MATHEMATICAL MODELLING OF HIV/AIDS CO-INFECTION WITH TUBERCULOSIS AND PNEUMONIA INCORPORATING PROTECTION

BY

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DECLARATION

This thesis is my own work and has not been presented for a degree award in any other institution.

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To God be the glory, honour and adoration for Holy is His mighty name.

DEDICATION

To my dear husband Mr. David Muraya
To my dear children, Amazing Grace Muraya and Prince Enoch Muraya
To my loving parents Mr.& Mrs. Gilbert Nthiiri Magiri

ABSTRACT

The synergistic relationship between HIV/AIDS and respiratory infections, such as tuberculosis(TB) and pneumonia not only results in high mortality rates but is also a source of economic burden borne by many nations in the sub-saharan Africa. The search for a cure or vaccine for HIV/AIDS has yielded no conclusive results so far. Treatment failure and lack of adherence to treatment schedule which results in the evolution of drug resistant strains of diseases are challenges to grapple with in the management of diseases such as HIV/AIDS and TB. Due to global economic recession, provision and access to subsidised medication may not be sustainable in the long run. Existing HIV/AIDS - TB models do not consider protection, which may be less costly as an intervention measure. Notably, the interaction between HIV/AIDS and pneumonia which contribute to a significant number of mortality cases in HIV/AIDS, has not been mathematically explored. In this work, two deterministic models based on systems of ordinary differential equations, one on the co-infection of HIV/AIDS with TB and the second on the co-infection between HIV/AIDS and pneumonia are formulated and analyzed to investigate protection as a control strategy. Using the next generation matrix approach the reproduction numbers for the models are determined and the respective disease free equilibrium points are shown not to be globally asymptotically stable. This implies that reoccurrence of the disease is possible especially when the conditions favoring such reoccurrence are prevailing. Four cases of maximum protection are considered. In all cases, the endemic states are shown to exist provided that the reproduction number is greater than unity. By use of Routh-Hurwitz criterion and suitable Lyapunov functions, the endemic states are shown to be locally and globally asymptotically stable respectively. This implies that with maximum protection against one infection, the other disease can be controlled with intervention measures possibly resulting in minimal deaths. This is illustrated by the numerical simulations which shows that protection as a strategy reduces the disease prevalence in all the cases considered. Thus, from the findings, emphasis should be placed on advocacy for protection against infection as a strategy for reducing disease prevalence.

TABLE OF CONTENTS

List of Tables

List of Figures

CHAPTER 1

INTRODUCTION

1.1 Background Information

Human immunodeficiency virus (HIV), whose discovery dates back to 1981[46], is a virus that overtime weakens the bodys immunity. Immunity system is the body's main defence against the threat of invasion by pathogenic organisms such as bacteria and viruses[22]. HIV destroys the $CD4^+$ T cells making the body unable to fight other infections and at this level, HIV leads to Acquired immunodeficiency syndrome (AIDS). With a compromised immune system, the body is at risk of opportunistic infections (OIs) such as TB and pneumonia [30, 32, 41]. Synergistic relationship between Malaria and HIV/AIDS has also been identified[28].

Respiratory infections such as TB and pneumonia account for a significant portion of illnesses among HIV/AIDS patients, since they take advantage of the weakened immune system. The mortality and morbidity associated with these illnesses is high in populations affected by poverty, social unrest and lack of proper health infrastructure, especially in the developing world[44].

TB is an airborne respiratory bacterial disease in humans caused by *Mycobacterium tuberculosis* (*Mtb*) [4]. It is a slow dynamics disease [26] and is mostly transmitted through the air when persons with pulmonary TB cough. The risk factors of TB infection are generally prolonged close interactions with infectious individuals and immunosuppression such as in HIV/AIDS[45]. The incubation period for TB is 2 to 10 weeks. Most TB infections in children and adolescents are asymptomatic [16]. When infection causes disease, signs or symptoms include; chronic cough, weight loss, fever, growth delay, night sweats and chills. Infection is often diagnosed by a positive TB skin test result. A chest x-ray film is needed for those with a positive skin test to determine the extent of the infection and the necessary treatment. In 2003, the estimated number of new TB cases was 8.8 million with 1.7 million deaths worldwide. Approximately, 27% of the new cases and 31.5 % of the deaths arose in Africa[19]. Thus there is need for protective measures to be put in place.

TB is the leading cause of death among people infected with HIV/AIDS[30]. According to the world health organization (WHO) estimates about 33% of HIV patients worldwide are co-infected with TB and about half of HIV infected persons are expected to acquire TB[45, 49]. Unfortunately three quarters of all dually infected people live in sub-saharan Africa [43]. HIV infected individuals with latent TB are more likely to progress to active TB faster than those who are sero-negative for HIV[41]. Furthermore the risk of recurrent TB disease is high in HIV infected patients due to treatment failure[1, 17, 41]. About 88% of recurrent TB is due to re-infection with a different strain of mycobacterium tuberculosis[20]. This may easily lead to drug resistant strains of TB.

Pneumonia is a lung infection involving the lung alveoli (air sacs), caused by microbes, including bacteria, viruses, or fungi. The viruses which cause pneumonia include influenza A and B viruses; respiratory syncytial virus (RSV); and *haemophilus parainfluenza* types 1, 2 and 3. *Streptococcus pneumoniae* is the most common cause of bacterial pneumonia. *Haemophilus influenzae* type b, group A *streptococcus*, and *Mycobacterium tuberculosis* are bacteria that also cause pneumonia. Pneumonia can be transmitted when airborne microbes from an infected individual are inhaled by a susceptible individual. Generally, the symptoms of pneumonia include: cough, difficult breathing, fever, muscle aches, loss of appetite and lethargy. Pneumonia mortality in children is very high especially in the developing world, with an estimate of 5,500 deaths per day [47].

Initially, intervention for HIV/AIDS was aimed at preventing new infections through creating awareness and advocating for change of behaviour. Currently, antiretroviral therapy(ARVs) is available as a treatment measure, which help to improve the quality of life of HIV infected individual hence reducing the morbidity and mortality related to HIV/AIDS. ARVs restore the immune system by maximal suppression of viral replication[33]. Unless coupled with counselling, the administration of ARVs can be counter productive since the individuals on ARVs can continue spreading the infection. The challenge of scarce economic resources is a threat to sustained access to ARV's. Furthermore, lack of adherence to treatment schedule is a challenge among HIV/AIDS patients. The search for HIV/AIDS vaccine has yielded no results so far. Thus effective programs to reduce HIV transmission are still needed[31]. Prevention against infection seems to be the viable alternative at the moment. Prevention against HIV/AIDS may include abstinence, being faithful, use of condoms, male circumcision among others.

TB treatment involves a 4-drug regimen for a minimum of six months with multiple antibiotics and regimens shorter than six months duration are not recommended by WHO for bacteriologically unconfirmed TB[13]. Due to this long period of treatment, in some cases, patients do not adhere to the treatment schedule and this leads to treatment failure and or drug resistance to TB. Pneumonia is generally treated by use of antibiotics. However it requires that the bacteria causing the pneumonia be identified so that the right antibiotic is administered. Severe pneumonia may lead to patients being place under intensive care unit due to difficulty in breathing.

1.2 Statement of the problem

The search for a cure or vaccine for HIV/AIDS has yielded no conclusive results so far. Treatment failure and lack of adherence to treatment schedule which results in the evolution of drug resistant strains of diseases are challenges to grapple with in the management of diseases such as HIV/AIDS and TB. Due to global economic recession, provision and access to subsidised medication may not be sustainable in the long run. Existing HIV/AIDS - TB models do not consider protection, which may be less costly as an intervention measure. Notably, the interaction between HIV/AIDS and pneumonia which contribute to a significant number of mortality cases in HIV/AIDS, has not been mathematically explored.

1.3 Objectives of the study

The broad objective of this study is to develop deterministic models to study the dynamics of HIV/AIDS co-infection with TB and pneumonia in the presence of protection.

The specific objectives of this research are:

(i) To formulate co-infection models for HIV/AIDS and TB, HIV/AIDS and pneumonia incorporating protection.

(ii) To determine the long term behaviour of the solutions by analyzing the equilibrium points.

(iii) To evaluate, through simulation, the role of protection in minimizing the effects of co-infection.

1.4 Scope of the study

This study will be carried out at Maseno University, Kenya, Africa. Data for simulation will be obtained from relevant sources.

1.5 Significance of the study

The findings of the study shall provide useful insights to policy makers and healthcare providers on the design and assessment of protection as an intervention strategy. The results also contribute to the body of knowledge and research on mathematical modelling of co-infections.

1.6 Justification of the study

Respiratory infections such as TB and pneumonia account for a significant portion of illnesses among HIV/AIDS patients, since they take advantage of the weakened immune system. The mortality and morbidity associated with these illnesses is high in populations affected by poverty, social unrest and lack of proper health infrastructure, especially in the developing world. In the light of scarce resources and failure to adhere to treatment schedule, protection as a strategy of control may be more viable than treatment.

1.7 Parameter values

Symbol	Parameter description
μ	Natural death rate
$\Lambda, \chi, \varpi, \nu, \gamma$	Recruitment rates
α_1, α_2	Loss of protection
ε	Treatment rate
$\delta_T, \delta_A, \delta_P$	Death rate due to TB, HIV/AIDS and Pneumonia
$\tau, \tau_1, \tau_2, \tau_3, \tau_4$	Rate of developing disease symptoms
π, θ, β	Probability of acquiring a disease
$\iota_T, \iota_H, \chi_P, \chi_H$	Probability of success of protection
C, η, θ	Contact rate with HIV/AIDS infectives, TB and Pneumonia
$\upsilon_1, \phi_1, \upsilon_2, \kappa_1, \kappa_2, \omega, \varphi_1, \varphi_2, \omega_1, \omega_2$	Modification parameters
$\phi_2, \phi_3, \nu_1, \nu_2, \sigma, \gamma, \varrho, \kappa, \omega_3, \phi_1, \phi_2$	Modification parameters
$\lambda_T, \lambda_H, \lambda_P$	Rate of infections
$\mathbb{R}$	Set of real numbers

1.8 Model assumptions

(i) The initial population comprises of uninfected individuals

(ii) No simultaneous infection of an individual with two diseases

(iii) No dual protection

(iv) There is successful treatment of TB and pneumonia

1.9 Model limitations

(i) The models cannot be generalized

(ii) The population used is closed i.e a population in which neither immigration nor emigration occurs. It is governed by rate of birth, growth and death

CHAPTER 2

LITERATURE REVIEW

The HIV/AIDS epidemic has become a major cause of mortality and has placed high demands on the world health system and economy since its discovery in 1984. It has affected all sections of the society such as the children, youths, adults women and men. In Kenya HIV prevalence is estimated based on demographic and health survey, AIDs indicator surveys and antenatal clinic sentinel surveillance. In 2011, several heads of states and governments during a high level meeting committed themselves to redouble efforts such as universal access to HIV prevention, treatment, care and support as a critical step towards ending the global HIV epidemic, with a view to achieving Millennium Development Goal 6 and to halt and begin to reverse the spread of HIV by 2015[24].

2.1 Interactions of HIV/AIDS with tuberculosis and pneumonia

About 1/3 of 39.5 million HIV infected people worldwide are co-infected with TB and up to 50 per cent of individuals living with HIV are expected to develop TB [9, 49]. Unfortunately three quarters of all dually infected people live in sub-saharan Africa[43, 50]. The risk of developing TB after an infectious contact is estimated to be 5-15%/year in HIV-1 infected patients compared to 5-10% during life time of non HIV-1 infected patients. HIV patients with latent TB progress faster to active TB due to compromised immune system [41, 50]. Tuberculosis incidences are increasing and its treatment has increasingly become more complex and difficult in HIV-1 infected patients due to the rising incidences of multi drug resistant tuberculosis (MDR-TB)[9] often related to non adherence to therapy, severe immunodeficiency, concurrent anti-fungal therapy and diarrhea.

As HIV infection progresses, immunity declines and patients tend to become more susceptible to common or even rare infections. The presence of other infections including TB and pneumonia tend to increase the rate of HIV replication. This acceleration may result in higher levels of infection and rapid HIV progression to the AIDS stage[28].

The study[25] assessed the incidence and clinical characteristics of patients with HIV infection with concurrent pneumocystis pneumonia (PCP) and TB. A retrospective record review of HIV infected patients admitted with pulmonary TB and PCP during the same

hospital admission from 1995 to 2004 was carried out. 2651 patients with HIV infection and possible TB or PCP were identified. There were 99 cases of PCP (81 presumptive and 18 confirmed) and 35 were new cases of TB. There were 17 patients who had a new, concurrent diagnosis of pulmonary TB and PCP. Approximately half of these patients were unaware of their HIV infections. Most were men and had a $CD4^+$ T count less than $100 cells/mm^3$.

2.2 Mathematical models for HIV/AIDS, tuberculosis and pneumonia

Mathematical models give epidemiologists a powerful tool for quantitatively assessing effectiveness of control methods and uncovering mechanisms of observed infection data [34]. Some of the models proposed by various authors for describing the epidemiology as well as the epidemiological consequences of the HIV/AIDS epidemic was reviewed by[39]. Their study highlight that mathematical models have been very useful in HIV research, particularly for empirical studies on people living with HIV/AIDS(PLWHA). The enormous public health burden inflicted by TB, pneumonia and HIV/AIDS necessitates the use of mathematical modelling to gain insights into their transmission dynamics and to evaluate the control measures in place. The primary disease is HIV/AIDS and host that are already infected with HIV/AIDS become co-infected with TB and pneumonia.

A mathematical model incorporating TB treatment and the use of ART for HIV/AIDS was presented by [11]. The major challenges in the process of treatment range from non-adherence to treatment, stigma and lack of accessibility to these drugs. Unless coupled with counselling, the administration of ARVs can be counter productive since the individuals on ARVs can continue spreading the infection. The challenge of scarce economic resources is a threat to sustained access to ARV's. The search for HIV/AIDS vaccine has yielded no results so far. Thus effective preventive programs to reduce HIV/AIDS transmission are still needed.

An HIV/AIDS model incorporating complacency for the adult population was formulated by [2]. The model analysis and simulation showed that complacency resulting from dependence of HIV transmission on the number of AIDS cases in a community leads to damped periodic oscillations in the number of infective with oscillations more marked at lower rates of progression to AIDS. Their model showed that prolonged survival of

AIDS cases lowers the endemic equilibrium level which is desirable. In a way this model advocates for protection which is the opposite of complacency as a means of lowering transmission rates.

A non linear mathematical model by [14] is proposed and analysed to study the transmission of HIV/AIDS in a population of varying size with treatments and vertical transmission. Stability analysis of the model showed that an increase in the rate of vertical transmission lead to an increase in the population of infectives which in turn increased the pre-AIDS and AIDS population. Vertical transmission of HIV has been significantly reduced especially for expectant mothers attending prenatal clinics. This is because those who are found to be HIV positive are placed on ARVs. Today HIV/AIDS is largely transmitted sexually[18].

A model on the spread of HIV/AIDS amongst a population of injecting drug users was developed and analysed by [15]. A threshold parameter R_o which determines the behaviour of the model was established. This model had a unique endemic equilibrium that was found to be locally stable. This model does not consider any intervention strategy. Findings from several studies have shown that drug abuse can exacerbate HIV disease progression and prevalence[21].

A non linear mathematical model of the spread of HIV/AIDS in a population of varying size with immigration of infectives was analyzed by [42]. The findings showed that the disease was always persistent if the direct immigration of infectives was allowed in the community. In the absence of inflow of infectives the endemicity of the disease is found to be higher if pre-AIDS individuals also interacted sexually in comparison to the case when they did not take part in sexual interactions. Currently there are no laws which prohibit immigration on the basis of one's HIV/AIDS status. This really poses a challenge especially in the light of sex tourism. Consequently, protection may be the best strategy in reducing new HIV/AIDS infections.

A deterministic model that incorporates the joint dynamics of TB and HIV/AIDS has been considered by [30]. They provided general insights into the potential effects of HIV infection on TB and vice versa. Their model did not include protection and treatment though they proposed that treatment be incorporated into models of HIV/TB co-infection. Synergistic interaction between HIV and mycobacterium tuberculosis using

a deterministic model, which incorporated many of the essential biological and epidemiological features of the two diseases was addressed by [40]. In their analysis, HIV only model was shown to have a globally asymptotically stable disease -free equilibrium whenever the reproduction number was less than unity and had a unique endemic equilibrium whenever the number exceeded unity. TB only model underwent backward bifurcation, where the stable free equilibrium coexisted with a stable endemic equilibrium when the associated reproduction threshold was less than unity. Their full model, with both HIV and TB was simulated to evaluate the impact of the various treatment strategies. The study showed that the HIV only strategy saved more cases of the mixed infection than the TB only strategy and for low treatment rates, the mixed only strategy saved the least number of cases in comparison to the other strategies. However, as already pointed out, treatment has its challenges namely; non-adherence, stigma and accessibility.

An HIV/AIDS and TB co-infection model which considers antiretroviral therapy for the AIDS cases and treatment of all forms of TB was presented by [11]. This model did not incorporate protection for the two diseases. They found out that treatment of AIDS cases resulted in a significant reduction of numbers of individuals progressing to active TB and treatment of latent and active forms of TB resulted in delayed onset of the AIDS stage of HIV infection. The danger of this delay is that in the absence of counselling people do not embrace protection and may be complacent. This may accelerate HIV incidence rates.

Review and comparison of mathematical models of TB dynamics was done by [6]. They presented a spartial stochastic individual based model and a set of delay differential equations encapsulating the same biological assumptions. They compared two different assumptions about partial immunity and explored the effect of treatment. The challenges that face TB treatment range from incorrect drug prescription to non adherence among others and this can lead to treatment failure. This model does not incorporate protection against TB.

A mathematical model for the co-infection of malaria and pneumonia was developed and analyzed by [23]. Protection as a strategy against infection was not incorporate. Deterministic model for malaria and HIV-coinfection, incorporating protection against malaria and HIV positive immigrants in the community was developed by [3]. There was no disease free point, but an initial infective immigration rate existed and a small perturbation around this point approached global stability if there was reduced susceptibility to HIV

by malaria infected individuals. Also, if HIV infectives are protected against malaria, the same attains global stability. They showed that protection against both diseases altered the qualitative behaviour of solutions. Motivated by these results, we propose to investigate the effect of protection on the transmission dynamics of HIV/AIDS, tuberculosis and pneumonia in two separate co infection models.

CHAPTER 3

HIV/TB Model

3.1 Model description and formulation

We formulate a model in which total human population at any time t, denoted by $N(t)$ is subdivided into classes, $S(t)$ the class of individuals susceptible to both TB and HIV/AIDS infection, P_T, individuals who are protected against TB, This protection is lost at the rate α_1. The class L_T consists of individuals who are asymptomatically infected with TB infection. This infection occurs at the rate λ_T, i.e the rate at which the disease spread among people. In the absence of treatment, TB symptoms are developed at the rate τ_1. The class I_T comprises of individuals symptomatically infected with TB. Treatment for TB is assumed to be successful and is done at the rate ε. Thus the class T_T consists of individuals who have recovered from TB infection. Mortality occurs among active TB patients at the rate δ_T, while natural death is assumed to occur in all classes at the rate μ.

The class P_H consist of individuals who are protected against HIV/AIDS infection. This protection may be lost due to risky behaviour at the rate α_2. Since the modes of transmission for the two diseases are different we do not assume simultaneous infection of an individual with the two diseases. Furthermore, for purposes of simplicity we do not assume dual protection for TB and HIV/AIDS. The class I_H is made up of individuals who are asymptomatically infected with HIV/AIDS. This infection occurs at the rate λ_H. In the absence of intervention (therapy), individuals develop symptoms of HIV/AIDS and progress from the class I_H to the class I_A at the rate τ_2. Mortality occurs among HIV/AIDS patients at the rate δ_A.

Individuals in the class I_H can acquire TB at the rate $\upsilon_1\lambda_T$ and progress to the class I_{HL}, where υ_1 is a modification parameter. This group of individuals develop TB symptoms at the rate τ_3, where $\tau_3 > \tau_1$, and progress to the class I_{HT}. Individuals in the class I_A can also acquire TB at the rate $\upsilon_2\lambda_T$, where $\upsilon_2 > \upsilon_1$ and progress to the class I_{AL}. This group of individuals develop TB symptoms at the rate τ_4, where $\tau_4 > \tau_3$, and progress to the class I_{AT}. In the absence of intervention (therapy), individuals develop symptoms of HIV/AIDS and progress from the class I_{HT} to the class I_{AT} at the rate

$\upsilon_3\tau_2$, where υ_3 is a modification. Upon effective TB treatment, treated individuals in the class I_{AT} will move back to the class I_A. Mortality occurs due to the dual infection of HIV/AIDS and TB at the rate δ_{AT}.

Individuals in the class I_L can acquire HIV/AIDS at a rate $\kappa_1\lambda_H$ and progress to the class I_{LH} Individuals in the class I_T can acquire HIV/AIDS at a rate $\kappa_2\lambda_H$ and progress to the class I_{TH}. κ_1 and κ_1 are modification parameters and $\kappa_2 > \kappa_1$.

The total human population at any time t is defined as

$$\begin{aligned} N(t) = S(t) + P_T(t) + P_H(t) + I_H(t) + I_{HL}(t) + I_L(t) + I_T(t) + T_T(t) \\ + I_{HT}(t) + I_A(t) + I_{AL}(t) + I_{AT}(t) \end{aligned} \tag{3.1.1}$$

We define the rate at which susceptible individuals acquire TB as

$$\lambda_T = \frac{\theta\eta[\phi_1 I_T + \phi_2 I_{TH} + \phi_3 I_{AT}]}{N(t)} \tag{3.1.2}$$

where θ is the probability that a susceptible individual will acquire TB upon contact with TB infected individuals and η is the contact rate with TB infected individuals while and $\phi_3 > \phi_2 > \phi_1$ are modification parameters.

The rate at which a susceptible individual acquire HIV/AIDS is defined as

$$\lambda_H = \frac{\pi C[I_H + \gamma[I_{LH} + \sigma I_{TH}] + \omega[I_A + \nu_1[I_{AL} + \nu_2 I_{AT}]]]}{N(t)} \tag{3.1.3}$$

where π is the probability that susceptible individuals will acquire HIV upon effective contact with an HIV infected individual and C is the effective contact rate with HIV/AIDS infected individuals. This effective contact rate may include, sexual intercourse with an infected individual, blood transfusion with infected blood, sharing sharp objects with HIV/AIDS infected individuals and vertical transmission from mother to child during birth and through breastfeeding. while γ, σ, ω, ν are modification parameters.

Disease prevalence is the number of people in a population who have a disease at a given time. For HIV/AIDS, this prevalence is given by

$$\frac{[I_H + \gamma[I_{LH} + \sigma I_{TH}] + \omega[I_A + \nu_1[I_{AL} + \nu_2 I_{AT}]]]}{N(t)} \tag{3.1.4}$$

It is assumed that an individual who is asymptomatic infected with HIV/AIDS and has latent TB is more infectious of HIV/AIDS than one asymptomatically infected with HIV/AIDS. The same assumption is made for an individual actively infected with TB and is asymptomatic with HIV/AIDS. Similarly AIDS individuals are more infectious than individuals asymptomatic with HIV due to high viral load[28].

The aim is to study the effect of protection for TB and HIV/AIDS in the co-infection model. Protection against these two infections involves limiting exposure to risk factors that can lead to infection. The risk factors for HIV involves; having unprotected anal or vaginal sex, having another sexually transmitted infection such as syphilis, herpes, chlamydia, gonorrhoea and bacterial vaginosis; sharing contaminated needles, syringes and other injecting equipment and drug solutions when injecting drugs; receiving unsafe injections, blood transfusions, medical procedures that involve unsterile cutting or piercing; and experiencing accidental needle stick injuries [7]. Persons at high risk for developing TB disease fall into two categories; persons who have been recently infected with TB bacteria and persons with medical conditions that weaken the immune system.

Let ι_T and ι_H denote the probability of success of protection against TB and HIV/AIDS respectively. The modified rate of infection for TB is λ_T^p

$$\lambda_T^p = \frac{\theta\eta(1-\iota_T)[\phi_1 I_T + \phi_2 I_{TH} + \phi_3 I_{AT}]}{N(t)} \tag{3.1.5}$$

and for HIV is

$$\lambda_H^p = \frac{\pi C(1-\iota_H)[I_H + \gamma[I_{LH} + \sigma I_{TH}] + \omega[I_A + \nu_1[I_{AL} + \nu_2 I_{AT}]]]}{N(t)} \tag{3.1.6}$$

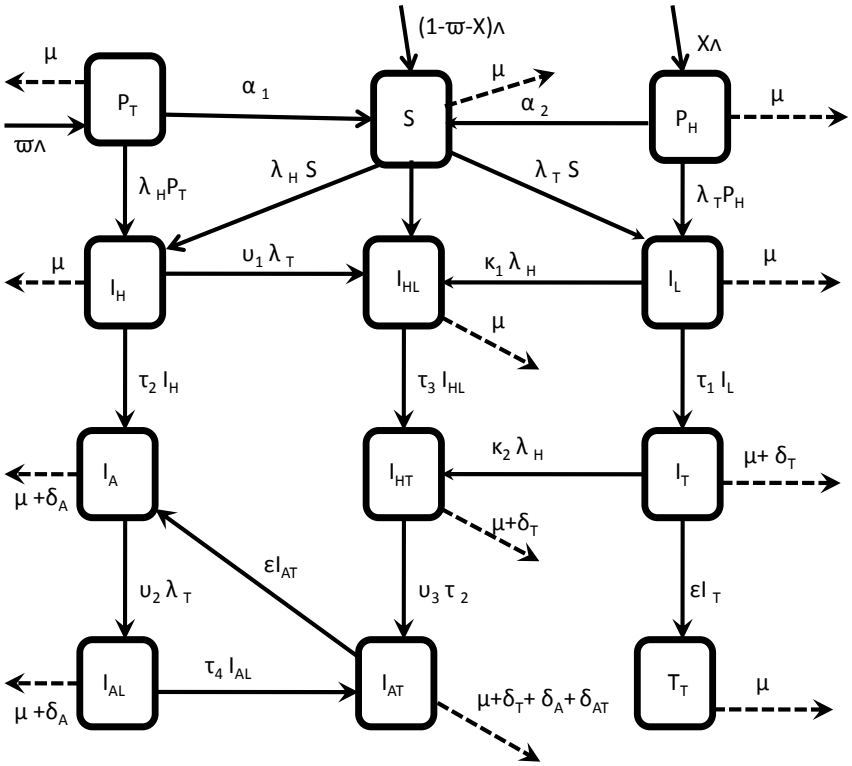

Figure 3.1.1: The flow diagram for tuberculosis and HIV/AIDS co-infection.

$$
\begin{aligned}
\frac{dS}{dt} &= (1-\varpi-\chi)\Lambda + \alpha_1 P_T + \alpha_2 P_H \\
&\quad -(\mu+\lambda_H+\lambda_T)S \\
\frac{dP_T}{dt} &= \varpi\Lambda - (\mu+\alpha_1+\lambda_H)P_T \\
\frac{dP_H}{dt} &= \chi\Lambda - (\alpha_2+\mu+\lambda_T+)P_H \\
\frac{dI_H}{dt} &= \lambda_H P_T + \lambda_H S - (\upsilon_1\lambda_T+\mu+\tau_2)I_H \\
\frac{dI_A}{dt} &= \tau_2 I_H + \varepsilon I_{AT} - (\mu+\delta_A+\upsilon_2\lambda_T)I_A \\
\frac{dI_L}{dt} &= \lambda_T P_H + \lambda_T S - (\mu+\kappa_1\lambda_H+\tau_1)I_L \\
\frac{dI_T}{dt} &= \tau_1 I_L - (\mu+\delta_T+\varepsilon+\kappa_2\lambda_H)I_T \\
\frac{dT_T}{dt} &= \varepsilon I_T - \mu T_T \\
\frac{dI_{HL}}{dt} &= \upsilon_1\lambda_T I_H + \kappa_1\lambda_H I_L - (\mu+\tau_3)I_{HL} \\
\frac{dI_{HT}}{dt} &= \kappa_2\lambda_H I_T + \tau_3 I_{HL} - (\mu+\delta_T+\upsilon_3\tau_2)I_{HT} \\
\frac{dI_{AL}}{dt} &= \upsilon_2\lambda_T I_A - (\mu+\delta_A+\tau_4)I_{AL} \\
\frac{dI_{AT}}{dt} &= \upsilon_3\tau_2 I_{HT} + \tau_4 I_{AL} - (\mu+\delta_T+\delta_A+\delta_{AT}+\varepsilon)I_{AT}
\end{aligned}
\tag{3.1.7}
$$

where $\varpi\Lambda$ is the constant recruitment rate into the class of individuals protected against TB, $\chi\Lambda$ is the constant recruitment rate into the class of individuals protected against HIV and $(1-\varpi-\chi)\Lambda$ is the constant recruitment rate into the class of susceptible individuals to both TB and HIV virus. Every individual is assumed to be susceptible to both infections. It is assumed that there is no simultaneous infection with HIV/AIDS and TB because of the different transmission routes. It is also assumed that when one is successfully treated against TB recovery does not not confer permanent immunity against TB infection.

3.2 Positivity and boundedness of solutions

Since the model deals with human population, all the state variables are positive at all time t. We show that our solutions are bounded in the set Γ where

$$\begin{aligned}\{S(t), P_H(t), P_T(t), I_H(t), I_{HL}(t), I_L(t), I_T(t), T_T(t),\\ I_{TH}(t), I_A(t), I_{AL}(t), I_{AT}(t)\} \in \Gamma \ \subset \mathbb{R}^{12}_{+}.\end{aligned} \tag{3.2.1}$$

Taking the time derivative of $N(t)$ from Equation (3.1.7), we have

$$\begin{aligned}\frac{dN(t)}{dt} &= \frac{dS}{dt}+\frac{dP_T}{dt}+\frac{dP_H}{dt}+\frac{dI_H}{dt}+\frac{dI_A}{dt}+\frac{dI_L}{dt}\\ &+\frac{dI_T}{dt}+\frac{dT_T}{dt}+\frac{dI_{HL}}{dt}+\frac{dI_{HT}}{dt}+\frac{dI_{AL}}{dt}+\frac{dI_{AT}}{dt}\\ &= \Lambda-\mu N-(\delta_T+\delta_A+\delta_{AT})I_{AT}-\delta_A I_{AL}\end{aligned} \tag{3.2.2}$$

$$\frac{dN(t)}{dt} = \Lambda-\mu N(t)-(\delta_T+\delta_A+\delta_{AT})I_{AT}-\delta_A I_{AL} \tag{3.2.3}$$

thus

$$\frac{dN(t)}{dt} \leq \Lambda-\mu N(t) \tag{3.2.4}$$

$$dN(t)+(\mu N(t)-\Lambda)dt \leq 0 \tag{3.2.5}$$

$$dN(t)e^{\mu_t}+(e^{\mu_t}\mu N(t)-e^{\mu_t}\Lambda)dt \leq 0 \tag{3.2.6}$$

Integrating we have

$$\int (N,t)dt = \int ((e^{\mu_t}\mu N(t) - e^{\mu_t}\Lambda))dt \leq 0 \tag{3.2.7}$$

$$(N,t) = e^{\mu_t}N(t) - e^{\mu_t}\frac{\Lambda}{\mu} \leq b \tag{3.2.8}$$

therefore

$$e^{\mu_t}N(t) - e^{\mu_t}\frac{\Lambda}{\mu} \leq b \tag{3.2.9}$$

at $t = 0$

$$N(t) - \frac{\Lambda}{\mu} = b \tag{3.2.10}$$

substituting b we get

$$e^{\mu_t}N(t) - e^{\mu_t}\frac{\Lambda}{\mu} = N(t) - \frac{\Lambda}{\mu} \tag{3.2.11}$$

dividing by e^{μ_t} we get

$$N(t) \leq \frac{\Lambda}{\mu} + (N(t) - \frac{\Lambda}{\mu})e^{-(\mu_t)} \tag{3.2.12}$$

as $t \to \infty$ we have

$$N(t) \leq \frac{\Lambda}{\mu} \tag{3.2.13}$$

which shows that the solutions are bounded . Having shown that our solutions are positive and bounded for all $t \geq 0$ in the region Γ, the model is well posed and biologically meaningful and may now be analyzed in the same region.

3.3 Reproduction number R_0

The basic reproduction number is the average number of secondary infections due to a single infectious individual in a fully susceptible population[38]. It is the spectral radius of a matrix

$$FV^{-1} \tag{3.3.1}$$

where F is the Jacobian of $\mathcal{F}$, where $\mathcal{F}$ is the rate of appearance of new infections in compartment and V is the Jacobian of $\mathcal{V}$, where $\mathcal{V}$ is the rate of transfer of individuals into and out of compartment. FV^{-1} is calculated by the method of next generation matrix [37]. The disease free equilibrium of Equation (3.1.7) is given by

$$E^0 = \{S, P_H, P_T, I_H, I_A, I_L, I_T, T_T, I_{HL}, I_{HT}, I_{AL}, I_{AT}\} = \\ (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0) \tag{3.3.2}$$

We define $\mathcal{F}$ as

$$\mathcal{F} = \begin{pmatrix} \lambda_H P_T + \lambda_H S \\ 0 \\ \lambda_T P_H + \lambda_T S \\ 0 \\ \upsilon_1 \lambda_T I_H + \kappa_1 \lambda_H I_L \\ \kappa_2 \lambda_H I_T \\ \upsilon_2 \lambda_T I_A \\ 0 \end{pmatrix} \tag{3.3.3}$$

We also define $\mathcal{V}$ as

$$\mathcal{V} = \mathcal{V}^- - \mathcal{V}^+ \tag{3.3.4}$$

where $\mathcal{V}^-$ is the rate of transfer of individuals out of a compartment and $\mathcal{V}^+$ is the rate of transfer of individuals into compartment. Thus $\mathcal{V}$ is given by

$$\mathcal{V} = \begin{pmatrix} (\upsilon_1 \lambda_T + \mu + \tau_2) I_H \\ -\tau_2 I_H - \varepsilon I_{AT} + (\mu + \delta_A + \upsilon_2 \lambda_T) I_A \\ (\mu + \kappa_1 \lambda_H + \tau_1) I_L \\ -\tau_1 I_L + (\mu + \delta_T + \varepsilon + \kappa_2 \lambda_H) I_T \\ (\mu + \tau_3) I_{HL} \\ -\tau_3 I_{HL} + (\mu + \delta_T + \upsilon_3 \tau_2) I_{HT} \\ (\mu + \delta_A + \tau_4) I_{AL} \\ -\upsilon_3 \tau_2 I_{HT} - \tau_4 I_{AL} + (\mu + \delta_T + \delta_A + \delta_{AT} + \varepsilon) I_{AT} \end{pmatrix} \tag{3.3.5}$$

The Jacobian of $\mathcal{F}$ at the disease free equilibrium denoted as F is given by

$$F = \begin{pmatrix} \vartheta_1 & \vartheta_2 & 0 & 0 & \vartheta_3 & \vartheta_4 & \vartheta_5 & \vartheta_6 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \vartheta_7 & 0 & \vartheta_8 & 0 & \vartheta_9 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{3.3.6}$$

where $\vartheta_1 = \pi c(1-\iota_H), \vartheta_2 = \pi c(1-\iota_H)\omega, \vartheta_3 = \pi C(1-\iota_H)\gamma, \vartheta_4 = \pi C(1-\iota_H)\gamma\sigma, \vartheta_5 = \pi C(1-\iota_H)\omega\nu_1, \vartheta_6 = \pi C(1-\iota_H)\omega\nu_2, \vartheta_7 = \theta\eta(1-\iota_T)\Omega, \vartheta_8 = \theta\eta(1-\iota_T)\Omega\phi_2, \vartheta_9 = \theta\eta(1-\iota_T)\Omega\phi_4$. Similarly, the Jacobian of $\mathcal{V}$ at the disease free equilibrium is denoted by V and is given by

$$V = \begin{pmatrix} \varphi_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -\tau_2 & \varphi_2 & 0 & 0 & 0 & 0 & 0 & -\varepsilon \\ 0 & 0 & \varphi_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\tau_1 & \varphi_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \varphi_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\tau_3 & \varphi_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \varphi_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & \upsilon_3\tau_2 & \tau_4 & \varphi_8 \end{pmatrix} \tag{3.3.7}$$

Where $\varphi_1{=}\mu+\tau_2$, $\varphi_2{=}\mu+\delta_A$, $\varphi_3{=}\mu+\tau_1$, $\varphi_4{=}\mu+\delta_T+\varepsilon$, $\varphi_5{=}\mu+\tau_3$, $\varphi_6{=}\mu+\upsilon_3\tau_2+\delta_T$, $\varphi_7{=}\mu+\delta_A+\tau_4$ and $\varphi_8{=}\mu+\delta_A+\delta_T+\delta_{AT}+\varepsilon$ Thus the eigenvalues of the matrix FV^{-1} are $R_T = \frac{\theta\eta(1-\iota_T)\tau_1\phi_1}{(\tau_1+\mu)(\delta_T+\mu+\varepsilon)}$ and $R_H = \frac{\pi C(1-\iota_H)(\tau_1\omega+\delta_A+\mu)}{(\delta_A+\mu)(\mu+\tau_2)}$. The spectral radius of FV^{-1} is $max\{R_T, R_H\}$. Therefore, the effective reproduction number of model (2.1.7) is denoted as R_{HT} and is defined as $R_0 = max\{R_T, R_H\}$.

The reproduction number R_T gives the expected number of secondary TB infection produced by a single TB infectious individual during his/her infectious period when introduced into a completely TB susceptible population. Similarly, the reproduction number R_H gives the expected number of secondary HIV/AIDS infection produced by a single HIV/AIDS infectious individual during his/her infectious period when introduced into a completely HIV/AIDS susceptible population. Since Equation (3.1.7) satisfy conditions $A1-A5$ [48],then the disease free equilibrium $E^0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0)$ is locally asymptotically stable if $R_{HT} < 1$ and unstable if $R_{HT} > 1$. In the absence of protection

$\iota_T = \iota_H = 0$, implying that the probability of success of protection is considered to be zero.

3.4 Global stability for the disease free equilibrium

For global stability of the DFE, the technique by [5] is used. There are two conditions that if met guarantee the global asymptotic stability of the disease free state. Equation (3.1.7) may be written in the form

$$\begin{aligned} \frac{dX}{dt} &= K(X,Z) \\ \frac{dZ}{dt} &= G(X,Z), G(X,0) = 0 \end{aligned} \tag{3.4.1}$$

where $X \in \mathbb{R}^4$ and $X = \{S, P_T, P_H, T_T\}$ denotes the number of uninfected individuals and $Z \in \mathbb{R}^8$ where $Z = \{I_H, I_A, I_L, I_T, I_{HL}, I_{HT}, I_{AL}, I_{AT}\}$ denotes the number of infected individuals . $E^O = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0)$ denotes the disease free equilibrium point of this system where

$$X^* = (\frac{\Lambda}{\mu})$$

conditions (2.4.2) may be met to guarantee global asymptotic stability

$$\begin{aligned} \frac{dX}{dt} &= K(X,0), X^* \text{is globally asymptotic stable} \\ G(X,Z) &= AZ - \widehat{G}(X,Z), \widehat{G}(X,Z) \geq 0 \forall (X,Z) \in \Gamma \end{aligned} \tag{3.4.2}$$

where $A = D_z G(X^*, 0)$ is an M matrix and Γ is the region where the model has biological meaning.

Theorem
If system (3.4.1) satisfies conditions (3.4.2), then the fixed point

$$E^0 = (X^*, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,)$$

is a globally asymptotically stable equilibrium of the system (3.4.1) provided that $R_{HT} < 1$ and the assumptions in (3.4.2) are satisfied .

Proof

Consider $K(X,0) = (\Lambda - \mu S)$ and $G(X,Z) = AZ - \widehat{G}(X,Z)$ where

$$A = \begin{pmatrix} -h_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ \tau_2 & -h_2 & 0 & 0 & 0 & 0 & 0 & \varepsilon \\ 0 & 0 & -h_3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \tau_1 & -h_4 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -h_5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \tau_3 & -h_6 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -h_7 & 0 \\ 0 & 0 & 0 & 0 & 0 & \upsilon_3\tau_2 & \tau_4 & -h_8 \end{pmatrix} \tag{3.4.3}$$

where $h_1 = \mu+\tau_2$, $h_2 = \mu+\delta_A$, $h_3 = \mu+\tau_1$,$h_4 = \mu+\delta_T+\varepsilon$,$h_5 = \mu+\tau_3$, $h_6 = \mu+\delta_T+\nu_3\tau_2$, $h_7 = \mu + \delta_A + \tau_4$, $h_8 = \mu + \delta_T + \delta_A + \delta_{AT} + \varepsilon$

and

$$\hat{G}(X,Z) = \begin{pmatrix} G_1 \\ G_2 \\ G_3 \\ G_4 \\ G_5 \\ G_6 \\ G_7 \\ G_8 \end{pmatrix} = \begin{pmatrix} -\lambda_H(P_T + S) + \upsilon_1\lambda_T \\ +\upsilon_2\lambda_T \\ -\lambda_T(P_H + S) + \kappa_1\lambda_H \\ \kappa_2\lambda_H \\ -(\upsilon_1\lambda_T + \kappa_1\lambda_H) \\ -(\kappa_2\lambda_H) \\ -(\upsilon_2\lambda_T) \\ 0 \end{pmatrix} \tag{3.4.4}$$

Since all the conditions in Equation (3.4.2) are not satisfied because $G_5, G_6, G_7 < 0$, the DFE E^0 may not be globally asymptotically stable, implying that we anticipate an outbreak when particular conditions which favour the outbreak of the disease are prevailing.

3.4.1 The case of maximum protection against TB

Suppose that there are no new TB infections and the only infection that spread in the population is that of HIV/AIDS. This can be achieved by ensuring that the probability of success of protection is high and can be considered as $\iota_T = 1$. Thus Equation (3.1.7)

will be reduced to

$$\begin{aligned}
\frac{dS}{dt} &= (1-\chi-\varpi)\Lambda + \alpha_2 P_H - (\mu+\lambda_H)S \\
\frac{dP_H}{dt} &= \chi\Lambda - (\alpha_2+\mu)P_H \\
\frac{dP_T}{dt} &= \varpi\Lambda - (\mu+\lambda_H)P_T \\
\frac{dI_H}{dt} &= \lambda_H(S+P_T) - (\mu+\tau_2)I_H \\
\frac{dI_A}{dt} &= \tau_2 I_H - (\mu+\delta_A)I_A
\end{aligned} \tag{3.4.5}$$

The rate of infection for Equation (3.4.5) is defined as

$$\lambda_H^h = \frac{\pi C(1-\iota_H)(I_H+\omega I_A)}{N(t)} \tag{3.4.6}$$

with the effective reproduction number

$$R_H = \frac{\pi C(1-\iota_H)(\delta_A+\mu+\omega\tau_2)(\mu(1-\chi)+\alpha_2)}{(\delta_A+\mu)(\mu+\tau_2)(\mu+\alpha_2)}. \tag{3.4.7}$$

An endemic state $I_H^* > 0$ where

$$I_H^* = \frac{\Lambda(R_H-1)(\delta_A+\mu)}{(C\pi)(1-\iota_H)(\delta_A+\mu+\omega\tau_2)-\delta_A\tau_2} \tag{3.4.8}$$

exists provided $R_H > 1$ with $\pi C < \pi C\iota_H + \tau_2$ since $(1-\iota_H) > 0$

3.4.2 Local stability of the endemic equilibrium

The first four equations in Equation (3.4.5) do not contain the class I_A, and so we can analyze the reduced system

$$\begin{aligned}
\frac{dS}{dt} &= (1-\chi-\varpi)\Lambda + \alpha_2 P_H - (\mu+\lambda_H^h)S \\
\frac{dP_H}{dt} &= \chi\Lambda - (\alpha_2+\mu)P_H \\
\frac{dP_T}{dt} &= \varpi\Lambda - (\mu+\lambda_H^h)P_T \\
\frac{dI_H}{dt} &= \lambda_H^h(S+P_T) - (\mu+\tau_2)I_H
\end{aligned} \tag{3.4.9}$$

The Jacobian matrix of equation (3.4.9) at $E^*(S^*, P_H^*, P_T^* I_H^*)$, denoted as $J(E^*)$ is given by

$$J(E^*) = \begin{pmatrix} -(\mu + \lambda_H^h) & \alpha_2 & 0 & \frac{-\beta C(1-\iota_H)S^*}{N(t)} \\ 0 & -(\alpha_2 + \mu) & 0 & 0 \\ 0 & 0 & -(\mu + \lambda_H^h) & \frac{-\beta C(1-\iota_H)P_T^*}{N(t)} \\ \lambda_H^h & 0 & \lambda_H^h & -(\mu + \tau_2) \end{pmatrix} \tag{3.4.10}$$

Clearly $-(\mu+\alpha_2)$ is an eigenvalue of Equation (3.4.10). The other eigenvalues are obtained from the reduced matrix B where

$$B = \begin{pmatrix} -(\mu + \lambda_H^h) & 0 & \frac{-\beta C(1-\iota_H)S^*}{N(t)} \\ 0 & -(\mu + \lambda_H^h) & \frac{-\beta C(1-\iota_H)P_T^*}{N(t)} \\ \lambda_H^h & \lambda_H^h & -(\mu + \tau_2) \end{pmatrix} \tag{3.4.11}$$

An important creterion by Routh-Hurwitz gives the necessary and sufficient conditions for all the roots of the characteristic polynomial (with real coefficients) to lie in the left half of the complex plane. In other words, all the roots of the polynomial are negative or have negative real roots iff the determinants of all Hurwitz matrices are positive [52].

Clearly, the trace of Equation (3.4.11) is negative and the determinant of Equation (3.4.11) is given by

$$\begin{aligned} detB = [\frac{I_H^*(1-\iota_H)\eta\theta}{N(t)} + \mu][\frac{I_H^*(1-\iota_H)(S^* - P_T^*)\eta\theta}{N^2(t)} \\ (I_H^*(\mu+\tau) - (1-\iota_H)\eta\theta + \mu + \tau) - \mu(\mu+\tau)] \end{aligned} \tag{3.4.12}$$

$detB > 0$ provided that

$$[\frac{I_H^*(1-\iota_H)(S^* - P_T^*)\eta\theta}{N^2(t)}(I_H^*(\mu+\tau) - (1-\iota_H)\eta\theta + \mu + \tau) \geq (\mu(\mu+\tau)) \tag{3.4.13}$$

Thus, by Routh-Hurwitz creteria, the endemic state $E^*(S^*, P_H^*, P_T^* I_H^*)$ is locally asymptotically stable provided that inequality (3.4.13) holds.

3.4.3 Global stability of the endemic equilibrium

We obtain the global stability by means of Lyapunov's direct method and LaSalle's invariance principle[12]. For Equation (3.4.5), consider the Lyapunov function

$$L : (S, P_H, P_T, I_H, I_A) \in \Gamma \subset \mathbb{R}^5_+ : S, P_H, P_T, I_H, I_A > 0 \tag{3.4.14}$$

where

$$\begin{aligned} L : (S, P_H, P_T, I_H, I_A) = \lambda^h_H(S - S^* - S^* \log \frac{S}{S^*}) + \lambda^h_H(P_H - P^*_H - P^*_H \log \frac{P_H}{P^*_H}) + \\ \lambda^h_H(P_T - P^*_T - P^*_T \log \frac{P_T}{P^*_T}) + \lambda^h_H(I_H - I^*_H - I^*_H \log \frac{I_H}{I^*_H}) + \\ \lambda^h_H(I_A - I^*_A - I^*_A \log \frac{I_A}{I^*_A}) \end{aligned} \tag{3.4.15}$$

L is C^1 in the interior of Γ. E^* is the global minimum of L on Γ and $L : (S, P_H, P_T, I_H, I_A) = 0$. The time derivative of L is given by

$$\begin{aligned} \frac{dL}{dt} = \dot{L} = \lambda^h_H(1 - \frac{S^*}{S})\frac{dS}{dt} + \lambda^h_H(1 - \frac{P^*_H}{P_H})\frac{dP_H}{dt} + \lambda^h_H(1 - \frac{P^*_T}{P_T})\frac{dP_T}{dt} + \\ \lambda^h_H(1 - \frac{I^*_H}{I_H})\frac{dI_H}{dt} + \lambda^h_H(1 - \frac{I^*_A}{I_A})\frac{dI_A}{dt} \\ = -\lambda^h_H(\frac{S - S^*}{S})[(\mu + \lambda^h_H)(S - S^*) + \alpha_2(P_H - P^*_H)] \\ -\lambda^h_H(\frac{P_H - P^*_H}{P_H})[(\alpha_2 + \mu)(P_H - P^*_H)] - \lambda^h_H(\frac{P_T - P^*_T}{P_T})[(\mu + \lambda^h_H)(P_T - P^*_T)] \\ -\lambda^h_H(\frac{I_H - I^*_H}{I_H})[(\mu + \tau_2)(I_H - I^*_H)] - \lambda^h_H(\frac{I_A - I^*_A}{I_A})[(\mu + \delta_A)(I_A - I^*_A)] \end{aligned} \tag{3.4.16}$$

hence $\dot{L} \leq 0$ is negative . We see that $\dot{L} = 0$ at E^*. Thus $\dot{L}$ is negative definite and the largest compact invariant set in $\{S, P_H, P_T, I_H, I_A\} \in \Gamma : \dot{L} = 0$ is the Singlet on E^*, where E^* is the endemic equilibrium. Thus E^* is globally asymptotically stable in the interior of Γ. Mathematically, we have shown that protection produces desired results in terms of disease intervention. Therefore, at this point, we see the positive impact protection against one disease has on the dynamics of the other disease.

3.4.4 Case of maximum protection against HIV/AIDS

Assuming that there is no new HIV/AIDS infections in the TB and HIV/AIDS co-infection model, the resulting model will be

$$\begin{aligned}
\frac{dS}{dt} &= (1-\varpi-\chi)\Lambda + \alpha_1 P_T - (\mu+\lambda_T)S \\
\frac{dP_T}{dt} &= \varpi\Lambda - (\mu+\alpha_1)P_T \\
\frac{dP_H}{dt} &= \chi\Lambda - (\mu+\lambda_T)P_H \\
\frac{dI_L}{dt} &= \lambda_T(S+P_H) - (\mu+\tau_1)I_L \\
\frac{dI_T}{dt} &= \tau_1 I_L - (\mu+\delta_T+\varepsilon)I_T \\
\frac{dT_T}{dt} &= \varepsilon I_T - \mu T_T
\end{aligned} \tag{3.4.17}$$

The rate of infection for Equation (3.4.17) is

$$\lambda_T^t = \frac{\theta\eta(1-\iota_T)I_T}{N(t)} \tag{3.4.18}$$

and the effective reproduction number is given by

$$R_T = \frac{\theta\eta(1-\iota_T)(\mu(1-\varpi)+\alpha_1)}{(\delta_T+\mu+\varepsilon)(\mu+\tau_1)(\mu+\alpha_1)} \tag{3.4.19}$$

An endemic state $I_L^* > 0$ where

$$I_L^* = \frac{\Lambda(\delta_A+\varepsilon+\mu)(R_T-1)}{(\eta\theta\tau_1)(1-\iota_T)} \tag{3.4.20}$$

exist provided that $R_T > 1$ with $(1-\iota_T) > 0$.

3.4.5 Local stability of the endemic equilibrium

Since the first five equations of Equation (3.4.17) are independent of T_T, we analyze the reduced system

$$\begin{aligned}
\frac{dS}{dt} &= (1-\varpi-\chi)\Lambda + \alpha_1 P_T - (\mu+\lambda_T^t)S \\
\frac{dP_T}{dt} &= \varpi\Lambda - (\mu+\alpha_1)P_T \\
\frac{dP_H}{dt} &= \chi\Lambda - (\mu+\lambda_T^t)P_H \\
\frac{dI_L}{dt} &= \lambda_T^t(S+P_H) - (\mu+\tau_1)I_L \\
\frac{dI_T}{dt} &= \tau_1 I_L - (\mu+\delta_T+\varepsilon)I_T
\end{aligned} \tag{3.4.21}$$

The Jacobian of Equation(3.4.21) at the endemic state $E^*(S^*, P_H^*, P_T^*, I_L^*, I_T^*)$ is given by

$$J(E^*) = \begin{pmatrix}
-(\mu+\lambda_T^t) & \alpha_1 & 0 & 0 & \frac{-\theta\eta S^*(1-\iota_T)}{N(t)} \\
0 & -(\mu+\alpha_1) & 0 & 0 & 0 \\
0 & 0 & -(\mu+\lambda_T^t) & 0 & \frac{-\theta\eta P_H^*(1-\iota_T)}{N(t)} \\
\lambda_T^t & 0 & \lambda_T^t & -(\mu+\tau_1) & 0 \\
0 & 0 & 0 & \tau_1 & -(\mu+\delta_T+\varepsilon)
\end{pmatrix} \tag{3.4.22}$$

Since $-(\mu+\alpha_1)$ is an eigenvalue of Equation (3.5.22). Next we consider the reduced matrix

$$B_1 = \begin{pmatrix}
-(\mu+\lambda_T^t) & 0 & 0 & \frac{-\theta\eta S^*(1-\iota_T)}{N(t)} \\
0 & -(\mu+\lambda_T^t) & 0 & \frac{-\theta\eta P_H^*(1-\iota_T)}{N(t)} \\
\lambda_T^t & \lambda_T^t & -(\mu+\tau_1) & 0 \\
0 & 0 & \tau_1 & -(\mu+\delta_T+\varepsilon)
\end{pmatrix} \tag{3.4.23}$$

The trace of Equation (3.4.23) is negative and the determinant is given by

$$\begin{aligned}
detB_1 = \frac{1}{N(t)}\{[I_T^*(1-\iota_T)\theta\eta + N\mu] \\
(I_T^*)^2(1+P_H^*)(1-\iota_T)^3\theta^3\eta^3 + (N(t))^2[(I_T^*)^2(1-\iota_T)\theta\eta + N(t)\mu](\mu+\delta_T+\varepsilon)(\mu+\tau_1)\}
\end{aligned} \tag{3.4.24}$$

Which is positive since $(1-\iota_T) > 0$. Thus, the endemic state $E^*(S^*, P_H^*, P_T^*, I_L^*, I_T^*)$ is locally asymptotically stable.

3.4.6 Global stability of the endemic equilibrium

Consider the non-linear Lyapunov function

$$L_e : (S, P_H, P_T, I_L, I_T, T_T) \in \Gamma \subset \mathbb{R}^6_+ : S, P_H, P_T, I_L, I_T, T_T > 0 \tag{3.4.25}$$

defined as

$$\begin{aligned} L_e : (S, P_H, P_T, I_L, I_T, T_T) = \lambda^t_T(S - S^* - S^* \log \frac{S}{S^*}) \\ +\lambda^t_T(P_H - P^*_H - P^*_H \log \frac{P_H}{P^*_H}) + \lambda^t_T(P_T - P^*_T - P^*_T \log \frac{P_T}{P^*_T}) + \lambda^t_T(I_L - I^*_L - I^*_L \log \frac{I_L}{I^*_L}) + \\ \lambda^t_T(I_T - I^*_T - I^*_T \log \frac{I_T}{I^*_T}) + \lambda^t_T(T_T - T^*_T - T^*_T \log \frac{T_T}{T^*_T}) \end{aligned} \tag{3.4.26}$$

where L_e is C^1 in the interior of Γ. E^* is the global minimum of L_e on Γ and $L_e : (S, P_H, P_T, I_L, I_T, T_T) = 0$. The time derivative of L_e is given by

$$\begin{aligned} \frac{dL_e}{dt} = \dot{L}_e = \lambda^t_T(1 - \frac{S^*}{S})\frac{dS}{dt} + \lambda^t_T(1 - \frac{P^*_H}{P_H})\frac{dP_H}{dt} + \lambda^t_T(1 - \frac{P^*_T}{P_T})\frac{dP_T}{dt} + \\ \lambda^t_T(1 - \frac{I^*_L}{I_L})\frac{dI_L}{dt} + \lambda^t_T(1 - \frac{I^*_T}{I_T})\frac{dI_T}{dt} + \lambda^t_T(1 - \frac{T^*_T}{T_T})\frac{dT_T}{dt} \\ = -\lambda^t_T(\frac{S - S^*}{S})[(\mu + \lambda^t_T)(S - S^*) + \alpha_1(P_T - P^*_T)] \\ -\lambda^t_T(\frac{P_T - P^*_T}{P_T})[(\alpha_1 + \mu)(P_T - P^*_T)] - \lambda^t_T(\frac{P_H - P^*_H}{P_H})[(\mu + \lambda^t_T)(P_H - P^*_H)] \\ -\lambda^t_T(\frac{I_L - I^*_L}{I_L})[(\mu + \tau_1)(I_L - I^*_L)] \\ -\lambda^t_T(\frac{I_T - I^*_T}{I_T})[(\mu + \delta_T + \varepsilon)(I_T - I^*_T)] - \lambda^t_T(\frac{T_T - T^*_T}{T_T})[\mu(T_T - T^*_T)] \end{aligned} \tag{3.4.27}$$

hence $\dot{L}_e < 0$. We see that $\dot{L}_e = 0$ iff $S = S^*, P_H = P^*_H, P_T - P^*_T, I_L = I^*_L, I_T = I^*_T \text{and} T_T = T^*_T$. Thus the largest compact invariant set in $\{S, P_H, P_T, I_L, I_T, T_T\} \in \Gamma : \dot{L}_e = 0$ is the Singlet on E^*, where E^* is the endemic equilibrium. Thus E^* is globally asymptotically stable in the interior of Γ.

3.4.7 Numerical simulations

Numerical simulations are carried out to graphically illustrate the effect of protection on the dynamics of infection.

Table 3.1: Parameter values used in simulation of HIV/AIDS and tuberculosis model

Parameter description	**Symbol**	**Value**	**Source**
Natural death rate	μ	$7.0 \times 10^{-3} days^{-1}$	[8]
Recruitment rate	Λ	$8.7 \times 10^{-3} days^{-1}$	[8]
Rate of recruitment into HIV protected class	χ	6.7×10^{-3}	Estimated
Rate of recruitment into TB protected class	ϖ	1.2×10^{-3}	Estimated
Loss of protection against HIV/AIDS	α_2	1.0×10^{-4}	Estimated
Death due to HIV/AIDS	δ_A	$2.3 \times 10^{-4} days^{-1}$	[29]
Rate of progression to AIDS stage	τ_2	$1.25 \times 10^{-1} days^{-1}$	[36]
Probability of acquiring HIV/AIDS	π	$1.1 \times 10^{-10} days^{-1}$	[10]
Probability of success of protection against HIV/AIDS	ι_H	9.0×10^{-1}	Estimated
Contact rate with HIV/AIDS infectives	C	8.0×10^{-2}	Estimated
Loss of protection against TB	α_1	0.1×10^{-3}	Estimated
Death due to TB	δ_T	$3.95 \times 10^{-1} days^{-1}$	[30]
Rate of progression to symptomatic TB	τ_1	$5.0 \times 10^{-1} days^{-1}$	[27]
Probability of acquiring TB	θ	1.1×10^{-4}	Estimated
Probability of success of protection against TB	ι_T	9.0×10^{-1}	Estimated
Contact rate with TB infectives	η	2.0×10^{-4}	Estimated

3.4.7.1 The effect of varying the protection term on HIV/AIDS infections

Numerical simulations were carried out to investigate the effect of protection on HIV/AIDS and TB prevalence. The following graphs were obtained for a given set on initial conditions and parameter values in table 3.1

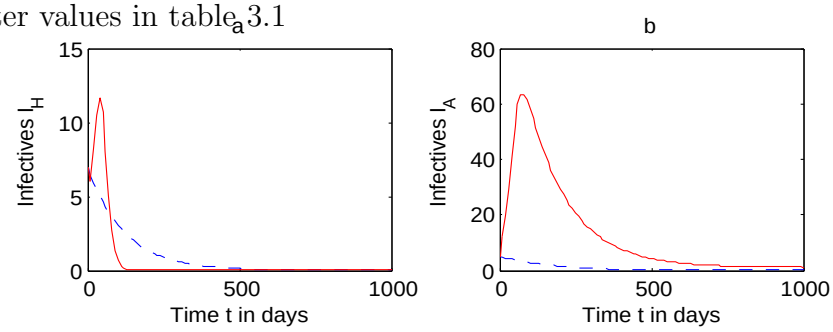

Figure 3.4.1: Simulation of model showing the evolution of HIV/AIDS against time

time; red Continuous line: $\pi = 1.1 \times 10^{-2}, \iota_H = 1.0 \times 10^{-4}$
blue dotted line: $\pi = 1.1 \times 10^{-10}, \iota_H = 9.0 \times 10^{-1}$

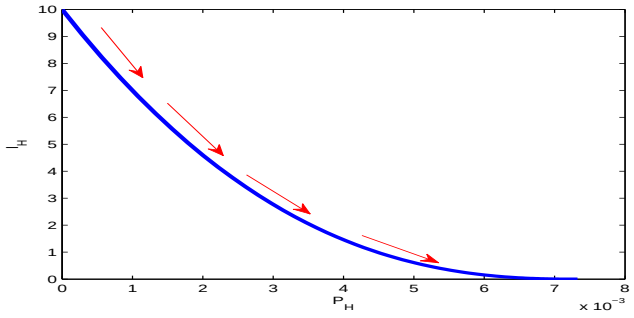

Figure 3.4.2: The graph of I_H against P_H

3.4.7.2 The effect of varying the protection term on TB infection

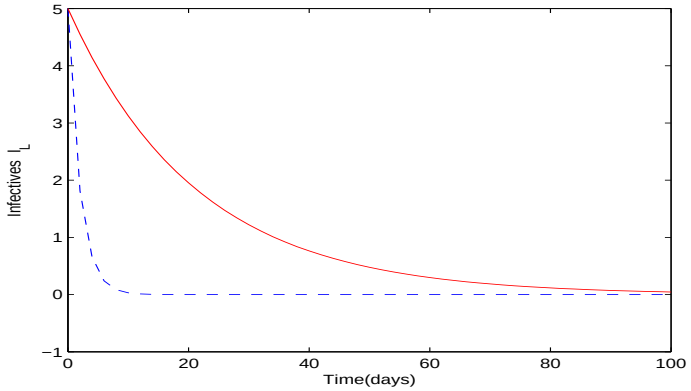

Figure 3.4.3: Evolution of TB against time

time; red Continuous line: $\theta = 1.1 \times 10^{-2}, \iota_T = 4.0 \times 10^{-1}$
blue dotted line: $\theta = 1.1 \times 10^{-4}, \iota_T = 9.0 \times 10^{-1}$

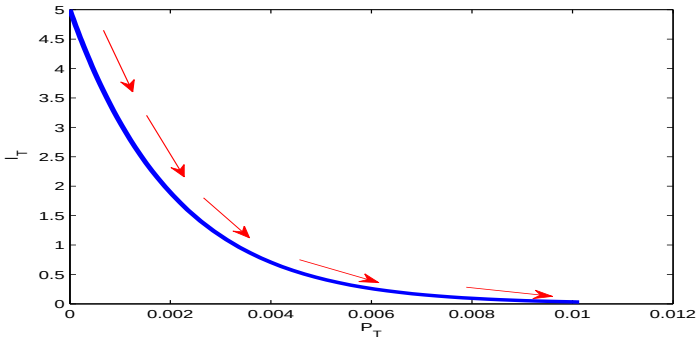

Figure 3.4.4: The graph of I_T against P_T

CHAPTER 4

HIV/Pneumonia model

4.1 Model description and formulation

We formulate a model in which the total human population at any time t denoted by $N(t)$, is subdivide into subclasses, $S(t)$ the class of individuals susceptible to both pneumonia and HIV/AIDS infection, P_P, individuals who are protected against pneumonia. The protection is lost at the rate α_1. The class I_P consists of individuals who are infected with pneumonia at a rate λ_P. Treatment for pneumonia is assumed to be successful and is done at the rate ε. The class T_P consists of individuals who have recovered from pneumonia infection. Mortality occurs among pneumonia patients at the rate δ_P, while natural death is assumed to occur in all classes at the rate μ.

The class P_H consist of individuals who are protected against HIV/AIDS infection. For various forms of protection against HIV/AIDS, see for instance[51, 46]. This protection may be lost due to risky behaviour at the rate α_2. Since the modes of transmission for the two diseases are different and also for purposes of simplicity we do not assume dual protection for pneumonia and HIV/AIDS. The class I_H is made up of individuals who are asymptomatically infected with HIV/AIDS. This infection occurs at the rate λ_H. In the absence of intervention (therapy), individuals develop symptoms of HIV/AIDS and progress from the class I_H to the class I_A at the rate τ. Mortality occurs among HIV/AIDS patients at the rate δ_A.

Individuals in the class I_H can acquire pneumonia at the rate $\varphi_1\lambda_P$ and progress to the class I_{HP}, where φ_1 is a modification parameter accounting for the fact that individuals who have HIV virus are more susceptible to pneumonia infection than HIV negative individuals due to immunosuppression. Individuals in the class I_A can also acquire pneumonia at the rate $\varphi_2\lambda_P$, where $\varphi_2 > \varphi_1$ and progress to the class I_{AP}. In the absence of intervention (therapy), individuals in the class I_{HP} develop symptoms of HIV/AIDS and progress to the class I_{AP} at the rate $\varrho\tau$, where ϱ is a modification parameter. Upon effective pneumonia treatment, individuals in the class I_{HP} and I_{AP} move to the classes I_H and I_A respectively. Mortality occurs due to the dual infection of HIV/AIDS and pneumonia at a rate δ_{AP}.

Individuals in the class I_P can acquire HIV/AIDS at a rate $\kappa\lambda_H$ and progress to the class I_{HP} where $0 < \kappa < 1$ is a modification parameter accounting for the fact that individuals infected with pneumonia, due to morbidity have reduced activity and are less susceptible.

The total population

$$N(t) = S(t) + P_P(t) + P_H(t) + I_H(t) + I_{HP}(t) + I_P(t) + T_P(t) + I_A(t) + I_{AP}(t) \tag{4.1.1}$$

We define the rate at which susceptible individuals acquire pneumonia as

$$\lambda_P = \frac{\pi\theta[I_P + \phi_1 I_{HP} + \phi_2 I_{AP}]}{N(t)}, \tag{4.1.2}$$

where π is the probability that one will acquire pneumonia upon contact with pneumonia infected individuals and θ is the contact rate with pneumonia infected individuals while $\phi_2 > \phi_1$ are modification parameters accounting for the assumed increased infectivity due to dual infection.

The rate at which susceptible individuals acquire HIV/AIDS is defined as

$$\lambda_H = \frac{\beta C[I_H + \omega_1 I_{HP} + \omega_2 I_A + \omega_3 I_{AP}]}{N(t)}, \tag{4.1.3}$$

where β is the probability that susceptible individuals acquire HIV upon contact with an HIV infected individual and C is the effective contact rate with HIV/AIDS infected individuals. $\omega_3 > \omega_2 > \omega_1$, are modification parameters showing the infectious rate per class.with the assumption that an individual who is asymptomatic with HIV/AIDS and has pneumonia is more infectious of HIV/AIDS than one asymptomatically infected with HIV/AIDS. Similarly AIDS individuals are more infectious than individuals asymptomatic with HIV/AIDS due to high viral load[28].

HIV/AIDS prevalence denoted by Φ will be

$$\Phi = \frac{\lambda_H}{\beta C}. \tag{4.1.4}$$

This study seeks to investigate the effect of protection for HIV/AIDS and pneumonia in the co-infection model. Let χ_P and χ_H denote the probability of success of protection

against pneumonia and HIV/AIDS respectively. The modified rates of infection λ_P^r and λ_H^p become

$$\lambda_P^r = \lambda_P(1 - \chi_P) \tag{4.1.5}$$

and

$$\lambda_H^p = \lambda_H(1 - \chi_H) \tag{4.1.6}$$

From the above definitions, the resulting flow diagram for the co-infection is given below.

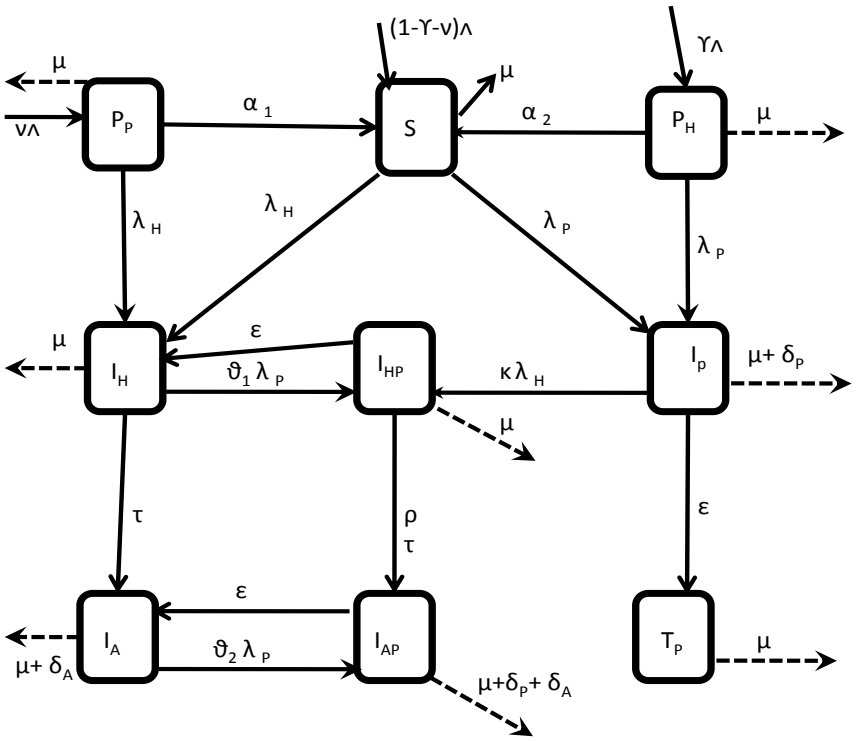

Figure 4.1.1: The flow diagram for the pneumonia and HIV/AIDS co-infection.

$$
\begin{aligned}
\frac{dS}{dt} &= (1-\nu-\gamma)\Lambda + \alpha_1 P_P + \alpha_2 P_H - (\mu + \lambda_H + \lambda_P)S \\
\frac{dP_P}{dt} &= \nu\Lambda - (\mu + \alpha_1 + \lambda_H)P_P \\
\frac{dP_H}{dt} &= \gamma\Lambda - (\alpha_2 + \mu + \lambda_P)P_H \\
\frac{dI_H}{dt} &= \lambda_H P_P + \lambda_H S + \varepsilon I_{HP} - (\varphi_1\lambda_P + \mu + \tau)I_H \\
\frac{dI_A}{dt} &= \tau I_H + \varepsilon I_{AP} - (\mu + \delta_A + \varphi_2\lambda_P)I_A \\
\frac{dI_P}{dt} &= \lambda_P P_H + \lambda_P S - (\mu + \kappa\lambda_H + \varepsilon + \delta_P)I_P \\
\frac{dT_P}{dt} &= \varepsilon I_P - \mu T_P \\
\frac{dI_{HP}}{dt} &= \varphi_1\lambda_P I_H + \kappa\lambda_H I_P - (\mu + \varrho + \delta_P + \varepsilon)I_{HP} \\
\frac{dI_{AP}}{dt} &= \varrho\tau I_{HP} + \varphi_2\lambda_P I_A - (\mu + \delta_A + \delta_P + \delta_{AP} + \varepsilon)I_{AP}
\end{aligned} \tag{4.1.7}
$$

where $\nu\Lambda$ is the constant recruitment rate into the class of individuals protected against pneumonia, $\gamma\Lambda$ is the constant recruitment rate into the class of individuals protected against HIV and $(1-\nu-\gamma)\Lambda$ is the constant recruitment rate into the class of susceptible individuals to both pneumonia and HIV virus.

4.2 Positivity and boundedness of solutions

The model Equation (4.1.7) is studied in the feasible region Ω such that

$$
\begin{aligned}
\{S(t), P_H(t), P_P(t), I_H(t), I_{HP}(t), I_P(t), T_P(t), \\
I_A(t), I_{AP}(t)\} \in \Omega \subset \mathbb{R}^9_+.
\end{aligned} \tag{4.2.1}
$$

Based on the fact that the model deal with human population, all the state variables and parameters are non-negative for all $t \geq 0$. It can be shown that the solutions are bounded such that

$$
0 \leq N \leq \frac{\Lambda}{\mu}
$$

Since the solutions are positive and bounded the two models are epidemiologically well posed.

4.3 Reproduction number R_0

The basic reproduction number is the average number of secondary infections due to a single infectious individual in a fully susceptible population[38]. It is the spectral radius of a matrix

$$FV^{-1} \tag{4.3.1}$$

where F is the Jacobian of $\mathcal{F}$, where $\mathcal{F}$ is the rate of appearance of new infections in compartment and V is the Jacobian of $\mathcal{V}$, where $\mathcal{V}$ is the rate of transfer of individuals into and out of compartment. FV^{-1} is calculated by the method of next generation matrix [37]. The disease free equilibrium of Equation (4.1.7) is given by

$$E_1^0 = \{S, P_P, P_H, I_H, I_A, I_P, T_P, I_{HP}, I_{AP}\} = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0) \tag{4.3.2}$$

We define $\mathcal{F}$ into a class as

$$\mathcal{F} = \begin{pmatrix} \lambda_H(P_P + S) \\ 0 \\ \lambda_P(P_H + S) \\ \vartheta_1\lambda_P + \kappa\lambda_H I_P \\ \vartheta_2\lambda_P I_A \end{pmatrix} \tag{4.3.3}$$

We also define $\mathcal{V}$ as

$$\mathcal{V} = \mathcal{V}^- - \mathcal{V}^+ \tag{4.3.4}$$

where $\mathcal{V}^-$ is the rate of transfer of individuals out of a compartment and $\mathcal{V}^+$ is the rate of transfer of individuals into compartment. Thus $\mathcal{V}$ is given by

$$\mathcal{V} = \begin{pmatrix} (\varphi_1\lambda_P + \mu + \tau)I_H - \varepsilon I_{HP} \\ -\tau I_H - \varepsilon I_{AP} + (\mu + \delta_A + \varphi_2\lambda_P)I_A \\ (\mu + \kappa\lambda_P + \varepsilon + \delta_P)I_P \\ (\mu + \varrho + \delta_P)I_{HP} \\ \varrho\tau I_{HP} + (\mu + \delta_A + \delta_P + \delta_{AP} + \varepsilon)I_{AP} \end{pmatrix} \tag{4.3.5}$$

The Jacobian of $\mathcal{F}$ at the disease free equilibrium denoted as F and is given by

$$F = \begin{pmatrix} \beta C(1-\chi_H) & \beta C(1-\chi_H)\omega_2 & 0 & \beta C(1-\chi_H)\omega_1 & \beta C(1-\chi_H)\omega_3 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \pi\theta(1-\chi_P) & \pi\theta(1-\chi_P)\phi_1 & \pi\theta(1-\chi_P)\phi_2 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} \tag{4.3.6}$$

Similarly, the Jacobian of $\mathcal{V}$ at the disease free equilibrium is denoted by V and is given by

$$V = \begin{pmatrix} \mu+\tau & 0 & 0 & -\varepsilon & 0 \\ -\tau & \mu+\delta_A & 0 & 0 & -\varepsilon \\ 0 & 0 & \mu+\varepsilon+\delta_P & 0 & 0 \\ 0 & 0 & 0 & \mu+\varrho+\delta_P & 0 \\ 0 & 0 & 0 & -\varrho\tau & \mu+\delta_P+\delta_A+\delta_{AP}+\varepsilon \end{pmatrix} \quad (4.3.7)$$

Thus the eigenvalues of the matrix FV^{-1} are

$$R_P = \frac{\pi\theta(1-\chi_P)}{\varepsilon+\mu+\delta_P}$$

and

$$R_H = C\beta(1-\chi_H)(\frac{\mu+\delta_A+\tau\omega_2}{(\mu+\tau)(\mu+\delta_A)})$$

where R_P is the reproduction number for pneumonia and R_H is the reproduction number for HIV/AIDS in the Equation (4.1.7). The spectral radius of FV^{-1} is $max\{R_P, R_H\}$. Therefore, the basic reproduction number of Equation (4.1.7) is denoted as R_0^1 and is defined as $R_0^1 = max\{R_P, R_H\}$.

The reproduction number R_P gives the expected number of secondary Pneumonia infection produced by a single pneumonia infectious individual during his/her infectious period when introduced into a completely Pneumonia susceptible population. Similarly,The reproduction number R_H gives the expected number of secondary HIV/AIDS infection produced by a single HIV/AIDS infectious individual during his/her infectious period when introduced into a completely HIV/AIDS susceptible population. Since Equation (4.1.7) satisfy conditions $A1 - A5$ [48],then the disease free equilibrium $E_1^0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0)$ is locally asymptotically stable if R_0^1 and unstable if R_0^1. in the absence of protection $\chi P = \chi H = 0$ and $R_0^1 = max\{R_P, R_H\}$.

4.4 Global stability for the disease free equilibrium

there are two conditions that if met they guarantee the global asymptotic stability of the disease free state. Equation (4.1.7) may be written in the form

$$\begin{aligned} \frac{dX}{dt} &= K(X,Z) \\ \frac{dZ}{dt} &= W(X,Z), W(X,0) = 0 \end{aligned} \quad (4.4.1)$$

where $X \in \mathbb{R}^4$ and $X = \{S, P_P, P_H, T_T\}$ denotes the number of uninfected individuals and $Z \in \mathbb{R}^5$ where $Z = \{I_H, I_A, I_P, I_{HP}, I_{AP}\}$ denotes the number of infected individuals . $E_1^O = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0)$ denotes the disease free equilibrium of this system where

$$X^* = (\frac{\Lambda}{\mu})$$

conditions (4.4.2) may be met to guarantee global asymptotic stability

$$\begin{aligned} \frac{dX}{dt} &= K(X,0), X^* \text{is globally asymptotic stable} \\ W(X,Z) &= BZ - \widehat{W}(X,Z), \widehat{W}(X,Z) \geq 0 \forall (X,Z) \in \Omega \end{aligned} \tag{4.4.2}$$

where $H = D_z N(X^*, 0)$ is an M matrix and Ω is the region where the model has biological meaning.

Theorem
If system (4.4.1) satisfies conditions (4.4.2), then the fixed point $E_1^O = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0)$ is a globally asymptotically stable equilibrium of the system (4.4.1) provided that $R_0^1 < 1$ and the assumptions in (4.4.2) are satisfied .

Proof
Consider $F(X,0) = (\Lambda - \mu S_H)$ and $W(X,Z) = AZ - \widehat{W}(X,Z)$ where

$$H = \begin{pmatrix} -y_1 & 0 & 0 & \varepsilon & 0 \\ \tau & -y_2 & 0 & 0 & \varepsilon \\ 0 & 0 & -y_3 & 0 & 0 \\ 0 & 0 & 0 & -y_4 & 0 \\ 0 & 0 & 0 & \varrho\tau & -y_5 \end{pmatrix} \tag{4.4.3}$$

Where $y_1 = (\mu + \tau), y_2 = (\mu + \delta_A), y_3 = (\mu + \varepsilon + \delta_P), y_4 = (\mu + \varrho + \delta_P + \varepsilon), y_5 = (\mu + \delta_A + \delta_P + \delta_{AP} + \varepsilon)$

and

$$\hat{W}(X,Z) = \begin{pmatrix} W_1 \\ W_2 \\ W_3 \\ W_4 \\ W_5 \end{pmatrix} = \begin{pmatrix} -\lambda_H(P_P + S) + \varphi_1\lambda_P \\ +\varphi_2\lambda_P \\ -\lambda_P(P_H + S) + \kappa\lambda_H \\ -(\varphi_1\lambda_P + \kappa\lambda_H) \\ -(\varphi_2\lambda_P) \end{pmatrix} \tag{4.4.4}$$

Since $W_4, W_5 < 0$,all the conditions in Equation (4.4.2) may not satisfied. Hence E_1^0 not globally asymptotically

4.4.1 The case of maximum protection against pneumonia

In this case the probability of the success of protection is unity, That is $\chi_P = 1$. Assuming that there are no new pneumonia infections in the population, then $\lambda_P = I_P = 0$. Therefore Equation (4.1.7) becomes

$$\begin{aligned}
\frac{dS}{dt} &= (1-\nu-\gamma)\Lambda + \alpha_2 P_H - (\mu+\lambda_H)S \\
\frac{dP_P}{dt} &= \nu\Lambda - (\mu+\lambda_H)P_P \\
\frac{dP_H}{dt} &= \gamma\Lambda - (\alpha_2+\mu)P_H \\
\frac{dI_H}{dt} &= \lambda_H P_P + \lambda_H S - (\mu+\tau)I_H \\
\frac{dI_A}{dt} &= \tau I_H - (\mu+\delta_A)I_A
\end{aligned} \tag{4.4.5}$$

The rate of infection for Equation (4.4.5) is given by

$$\lambda_H^h = \frac{C\beta(1-\chi_H)(I_H+\theta I_A)}{N(t)} \tag{4.4.6}$$

The effective reproduction numberR_H, computed using the next generation matrix method approach[37] for Equation (4.4.5) is given by

$$R_H = \frac{C\beta(1-\chi_H)(\delta_A+\mu+\theta\chi_H)(\mu(1-\gamma)+\alpha_2)}{(\delta_A+\mu)(\mu+\tau)(\mu+\alpha_2)} \tag{4.4.7}$$

The endemic state is defined as

$$I_H^* = \frac{\Lambda(\delta_A+\mu)(R_H-1)}{(1-\chi_H)(\delta_A+\mu+\theta\tau)-\delta_A\tau}. \tag{4.4.8}$$

For an infection to be endemic in a population, $I_H^* > 0$. This inequality holds provided that $R_H > 1$ with $(1-\chi_H) > 0$ and $[(1-\chi_H)(\delta_A+\mu+\theta\tau)] > (\delta_A\tau)$

4.4.2 Local stability of the endemic equilibrium

The long term behaviour of Equation (4.4.5) can be deduced from its stability analysis. From Equation (4.4.5) $N(t) = S + P_P + P_H + I_H + I_A$. We can study the first four

equations of Equation (4.4.5) since $I_A = N(t) - (S + P_P + P_H + I_H)$. Thus

$$\begin{aligned}
\frac{dS}{dt} &= (1-\nu-\gamma)\Lambda + \alpha_2 P_H - (\mu + \lambda_H^h)S \\
\frac{dP_P}{dt} &= \nu\Lambda - (\mu + \lambda_H^h)P_P \\
\frac{dP_H}{dt} &= \gamma\Lambda - (\alpha_2 + \mu)P_H \\
\frac{dI_H}{dt} &= \lambda_H^h P_P + \lambda_H^h S - (\mu + \tau)I_H
\end{aligned} \tag{4.4.9}$$

The Jacobian of Equation (4.4.9) at the endemic state $E_1^*(S^*, P_P^*, P_H^*, I_H^*)$, denoted as $J(E_1^*)$ is given by

$$J(E_1^*) = \begin{pmatrix} -(\mu + \lambda_H^h) & 0 & \alpha_2 & \frac{-C\beta S^*(1-\chi_H}{N} \\ 0 & -(\mu + \lambda_H^h) & 0 & \frac{-C\beta P_P^*(1-\chi_H}{N} \\ 0 & 0 & -(\alpha_2 + \mu) & 0 \\ \lambda_H^h & \lambda_H^h & 0 & -(\mu + \tau) \end{pmatrix} \tag{4.4.10}$$

Clearly $-(\alpha_2 + \mu)$ is an eigenvalue of Equation (4.4.10). The other eigenvalues can be obtained from the reduced matrix defined by

$$B_2 = \begin{pmatrix} -(\mu + \lambda_H^h) & 0 & \frac{-C\beta S^*(1-\chi_H)}{N(t)} \\ 0 & -(\mu + \lambda_H^h) & \frac{-C\beta P_P^*(1-\chi_H)}{N(t)} \\ \lambda_H^h & \lambda_H^h & -(\mu + \tau) \end{pmatrix} \tag{4.4.11}$$

The trace of Equation (4.4.11) is negative and its determinant is given by

$$\begin{aligned}
detB_2 = [\frac{I_H^*(1-\chi_H)\beta C}{N(t)} + \mu][\frac{I_H^*(1-\chi_H)(S^* - P_P^*)\beta C}{N^2} \\
(I_H^*(\mu+\tau) - (1-\chi_H)\beta C + \mu + \tau) - \mu(\mu+\tau)]
\end{aligned} \tag{4.4.12}$$

$detB_2 > 0$ provided that

$$[\frac{I_H^*(1-\chi_H)(S^* - P_P^*)\beta C}{N^2}(I_H^*(\mu+\tau) - (1-\chi_H)\beta C + \mu + \tau) \geq (\mu(\mu+\tau)) \tag{4.4.13}$$

Since the trace is negative and the determinant is positive provided that inequality (4.4.13) hold, the eigenvalues of Equation (4.4.11) will have negative real parts. Therefore the endemic equilibrium $E_1^*(S^*, P_P^*, P_H^*, I_H^*)$ is locally asymptotically stable.

4.4.3 Global stability of the endemic equilibrium

The global stability of the equilibria are obtained by means of Lyapunov's direct method and LaSalle's invariance principle[12]. Consider the non-linear Lyapunov function

$$V_e : (S, P_P, P_H, I_H, I_A) \in \Omega \subset \mathbb{R}^5_+ : S, P_P, P_H, I_H, I_A > 0 \tag{4.4.14}$$

defined as

$$\begin{aligned} V_e : (S, P_P, P_H, I_H, I_A) = \lambda^h_H(S - S^* - S^* \log \frac{S}{S^*}) + \lambda^h_H(P_P - P^*_P - P^*_P \log \frac{P_P}{P^*_P}) + \\ \lambda^h_H(P_H - P^*_H - P^*_H \log \frac{P_H}{P^*_H}) + \lambda^h_H(I_H - I^*_H - I^*_H \log \frac{I_H}{I^*_H}) + \\ \lambda^h_H(I_A - I^*_A - I^*_A \log \frac{I_A}{I^*_A}) \end{aligned} \tag{4.4.15}$$

where V_e is C^1 in the interior of the region Ω. E^*_1 is the global minimum of V_e on Ω and $V_e : (S, P_P, P_H, I_H, I_A) = 0$. The time derivative of Equation(4.4.15) is given by

$$\begin{aligned} \frac{dV_e}{dt} = \dot{V_e} = \lambda^h_H(1 - \frac{S^*}{S})\frac{dS}{dt} + \lambda^h_H(1 - \frac{P^*_P}{P_P})\frac{dP_P}{dt} + \lambda^h_H(1 - \frac{P^*_H}{P_H})\frac{dP_H}{dt} + \\ \lambda^h_H(1 - \frac{I^*_H}{I_H})\frac{dI_H}{dt} + \lambda^h_H(1 - \frac{I^*_A}{I_A})\frac{dI_A}{dt} \\ = -\lambda^h_H(\frac{S - S^*}{S})[(\mu + \lambda^h_H)(S - S^*) + \alpha_2(P_H - P^*_H)] \\ -\lambda^h_H(\frac{P_H - P^*_H}{P_H})[(\alpha_2 + \mu)(P_H - P^*_H)] - \lambda^h_H(\frac{P_P - P^*_P}{P_P})[(\mu + \lambda^h_H)(P_P - P^*_P)] \\ -\lambda^h_H(\frac{I_H - I^*_H}{I_H})[(\mu + \tau_2)(I_H - I^*_H)] - \lambda^h_H(\frac{I_A - I^*_A}{I_A})[(\mu + \delta_A)(I_A - I^*_A)] \end{aligned} \tag{4.4.16}$$

Hence $\dot{V_e} < 0$. We see that $\dot{V_e} = 0$ iff $S = S^*, P_H = P^*_H, P_P = P^*_P, I_H = I^*_H$ and $I_A = I^*_A$. Thus the largest compact invariant set in $\{S, P_H, P_P, I_H, I_A\} \in \Omega : \dot{V_e} = 0$ is the Singleton E^*_1, where E^*_1 is the endemic equilibrium. Thus E^*_1 is globally asymptotically stable in the interior of the region Ω.

4.4.4 Case of maximum protection against HIV/AIDS

In this case the probability of the success of protection is unity, i.e $\chi_H = 1$. Assuming that there are no new HIV/AIDS infections in the population, then $\lambda_H = I_H = I_A = 0$.

Therefore Equation (4.1.7) becomes

$$\begin{aligned}
\frac{dS}{dt} &= (1-\nu-\gamma)\Lambda + \alpha_1 P_P - (\mu+\lambda_P)S \\
\frac{dP_P}{dt} &= \nu\Lambda - (\mu+\alpha_1)P_P \\
\frac{dP_H}{dt} &= \gamma\Lambda - (\mu+\lambda_P)P_H \\
\frac{dI_P}{dt} &= \lambda_P P_H + \lambda_P S - (\mu+\varepsilon+\delta_P)I_P \\
\frac{dT_P}{dt} &= \varepsilon I_P - \mu T_P
\end{aligned} \tag{4.4.17}$$

The rate of infection Equation (4.4.17) is now defined as

$$\lambda_P^p = \frac{\pi\theta(1-\chi_P)I_P}{N(t)} \tag{4.4.18}$$

while the effective reproduction number is given by

$$R_P = \frac{\pi\theta(1-\chi_P)(\mu(1-\nu)+\alpha_1)}{(\delta_P+\mu+\varepsilon)(\mu+\alpha_1)}. \tag{4.4.19}$$

For the infection to be endemic in a population $I_P^* > 0$ where

$$I_P^* = \frac{\Lambda(R_P-1)}{(\pi\theta)(1-\chi_P)-\delta_P} > 0 \tag{4.4.20}$$

provided $R_P > 1$ with $\delta_P < \pi\theta(1-\chi_P)$.

4.4.5 Local stability of the endemic equilibrium

The total population $N(t)$ from Equation (4.4.17) is $N(t) = S + P_P + P_H + I_P + T_P$ for which $T_P = N(t) - S + P_P + P_H + I_P$. Thus we study the first four equations of Equation (4.4.17) at the endemic state $E_2^*(S^*, P_H^*, P_P^* I_P^*)$.

$$\begin{aligned}
\frac{dS}{dt} &= (1-\nu-\gamma)\Lambda + \alpha_1 P_P - (\mu+\lambda_P^p)S \\
\frac{dP_P}{dt} &= \nu\Lambda - (\mu+\alpha_1)P_P \\
\frac{dP_H}{dt} &= \gamma\Lambda - (\mu+\lambda_P^p)P_H \\
\frac{dI_P}{dt} &= \lambda_P^p P_H + \lambda_P^p S - (\mu+\varepsilon+\delta_P)I_P
\end{aligned} \tag{4.4.21}$$

The Jacobian of Equation (4.4.21) is given by

$$J(E_2^*) = \begin{pmatrix} -(\mu+\lambda_P^p) & \alpha_1) & 0 & \frac{-\pi\theta S^*(1-\chi_P^p)}{N} \\ 0 & -(\mu+\alpha_1 & 0 & 0 \\ 0 & 0 & -(\mu+\lambda_P^p) & \frac{-\pi\theta P_H^*(1-\chi_P)}{N} \\ \lambda_P^p & 0 & \lambda_P^p & -(\mu+\varepsilon+\delta_P) \end{pmatrix} \tag{4.4.22}$$

Clearly $-(\mu+\alpha_1)$ is an eigenvalue of Equation (4.4.22). To obtain the other eigenvalues, we analyze the system

$$B_3 = \begin{pmatrix} -(\mu+\lambda_P^p) & 0 & \frac{-\pi\theta S^*(1-\chi_P)}{N} \\ 0 & -(\mu+\lambda_P^p) & \frac{-\pi\theta P_H^*(1-\chi_P)}{N} \\ \lambda_P^p & \lambda_P^p & -(\mu+\varepsilon+\delta_P) \end{pmatrix} \tag{4.4.23}$$

$trB_3 < 0$ and

$$detB_3 = \frac{1}{N^2(t)}[\frac{I_P^*(1-\chi_P)\pi\theta}{N(t)} + \mu][(1-\chi_P)^2\pi^2\theta^2 I_P^*(P_H^* + S^*) + N(t)(I_P^*(1-\chi_P)\pi\theta + N(t)\mu)(\varepsilon+\mu+\tau)] \tag{4.4.24}$$

$detB_3$ is positive since $(1-\chi_P) > 0$. Therefore the endemic equilibrium $E_2^*(S^*, P_H^*, P_P^* I_P^*)$ is locally asymptotically stable.

4.4.6 Global stability of the endemic equilibrium

Consider the non-linear Lyapunov function

$$V : (S, P_P, P_H, I_P, T_P) \in \Omega \subset \mathbb{R}_+^5 : S, P_P, P_H, I_P, T_P > 0 \tag{4.4.25}$$

defined as

$$\begin{aligned} V : (S, P_P, P_H, I_P, T_P) = \lambda_P^p(S - S^* - S^* \log \frac{S}{S^*}) + \\ \lambda_P^p(P_P - P_P^* - P_P \log \frac{P_P}{P_P^*}) + \lambda_P^p(P_H - P_H^* - P_H^* \log \frac{P_H}{P_H^*}) + \\ \lambda_P(I_P - I_P^* - I_P^* \log \frac{I_P}{I_P^*}) + \\ \lambda_P^p(T_P - T_P^* - T_P^* \log \frac{T_P}{T_P^*}) \end{aligned} \tag{4.4.26}$$

where V is C^1 in the interior of the region Ω. E_2^* is the global minimum of V on Ω and $V : (S, P_P, P_H, I_P, T_P) = 0$. The time derivative of Equation (4.4.26) is given by

$$\frac{dV}{dt} = \dot{V} = \lambda_P^p(1 - \frac{S^*}{S})\frac{dS}{dt} + \lambda_P^p(1 - \frac{P_P^*}{P_P})\frac{dP_P}{dt} + \lambda_P^p(1 - \frac{P_H^*}{P_H})\frac{dP_H}{dt} + \lambda_P^p(1 - \frac{I_P^*}{I_P})\frac{dI_P}{dt} + \lambda_P^p(1 - \frac{T_P^*}{T_P})\frac{dT_P}{dt} \tag{4.4.27}$$

with the derivatives of Equation S, P_P, P_H, I_P, T_P defined in Equation (4.4.17) and by using

$(1-\nu-\gamma)\Lambda = -\alpha_1 P_P^* + (\mu+\lambda_P^p)S^*, \nu\Lambda = (\mu+\alpha_1)P_P^*, \gamma\Lambda = (\mu+\lambda_P^p)P_H^*, \lambda_P^p(P_H+S) = (\mu+\varepsilon+\delta_P)I_P^*$, and $\varepsilon I_P = \mu T_P$ into Equation (4.4.27) we obtain

$$\begin{aligned}\dot{V} = -\lambda_P^p(\frac{S-S^*}{S})[(\mu+\lambda_P^p)(S-S^*) + \alpha_1(P_P - P_P^*)] \\ -\lambda_P^p(\frac{P_P - P_P^*}{P_P})[(\alpha_1+\mu)(P_P - P_P^*)] - \lambda_P^p(\frac{P_H - P_H^*}{P_H})[(\mu+\lambda_P^p)(P_H - P_H^*)] \\ -\lambda_P^p(\frac{I_P - I_P^*}{I_P})[(\mu+\varepsilon+\delta_P)(I_L - I_L^*)] - \lambda_P^p(\frac{T_P - T_P^*}{T_P})[\mu(T_P - T_P^*)]\end{aligned} \tag{4.4.28}$$

hence $\dot{V} < 0$. Thus E_2^* is globally asymptotically stable in the interior of the region Ω.

4.4.7 Numerical simulations

To graphically illustrate the effect of protection on the dynamics of infection, numerical simulations are carried out.

Table 4.1: Parameter values used in simulation of HIV/AIDS and pneumonia model

Parameter description	**Symbol**	**Value**	**Source**
Natural death rate	μ	$7.0 \times 10^{-3} days^{-1}$	[8]
Recruitment rate	Λ	$8.7 \times 10^{-3} days^{-1}$	[8]
Rate of recruitment into pneumonia protected class	γ	1.2×10^{-3}	Estimated
Rate of recruitment into HIV/AIDS protected class	ν	5.97×10^{-1}	[35]
Loss of protection against pneumonia	α_2	5.0×10^{-3}	Estimated
Death due to pneumonia	δ_A	$3.4 \times 10^{-2} days^{-1}$	[35]
Probability of acquiring pneumonia	π	1.1×10^{-9}	Estimated
Probability of success of protection against pneumonia	χ_P	9.0×10^{-1}	Estimated
Contact rate with pneumonia infective	θ	8.0×10^{-1}	Estimated

4.4.7.1 The effect of varying the protection term on pneumonia infection against time

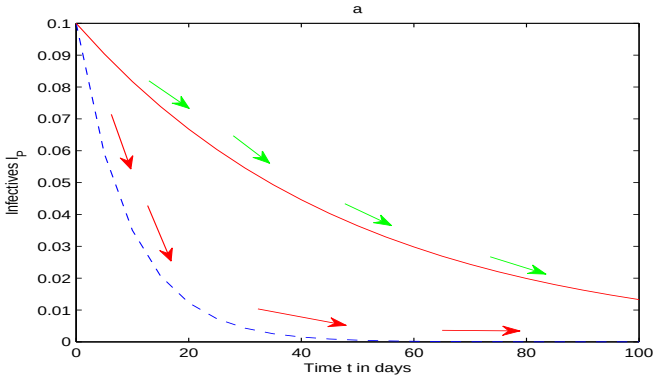

Figure 4.4.1: Simulation of Equation (4.4.17) showing the evolution of pneumonia

Continuous line: $\pi = 1.1 \times 10^{-3}, \chi_P = 6.0 \times 10^{-3}$
Broken line: $\pi = 1.1 \times 10^{-9}, \chi_P = 9.0 \times 10^{-1}$

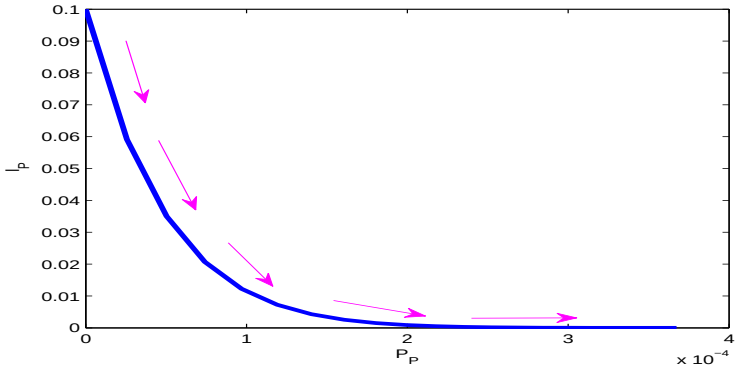

Figure 4.4.2: The graph of I_P against P_P

CHAPTER 5

Discussion, conclusion and recommendations

5.1 Discussion

The disease free equilibrium points for Equation(3.1.7) and Equation (4.1.7) are shown not to be globally asymptotically stable. This implies that reoccurrence of the disease is possible especially when the conditions favoring such reoccurrence are prevailing. Four cases of maximum protection are considered. In all cases, the endemic states are shown to exist provided that the reproduction number is greater than unity. By use of Routh-Hurwitz criterion and suitable Lyapunov functions, the endemic states are shown to be locally and globally asymptotically stable respectively. This implies that disease transmission levels can be kept quiet low or manageable with minimal deaths in the presence of protection.

From Figure 3.4.1(a), we see that , with a low protection rate the probability of infection is high and therefore the number of infectives I_H rises sharply in a short span before drastically dropping. This sharp drop may be attributed to the depletion of susceptibles or the susceptibles embracing protective measures. From the same figure a very high protection rate with a low probability of transmission results in reduced disease prevalence. The time evolution of I_A, is lower than that of I_H as depicted by Figure 3.4.1(b) since it takes time to progress from I_H to I_A as the body's immunity tries to fight the HIV virus. From Figure 3.4.3, with a high rate of protection, and a low probability of disease transmission, the diseases prevalence for TB also goes down. On the other hand, a low protection rate leads to a high disease prevalence. From Figure 3.4.2, we observe that the number of I_H infections reduces with increased protection. Similarly, Figure 3.4.4 shows that the number of I_T infectives reduces with increased protection. From Figure 4.4.1, a high rate of protection against pneumonia leads to a low probability of disease transmission and a low protection rate leads to a high disease prevalence. Figure 4.4.2 shows that the number of I_P infectives reduces with increased protection. This is consistent with reality[3] and the mathematical analysis which shows the attainment of local and global stability of the endemic equilibrium in the presence of protection.

In order to reduce the number of new HIV/AIDS and TB infections, and reduce the

impact of HIV/AIDS on individual, families and communities, there is need to employ strategies such as increasing the public awareness drive to behaviour change and encourage openness, increasing access to voluntary HIV testing and counselling, promoting increased condom use to reduce the spread of HIV infection, improving access to antiretroviral drugs (ARV's) for people living with AIDS, practising proper hygiene in the case of TB and avoiding clouded places. These strategies will help in reducing the economic burden that are borne by a country in giving care and treating the infected individuals. As evidence from these results, it is indeed true that prevention is better than cure.

5.2 Conclusion

In this work, we first formulated a model for the co-infection of HIV/AIDS with TB incorporating protection. To investigate the effect of protection, two cases were considered. That is, case of maximum protection against HIV/AIDS and the case of maximum protection against TB. The existence of the endemic equilibrium for the two cases was established and the stability of the same was analysed. In both cases the endemic equilibrium is found to be globally asymptotically stable.

Secondly, we formulated a model for the co-infection of HIV/AIDS with pneumonia incorporating protection. To investigate the effect of protection, two cases were considered, namely the case of maximum protection against HIV/AIDS and the case of maximum protection against pneumonia. The existence of the endemic equilibrium for the two cases was established and the stability of the same was analysed. From the numerical simulations, we observe that protection against a disease has the effect of reducing the disease prevalence. This is in agreement with the mathematical analysis which shows that in the presence of protection, the endemic equilibria are both locally and globally asymptotically stable.

5.3 Recommendations

The government, through the relevant people in the health sector, need to sensitize the public on the need of embracing protective measures in the view of reducing disease

prevalence in the population. Since protection has been used in a general sense, further research may be carried out to analyze the contribution of specific protective measures in the overall reduction of disease prevalence rates

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Appendix A
Matlab code for HIV/AIDS infectives against time

```
clear
options=odeset('RelTol',1e-4,'AbsTol',[1e-6 1e-4 1e-6 1e-4 1e-6]);
[T1,Y1]=ode45('JOYCE512', [0:10:1000],[100,0 , 8, 7, 5],options);
[T2,Y2]=ode45('JOYCE513', [0:10:1000],[100,0 , 8, 7, 5],options);
subplot(2,2,1)
plot(T1,Y1(:,4),'--',T2,Y2(:,4),'-r');
title('a');
xlabel 'Timet in days';
ylabel 'Infectives at I_H';
hold on
subplot(2,2,2)
plot(T1,Y1(:,5),'--',T2,Y2(:,5),'-r');
title('b');
xlabel 'Time t in days';
ylabel 'Infectives at I_A';
hold off
function dy=JOYCE512,JOYCE513(t,y)
dy=[10000 400 400 200 200]';
dy(1)=(1-a(1)-a(2))*a(3)+a(4)*y(2)-(a(5)+a(6))*y(1);
dy(2)=a(1)*a(3)-(a(4)+a(5))*y(2);
dy(3)=a(2)*a(3)-(a(5)+a(6))*y(3);
dy(4)=a(6)*(y(1)+y(3))-(a(5)+a(7))*y(4);
dy(5)=a(7)*y(4)-(a(5)+a(8))*y(5);
```

Appendix B
Matlab code for HIV/AIDS infectives against protection

```
[T,Y]=ode45('p3', (0:2:1000),[800,100 , 0, 45, 55]);
plot(Y(:,3),Y(:,4),'LineWidth',3);
xlabel 'P_H';
ylabel ' I_H';
function dy=p3(t,y)
dy=[10000 400 400 200 200]';
dy(1)=(1-h(1)-h(2))*h(3)+h(4)*y(3)-(h(5)+h(6))*y(1);
dy(2)=h(1)*h(3)-(h(5)+h(6))*y(2);
dy(3)=h(2)*h(3)-(h(4)+h(5))*y(3);
dy(4)=h(6)*(y(1)+y(2))-(h(5)+h(7))*y(4);
dy(5)=h(7)*y(4)-(h(5)+h(8))*y(5);
```

Appendix C
Matlab code for tuberculosis infectives against time

```
%options=odeset('RelTol',1e-,'AbsTol',[1e-6 1e-4 1e-6]);
[T1,Y1]=ode45('KJNNN2', (0:2:100),[50,0,5,5,5,10]);
[T2,Y2]=ode45('KJN22', (0:2:100),[50,0,5,5,5,10]);
plot(T1,Y1(:,4),'--',T2,Y2(:,4),'-r');
xlabel 'Time(days)';
ylabel 'Infectives  I_L';
function dy=KJNNN2,KJN22(t,y)
dy=[1000 600 500 400 300 200]';
dy(1)=(1-d(1)-d(2))*d(3)+d(4)*y(2)-(d(5)+d(6))*y(1);
dy(2)=d(1)*d(3)-(d(4)+d(5))*y(2);
dy(3)=d(2)*d(3)-(d(5)+d(6))*y(3);
dy(4)=d(6)*(y(1)+y(3))-(d(5)+d(7))*y(4);
dy(5)=d(7)*y(4)-(y(5)+d(9)+d(8))*y(5);
dy(6)=d(8)*y(5)-d(5)*y(6);
```

Appendix D
Matlab code for tuberculosis infectives against protection

```
[T,Y]=ode45('KJNNN', (0:10:10),[50,0,5,5,5,10]);
plot(Y(:,2),Y(:,4),'LineWidth',3);
xlabel 'P_T';
ylabel ' I_T';
function dy=KJNNN(t,y)
dy=[1000 600 500 400 300 200]';
dy(1)=(1-d(1)-d(2))*d(3)+d(4)*y(2)-(d(5)+d(6))*y(1);
dy(2)=d(1)*d(3)-(d(4)+d(5))*y(2);
dy(3)=d(2)*d(3)-(d(5)+d(6))*y(3);
dy(4)=d(6)*(y(1)+y(3))-(d(5)+d(7))*y(4);
dy(5)=d(7)*y(4)-(y(5)+d(9)+d(8))*y(5);
dy(6)=d(8)*y(5)-d(5)*y(6);
```

Appendix E
Matlab code for pneumonia infectives against time

```
[T1,Y1]=ode45('JK', (0:5:100),[50,0 , 1, 0.1, 4]);
[T2,Y2]=ode45('JK1', (0:5:100),[50,0 , 1, 0.1, 4]);
subplot(1,1,1)
plot(T1,Y1(:,4),'--',T2,Y2(:,4),'-r');
title('a');
xlabel 'Timet in days';
ylabel 'Infectives I_P';
xlabel 'Time t in days' ;
function dy=JK,JK1 (t,y)
dy=[1000 100 100 50 50]';
dy(1)=(1-b(1)-b(2))*b(3)+ b(4)*y(2)-(b(5)+b(6))*y(1);
dy(2)=b(1)*b(3)-(b(4)+b(5))*y(2);
dy(3)=b(2)*b(3)-(b(5)+b(6))*y(3);
dy(4)=b(6)*(y(1)+y(3))-(b(5)+b(7)+b(8))*y(4);
dy(5)=b(7)*y(4)-b(5)*y(5);
```

Appendix F
Matlab code for pneumonia infectives against protection

```
[T,Y]=ode45('JK', (0:5:100),[50,0 , 1, 0.1, 4]);
plot(Y(:,2),Y(:,4),'LineWidth',3);
xlabel 'P_P';
ylabel ' I_P';
function dy=JK(t,y)
b(1)=0.00597;
b(2)=0.00067;
b(3)=0.0008748;
b(4)=0.0005;
b(5)=0.007;
b(6)=(0.0000000011*0.000008*(1-0.9)*y(4))/(y(1)+y(2)+y(3)+y(4)+y(5));
b(7)=0.098;
b(8)=0.0000034;
dy=[1000 100 100 50 50]';
dy(1)=(1-b(1)-b(2))*b(3)+ b(4)*y(2)-(b(5)+b(6))*y(1);
dy(2)=b(1)*b(3)-(b(4)+b(5))*y(2);
dy(3)=b(2)*b(3)-(b(5)+b(6))*y(3);
dy(4)=b(6)*(y(1)+y(3))-(b(5)+b(7)+b(8))*y(4);
dy(5)=b(7)*y(4)-b(5)*y(5);
```