I_2)S \\
&\quad -(\mu + k_1)I_1 + \alpha I_2\Big)\Big] + \Big[(1 - \frac{1}{I_2})(k_1 I_1 - (\mu + k_2 + \alpha)I_2)\Big] \\
&\quad + \Big[(1 - \frac{1}{A})(k_2 I_2 - (\mu + \delta)A)\Big] + \Big[(1 - \frac{1}{E})(\phi S - (\mu + \theta)E)\Big] \\
&= \mu K - \frac{a_0}{S}\mu K - \mu(S + I_1 + I_2 + A + E) - \frac{a_0}{S}\theta E + a_0(\mu + \phi) + a_0 c(\beta_1 I_1 + \beta_2 I_2) \\
&\quad -\frac{1}{I_1}c(\beta_1 I_1 + \beta_2 I_2)S + (\mu + k_1) - \frac{1}{I_1}\alpha I_2 + (\mu + k_2 + \alpha) - \frac{1}{A}k_2 I_2 + (\mu + \delta) \\
&\quad -\frac{1}{E}\phi S + (\mu + \theta) \\
&\leq \mu K - \mu(I_1 + I_2) + a_0 c(\beta_1 I_1 + \beta_2 I_2) + 4\mu + a_0(\mu + \phi) + k_1 + k_2 + \alpha + \delta + \theta.
\end{aligned}$$

Note that by the choice of a_0 we have:

$$a_0 c\beta_1 I_1 - \mu I_1 = I_1\,(a_0 c\beta_1 - \mu) < 0 \text{ and } a_0 c\beta_2 I_2 - \mu I_2 = I_2\,(a_0 c\beta_2 - \mu) < 0.$$

Therefore

$$\dot{V}_1(t) \leq C,$$

where $C = \mu K + 4\mu + a_0(\mu + \phi) + k_1 + k_2 + \alpha + \delta + \theta$.

Integrating from 0 to t yields

$$V_1(t) = V_1(0) + \int_0^t \dot{V}_1(s)ds \leq V_1(0) + Ct \leq V_1(0) + CT. \tag{6.3}$$

However, we note that for any positive constant q,

$$\lim_{x\to 0^+} \left(x - q\ln\frac{x}{q}\right) = \infty.$$

Now further, due to positivity of the bracketed terms on the right hand side of equation (6.2), it follows that

$$\lim_{t\to T} V_1(t) = \infty. \tag{6.4}$$

The equation (6.4) is in conflict with the inequality (6.3). Thus we have arrived at a contradiction.

□

6.3 Stability analysis

6.3.1 Global stability of the disease-free equilibrium

The following positive numbers are useful in the proof of the global stability of disease-free equilibrium.

$$\xi_1 = \mu + k_2 + \alpha + k_1\frac{\beta_2}{\beta_1}, \quad \xi_2 = \alpha + \frac{\beta_2}{\beta_1}(\mu + k_1), \quad \xi_4 = (\mu + k_1)(\mu + k_2) + \alpha\mu.$$

Theorem 6.3.1. *If $\mathcal{R}_0 < 1$, then the disease-free equilibrium Σ_0 of system (6.1) is globally asymptotically stable.*

Proof. We introduce a number Λ as:

$$\Lambda = \frac{(\mu + \theta)K}{\mu + \phi + \theta}.$$

Assuming that $\mathcal{R}_0 < 1$, it is possible to find positive numbers ξ_0 and ξ_3 sufficiently small such as to have the following inequality:

$$C_2 = \xi_0 c\beta_2\Lambda + \xi_3 k_2 + \xi_4(\mathcal{R}_0 - 1) < 0.$$

Using such ξ_0 and ξ_3, together with the numbers ξ_i introduced already, we define a function V_2 as follows.

$$V_2(t) = \xi_0[K - (S + E)] + \xi_1 I_1 + \xi_2 I_2 + \xi_3 A. \tag{6.5}$$

The time derivative of $V_2(t)$ is given by:

$$\begin{aligned}\dot{V}_2(t) &= \xi_0[-\mu(K - (S + E)) + c(\beta_1 I_1 + \beta_2 I_2)S] + \xi_1 [c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2] \\ &\quad + \xi_2 [k_1 I_1 - (\mu + k_2 + \alpha)I_2] + \xi_3 [k_2 I_2 - (\mu + \delta)A] .\end{aligned}$$

Grouping some terms we have:

$$\dot{V}_2(t) \leq C_0[K - (S + E)] + C_1 I_1 + C_2 I_2 + C_3 A$$

where

$$\begin{aligned}C_0 &= -\mu\xi_0 < 0, \\ C_1 &= \xi_0 c\beta_1\Lambda + \xi_1 c\beta_1\Lambda - (\mu + k_1)\xi_1 + \xi_2 k_1, \\ C_2 &= \xi_0 c\beta_2\Lambda + \xi_1 c\beta_2\Lambda - (\mu + k_2 + \alpha)\xi_2 + \xi_3 k_2 + \xi_1\alpha, \\ C_3 &= -(\mu + \delta)\xi_3 < 0.\end{aligned}$$

Now we show that the coefficients C_1, C_2 are also negative. Firstly, it is easy to see that

$$-(\mu + k_1)\xi_1 + \xi_2 k_1 = -\xi_4 = -((\mu + k_1)(\mu + k_2) + \alpha\mu).$$

It follows that

$$C_1 = \xi_0 c\beta_1\Lambda + \xi_1 c\beta_1\Lambda - \xi_4 = \xi_0 c\beta_1\Lambda + \xi_4(\mathcal{R}_0 - 1) < 0.$$

Further, notice that

$$-(\mu + k_2 + \alpha)\xi_2 + \xi_1\alpha = -\xi_4\frac{\beta_2}{\beta_1}.$$

Thus, we have

$$\xi_1 c\beta_2\Lambda - \xi_4\frac{\beta_2}{\beta_1} = \xi_4(\mathcal{R}_0 - 1).$$

Therefore,

$$C_2 = \xi_0 c\beta_2\Lambda + \xi_3 k_2 + \xi_4(\mathcal{R}_0 - 1) < 0,$$

confirming that V_2 is a Lyapunov function. This completes the proof. □

6.4 Global stability of the endemic equilibrium

We investigate global stability of the endemic equilibrium of model (6.1) in the general case, that is when $\theta \neq 0$ and in particular case, when $\theta = 0$.

Theorem 6.4.1. *Assume that $\mathcal{R}_0 > 1$ and $\theta E^* < c\beta_1 I_1^* S^*$. Then the endemic equilibrium Σ_* of system (6.1) is globally asymptotically stable .*

Proof. Consider a function V_3 of the form:

$$
\begin{aligned}
V_3(t) &= \left(S - S^* - S^* \ln \frac{S}{S^*}\right) + D_1 \left(I_1 - {I_1}^* - {I_1}^* \ln \frac{I_1}{{I_1}^*}\right) \\
&\quad + D_2 \left(I_2 - I_2^* - {I_2}^* \ln \frac{I_2}{{I_2}^*}\right) + D_3 \left(A - A^* - A^* \ln \frac{A^*}{A}\right) \\
&\quad + D_4 \left(E - E^* - E^* \ln \frac{E^*}{E}\right),
\end{aligned}
$$

where D_1, D_2, D_3 and D_4 are positive constants, to be determined at a later stage.

The (endemic) equilibrium values of the system (6.1) satisfy the following equations:

$$
\begin{aligned}
\mu K &= S^*(\beta_1 {I_1}^* + \beta_2 {I_2}^*)c + (\mu + \phi)S^* - \theta E^* \\
(\mu + k_2 + \alpha) &= k_1 \frac{{I_1}^*}{{I_2}^*} \\
(\mu + k_1) &= \frac{S^*}{{I_1}^*}(\beta_1 {I_1}^* + \beta_2 {I_2}^*)c + \alpha \frac{{I_2}^*}{{I_1}^*} \\
(\mu + \delta) &= k_2 \frac{I_2^*}{A^*} \\
(\mu + \theta) &= \phi \frac{S^*}{E^*}.
\end{aligned}
$$

The time derivative of $V_3(t)$ is given by

$$
\begin{aligned}
\dot{V}_3(t) &= \mathrm{c}\beta_1 \left(1 - \frac{S^*}{S}\right)(I_1^* S^* - I_1 S) + c\beta_2 \left(1 - \frac{S^*}{S}\right)(I_2^* S^* - I_2 S) \\
&\quad + \left(2 - \frac{S}{S^*} - \frac{S^*}{S}\right) S^*(\mu + \phi) + \left(1 - \frac{I_1^*}{I_1}\right) D_1 c\beta_1 (I_1 S - I_1 S^*) \\
&\quad + \left(1 - \frac{I_1^*}{I_1}\right) D_1 \mathrm{c}\beta_2 \left(I_2 S - I_2^* S^* \frac{I_1}{I_1^*}\right) + (E - E^*)\,\theta \left(1 - \frac{S^*}{S}\right) \\
&\quad + D_3 \left(1 - \frac{A^*}{A}\right) k_2 \left(I_2 - I_2^* \frac{A}{A^*}\right) + D_2 \left(I_1 - I_1^* \frac{I_2}{I_2^*}\right) \left(1 - \frac{I_2^*}{I_2}\right) k_1 \\
&\quad + \left(1 - \frac{E^*}{E}\right) D_4 \left(S - S^* \frac{E}{E^*}\right) \phi. \qquad (6.6)
\end{aligned}
$$

Let

$$
x = \frac{S}{S^*},\ y = \frac{I_1}{I_1^*},\ z = \frac{I_2}{I_2^*},\ v = \frac{A}{A^*},\ w = \frac{E}{E^*}.
$$

Then (6.6) becomes

$$\begin{aligned}\dot{V}_3(t) &= S^*(\mu+\phi)\left(2-\frac{1}{x}-x\right)+D_1c\beta_1I_1^*S^*\left(1-\frac{1}{y}\right)(xy-y)+D_1c\beta_2I_2^*S^*\left(1-\frac{1}{y}\right)(xz-y)\\ &+D_2I_1^*k_1\left(1-\frac{1}{z}\right)(y-z)+D_3I_2^*k_2\left(1-\frac{1}{v}\right)(z-v)+\alpha D_1I_2^*\left(1-\frac{1}{y}\right)(z-y)\\ &+D_4k_2\left(1-\frac{1}{w}\right)\phi S^*(x-w)+c\beta_1I_1^*S^*\left(1-\frac{1}{x}\right)(1-xy)\\ &+c\beta_2I_2^*S^*\left(1-\frac{1}{x}\right)(1-xz)+\left(1-\frac{1}{x}\right)(x-1)\theta E^*. \qquad (6.7)\end{aligned}$$

This equation informs a choice of values for the numbers D_i, in order to render V_3 a Lyapunov function. For making our choices, we require the numbers D_i to satisfy the following equations.

$$\begin{aligned}&(D_1-1)=0\\ &-D_2I_1^*k_1+\alpha D_1I_2^*+D_3I_2^*k_2+c\beta_2I_2^*S^*=0\\ &-D_1c\beta_1I_1^*S^*-D_1c\beta_2I_2^*S^*+D_2I_1^*k_1-\alpha D_1I_2^*+c\beta_1I_1^*S^*=0\\ &-D_1c\beta_1I_1^*S^*+D_4k_2\phi S^*+\theta E^*=0\end{aligned}$$

This leads to the following D_i-values:

$$D_1=1,\quad D_2=\frac{c\beta_2S^*{I_2}^*+\alpha{I_2}^*}{k_1{I_1}^*},\quad D_3=\frac{D_2k_1I_1^*-(c\beta_2S^*{I_2}^*+\alpha I_2^*)}{k_2I_2^*}\ .$$

$$D_4=\frac{c\beta_1I_1^*S^*-\theta E^*}{k_2\phi S^*}.$$

Substituting back the D_i terms in (6.7), we have

$$\begin{aligned}\dot{V}_3(t) &= S^*(\mu+\phi)\left(2-\frac{1}{x}-x\right)+c\beta_2S^*{I_2}^*\left(3-\frac{1}{x}-\frac{xz}{y}-\frac{y}{z}\right)\\ &+\alpha{I_2}^*\left(2-\frac{z}{y}-\frac{y}{z}\right)+(c\beta_1I_1^*S^*-\theta E^*)\left(3-w-\frac{1}{x}-\frac{x}{w}\right)\le 0.\end{aligned}$$

This complete the proof. □

In particular, we have the following corollary:

Corollary 6.4.2. *If $\theta = 0$, then the endemic equilibrium Σ_* of system (6.1) is globally asymptotically stable for $\mathcal{R}_0 > 1$.*

6.5 Numerical simulation

The model can be used to test the efficiency of a given intervention. In particular, authorities may want to see the effect of, for example, expanding the use of PrEP. Thus, simulations in this context will also be shown.

We illustrate the analytical results by way of numerical simulations with the parameters applicable to South Africa as in Table 1 below:

Table 6.1: Estimating initial values for model system (6.1) based on parameters and their fixed values

Parameters	Value	Source
α	0.33	[9]
k_1	0.125	[41]
k_2	0.1	[9]
c	3	cf. [40, 71]
δ	0.279	[90]
μ	$\frac{1}{62.4}$	[90]
ϕ	0.01	Nominal
θ	0.001	Nominal

6.5.1 Details on the description of parameters and their values

In [40, 71] for instance, the average number of sexual partners per given time denoted by c is determined; values ranging from 1 to 2 for a specific case. In our case we find it convenient to take $c = 3$. We expect the following inequality, $\beta_1 < \beta_2$, to hold since the intensity of disease transmission in the symptomatic phase exceeds that of the asymptomatic phase. In the year 2016, the life expectancy in South Africa was estimated at 62.4 years, see for instance [90]. The mortality rate μ is simply the inverse of the life expectancy, and thus $\mu = \frac{1}{62.4}\text{year}^{-1}$. The parameter K is the size of the population when it is free from HIV. According to [90], in 2016 South Africa had an estimated total population 55.91 million. Thus we consider it reasonable to choose $K = 56$ million. We assume that 1% of the susceptible individuals take PrEP, that is, $\phi = 0.01$ and the default rate takes the value $\theta = 0.001$.

6.5.2 Initial conditions

For initial conditions, we first refer to the South African statistical release [90] of 2016 in order to do some projections. Let us denote the time 25 August 2016 by t_0. We note that

$$N(t_0) = S(t_0) + I_1(t_0) + I_2(t_0) + A(t_0) + E(t_0).$$

An estimated 7.03 million of the total population were infected with HIV/AIDS in 2016. This number can be split between the classes of $I_1(t_0)$, $I_2(t_0)$ and $A(t_0)$. We shall then use the parameters listed in Table 1 below to find a suitable equilibrium point to split the numbers between the classes of $I_1(t_0)$, $I_2(t_0)$ and $A(t_0)$. In this process we keep varying the value of β_1 and β_2 in order to vary the value of the basic reproduction number. This method leads to the following initial values for our simulations:

$$I_{1,0} = 5.11, \quad I_{2,0} = 1.43, \quad A_0 = 0.48.$$

We note that in endemic equilibrium,

$$E^* = \frac{\phi}{\mu + \theta} S^*.$$

Therefore, we consider it reasonable to use the initial value

$$E(t_0) = \frac{1}{50} \frac{\phi}{\mu + \theta} S(t_0).$$

This consideration leads us to assign initial values to S_0 and E_0, and thus our initial state for these two initial values are taken as:

$$S_0 = 46.18, \quad E_0 = 1.12 \ .$$

6.5.3 Simulations on the effect of PrEP

In the following we show the trajectories of $I_1(t), I_2(t), A(t)$ of the model for $\phi = 0.01$ in Fig. 6.1, and in Fig. 6.2 the trajectories of $I_2(t)$ for different values of ϕ, $\phi = 0.01,\ 0.02,\ 0.03$. For the different values of ϕ, the corresponding value of $\mathcal{R}_0$ will be denoted by $\mathcal{R}_0(\phi)$.

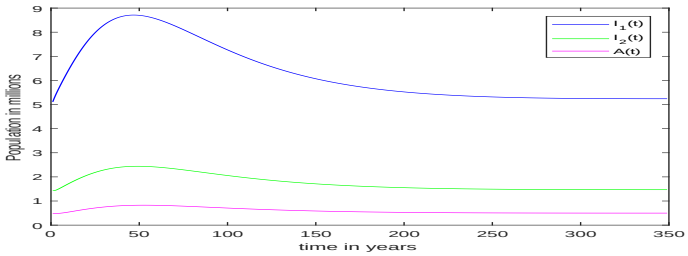


Figure 6.2: Population dynamics of the model for the case $\phi = 0.01$.

In both Figure 6.1 and Figure 6.2 we have chosen the values: $\beta_1 = 0.000481, \beta_2 = 0.000581$. In figure 6.1 we compute the basic reproduction number, $\mathcal{R}_0(0.01) = 1.401 > 1$. The trajectories show that the disease is prevailing at the endemic level. We also compute the endemic equilibrium points $I_1^* = 5.28, I_2^* = 1.48$ and $A^* = 0.50$ (in millions). In Figure 6.2, we show the graph of $I_2(t)$ with different values of ϕ. In the case $\phi = 0.02$, the basic

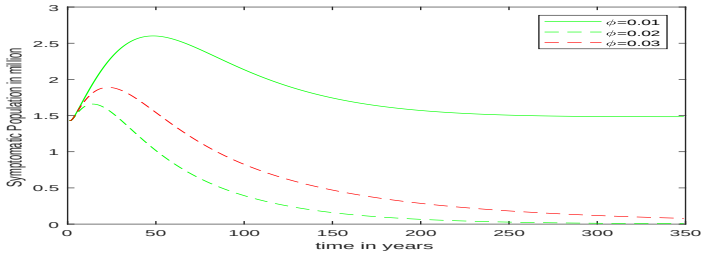


Figure 6.3: Comparing the class of symptomatic infectives, I_2, for different values of ϕ.

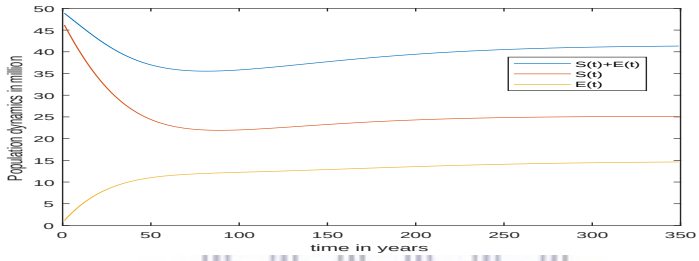


Figure 6.4: Population of susceptibles and individuals with PrEP

Chosen values: $\beta_1 = 0.000481, \beta_2 = 0.000581, \phi = 0.01$. Calculated values: $\mathcal{R}_0(0.01) = 1.414, S^* = 25.1157, E^* = 14.7739$.

reproduction number reduces to $\mathcal{R}_0(0.02) = 1.021$. This is due to increasing uptake of PrEP from 0.01 to 0.02, and we observe the increase in the uptake of PrEP has decreased the basic reproduction number and the class of $I_2(t)$. The equilibrium value is computed by $I_2^* = 0.12$. The same scenario is also very well observed in the simulation for the case where $\phi = 0.03$. In this case, the basic reproduction number is found to be below unity, that is, $\mathcal{R}_0(0.02) = 0.8039$. The class of $I_2(t)$ converges to zero. We note I_2^* is a decreasing function of ϕ. We note that also the long term (or asymptotic) values of I_1 and A are decreasing functions of ϕ. In Fig. 6.3 we show the dynamics of the population of susceptibles and of the individuals with PrEP.

6.6 Concluding remarks

In this paper, we have investigated a model describing the population dynamics of HIV/AIDS including treatment and pre-exposure prophylaxis (PrEP) in the context of South Africa. We proved global stability of disease-free and endemic equilibria, Theorem 6.3.1 and Theorem 6.4.1 respectively. Our analytical results and our sample simulations are quite meaningful as we work with the current HIV trend in South Africa. We showed the substantial impact that treatment has on the incidence, prevalence and mortality due to AIDS. Managing HIV with early treatment can decrease transmission and possibly decrease the number of AIDS related deaths. Our model quantifies how the use of PrEP can potentially reduce the number of new HIV infections, and this has been well observed in the sample simulations. South Africa has a wide range of its population being exposed to HIV. Its high-risk sections of the population include adolescent girls and young women, sex workers, men who have sex with men (MSM), discordant couples and truckers, all of whom face various barriers to access including stigma, criminalisation and lack of supportive service delivery infrastructure [21].

Chapter 7

A Stochastic HIV/AIDS epidemic treatment model with saturated incidence rate

7.1 Introduction

Mathematical modeling of epidemiological phenomena has become an important issue for modern society. The needs of this modeling has far increased recently. Most of these models are crucial and necessary to inform planning and policy formulation. In the mathematical study of epidemiological problems, the incidence rate that measures the rate of new infection is considered to be a very crucial parameter. It is assumed to be, in most classical disease transmission models, of mass action type with bilinear interactions given by βSI, where β is the per capita contact rate, and S and I represent the susceptible and infected populations, respectively. However, the actual incidence S and I may not be linear relationship. In [15], the following nonlinear incidence rate is used $g(I) = \frac{\beta I}{(1+\alpha I)}$ to the modeling of cholera. Nonlinearities can be approximated by a variety of forms $\frac{kSI}{(1+aI^2)}$ where kI measures the infection force of the disease and $\frac{1}{(1+\alpha I^2)}$ describes the psychological or inhibitory effect from the behavioural change of the susceptible individuals when the

number of infectives is very large ($k, \alpha > 0$). We investigate the stochastic dynamics of an HIV/AIDS epidemic treatment model with saturated incidence rate and we will restrict our attention the following saturated incidence rate and we refer to [48]

$$\lambda_{\text{sat}} = \beta_i \lambda$$

where

$$\lambda = \frac{c(\beta_1 I + \beta_2 J)}{(1 + \phi(I + J))}$$

and with $\frac{1}{(1+\phi(I+J))}$ measures the inhibition effect from behavioural change of susceptible individuals when their number increases or from the crowing effect of the infective individuals [112]. The constant parameter ϕ measures the extent of psychological or inhitory effect (detriment effect if $0 < \phi < 1$, beneficial or positive effect if $\phi > 1$) [48]. For a very large number of infective individuals, the force of infection may decrease as this number increases due to the fact that in the presence of large number of infectives, the population may tend to reduce the number of contacts per unit of time [112].

7.2 Preliminaries

Let us denote by $\mathbb{R}^n_+$ (resp. $\mathbb{R}^n_{++}$) the set of points in $\mathbb{R}^n$ having only non-negative (resp. strictly positive) coordinates.

Throughout this paper we assume to have a complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ with a filtration, $\{\mathcal{F}_t\}_{t\geq 0}$, that is right continuous and with $\mathcal{F}_0$ containing all the subsets having measure zero.

Remark 7.2.1. *We study the effect of stochastic noise in the transmission of HIV by adding randomly fluctuation affecting directly the deterministic model. Suppose that infection rate β_1 and β_2 are stochastically perturbed with $\beta_1 \to \beta_1 + \sigma\dot{W}(t)$ and $\beta_2 \to \beta_2 + \sigma\dot{W}(t)$.*

7.3 HIV/AIDS stochastic model

Model system (7.1)

$$\begin{aligned} dS &= [\mu K - \lambda S - \mu S]\,dt - \frac{c(I+J)S\sigma}{(1+\phi(I+J))}dW(t) \\ dI &= [\lambda S - (\mu + k_1)I + \alpha J]\,dt + \frac{cIS\sigma}{(1+\phi(I+J))}dW(t), \\ dJ &= [k_1 I - (\mu + k_2 + \alpha)J]\,dt + \frac{cJS\sigma}{(1+\phi(I+J))}dW(t), \\ dA &= [k_2 J - (\mu + \delta)A]\,dt. \end{aligned} \tag{7.1}$$

Let us define the following sets:

$$\begin{aligned} \Delta &= \left\{x \in \mathbb{R}^4_{++} :\ x_1 > 0,\ x_2 > 0,\ x_3 > 0,\ x_4 > 0, \text{ and } x_1 + x_2 + x_3 + x_4 \leq K\right\} \\ \Omega_0 &= \{w \in \Omega|\ A(t, w(t)) > 0 \text{ for all } t \geq 0\} \\ \Omega_1 &= \{w \in \Omega|\ (S(t, w(t)), I(t, w(t)), J(t, w(t)), A(t, w(t)) \in \Delta \text{ for } t \geq 0\}. \end{aligned}$$

Remark 7.3.1. *Let us write $N(t) = S(t) + I(t) + J(t) + A(t)$. Then $N(t)$ is the total population size, and satisfies the ordinary differential equation*

$$\frac{d}{dt}(K - N(t)) = \mu(K - N(t)) - \delta A(t).$$

Therefore it follows from solving the ordinary differential equation, that for any sample path $w \in \Omega_0$, if we have $N(0) \in \Delta$ then $N(t) \in \Delta$. Note also that $\Omega_1 \subseteq \Omega_0$.

Theorem 7.3.2. *For model (7.1) and an initial value $(S(0), I(0), J(0), A(0)) \in \Delta$ with all coordinates positive, there is a unique solution $X(t) = (S(t), I(t), J(t), A(t))$ with $X(t) \in \Delta$ for all $t \geq 0$ with probability one.*

Proof. The coefficients of the system (7.1) are locally Lipschitz continuous. Thus there exists a unique local solution on $t \in [0, \tau_{en})$, where τ_{en} is the explosion time. Suppose that we choose a number $m_0 \in \mathbb{N}$ sufficiently large so that $S(0), I(0), J(0), A(0)$ all lie within the interval $(\frac{1}{m_0}, K)$. For each $n \in \mathbb{N} \cap [m_0, \infty)$, let us write

$$D_n = \left\{ t \in [0, \tau_{en}) : \ S(t) \leq \frac{1}{n} \text{ or } I(t) \leq \frac{1}{n} \text{ or } J(t) \leq \frac{1}{n} \text{ or } A(t) \leq \frac{1}{n} \right\}.$$

Then we define stopping times τ_n and τ_∞ by taking τ_n to be the infimum of D_n if $D_n \neq \emptyset$ and otherwise $\tau_n = \infty$. The set D_∞ and the random variable τ_∞ are defined as:

$$\begin{aligned} D_\infty &= \{t \in [0, \tau_{en}) : \ S(t) \leq 0 \text{ or } I(t) \leq 0 \text{ or } J(t) \leq 0 \text{ or } A(t) \leq 0\} \\ \tau_\infty &= \lim_{n \to \infty} \tau_n = \inf D_\infty. \end{aligned}$$

For each $\gamma > 0$, let $\Omega_{(\gamma)}$ be the subset of Ω defined below.

$$\Omega_{(\gamma)} = \{\omega \in \Omega | \tau_\infty(\omega) \leq \gamma\}$$

We shall prove by contradiction that $\tau_{en} = \infty$ (a.s.). So let us assume to the contrary that there exists $T, C \in \mathbb{R}$ with $C > 0$, and with $T < \tau_{en}$ such that $\mathbb{P}(\Omega_{(T)}) = C$.
Let us define the function $V(X)$, for $X = (S, I, J, R)$, by the formula:

$$V(X) = \ln\left(\frac{K^4}{SIJA}\right) = \ln\frac{K}{S} + \ln\frac{K}{I} + \ln\frac{K}{J} + \ln\frac{K}{A}$$

By remark 7.3.1, each of the four terms of $V(X(t))$ are non-negative for every $t \in [0, \tau_\infty)$. We set up a contradiction by calculating upper and lower bounds on expectations of V. Firstly we calculate an upper bound. For every $u \in [0, \tau_\infty \wedge T)$ we have:

$$
\begin{aligned}
dV(X(u)) &= -\frac{1}{S(u)}\left\{[\mu K-\lambda(u)S(u)-\mu S(u)]\,du-\frac{c(I(u)+J(u))S(u)\sigma}{(1+\phi(I(u)+J(u)))}dW(u)\right\}\\
&\quad+\frac{1}{2S^2(u)}\left[\frac{c^2(I(u)+J(u))^2S^2(u)\sigma^2}{(1+\phi(I(u)+J(u)))^2}\right]du-\frac{1}{I(u)}\{[\lambda(u)S(u)\\
&\quad-(\mu+k_1)I(u)+\alpha J(u)]\,du+\frac{cI(u)S(u)\sigma}{(1+\phi(I(u)+J(u)))}dW(u)\Big\}\\
&\quad+\frac{1}{2I^2(u)}\left[\frac{c^2(I^2(u)S^2(u)\sigma^2}{(1+\phi(I(u)+J(u)))^2}\right]du\\
&\quad-\frac{1}{J(u)}\left\{[k_1I(u)-(\mu+k_2+\alpha)J(u)]\,du+\frac{cJ(u)S(u)\sigma}{(1+\phi(I(u)+J(u)))}dW(u)\right\}\\
&\quad+\frac{1}{2J^2(u)}\left[\frac{c^2(J^2(u)S^2(u)\sigma^2}{(1+\phi(I(u)+J(u)))^2}\right]du\\
&\quad-\frac{1}{A(u)}\left[k_2J(u)-(\mu+d)A(u)\right]du. \qquad (7.2)
\end{aligned}
$$

Removing some of the negative terms on the right hand side, we obtain the following inequality.

$$
\begin{aligned}
dV(X(u)) &\leq \left[\lambda(u)+4\mu+k_1+k_2+\alpha+\delta+\frac{1}{2}\frac{c^2(I(u)+J(u))^2\sigma^2}{(1+\phi(I(u)+J(u)))^2}\right.\\
&\quad\left.+\frac{c^2S^2(u)\sigma^2}{(1+\phi(I(u)+J(u)))^2}\right]du\\
&\quad+\left[\frac{c(I(u)+J(u))\sigma}{(1+\phi(I(u)+J(u)))}-2\frac{cS(u)\sigma}{(1+\phi(I(u)+J(u)))}\right]dW(u) \qquad (7.3)
\end{aligned}
$$

Note that since

$$
\frac{1}{(1+\phi(I(u)+J(u)))}<1,\ \frac{I}{(1+\phi(I(u)+J(u)))}<K,\ \frac{J}{(1+\phi(I(u)+J(u)))}<K
$$

, then (7.3) becomes

$$
dV(X(u))\leq\rho du+\left[\frac{c(I(u)+J(u))\sigma}{(1+\phi(I(u)+J(u)))}-2\frac{cS(u)\sigma}{(1+\phi(I(u)+J(u)))}\right]dW(u) \qquad (7.4)
$$

where

$$\begin{aligned}\rho &= cK(\beta_1+\beta_2)+4\mu+k_1+k_2+\alpha+\delta+\frac{1}{2}c^2(2K)^2\sigma^2+c^2K^2\sigma^2\\ &= cK(\beta_1+\beta_2)+4\mu+k_1+k_2+\alpha+\delta+3c^2K^2\sigma^2,\end{aligned}$$

and for $t\in[0,\tau_\infty\wedge T]$, let $M(t)$ be as below.

$$M(t)=\sigma\int_0^t\left[\frac{c(I(u)+J(u))}{(1+\phi(I(u)+J(u)))}-2\frac{cS(u)}{(1+\phi(I(u)+J(u)))}\right]dW(u).$$

Now we have the following inequality:

$$\int_0^t dV(X(u))\leq\rho t+M(t).$$

Therefore, for any $k\in\mathbb{N}\cap[m_0,\infty)$ we have

$$V(X(t\wedge\tau_k))-V(X(0))\leq\rho(t\wedge\tau_k)+M(t\wedge\tau_k)\text{ (a.s.)}$$

The stochastic process $M(t)$ is a local martingale and therefore for any $m\in\mathbb{N}\cap[m_0,\infty)$ we have $\mathbb{E}[M(t\wedge\tau_m)]=M(0)=0$. Consequently,

$$\mathbb{E}[V(X(T\wedge\tau_m))]\leq\rho(T\wedge\tau_m)+V(X(0)\leq\rho T+V(X(0)),$$

and we have the upper bound which we set out to find. We now search for a lower bound for $\mathbb{E}[V(X(T\wedge\tau_m))]$. Note that if $\omega\in\Omega_{(T)}$ and we evaluate $V(X(\zeta))$ for $\zeta=\omega(\tau_m)$, then we get:

$$V(X(\zeta))\geq\ln(mK).$$

We can deduce the lower bound:

$$\mathbb{E}[V(X(T\wedge\tau_m))]\geq C\ln(mK).$$

These two bounds yield

$$C\ln(mK) \leq \mathbb{E}[V(X(T \wedge \tau_m))] \leq \rho T + V(X(0)).$$

We can choose a value of m sufficiently big, so that

$$C\ln(mK) > \rho T + V(X(0)),$$

leading to a contradiction. Therefore we must have $\tau_\infty = \infty$ almost surely. This complete the proofs.

□

7.4 Exponential stability under large perturbation

Theorem 7.4.1. *Assume that* $\beta = \max\{\beta_1, \beta_2\}$. *If* $\frac{1}{2}\sigma^2 > \frac{\beta^2}{(\mu+\delta)}$, *then disease-free equilibrium* $E_0 = (K, 0, 0, 0)$ *is almost surely exponentially stable in* Δ.

Proof. Let $(S_0, I_0, J_0, A_0) \in \Delta$. In virtue of theorem 7.3.2, the solution of the system 7.1 remains in Δ. Then let us define the function

$$V_2 = \ln\left[(K - S) + I + J + A\right].$$

With the application of the multi-dimensional Itô's formula, it will result in the following

$$\begin{aligned} dV_2 &= \frac{1}{[(K-S)+I+J+A]}\left[-dS + dI + dJ + dA\right] \\ &\quad -\frac{1}{2}\sigma^2\left(\frac{c(I+J)S}{[(K-S)+I+J+A]\left[1+\phi(I+J)\right]}\right)^2 dt \\ &\quad -\frac{1}{2}\sigma^2\left(\frac{cIS}{[(K-S)+I+J+A]\left[1+\phi(I+J)\right]}\right)^2 dt \\ &\quad -\frac{1}{2}\sigma^2\left(\frac{cJS}{[(K-S)+I+J+A]\left[1+\phi(I+J)\right]}\right)^2 dt \end{aligned} \tag{7.5}$$

.

Further we have

$$\begin{aligned}
dV_2 &= -\frac{[\mu((K-S)+(I+J+A))+\delta A]}{[(K-S)+I+J+A]} - \frac{1}{2}\sigma^2\left(\frac{c(I+J)S}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}\right)^2 dt \\
&\quad -\frac{1}{2}\sigma^2\left(\frac{cIS}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}\right)^2 dt \\
&\quad -\frac{1}{2}\sigma^2\left(\frac{cJS}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}\right)^2 dt \\
&\quad +\frac{2\sigma c(I+J)S}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}dW \\
&\quad +\left(\frac{2c(\beta_1 I+\beta_2 J)S}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}\right)dt \\
&\leq -\frac{[\mu((K-S)+(I+J+A))+\delta A]}{[(K-S)+I+J+A]} - \frac{1}{2}\sigma^2\left(\frac{c(I+J)S}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}\right)^2 dt \\
&\quad +\frac{2\sigma c(I+J)S}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}dW \\
&\quad +\left(\frac{2c(\beta_1 I+\beta_2 J)S}{[(K-S)+I+J+A]\,[1+\phi(I+J)]}\right)dt \qquad (7.6)
\end{aligned}$$

Letting $Z = \left(\frac{c(I+J)S}{[(K-S)+I+J+A][1+\phi(I+J)]}\right)$. Then we write 7.6 by

$$\begin{aligned}
dV_2 &\leq \left[-\frac{1}{2}\sigma^2 Z^2 + 2\beta Z - \frac{[\mu((K-S)+(I+J+A))+\delta A]}{(K-S)+I+J+A}\right]dt + 2\sigma Z dW \\
&\leq \left[-\frac{1}{2}\sigma^2 Z^2 + 2\beta Z - (\mu+\delta)\right]dt + 2\sigma Z dW. \qquad (7.7)
\end{aligned}$$

where

$$\beta = \max\{\beta_1, \beta_2\}.$$

Thus since $-\frac{1}{2}\sigma^2 Z^2 + 2\beta Z - (\mu+\delta) = -\frac{1}{2}\sigma^2\left(Z - \frac{2\beta}{\sigma^2}\right)^2 + \frac{2\beta^2-(\mu+\delta)\sigma^2}{\sigma^2}$, it can be deduced that

$$dV \leq \frac{2\beta^2-(\mu+\delta)\sigma^2}{\sigma^2} + 2\sigma Z dW\ ,$$

and integrating we get

$$\begin{aligned}
&\ln\left[(K-S(t))+I(t)+J(t)+A(t)\right] \\
&\quad \leq \ln\left[(K-S_0)+I_0+J_0+A_0\right] + \tfrac{2\beta^2-(\mu+\delta)\sigma^2}{\sigma^2}t + \textstyle\int_0^t 2\sigma Z dW.
\end{aligned}$$

Note that the quadratic variation of the stochastic integral $\int_0^t Z(s)dW_0(s)$ is $\int_0^t Z^2 ds \leq Ct$; for some constant C. Then by the strong law of large number for local martingales, see [60], we have

$$\lim_{t\to\infty} \frac{1}{t} \int_0^t Z(s)dW(s) = 0 \ a.s. \tag{7.8}$$

Therefore, it can be concluded that

$$\lim_{t\to\infty} \sup \frac{1}{t} \ln\left[(K - S(t)) + I(t) + J(t) + A(t)\right] \leq \frac{2\beta^2 - (\mu+\delta)\sigma^2}{\sigma^2} < 0$$

This completes the proof. □

Remark 7.4.2. *Assuming that $\phi = \sigma = 0$, then the model system has the same basic reproduction given in (3.3).*

Theorem 7.4.3. *If $\mathcal{R}_0 < 1$, then $I(t), J(t)$ and $A(t)$ converges exponentially to $(0, 0, 0)$.*

Proof. Let $(S(0), I(0), J(0), A(0)) \in \Delta$. Since $\mathcal{R}_0 < 1$, let $\theta > 0$ such that

$$\theta k_2 < \pi(1 - \mathcal{R}_0)\beta_2$$

where $\pi = (\mu + k_1)(\mu + k_2) + \alpha\mu$.

Consider the following

$$V_3 = \ln(\xi_1 I(t) + \xi_2 J(t) + \theta A(t)) \tag{7.9}$$

where ξ_1 and ξ_2 as defined in chapter 5.

By Itô's formula, we have the following

$$
\begin{aligned}
dV_3 &= \frac{1}{\xi_1 I(t)+\xi_2 J(t)+\theta A(t)}\left[\xi_1 dI(t)+\xi_2 dJ(t)+\theta dA(t)\right] \\
&\quad -\frac{1}{2\{[\xi_1 I(t)+\xi_2 J(t)+\theta A(t)][1+\phi(I+J)]\}^2}(\xi_1\sigma cIS)^2 \\
&\quad -\frac{1}{2\{[\xi_1 I(t)+\xi_2 J(t)+\theta A(t)][1+\phi(I+J)]\}^2}(\xi_2\sigma cJS)^2 \\
&\leq \frac{1}{\xi_1 I(t)+\xi_2 J(t)+\theta A(t)}\left[\xi_1 dI(t)+\xi_2 dJ(t)+\theta dA(t)\right] \\
&\leq \frac{1}{\xi_1 I(t)+\xi_2 J(t)+\theta A(t)}\left(\pi(\mathcal{R}_0-1)(\beta_1 I+\beta_2 J)+\theta dA(t)\right) \\
&+ \frac{\sigma c(\xi_1 I+\xi_2 J)S}{[\xi_1 I(t)+\xi_2 J(t)+\theta A(t)][1+\phi(I+J)]}dW \\
&\leq \frac{1}{\xi_1 I(t)+\xi_2 J(t)+\theta A(t)}\left[-\pi(1-\mathcal{R}_0)I\beta_1-(\pi(1-\mathcal{R}_0)\beta_2-\theta k_2)J-(\mu+k_2)\theta A\right] \\
&\quad \frac{\sigma c(\xi_1 I+\xi_2 J)S}{[\xi_1 I(t)+\xi_2 J(t)+\theta A(t)][1+\phi(I+J)]}dW \\
&\leq -\bar{\theta}dt+\frac{1}{[\xi_1 I(t)+\xi_2 J(t)+\theta A(t)][1+\phi(I+J)]}\sigma c(\xi_1 I+\xi_2 J)SdW \qquad (7.10)
\end{aligned}
$$

Where $\bar{\theta}=\max(\pi(1-\mathcal{R}_0)\beta_1,(\pi(1-\mathcal{R}_0)\beta_2-\theta k_2),(\mu+k_2)\theta)$. By integrating we check

$$
\begin{aligned}
&\ln(\xi_1 I(t)+\xi_2 J(t)+\theta A(t)) \\
&\leq \ln(\xi_1 I_0+\xi_2 J_0+\theta A_0)-\bar{\theta}t \\
&+\int_0^t \frac{\sigma c(\xi_1 I(s)+\xi_2 J(s))S(s)}{[\xi_1 I(s)+\xi_2 J(s)+\theta A(s)][1+\phi(I(s)+J(s))]}dW(s) \qquad (7.11)
\end{aligned}
$$

We note in particular that in view of the strong law of large number for local martingales [60], the last terms of (7.11) will vanish a.s.

Therefore, we can deduce that

$$
\lim_{t\to\infty}\sup\frac{1}{t}\ln(\xi_1 I(t)+\xi_2 J(t)+\theta A(t))\leq -\bar{\theta}<0.
$$

This complete the proof.

□

7.5 Numerical simulations

We present some numerical simulations and we refer to the table 5.1. In order to find the equilibrium point, let us first consider the following equilibrium values for I and J:

$$I = \frac{(\alpha+\mu+k_2)K\lambda\mu}{(\lambda+\mu)\ ((\mu+k_1)\ (\mu+k_2)+\alpha\mu)}$$

and

$$J = \frac{1}{(\alpha+\mu+k_2)}\left[k_1\frac{(\alpha+\mu+k_2)K\lambda\mu}{(\lambda+\mu)\ ((\mu+k_1)\ (\mu+k_2)+\alpha\mu)}\right]$$

where

$$\lambda = \frac{c(\beta_1 I+\beta_2 J)}{[1+\phi(I+J)]}.$$

Thus, our initial state is taken as:

$$S_0 = 49.12, I_0 = 5.11, J_0 = 1.35, A_0 = 0.23.$$

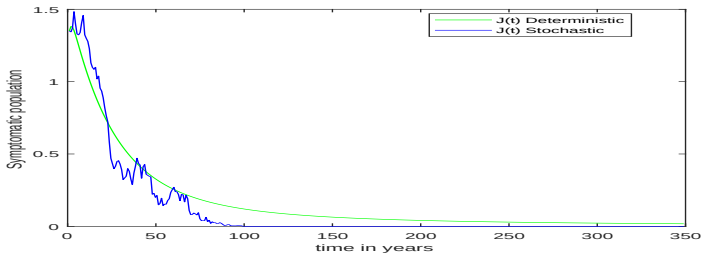


Figure 7.1: Stochastic perturbation with $\phi = 0.90$

Chosen values: $\beta_1 = 0.000176, \beta_2 = 0.00037, \sigma = 0.03$. Calculated value: $\mathcal{R}_0 = 0.9616$.

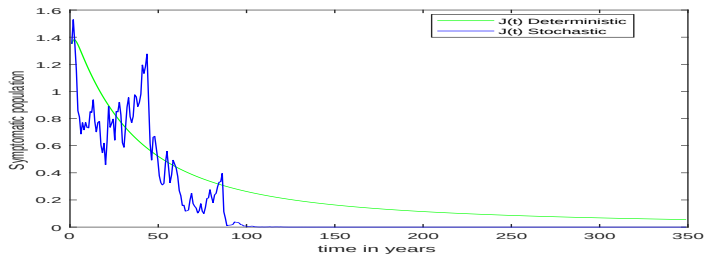


Figure 7.2: Decreasing ϕ by 0.20

Chosen values: $\beta_1 = 0.000176, \beta_2 = 0.00037, \sigma = 0.03$. Calculated value: $\mathcal{R}_0 = 0.9616$.

In both figures 7.1 and 7.2, we choose the same value of stochastic perturbation $\sigma = 0.03$. The basic reproduction number is found to be $\mathcal{R}_0 < 1$. In this case, the disease-free equilibrium is almost surely exponential stable. It can be seen that the number of infected individuals in figure 7.2 is higher than in figure 7.1 due to decreasing the value of ϕ by 0.20, but in both cases the requirements of Theorem 7.4.1 are satisfied.

7.6 Conclusion

This paper presents a stochastic model describing the population dynamics of an HIV/AIDS epidemic. Our aim is to study the effect of stochastic noise and that of the saturated incidence rate in the transmission of HIV, i.e., stochasticity associated with the parameters β_1 and β_2. We proved the almost sure exponential stability of the model system under suitable conditions. In particular, we proved that the stochastic perturbation does not destabilize the disease-free equilibrium, that is to say, whenever $\mathcal{R}_0 < 1$, then the disease-free equilibrium is almost surely exponentially stable. Our future work should analyze other types of stability such as the pth moment exponential stability and in more complex compartmental models.

Chapter 8

Exponential stability of a disease-free for an HIV epidemic model with the use of prophylaxis

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Submitted for publication.

8.1 Introduction

Pre-exposure prophylaxis has become a very promising approach for the HIV prevention from infected individuals. However, the risk infection with HIV after exposure to a virus can be better understood through a stochastic framework. In this research, we present a stochastic model for HIV/AIDS epidemic with the use of prophylaxis and we show that the model with random perturbation has a unique global positive solution. Thereafter, we introduce an analogue of the basic reproduction number, call it $\mathcal{R}_\sigma$ to support a theorem on almost sure exponential stability. The latter asserts that the disease free goes extinct exponentially almost surely whenever $\mathcal{R}_\sigma < 1$. The results show that small stochastic perturbations predict disease extinction rather than persistence.

The following papers, see for instance in [26, 38, 105, 106, 16] show that stochastic perturbations can further improve the quality stability of the disease-free equilibrium for the specific models. However, stochastic models of HIV/AIDS population dynamics including ARV treatment and Pre-exposure prophylaxis have not been intensively studied. The current paper aims to demonstrate how the use of PrEP may lead to reducing new infections for instance, and even in the presence of minor stochastic perturbations. Our motivation in this chapter comes from the fact that stochastic framework may have the ability to predict efficacy of prophylaxis against HIV.

In section 8.2 , we show the model and prove positivity. In Section 8.3 we present a theorem on almost sure exponential stability. We provide numerical simulations to in Section 8.4 . In Section 8.5 we present some concluding remarks.

8.2 HIV stochastic Model

Throughout this paper we assume to have a complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ with a filtration, $\{\mathcal{F}_t\}_{t\geq 0}$, that is right continuous and $\mathcal{F}_0$ containing all the subsets having measure zero.

Let $B(t) = (B_0(t), B_1(t), B_2(t), B_3(t), B_4(t))$ be a 5-dimensional Wiener process defined on the given probability space. The non-negative constants $\sigma_0, \sigma_1, \sigma_2$, σ_3 and σ_4 denote the intensities of the stochastic perturbations. We shall assume that the components of the 5-dimensional Wiener process B_i are mutually independent. In the model, we also introduce two positive constants r and q such that $r^2 + q^2 = 1$ and $r > \frac{\sqrt{2}}{2}$. We have the following model system:

$$
\begin{aligned}
dS(t) &= [\mu K - \lambda S(t) - (\mu+\phi)S + \theta E]dt + \sigma_0 S(t)dB_0(t),\\
dI_1(t) &= [\lambda S(t) - (\mu+k_1)I_1(t) + \alpha I_2(t)]dt + \sigma_1 r I_1(t)dB_1(t),\\
dI_2(t) &= [k_1 I_1(t) - (\mu+k_2+\alpha)I_2(t)]dt + \sigma_2 q I_2(t)dB_2(t),\\
dA(t) &= [k_2 I_2 - (\mu+\delta)A]dt + \sigma_3 A(t)dB_3(t)\\
dE(t) &= [\phi S - (\mu+\theta)E]dt + \sigma_4 E(t)dB_4(t) \qquad (8.1)
\end{aligned}
$$

where

$$\lambda = c(\beta_1 I_1(t) + \beta_2 I_2(t)).$$

We now show that solutions of (8.1) exist globally and are positive, but first let us write:

$$\mathbb{R}^n_{++} = \{x \in \mathbb{R}^n | x_i > 0 \text{ for all } i = 1, 2, .., n\}. \qquad (8.2)$$

Theorem 8.2.1. *For model* (8.1) *and any initial value* $(S(0), I_1(0), I_2(0), A(0), E(0)) \in \mathbb{R}^5_{++}$, *there is a unique solution* $(S(t), I_1(t), I_2(t), A(t), E(t))$ *on* $t \geq 0$ *which remains in* $\mathbb{R}^5_{++}$ *with probability one.*

Proof. Consider the function V_1 as defined below

$$
\begin{aligned}
V_1(S, I_1, I_2, A, E) = \Big(S - a_0 - a_0 \ln \frac{S}{a_0}\Big) + \Big(I_1 - 1 - \ln I_2\Big) + \Big(I_2 - 1 - \ln I_2\Big)\\
+\Big(A - 1 - \ln A\Big) + \Big(E - 1 - \ln E\Big).
\end{aligned}
$$

By applying Itô's formula as in the proof Theorem 4.3.1, we have:

$$
\begin{aligned}
dV_1(S, I_1, I_2, A, E) &= \mathcal{L}V_1 dt + (S - a_0)\sigma_0 dB_0(t) + (I_1 - 1)r\sigma_1 dB_1(t)\\
&\quad +(I_2 - 1)q\sigma_2 dB_2(t) + (A - 1)\sigma_3 dB_3(t)\\
&\quad +(E - 1)\sigma_4 dB_4(t), \qquad (8.3)
\end{aligned}
$$

where

$$\begin{aligned}
\mathcal{L}V_1 &= \Big[\Big(1-\frac{a_0}{S}\Big)\Big(\mu K - c(\beta_1 I_1+\beta_2 I_2)S-(\mu+\phi)S+\theta E\Big)\Big]+\Big[\Big(1-\frac{1}{I_1}\Big)\Big(c(\beta_1 I_1+\beta_2 I_2)S\\
&\quad -(\mu+k_1)I_1+\alpha I_2\Big)\Big]+\Big[(1-\frac{1}{I_2})(k_1 I_1-(\mu+k_2+\alpha)I_2)\Big]\\
&\quad +\Big[(1-\frac{1}{A})(k_2 J-(\mu+\delta)A)\Big]+\Big[(1-\frac{1}{E})(\phi S-(\mu+\theta)E)\Big]\\
&\quad +\frac{1}{2}\left(a_0\sigma_0^2+r^2\sigma_1^2+q^2\sigma_2^2+\sigma_3^2+\sigma_4^2\right)\\
&= \mu K-\frac{a_0}{S}\mu K-\mu(S+I_1+I_2+A+E)-\frac{a_0}{S}\theta E+a_0(\mu+\phi)+a_0 c(\beta_1 I_1+\beta_2 I_2)\\
&\quad -\frac{1}{I_1}c(\beta_1 I_1+\beta_2 I_2)S+(\mu+k_1)-\frac{1}{I_1}\alpha I_2+(\mu+k_2+\alpha)-\frac{1}{A}k_2 J+(\mu+\delta)\\
&\quad -\frac{1}{E}\phi S+(\mu+\theta).
\end{aligned}$$

Now we note that we have an upper bound for $\mathcal{L}V_1$

$$\begin{aligned}
\mathcal{L}V_1 &\leq \mu K-\mu(I_1+I_2)+a_0 c(\beta_1 I_1+\beta_2 I_2)+4\mu+a_0(\mu+\phi)+k_1+k_2+\alpha+\delta+\theta\\
&\quad +\frac{1}{2}\left(a_0\sigma_0^2+r^2\sigma_1^2+q^2\sigma_2^2+\sigma_3^2+\sigma_4^2\right).
\end{aligned}$$

We choose $a_0>0$ sufficiently small in order to have

$$a_0 c\beta_1 I_1-\mu I_1=I_1\left(a_0 c\beta_1-\mu\right)<0 \text{ and } a_0 c\beta_2 I_2-\mu I_2=I_2\left(a_0 c\beta_2-\mu\right)<0.$$

Therefore

$$\mathcal{L}V_1\leq C,$$

where $C=\mu K+4\mu+a_0(\mu+\phi)+k_1+k_2+\alpha+\delta+\theta+\frac{1}{2}\left(a_0\sigma_0^2+r^2\sigma_1^2+q^2\sigma_2^2+\sigma_3^2+\sigma_4^2\right)$ is a constant.

The rest of the proof follows readily. □

The following subset Φ of sample paths will be of interest.

$$\Phi = \left\{\omega \in \Omega | \, (S(t,\omega), I_1(t,\omega), I_2(t,\omega), A(t,\omega), E(t,\omega)) \in \mathbb{R}^5_{++} \text{ for all } t \geq 0\right\}.$$

From Theorem 8.2.1 it follows that $\mathbb{P}(\Omega \backslash \Phi) = 0$. In the remainder of this section we assume that sample paths are restricted to Φ.

8.3 Almost sure exponential stability

In the following, we introduce some more concepts leading to the preparation of our main theorem on almost sure exponential stability.

Let us first assume that $\sigma_0 = \sigma_4 = 0$, then the model system (8.1) exhibits a disease-free equilibrium $E_0 = (\frac{(\mu+\theta)K}{(\mu+\phi+\theta)}, 0, 0, 0, \frac{\phi K}{(\mu+\phi+\theta)})$. Note that condition $\sigma_0 = \sigma_4 = 0$ is also in line with section 5.4. In this case the basic reproduction number is computed by

$$\mathcal{R}_0 = \frac{c(\mu+\theta)K\beta_1 b_1}{(\mu+\phi+\theta)b_4} \tag{8.4}$$

where

$$b_1 = (\mu + k_2 + \alpha + k_1\frac{\beta_2}{\beta_1}), \; b_4 = ((\mu+k_1)(\mu+k_2) + \alpha\mu).$$

Remark 8.3.1. *The function that we now introduce links $\mathcal{R}_0$ and $\mathcal{R}_\sigma$. Let us define*

$$h : \mathbb{R}_{++} \to \mathbb{R}_+ \text{ by the rule } x \to \frac{1}{x}[r^2x^2b_1^2 + q^2(1 - b_1^2x^2)] \tag{8.5}$$

with b_1 as in (8.4).

If $r = q = \frac{\sqrt{2}}{2}$, then $h(x) = \frac{1/2}{x}$. In this case h tends 0^+ as x approaches $+\infty$. In our proof, we omit the case where both are equal. Further, it is easy to see that for $r \neq q$, then h tends $+\infty$ as x tends $+\infty$; h tends to $+\infty$ as x tends to 0^+. Therefore, $h'(x)$ is continuous on $\mathbb{R}_{++}$ and has the following root denoted by $x_0 = \frac{q^2}{b_1\sqrt{2r^2-1}}$. Therefore, $h''(x_0) > 0$ to indicate that $h(x)$ has a minimum given by

$$h(r^*) = \frac{b_1 r^2}{\sqrt{2r^2-1}}.$$

At the end of the proof for our main theorem, we shall use the fact that

$$\mathcal{R}_\sigma = \frac{c(\mu+\theta)K\beta_1 b_1}{(\mu+\phi+\theta)(b_4 + \min\{\sigma_2^1, \sigma_2^2\}h(r^*))}. \tag{8.6}$$

Proposition 8.3.2. *If* $(S(0), I_1(0), I_2(0), A(0), E(0)) \in \mathbb{R}^5_{++}$, *then almost surely,* $S(t) + E(t) \leq K$ *for all* $t > 0$.

Proof. Given any path (in Φ), then

$$\frac{d((S+E)-K)}{dt} = -\mu((S+E)-K) - c(\beta_1 I_1 + \beta_2 I_2)S \leq -\mu((S+E)-K).$$

Therefore $S(0) + E(0) < K$ implies that $S(t) + E(t) < K$ for all $t > 0$.

□

Consider the numbers b_0, b_1, b_2, b_3, b_4 and b_5

where

$$\begin{aligned} b_1 &= (\mu + k_2 + \alpha + k_1\frac{\beta_2}{\beta_1}),\ b_2 = \alpha + \frac{\beta_2}{\beta_1}(\mu + k_1) + b_5 \\ b_3 &= b_4\frac{(1-\mathcal{R}_0)}{k_2}, b_4 = ((\mu+k_1)(\mu+k_2) + \alpha\mu) \\ b_5 &= \frac{(1-\mathcal{R}_0)}{k_1}. \end{aligned} \tag{8.7}$$

Note that we choose b_0 sufficiently small such that

$$b_0 c\beta_1 \Lambda + \frac{b_4}{2}(\mathcal{R}_0 - 1) < 0$$

and

$$b_0 c\beta_2 \Lambda - b_5(\mu + k_2 + \alpha) < 0,$$

where $\Lambda = \frac{(\mu+\theta)K}{(\mu+\phi+\theta)}$.

Using the numbers b_i introduced, we can now define a function $Z(t)$ below. Recall that as we work with sample paths in Φ, this implies in particular that $Z(t) > 0$ for all $t \geq 0$.

Thus we define

$$Z(t) = b_0(K - (S(t) + E(t)) + b_1 I_1(t) + b_2 I_2(t) + b_3 A(t) \tag{8.8}$$

and let

$$V_2(t) = \ln Z(t).$$

For a stochastic process $x(t)$ we write

$$\langle x \rangle_t = \frac{1}{t}\int_0^t x(s)ds.$$

Proposition 8.3.3. *The disease-free equilibrium of model system (8.1) is almost surely exponentially stable if*

$$\limsup_{t\to\infty} \langle \mathcal{L}V_2(X) \rangle_t < 0 \quad \text{(a.s.)}.$$

Proof. We start off by noting that

$$V_2(X(t)) = V_2(X(0)) + \int_0^t \mathcal{L}V_2(X(u))du + M_t,$$

where

$$
\begin{aligned}
M_t &= \int_0^t \left(-b_0\sigma_0 \frac{S(u)}{z(X(u))} dB_0(u) + b_1 r\sigma_1 \frac{I_1(u)}{z(X(u))} dB_1(u) + b_2 q\sigma_2 \frac{I_2(u)}{z(X(u))} dB_2(u) \right. \\
&\quad \left. + b_3\sigma_3 \frac{A(u)}{z(X(u))} dB_3(u) - b_0\sigma_4 \frac{E(u)}{z(X(u))} dB_4(u) \right)
\end{aligned}
$$

The strong law of large numbers for local martingales, see [60, p12] for instance, implies that

$$\lim_{t\to\infty} \frac{1}{t} M_t = 0 \text{ (a.s.).}$$

Also, we observe that

$$\lim_{t\to\infty} \frac{1}{t} V_2(X(0)) = 0.$$

Therefore

$$\limsup_{t\to\infty} \frac{1}{t} V_2(X(t)) = \limsup_{t\to\infty} \frac{1}{t} \int_0^t \mathcal{L}V_2(X(u)) du = \limsup_{t\to\infty} \langle \mathcal{L}V_2(X) \rangle_t \quad \text{(a.s.).}$$

This completes the proof. □

We now calculate $\mathcal{L}V_2$.

$$
\begin{aligned}
\mathcal{L}V_2 &= -\mu b_0 \frac{[K-(S+E)]}{Z} + \frac{I_1}{Z}[(b_0+b_1)c\beta_1 S - b_1(\mu+k_1) + b_2 k_1] \\
&\quad + \frac{I_2}{Z}[(b_0+b_1)c\beta_1 S + b_1\alpha - b_2(\mu+k_2+\alpha) + b_3 k_2] \\
&\quad - b_3(\mu+\delta)\frac{A}{Z} - \frac{1}{2Z^2}\left(r^2 b_1^2\sigma_1^2 I_1^2 + q^2 b_2^2\sigma_2^2 I_2^2 + b_3^2\sigma_3^2 A^2 \right) \\
&\leq C_0 \frac{[K-(S+E)]}{Z} + C_1 \frac{I_1}{Z} + C_2 \frac{I_2}{Z} + C_3 \frac{A}{Z} - \frac{1}{2Z^2}\left(r^2 b_1^2\sigma_1^2 I_1^2 + q^2 b_2^2\sigma_2^2 I_2^2 \right).
\end{aligned}
$$

By Lemma 2.3 in [106], we can find, for every sample path w of the Wiener process $W(t)$, there exists an unbounded increasing sequence t_n of positive time values for which

$$\limsup_{t\to\infty} \mathcal{L}V_2(t,w) = \lim_{n\to\infty} \mathcal{L}V_2(t_n,w),$$

and for which we can define the following limits:

$$s = \lim_{n\to\infty} \langle S\rangle_{t_n}, \quad i_1 = \lim_{n\to\infty} \left\langle \frac{I_1}{Z} \right\rangle_{t_n}, \quad i_2 = \lim_{n\to\infty} \left\langle \frac{I_2}{Z} \right\rangle_{t_n}, \quad a = \lim_{n\to\infty} \left\langle \frac{A}{Z} \right\rangle_{t_n},$$

and

$$q = \lim_{n\to\infty} \left\langle \frac{K-(S+E)}{Z} \right\rangle_{t_n}.$$

In particular we note the identity

$$b_0 q + b_1 i_1 + b_2 i_2 + b_3 a = 1 \tag{8.9}$$

and

$$b_0 q, b_1 i, b_2 j, b_3 a \in [0,1].$$

We define $F(b)$ as:

$$F(b) = F(b_0,b_1,b_2,b_3) = \limsup_{t\to\infty} \mathcal{L}V_2(t).$$

Then $F(b)$ takes the form:

$$\begin{aligned} F(b) &= C_0 q + C_1 i_1 + C_2 i_2 + C_3 a - \frac{1}{2}\left(r^2 b_1^2 \sigma_1^2 i_1^2 + q^2 b_2^2 \sigma_2^2 i_2^2\right) \\ &\leq C_0 q + C_1 i_1 + C_2 i_2 + C_3 a - \frac{1}{2}\min\{\sigma_2^1, \sigma_2^2\}\left(r^2 b_1^2 i_1^2 + q^2 b_2^2 i_2^2\right) \end{aligned} \tag{8.10}$$

with $s < \frac{(\mu+\theta)K}{(\mu+\phi+\theta)} = \Lambda$ and where

$$
\begin{aligned}
C_0 &= -b_0\mu < 0 \\
C_1 &= b_0c\beta_1\Lambda + b_4(\mathcal{R}_0 - 1) + k_1b_5 \\
&= b_0c\beta_1\Lambda + \frac{b_4}{2}(\mathcal{R}_0 - 1) < 0 \\
C_2 &= b_0c\beta_2\Lambda + b_4(\mathcal{R}_0 - 1) + k_2b_3 - b_5(\mu + k_2 + \alpha) \\
&= b_0c\beta_2\Lambda - b_5(\mu + k_2 + \alpha) < 0 \\
C_3 &= -(\mu + \delta)b_3 < 0.
\end{aligned}
$$

Remark 8.3.4. *From the identity (8.9), we also have the inequality*

$$
\begin{aligned}
(b_2i_2)^2 &\leq (1 - b_1i_1)^2 \\
&\leq (1 - b_1^2i_1^2),
\end{aligned}
$$

and with $h(.)$ being the function as in equation (8.6), then the last term of (8.10) can be written as:

$$(r^2b_1^2i_1^2 + q^2b_2^2i_2^2) = i_1h(i_1).$$

Therefore from C_1 we have the inequality

$$b_0c\beta_1\Lambda + \frac{1}{2}[b_4 + \min\{\sigma_2^1, \sigma_2^2\}h(r^*)](\mathcal{R}_\sigma - 1) < 0.$$

Theorem 8.3.5. *Assuming $\mathcal{R}_\sigma < 1$, then $(I_1(t), I_2(t), A(t))$ almost surely converge exponentially to 0.*

Proof. Note that by the choice of b_0, it follows that

$$b_0c\beta_1\Lambda + \frac{1}{2}\frac{cK(\mu + \theta)b_1}{(\mu + \phi + \theta)} - \frac{1}{2}b_4 - \frac{1}{2}\min\{\sigma_2^1, \sigma_2^2\}h(r^*) < 0.$$

Thus

$$
\begin{aligned}
F(b) \quad \leq \quad & -b_0\mu q + i_1[b_0 c\beta_1\Lambda + \frac{1}{2}(b_4 + \min\{\sigma_2^1, \sigma_2^2\}h(r^*))(\mathcal{R}_\sigma - 1)] - i_2 b_5(\mu + k_2 + \alpha) \\
& -a(\mu + \delta)b_3 < 0.
\end{aligned}
$$

This completes the proof. □

8.4 Numerical simulation

We use parameters and initial states values given in [70]. The parameters values are as follows:

Table 8.1: List of parameters and their values chosen to simulate the model system (8.1) based on the South African historical HIV trend.

Parameters	Value	Source
α	0.33	[9]
k_1	0.125	[41]
k_2	0.1	[9]
c	3	cf. [40]
δ	0.279	[90]
μ	$\frac{1}{62.4}$	[90]
ϕ	0.01	Nominal
θ	0.001	Nominal

We assign the following initial values:

$$S_0 = 56.18, \quad E_0 = 1.12, \quad I_{1,0} = 5.11, \quad I_{2,0} = 1.43, \quad A_0 = 0.48$$

In the following we only show the trajectories of $I_2(t)$ for different values of ϕ, $\phi = 0.02,\ 0.021$. For the different values of ϕ, the corresponding value of $\mathcal{R}_0$ will be denoted by $\mathcal{R}_0(\phi)$.

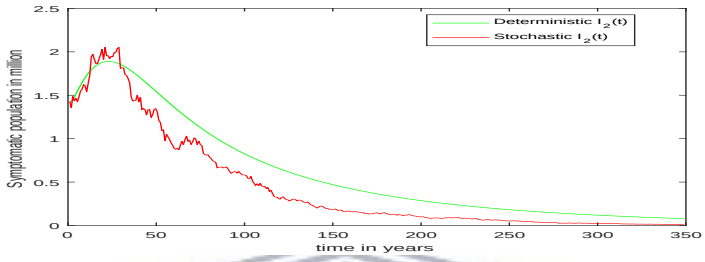

Figure 8.1: Convergence beyond $\mathcal{R}_0(\phi) < 1$.

Chosen values: $\beta_1 = 0.000481, \beta_2 = 0.000581, \sigma_1 = 0.03, \sigma_2 = 0.03$. Calculated values: $\mathcal{R}_0(0.02) = 1.021, \mathcal{R}_\sigma = 0.726$

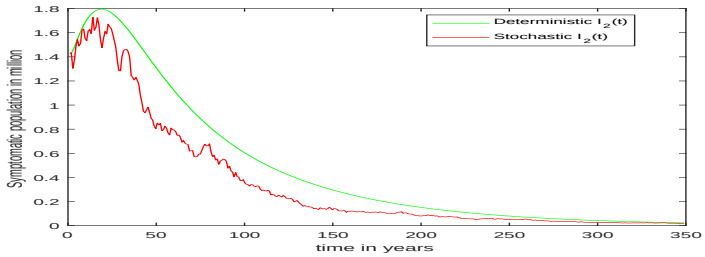

Figure 8.2: Convergence to the disease-free equilibrium.

Chosen values: $\beta_1 = 0.000481, \beta_2 = 0.000581, \sigma_1 = 0.03, \sigma_2 = 0.03$. Calculated values: $\mathcal{R}_0(0.021) = 0.9975, \mathcal{R}_\sigma = 0.7124$.

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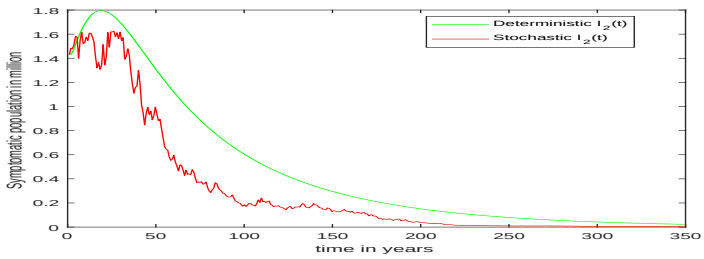

Figure 8.3: Improving stability of the disease-free equilibrium.
Chosen values: $\beta_1 = 0.000481, \beta_2 = 0.000581, \sigma_1 = 0.04, \sigma_2 = 0.05$. Calculated values: $\mathcal{R}_0(0.021) = 0.9975, \mathcal{R}_\sigma = 0.5872$.

In Figure 8.1, for $\phi = 0.02$ and $\sigma_1 = \sigma_2 = 0.03$, $\mathcal{R}_0(0.02) = 1.021$ while $\mathcal{R}_\sigma = 0.726 < 1$. In this case, Theorem 8.3.5 guarantees almost sure exponential stability. Indeed there is convergence to the disease-free equilibrium even beyond $\mathcal{R}_0(\phi) < 1$. The substantial change which occurred in the value of the basic reproduction number is due to both increasing uptake of PrEP and the stochastic perturbations, which led to decreasing the value of the the class of $I_2(t)$. In Figure 8.2, for $\sigma_1 = \sigma_2 = 0.03$ and an increase in the uptake of PrEP to $\phi = 0.021$ results in decreasing the basic reproduction number to $\mathcal{R}_0(0.02) = 0.9975 < 1$ while $\mathcal{R}_\sigma = 0.726 < 1$. The disease-free equilibrium is almost sure exponentially stable. In Figure 8.3, we increase the values $\sigma_1 = 0.04, \sigma_2 = 0.05$ and $\mathcal{R}_\sigma = 0.5872 < 1$. In this case, we have expected the disease to converge faster to zero according to the theorem.

8.5 Concluding remarks

In this chapter, we investigated a stochastic model describing the population dynamics of HIV with pre-exposure prophylaxis (PrEP). We proved existence of solutions which are almost surely global and positive by using Lyapunov techniques. We also proved a theorem (Theorem 8.3.5) on almost exponential stability. From the main theorem (Theorem 8.3.5), we found that the disease-free equilibrium is almost surely exponentially

stable whenever the requirement is fulfilled. The simulations show that minor stochastic perturbations on the model may not always be catastrophic, and this has been observed in the simulations. Thus, minor environmental perturbations may not stop public health authorities from deciding on launching of a certain programme. Our model has attempted to show how the use of PrEP can potentially reduce the number of new HIV infections, and even when minor stochastic perturbations are considered.

Chapter 9

Concluding remarks and scope for future research

It has been shown throughout the literature that the greatest burden of HIV/AIDS is still in sub-Saharan Africa and in this region, especially women are severely affected. South Africa has more people infected with HIV, but the country has kept more HIV-infected people alive than any other country by providing access to anti-retroviral therapy (ART) in the public sector and negotiating drug prices [104]. Anti-retroviral Treatment (ART) can help to reduce HIV transmission. The substantial impact of treatment on the incidence, prevalence and mortality shows how it is imperative to make ARV treatment available to everyone, regardless of $CD4^+$ cell counts. It is also known that early ARV treatment eliminates HIV transmission and possibly eliminates AIDS related deaths. Thus, HIV/AIDS can be considered as a chronic manageable disease rather than a fatal one.

However, the HIV/AIDS epidemic addresses a complex challenge to the public policy of South Africa, with implications for some of the government's key policy objectives (notably health, education, social development), and impacts on public finance and macroeconomic. There is a range of fiscal consequences resulting from HIV/AIDS beyond the

costs of the policy response. An important aspect of the fiscal costs of HIV/AIDS is the fact that the costs of HIV/AIDS impacts and its national response are highly persistent-not only absorbing a considerable share of fiscal resources at present, but projected to continue doing so over many years [24].

Our dissertation deals with stochastic modeling an HIV/AIDS epidemic disease with treatment. The dynamics of the model are also studied when there is a massive inflow of HIV infectives.

We start off with the underlying deterministic model in Chapter 3. We extend the paper of cai et al. [14] and we prove both global stability of endemic and disease-free equilibrium with and without the inflow of infectives respectively. We prove existence of the endemic equilibrium as well. We carry out with stability analysis and we support our theoretical results by way of numerical simulations. Through the numerical simulations, we show the impact that the inflow have on the transmission of HIV. The disease in this case remain at the endemic level and the model system does not exhibit a disease-free equilibrium.

Explicit inclusion of stochastic perturbations into epidemiological models by way of Brownian motion shows much insight into the problem since randomness does feature in real life. Stochasticity has been introduced in various biological models such as for instance, natural resource management or the ecological studies or the epidemics in human populations. In Chapter 4, a stochastic model for the population dynamics of HIV/AIDS is introduced and we show that there are feasible solutions (almost surely) in every sense that we have explored. We also investigate the asymptotic behaviour of the solutions with respect to the disease-free equilibrium of the underlying deterministic model. Our results have shown that minor random noise predicts extinction of the disease rather than persistence.

In Chapter 5, We have presented an *sde* model of HIV with inflow of infectives. In the

special case that we have no inflow of infectives into the system and $\sigma_0 = 0$, and for sufficiently small values of the perturbation parameter, stability of the disease-free equilibrium is obtained for a bigger range of values of the basic reproduction number $\mathcal{R}_0$ of the deterministic model, i.e., beyond the range $\mathcal{R}_0 < 1$. This is sufficiently significant that it can be observed in simulations. The almost sure exponential stability is a fairly strong type of stability, it being a stochastic version of global asymptotic stability. For the public health authorities it is comforting to know that the presence of minor stochasticity on their model will not be a hindrance if eradication strategies should be launched. In the case of stochastic HIV/AIDS model with inflow of infectives, we have been able to study stability in the mean. The theorem asserts that asymptotically the stochastic solutions stay within a certain bound from the (non-trivial) equilibrium point of the underlying deterministic model.

In Chapter 6, we have established a model describing the population dynamics of HIV/AIDS including treatment and pre-exposure prophylaxis (PrEP) in the context of South Africa. Our analytical results and our sample simulations are quite meaningful as we work with the current HIV trend in South Africa. Our model quantifies how the use of PrEP can potentially reduce the number of new HIV infections, and this has been well observed in the sample simulations. South Africa has a wide range of its population being exposed to HIV. Its high-risk sections of the population include adolescent girls and young women, sex workers, men who have sex with men (MSM), discordant couples and truckers, all of whom face various barriers to access including stigma, criminalisation and lack of supportive service delivery infrastructure [21]. If they are to be the focal point for PrEP, it will be imperative to assess how best to introduce PrEP into programmes where these high risk sections of the population can be supported [22].

The incidence rate that measures the rate of new infection is considered to be a very crucial parameter. In Chapter 7 we introduce a stochastic model for HIV/AIDS with incidence rate., stochasticity associated with the parameter β. Thus by constructing

suitable Lyapunov functions and applying Itô's formula, some other properties such as existence of global positive solution, convergence, almost sure exponential stability are proved. Our theoretical results are supported by ways of numerical simulations. Our results show stochastic perturbation can predict extinction rather than persistence. We also show that when inhibitory effect from the behavioural change of the susceptible individuals is large then the force of infections becomes small.

In chapter 8, we present a stochastic model for HIV/AIDS epidemic with the use of prophylaxis and we show that the model with random perturbation has a unique global positive solution. Our motivation in this research comes from the fact that stochastic framework may have the ability to predict efficacy of prophylaxis against HIV.

The effects of different environmental noises from the underlying deterministic model may lead to different dynamical outcomes. In the case of HIV models, we may have to extend to the approach in [84] to illustrate the different dynamical outcomes of two stochastic differential equation models based on simulation observations and the theorems obtained from previous sections. Following the approach for instance in [84], then the HIV/AIDS perturbed can be written as

$$\begin{aligned}
dS &= [\mu K - c(\beta_1 I_1 + \beta_2 I_2)S - \mu S]\,dt + \sigma_{00} S dW_{00}(t) + \sigma_{01} I_1 dW_{01}(t) \\
&\quad + \sigma_{02} I_2 dW_{02}(t) + \sigma_{03} A dW_{03}(t) \\
dI_1 &= [c(\beta_1 I_1 + \beta_2 I_2)S - (\mu + k_1)I_1 + \alpha I_2]\,dt + \sigma_{10} S dW_{10}(t) + \sigma_{11} I_1 dW_{11}(t) \\
&\quad + \sigma_{12} I_2 dW_{12}(t) + \sigma_{13} A dW_{13}(t) \\
dI_2 &= [k_1 I_1 - (\mu + k_2 + \alpha)I_2]\,dt + \sigma_{20} S dW_{20}(t) + \sigma_{21} I_1 dW_{21}(t) \\
&\quad + \sigma_{22} I_2 dW_{22}(t) + \sigma_{23} A dW_{23}(t) \\
dA &= [k_2 I_2 - (\mu + \delta)A]\,dt + \sigma_{30} S dW_{30}(t) + \sigma_{31} I_1 dW_{31}(t) \\
&\quad + \sigma_{32} I_2 dW_{32}(t) + \sigma_{33} A dW_{33}(t).
\end{aligned}$$

where $\sigma_{ij}, i, j = 0, 1, 2, 3$ are real constants and known as the intensity of environmental fluctuations, $W_{ij}(t), i, j = 0, 1, 2, 3$ independent standard Brownian motion. For simplicity, the dynamics of the model can also be studied when the values of $\sigma_{ij} = \sigma_j, i = 0, 1, 2, 3$.

Mathematical modeling has been such an important approach to control the population dynamics of infectious diseases. Optimal control has been applied by many mathematicians in the analysis and control of infectious diseases both qualitatively and quantitatively. In particular, the study on optimal control aims to determine the best method of controlling the outbreak of certain disease for instance within a specific time frame. Our future work will formulate an optimal control problem for both deterministic and stochastic cases where the objective would be to determine the ARV treatment strategy and PrEP strategy that minimize the class of individuals with HIV as well as the costs associated with ARV treatment and PrEP. The outbreak of HIV/AIDS has led to an increasing awareness among economists of the need to study their impact on the economy in terms of the resources allocation and cost. This question arises when the resources available for public healthcare are strictly limited. If resources are unlimited, then the optimal way to allocate prevention funds is to spend enough to eradicate the disease. Another approach that we aim to research on is the cost-effectiveness analysis (CEA). CEA is a type of economic analysis where both the cost and the outcome (impact, result, effect, benefit, health gain) of an intervention are evaluated and then expressed in the form of a cost-effectiveness ratio. The numerator of the cost-effectiveness (CE) ratio represents the cost of the intervention associated with one unit of outcome. The denominator is the unit of outcome. It can be expressed using many types of measures including: years of life gained, quality-adjusted life years gained ($QALYs$), new diagnoses, infections averted, and deaths averted. CEA is usually conducted on interventions that are known to be effective. In recent years, mathematical models with the inclusion of latent infected T-cells have been developed to investigate the models behaviors. Many of these models do not consider the effect of stochastic fluctuation factor which is such an important component in epidemiological modeling. Research related to stochastic differential equation model of the dynamics mechanism of HIV virus can be very meaningful with experimental data.

Stochastic models of HIV co-infection with malaria, Tuberculosis or flu will also be at centre of our future research. Another version of stochastic model can also be formulated by using the continuous-time discrete state Galton-Watson branching process (GWbp). The branching process helps to determine disease invasion and extinction probabilities.

Bibliography

[1] H. Abbey. An examination of the Reed-Frost theory of epidemics. *Hum. Biol.* (1952), **24**, 201-233.

[2] L.J. Allen, T. Lewis, C.F. Martin, M.A. Jones, C.K. Lo, M. Stamp, G. Mundel, A.B. Way. Analysis of a measles epidemic. *Stat. Med.* (1993), **12**, 229-239.

[3] R. Anderson, R. May. Infectious Diseases of Humans: Dynamics and Control; Oxford University Press: New York, NY, USA, 1991.

[4] E. J. Arts and D. J. Hazuda. HIV-1 Antiretroviral Drug Therapy. *Cold Spring Harb. Perspect. Med.*, **2(4)**(2012) 1-23.

[5] M. Bachar, A. Dorfmayr. HIV treatment models with time delay. *C.R. Biologies* **327** (2004) 983 – 994.

[6] U.S. Basak, B.K. Datta, P.K. Ghose. Mathematical Analysis of an HIV/AIDS Epidemic Model. *American Journal of Mathematics and Statistics*, (2015) 5(5), 253-258.

[7] S. Blower. Calculating the consequences: HAART and risky sex. *AIDS* **15**, (2001) 1309 – 1310.

[8] C.P. Bhunu. Assessing the impact of homelessness on HIV/AIDStransmission dynamics. *Cogent Mathematics* (2015) **2**: 1021602.

[9] C.P Bhunu, S. Mushayabasa, H. Kojouharov, J.M. Tchuenche. Mathematical analysis of an HIV/AIDS model: impact of educational programs and abstinence in sub-Sahara Africa. *J. Math. Model. Algorithms* **10** (2011) no.**1**, 31 – 55.

[10] J. Bor, A. J Herbst, ML. Newell, T. Bärnighausen. Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. *Science*, 2013, **339**:961-965.

[11] F. Brauer, P. Van den Driessche and W.U Jianhorg. *Mathematical Epidemiology*. Mathematical Biosciences subseries. PK Maimi Oxford 2008.

[12] R. Singh, S. Ali, M. Jain, Rakhee. Epidemic Model of HIV/AIDS Transmission Dynamics with Different Latent Stages Based on Treatment. *American Journal of Applied Mathematics* **4(5)** (2016) 222-234.

[13] B. Buonomo. A simple analysis of vaccination strategies for rubella. *Math. Biosci. Eng.* (2011), **8**, 677-687.

[14] L. Cai, X. Li, M. Ghosh, B. Guo. Stability analysis of an HIV/AIDS epidemic model with treatment. *Journal of Computational and Applied Mathematics* **229** (2011) 313−323.

[15] V. Capasso, G. Serio, A generalization of the Kermack–Mckendrick deterministic epidemic model, *Math. Biosci*, **42**, 41 – 61, 1978.

[16] L. Chen, J. Chen. *Nonlinear Biological Dynamical System*, Beijing, Science Press, 1993.

[17] S.C. Chen, C.F. Chang, L.J. Jou,C.M. Liao. Modelling vaccination programmes against measles in Taiwan. *Epidemiol. Infect.* (2007), **135**, 775-786.

[18] S.C. Chen, C.M. Liao. Modelling control measures to reduce the impact of pandemic influenza among schoolchildren. *Epidemiol. Infect.* (2008), **136**, 1035-1045.

[19] N. Dalal, D. Greenhalgh and X.R. Mao. A stochastic model of AIDS and condom use. *J. Math. Anal. Appl.* **325** (2007)

[20] R. Derrick William, I. Grossman Stanley. *Elementary Differential Equations with Applications*, Addison-Wesley, 1976, 537 pages.

[21] Desmond Tutu HIV Foundation. Key Populations, Key Responses: A Gap Analysis for Key Populations and HIV in South Africa, and Recommendations for the National Strategic Plan for HIV/AIDS, STIs and TB (2012-2016). 2011. http://www.desmondtutuhivfoundation.org.za/documents/Key-Populations-Key-Solutions-report.pdf (accessed 17 January 2013).

[22] R. Eakle, W. D. F. Venter, H. Rees. Pre-exposure prophylaxis for HIV prevention: Ready for prime time in South Africa? *South African Medical Journal*, **103(8)** (2013) 515-516

[23] J.W. Eaton, L.F. Johnson, J.A. Salomon, T. Bärnighausen, E. Bendavid et al. (2012) HIV Treatment as Prevention: Systematic Comparison of Mathematical Models of the Potential Impact of Antiretroviral Therapy on HIV Incidence in South Africa.. PLoS Med, 9(7), e1001245.

[24] L. Elizabeth, H. Markus. *the fiscal dimension of HIV/AIDS in Botswana, South Africa, Swaziland and Uganda*, The World Bank, 2012.

[25] European Medicines Agency, First medicine for HIV pre-exposure prophylaxis recommended for approval in the EU (Accessed 22/06/2017).

[26] N. Dalal, D. Greenhalgh, X. Mao. A stochastic model of AIDS and condom use. *J. Math. Anal. Appl.*, **325** (2007) 36-53.

[27] R. Derrick William, I. Grossman Stanley. *Elementary Differential Equations with Applications*, Addison-Wesley, 1976, 537 pages.

[28] Y. Ding, M. Xu, L. Hu. Asymptotic behavior and stability of a stochastic model for AIDS transmission. *Applied Mathematics and Computation* **204**, (2008) 99 − 108.

[29] E. F. Drabo, J. W. Hay, R. Vardavas, Z. R. Wagner and N. Sood. A cost-effectiveness analysis of pre-exposure prophylaxis for the prevention of HIV among Los Angeles County: Men who have sex with men. *Clin. Infect. Dis.*, **63(11)** (2016) 1495-1504.

[30] A. Friedman-Kien, L. Laubenstein, M. Marmor, K. Hymes, J. Green, A. Ragaz, J. Gottleib, F.Muggia, R. Demopoulos, M. Weintraub, Kaposi's sarcoma and pneumocystis pneumonia among homosexual men-New York City and California. *Morb. Mortal.Wkly.Rep.***30**, (1981) 305-308.

[31] L. Gao, H. Hethcote. Simulations of rubella vaccination strategies in China. **Math. Biosci**., **202**, (2006) 371-385.

[32] Global report: UNAIDS report on the global AIDS epidemic: 2012. UNAIDS, 2012.

[33] M. S. Gottlieb, R. Schroff, H.M Schanker, J.D. Weisman, P.T. Fan, R.A. Wolf, A. Saxon. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. *N. Engl. J. Med.* **305**, 1425 – 1431 (1981).

[34] Government of South Africa (January,2010) 'The National Communication Survey on HIV/AIDS 2009'.

[35] R. Grais, J. Ellis, G. Glass. Assessing the impact of airline travel on the geographic spread of pandemic influenza. *Eur. J. Epidemiol.* **18**,(2003) 1065-1072.

[36] R. Granich, J.G. Kahn, R. Bennett, CB. Holmes, N. Garg et al. (2012) Expanding ART for Treatment and Prevention of HIV in South Africa: Estimated Cost and Cost-Effectiveness 2011 – 2050. PLoS ONE 7(2): e30216. doi:10.1371/journal.pone.0030216

[37] H. Grant, Z. Mukandavire, R. Eakle, H. Prudden, G. B Gomez, H. Rees, C. Watts. When are declines in condom use while using PrEP a concern? Modelling insights from a Hillbrow, South Africa case study. *Journal of the International AIDS Society*, **20(1)** (2017).

[38] A. Gray, D. Greenhalgh, L. Hu, X. Mao, and J. Pan. A stochastic differential equation SIS epidemic model. *SIAM Journal of Applied Mathematics* **71(3)**, (2011) 876 – 902.

[39] R. Gwandure, E Ross, J Gardner, Parents' perceptions of HIV counselling and testing in schools: Ethical, legal and social implications, *S Afr Med J* **104(1)**, (2014) 40−42.

[40] S.D. Hove-Musekwa, F. Nyabadza. The dynamics of an HIV/AIDS model with screened disease carriers. *Computational and Mathematical Methods in Medicine*, **10(4)** (2009) 287-305.

[41] J.M. Hyman, J. Li, E.A. Stanley. The differential infectivity and staged progression models for the transmission of HIV. *Mathematical Biosciences*, **155** (1999) 77-109.

[42] Human Sciences Research Council (2009), 'South African National HIV Prevalence, Incidence, Behaviour and Communication Survey, 2008: A Turning Tide Among Teenagers?'

[43] Z. Jia et al., Modeling the impact of immigration on the epidemiology of tuberculosis. *theoretical population biology*, Vol **73**, (2008) 437 − 448

[44] Joint United Nations Programme on HIV/AIDS. (2012). World AIDS Day report, 2011. Geneva, Switzerland: UNAIDS, 2011.

[45] Joint United Nations Programme on HIV/AIDS. (2016). Global AIDS update 2016. Geneva: UNAIDS.

[46] Joint United Nations Programme on HIV/AIDS. (2017). UNAIDS DATA 2017.

[47] A. Kamina, R.W. Makuch, H. Zhao. A stochastic modeling of early HIV-1 population dynamics. *Mathematical Biosciences*, **170** (2001) 187-198.

[48] E. L. Kateme, J.M. Tchuenche, S.D. Hove-Musekwa (2012). HIV/AIDS Dynamics with Three Control Strategies: The Role of Incidence Function. *ISRN Applied Mathematics*, 2012.

[49] M.J. Keeling, P. Rohani. Modeling Infectious Diseases in Humans and Animals; Princeton University Press: Princeton, NJ, USA, 2008.

[50] D. Kerrigan, A. Wirtz A, S. Baral et al. The global HIV epidemics among sex workers. The World Bank Publications, 2012.

[51] A. Lahrouz, L. Omari, A. Settati, A. Belmaâti. Comparison of deterministic and stochastic SIRS epidemic model with saturating incidence and immigration. *Arabian Journal of Mathematics*, **4(2)** (2014) 101 − 116.

[52] A. Lahrouz, L. Omari, D. Kiouach. Global analysis of a deterministic and stochastic nonlinear SIRS epidemic model. Nonlinear Analysis: Modelling and Control **16** (2011) 59 − 76.

[53] S. Leland, X. Rickman, Pneumocystis pneumonia-Los Angeles. *Morb. Mort. Wkly.Rep.* **30**, 250 − 252 (1981).

[54] D. Lestari. (2016, February). Local Stability of AIDS Epidemic Model Through Treatment and Vertical Transmission with Time Delay. In *Journal of Physics: Conference Series* (**Vol. 693**, No. 1, p. 012010). IOP Publishing.

[55] G. Li, W. Wang, Z. Jin. Global stability of an SEIR epidemic model with constant immigration, *Chaos Solitons Fractals*, **30**, (2006) 1012 − 1019.

[56] M. Lipsitch, T. Cohen, B. Cooper, J. Robins, S. Ma, L. James, G. Gopalakrishna, S. Chew, C. Tan, M. Samore, D. Fisman, M. Murray. Transmission dynamics and control of severe acute respiratory syndrome. *Science*, **300**, (2003) 1966-1970.

[57] Z. Liu, Dynamics of positive solutions to SIR and SEIR epidemic models with saturated incidence rates, *Nonlinear Analysis: Real World Applications*, **14** (2013) 1286-1299.

[58] Q. Lu. Stability of SIRS system with random perturbations. *Physica A* **388**, (2009) 3677 − 3686.

[59] Z. Ma, Y. Zhou, J. Wu. *Modeling and Dynamics of Infectious Diseases*. Higher Education Press, Beijing, China, 2009.

[60] X. Mao. *Stochastic differential equations and applications*. Elsevier, 2007.

[61] H.J. Marquez. *Nonlinear control systems: analysis and design*. Hoboken: Wiley-Interscience. **Vol.1**, 2003.

[62] H. Masur, *et al.* An outbreak of community-acquired pneumocystis carinii pneumonia: initial manifestation of cellular immune dysfunction. *N. Engl. J. Med.* **305**, 143 − 1438 (1981).

[63] Mid year estimates, Statistics South Africa, 2014.

[64] J. McNeil. A history of official government HIV/AIDS policy in South Africa. South African History Archives. http://www.sahistory.org.za/topic/history-official-government-hivaids-policy-south-africa (accessed 30 January 2014).

[65] Z. Mukandavire, W. Garira. Effects of public health educational campaigns and the role of sex workers on the spread of HIV/AIDS among heterosexuals. *Theoretical Population Biology* **72** (2007) 346 − 365.

[66] Z. Mukandavire, K.M. Mitchell, P. Vickerman. Comparing the impact of increasing condom use or HIV pre-exposure prophylaxis (PrEP) use among female sex workers. *Epidemics*, **14** (2016) 62-70.

[67] Z. Mukandavire, P. Das, C. Chiyaka, N.H. Gazi, K. Das, T. Shiri. HIV/AIDS Model with Delay and the Effects of Stochasticity. *J. Math. Model. Algor.* **10** (2011) 181-191.

[68] R. Naresh, A. Tripathi, D. Sharma. Modelling and analysis of the spread of AIDS epidemic with immigration of HIV infectives. *Journal of Mathematical and Computer Modelling*, Vol **49**, (2009) 880 − 892.

[69] M. U Nsuami, P. J Witbooi. Stochastic dynamics of an HIV/AIDS epidemic model with treatment. *Quaestiones Mathematicae*, (2018)1-17.

[70] M. U Nsuami and P. J Witbooi. A model of HIV/AIDS population dynamics including ARV treatment and pre-exposure prophylaxis. *Advances in Difference*

Equations (2018) 2018:11 https://doi.org/10.1186/s13662-017-1458-x

[71] F. Nyabadza, Z. Mukandavire . Modelling HIV/AIDS in the presence of an HIV testing and screening campaign. *Journal of theoretical biology*, **280(1)** (2011)167-179.

[72] B. Øksendal. *Stochastic Differential Equations: An introduction with applications*, 4th Edition. Springer, Berlin, 1995.

[73] C. Pukdeboon. A review of fundamentals of Lyapunov theory. *The Journal of Applied Science*, **10(2)**, (2011) 55-61.

[74] R. Rudnicki, K. Pichór. Influence of stochastic perturbation on prey-predator systems, *Mathematical Biosciences*, **206** (2007) 108-119.

[75] Z. Osman, X. Abdurahman. Stability Analysis of a Delayed HIV/AIDS Epidemic Model with Treatment and Vertical Transmission. *Applied Mathematics*, **6(10)**, (2015) 1781.

[76] H. Qiu, J. Lv, K. Wang.(2013). Two types of permanence of a stochastic mutualism model. *Advances in Difference Equations*, **2013(1)**, 1-17.

[77] F. Rao. Dynamical analysis of a stochastic predator-prey model with an Allee effect. *Abstract and Applied Analysis*, **Vol. 2013**, Article ID 340980, 10 pages, 2013.

[78] F.Rao, Dynamics of a stochastic SIR Epidemic Model, *Abstract and Applied Analysis*, Volume **2014**, Article ID 356013, 9 pages

[79] GJ. Ras, W. Simson, R. Anderson, OW. Prozesky, T. Hamnersma. Acquired immunodeficiency syndrome: A report of 2 South African cases. *S Afr Med J* 1983;

[80] S. Rerks-Ngarm, P. Pitisuttithum, S. Nitayaphan, J. Kaewkungwal, J. Chiu, R. Paris ... M. Benenson (2009). Vaccination with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. *New England Journal of Medicine*, **361(23)**, 2209-2220.

[81] S. Resch, E. Korenromp, J, Stover, M. Blakley, C. Krubiner, et al. (2011) Economic Returns to Investment in AIDS Treatment in Low and Middle Income Countries. PLoS ONE 6(10): e25310. doi:10.1371/journal.pone.0025310.

[82] T. Roy, C. Anderson, C. Evans, M. S Rahman,. Sexual risk behaviour of rural-to-urban migrant taxi drivers in Dhaka, Bangladesh: A cross-sectional behavioural survey. *Journal of Public Health*, Vol **124**, (2010) 648 − 658.

[83] H. Schmidt, K.H. Johansson, K. Jacobsson, B. Wahlberg, B. (2009). EL2620 Nonlinear Control.

[84] S. J. Schreiber, M. Benam, and K.A.S. Atchadé. Persistence in fluctuating environments. *Journal of Mathematical Biology*, **62(5)**:655-683, 2011.

[85] B. Seidu, O.D. Makinde, (2014). Optimal Control of HIV/AIDS in the Workplace in the Presence of Careless Individuals. *Computational and mathematical methods in medicine*, 2014.

[86] C. J. Silva, D. F. Torres (2017). Modeling and optimal control of HIV/AIDS prevention through PrEP. arXiv preprint arXiv:1703.06446.

[87] N. P. Simelela, W.D.F. Venter, A brief history of South Africa's response to AIDS." SAMJ: South African Medical Journal 104.3 (2014): 249-251.

[88] R. Singh, S. Ali, M. Jain, Rakhee. Epidemic Model of HIV/AIDS Transmission Dynamics with Different Latent Stages Based on Treatment. *American Journal of Applied Mathematics* **4(5)** (2016) 222-234.

[89] Statistical release, Mid-year population estimates, Statistics South Africa, 2013. 36 − 53.

[90] Statistics, S.A. Mid-year population estimates 2016 ; Statistical Release P0302.

[91] U. Skwara. A stochastic model of symbiosis, *Annales Polonici Mathematici*, **Vol. 97** (2010), 257-272.

[92] F. Tanser, T. Bärnighausen, E. Grapsa, J. Zaidi, ML. Newell ML., High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science*, 2013, 339:966-971.

[93] E. Tornatore, S.M. Buccellato, P. Vetro. Stability of a stochastic SIR system, *Physica A* **354**, (2005) 111 − 126.

[94] Treatment 2015, UNAIDS.

[95] A. Tripathi, R. Naresh, J.M.Tchuenche, Dileep Sharma, Modeling the Spread of HIV/AIDS with Infective Immigrants and Time Delay, *International Journal of Nonlinear Science*, Vol.**16** (2013) No.4,pp.313 − 3224.

[96] UNAIDS 2015, Biomedical AIDS research: Recent and upcoming advances.

[97] B. Van den Broek, W. Wiegernck, B. Kappen, Graphical Model Inference in Optimal Control of Stochastic Multi-Agent Systems, *Journal of Artificial Intelligence Research* **32** (2008) 95-122.

[98] P. Van den Driessche and J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. *Math. Biosci.* **180** (2002) 29-48.

[99] L.Y. Wang, H. L. Huang, A. C. Xu, and W.M.Wang, Stochastic extinction in an SIRS epidemic model incorporating media coverage, *Abstract and Applied Analysis*, vol. 2013, Article ID891765, 8 pages, 2013.

[100] X. X. Wang, H. L. Huang, Y. L. Cai, and W. M. Wang, The complex dynamics of a stochastic predator-prey model, *Abstract and Applied Analysis*, vol. **2012**, Article ID 401031, 24 pages, 2012.

[101] J. Wang, A.J. McMichael, B. Meng, N.G. Becker, W. Han, K. Glass, J. Wu, X. Liu, J. Liu, X. Li, X. Zheng. Spatial dynamics of an epidemic of severe acute respiratory syndrome in an urban area. **Bull. World Health Organ**. (2006), **84**, 965-968.

[102] J.L. Weinberg, C.L. Kovarik, (2010). The WHO clinical staging system for HIV/AIDS. *Virtual Mentor*, 12(3), 202.

[103] WHO and UNAIDS. Global update on HIV treatment: results, impact and opportunities. Geneva, World Health Organization, 2013.

[104] Williams, G. Brian and Eleanor Gouws. "Ending AIDS in South Africa: How long will it take? How much will it cost?." arXiv preprint arXiv:1311.1815 (2013).

[105] P. J. Witbooi. An SEIRS epidemic model with stochastic transmission. *Advances in Difference Equations*, **2017(1)**, (2017): 109.

[106] P.J. Witbooi. Stability of an SEIR epidemic model with independent stochastic perturbations. *Physica A*, **392** (2013) 4928 – 4936.

[107] P.J. Witbooi. Stability of an SEIR epidemic model with independent stochastic perturbations. *Physica A*, **392** (2013) 4928 – 4936.

[108] P. J. Witbooi. Stability of a Stochastic Model of an SIR Epidemic with Vaccination. *Acta Biotheoretica*, **65.2** (2017) 151-165.

[109] World Health Organization. (2010). Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach-2010 revision.

[110] World Health Organization. (2015). WHO expands recommendation on oral preexposure prophylaxis of HIV infection (PrEP): Policy brief. Geneva: WHO.

[111] www.aids.gov/hiv-aids-basics/prevention/reduce-your-risk/pre-exposure-prophylaxis

[112] D. Xiao and S. Ruan, Global analysis of an epidemic model with nonmonotone incidence rate, *Mathematical Biosciences*, **vol. 208, no. 2**, 419-429, 2007.

[113] J. Yang, X. Wang, X. Li. Global stability of an HIV/AIDS model with stochastic perturbation. *Asian-European Journal of Mathematics*, **4(2)** (2011) 349-358.

[114] Y. Zhao, D. Jiang. The Behavior of an SVIR Epidemic Model with Stochastic Perturbation. *Abstract and Applied Analysis*, **Vol 2014** (2014), Article ID 742730, 7 pages http://dx.doi.org/10.1155/2014/742730.

[115] T. Zhang and Z. D. Teng. Permanence and extinction for a nonautonomous SIRS epidemic model with time delay, *Applied Mathematical Modelling*, **33(2)** (2009) 1058 – 1071.

[116] Y. Zhou, W. Zhang, S.Yuan, H. Hu. Persistence and extinction in stochastic SIRS models with general nonlinear incidence rate. *Electronic Journal of Differential Equations*, **2014(42)** (2014) 1-17.

[117] L. Zhu, H. Hu. A stochastic SIR epidemic model with density dependent birth rate. *Advances in Difference Equations*, **2015(1)**, (2015) 1-12.

[118] L. Zu, D. Jiang, D. O'Regan. Stochastic Permanence, Stationary Distribution and Extinction of a Single-Species Nonlinear Diffusion System with Random Perturbation. *Abstract and Applied Analysis*, **Vol. 2014** (2014), Article ID 320460, 14 pages.