BSc Final Project

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Mathematical Epidemiology - Continuous Models: Calculating $\mathcal{R}_0$ values of 2 models concerning HIV/AIDS infection

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April 10, 2022

Abstract

Background: In our project we look at the basic reproduction number $\mathcal{R}_0$, it is a very important tool that is used to measure the potential of an epidemic in a susceptible population. Here we calculate $\mathcal{R}_0$ for 2 models, one based on a simple early model used for HIV infection in homosexual populations and the latter based on a more complex model with different age groups used for modelling HIV infection in a heterosexual population in Kenya.

Methods: The calculation of the $\mathcal{R}_0$ values was done by closely following the method use in the well cited paper [VdDW02]; this method is called the Next Generation Operator method. For one of our models we used Mathematica to create a plot which simulated the usefulness of the $\mathcal{R}_0$ value in predicting epidemics.

Results: Calculated the reproduction number of the model from [Mur02] to be $\mathcal{R}_0 = \frac{\beta c}{\upsilon+\mu}$ and demonstrated the importance of the average number of sexual partners, c, in causing an outbreak. For the HIV model lifted from [OL19] we calculated the reproduction number in the young adult population and adult population to be $\mathcal{R}_{0d} = \sqrt{\left[\frac{\beta_1\gamma_1(\delta_1\theta_2+\mu_d)}{\mu_d(\mu_d+\delta_1)}\right]\left[\frac{\beta_2\gamma_2(\mu_d+\theta_5\phi_1)}{\mu_d(\mu_d+\phi_1)}\right]}$ and $\mathcal{R}_{0a} = \sqrt{\left[\frac{\beta_3\gamma_3(\delta_2\eta_3+\eta_1\mu_a)}{\mu_a(\mu_a+\delta_2)}\right]\left[\frac{\beta_4\gamma_4(\eta_4\mu_a+\eta_6\phi_2)}{\mu_a(\mu_a+\phi_2)}\right]}$ respectively. Next we calculated the basic reproduction number between the age groups getting $\mathcal{R}_{0mdfa} = \sqrt{\left[\frac{\alpha\beta_4\gamma_4(\eta_5\phi_1+\alpha+\mu_d)}{(\mu_d+\alpha)(\mu_d+\phi_1+\alpha)(\mu_a+\alpha)}\right]\left[\frac{\beta_1\gamma_1(\theta_1\mu_a+\delta_2\theta_3)}{(\delta_2+\mu_a)(\mu_a+\alpha)}\right]}$ for between young male adults and adult females and $\mathcal{R}_{0fdma} = \sqrt{\left[\frac{\beta_2\gamma_3(\theta_4\mu_a+\theta_6\phi_2)}{(\mu_a+\alpha)(\mu_a+\phi_2)}\right]\left[\frac{\alpha\beta_3\gamma_3(\alpha+\delta_1\eta_2+\mu_d)}{(\delta_1+\mu_d+\alpha)(\mu_a+\alpha)(\alpha+\mu_d)}\right]}$ for between young female adults and adult males. We also established that the basic reproduction number between age groups is $\mathcal{R}_0 = max\{\mathcal{R}_{0fdma}, \mathcal{R}_{0mdfa}\}$.

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Chapter 1

Introduction

HIV/AIDS has been a well talked about subject over the last 5 decades, as with all diseases; scientists wish to create models which can be used to predict an outbreak of the disease, this also allows scientists to see what can prevent an epidemic. An important model often used when beginning to model a disease is the SIR compartmental model, often as we learn more about the disease we can add more 'compartments' to this model, making it even more complex and more accurate.

In this project we will be making use of the SIR model [Wei13], this then will lead to us to bringing in the concept of the basic reproduction number ($\mathcal{R}_0$) which we will then calculate for 2 models. Calculating the basic reproduction number allows us to observe and identify what will cause an outbreak in an entirely susceptible population (this occurs when $\mathcal{R}_0 > 1$); this in turn allows us to advise on how to prevent an epidemic.

Firstly, we look at a simple model for HIV infection in a homosexual population (from [Mur02]) which would reflect an early model used by scientists at the beginning of the HIV/AIDS epidemic in homosexual communities, looking at what would cause an epidemic and how to avoid one. Secondly, we will move onto a more complex recent day model (from [OL19]), used to model HIV infection in an age-grouped heterosexual population in Kenya. We see that the model from [Mur02] is from early days in the HIV/AIDS epidemics, thus it does not include a compartment for treatment like [OL19] does; something both models do not take into account is the use of condoms in the prevention of HIV infection, the article [GDL01] examines the impact of condom use on the sexual transmission of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). These models have been built upon as knowledge of HIV and AIDS increases leading to much more complex models such as multi-modelling approaches which allow us to help eliminate other diseases among HIV infected men, the paper [SSW+18] investigates how to eliminate the hepatitis c virus as a public health threat among HIV positive-men.

Chapter 2

The basic reproduction number

2.1 Understanding $\mathcal{R}_0$

In mathematical epidemiology, the basic reproduction number denoted as $\mathcal{R}_0$, is defined as: the expected number cases an infected individual can produce in an entirely susceptible population. Effectively, this means that if $\mathcal{R}_0 = 23$, then on average, an infected individual would infect 23 others, how ever, $\mathcal{R}_0$ does not take into account cases produced by secondary cases. The $\mathcal{R}_0$ value depends on a number of parameters, such as parameters which account for the infectivity of the disease, the death rate of the disease, the recovery rate of the population and so on. As a result of this, $\mathcal{R}_0$ is not a biological constant for a disease as it's directly affected by parameters such as the socio-behavioural actions of the infected population, thus the $\mathcal{R}_0$ values obtained are estimated and are to be taken with a grain of salt. We see that generally as $\mathcal{R}_0 > 1$, the disease-free equilibrium is unstable and an outbreak occurs, the larger the $\mathcal{R}_0$ value the larger the outbreak; this coincides with our definition of $\mathcal{R}_0$. The converse is true, if $\mathcal{R}_0 < 1$, the disease-free equilibrium is locally asymptotically stable and thus no outbreak occurs.

2.2 Calculating $\mathcal{R}_0$ for a simple SIR model

Next, we wish to show how $\mathcal{R}_0$ is calculated for a simple SIR model, SIR is an acronym for Susceptible Infected Removed. This is a compartmental model which can be added to match the disease you wish to study. Below we are given 3 differential equations:

$$\begin{aligned}
\dot{S} &= -\frac{\beta SI}{N} \\
\dot{I} &= \frac{\beta SI}{N} - \gamma I \\
\dot{R} &= \gamma I
\end{aligned}$$

with

$$N(t) = S(t) + I(t) + R(t)$$

where $S(t)$, $I(t)$ and $R(t)$ is the number of susceptible, infective and removed individuals at time $t \geq 0$, respectively. Also, $\beta, \gamma \in R^+$ where β is the infectivity of the disease and γ is the recovery rate. We also have $N \in R$ is the size of the population.
When we are looking at what causes an outbreak, then the rate of infections, $\dot{I} > 0$, that is:

$$\begin{aligned}
\frac{\beta SI}{N} - \gamma I > 0 \\
(\frac{\beta S}{N} - \gamma)I > 0
\end{aligned}$$

Here we have assumed the number of infected $I(t) > 0$, thus $(\frac{\beta S}{N} - \gamma) > 0$. Now, using this assumption we see that:

$$\frac{\beta S}{N} - \gamma > 0$$
$$\frac{\beta}{\gamma}\frac{S}{N} > 0$$

Initially when $t = 0$, if we have a large susceptible population $S(t)$ and a relatively low infected population $I(t)$, that is $S(t) >> I(t)$, then we have that the total size of the population $N(t) \simeq S(t)$. Meaning $\frac{S}{N} \simeq 1$, giving:

$$\mathcal{R}_0 = \frac{\beta}{\gamma} > 1$$

When we are calculating $\mathcal{R}_0$ we assume that no one enters or leaves the population, that is $N(t) = S(t) + I(t) + R(t)$. Using this assumption we observe that:

$$\begin{aligned}\frac{dN}{dt} &= \frac{d}{dt}(S + I + R)\\ &= \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = \dot{S} + \dot{I} + \dot{R}\\ &= -\frac{\beta SI}{N} + (\frac{\beta SI}{N} - \gamma I) + \gamma I = 0\end{aligned}$$

Thus from above, we see that $N(t)$ is a constant $\equiv N$.

Chapter 3

Basic Epidemic Model for HIV Infection in a Homosexual Population

3.1 The model

This is an early model lifted from [Mur02], a common way of constructing an epidemic model is via a flow chart, in this model we are interested in the development of an AIDS epidemic in a homosexual population. Below we can see the flow chart for such a model: Assumptions we make

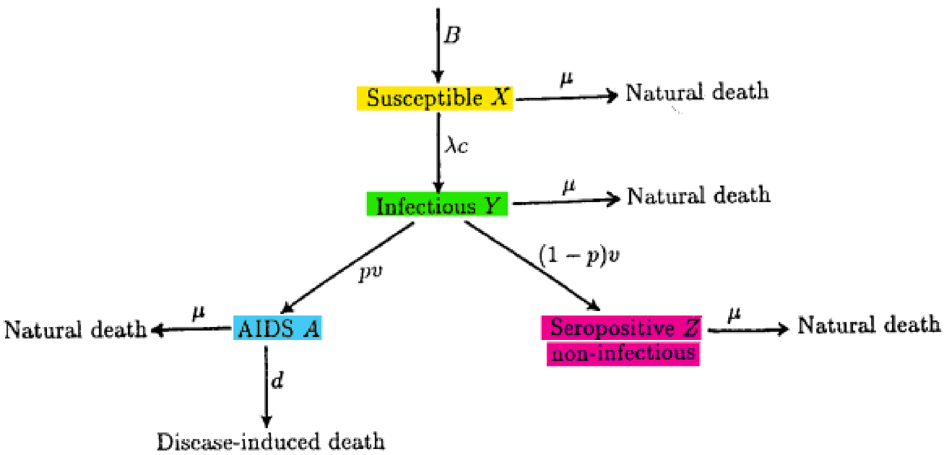

Figure 3.1: Flow chart HIV infection in model 1 for which we will be using to create our model system.

are that there is a constant rate of immigration, B of susceptible males into a population of size $N(t)$, we also let $X(t)$, $Y(t)$, $A(t)$ and $Z(t)$ denote the number of susceptible males, infectious males, AIDS patients and the number of HIV-positive/seropositive men who are noninfectious respectively. We assume that susceptible men have a natural death rate of μ. We also assume that AIDS patients die at a rate d where $1/d$ is of the order of months to years, most often it's the latter. From 3.1 we can establish the model system as:

$$\begin{aligned}
\dot{Y} &= \lambda(t)cX(t) - (\upsilon + \mu)Y(t), \\
\dot{A} &= p\upsilon\lambda Y(t) - (d + \upsilon)A(t), \\
\dot{X} &= B - \mu X(t) - \lambda(t)cX(t), \\
\dot{Z} &= (1 - p)\upsilon Y(t) - \mu A(t)
\end{aligned}$$

where

$$\lambda(t) = \beta \frac{1}{N(t)} Y(t)$$

β is the transmission probability, c is the number of sexual partners, p is the proportion of HIV-positives who are infectious and v is the rate of conversion from infection to AIDS here taken to be constant. We also have that $1/v$ is the average incubation time of the disease. It's important to note in this model the total population $N(t)$ is not constant, this can be checked by adding $\dot{Y}, \dot{A}, \dot{X}, \dot{Z}$ which gives:

$$\frac{dN}{dt} = B - \mu N - dA$$

3.2 Calculating $\mathcal{R}_0$

In order to calculate $\mathcal{R}_0$ we will be closely following the method used in [VdDW02]. This method uses the Next Generation Operator and utilises the aforementioned disease-free equilibrium. The disease-free equilibrium (DFE) is when $\dot{Y} = 0$, we can utilise this to calculate the DFE as follows:

$$\begin{aligned} \frac{\beta Y}{N} cX - (v + \mu)Y &= 0 \\ Y(\frac{\beta}{N} cX - (v + \mu)) &= 0 \end{aligned}$$

Thus $Y = 0$, also at the DFE, the size of the susceptible population is not changing that is $\dot{X} = 0$, now looking at the $\dot{X}$ differential equation:

$$\begin{aligned} \dot{X} &= B - \mu X - \frac{\beta Y}{N} cX \\ 0 &= B - \mu X \\ X &= \frac{B}{\mu} = N \end{aligned}$$

We also know that since there are no infections (Y) then there can't be any AIDS patients (A) or seropositive patients, thus $A = 0$ and $Z = 0$, that is the DFE is the vector:

$$DFE = (0, 0, N, 0)^T$$

Now, Let f be vector of infected classes, thus

$$\frac{df}{dt} = \mathcal{F}(Y, A) - \mathcal{V}(Y, A)$$

Where $\mathcal{F}(Y, A)$ is the vector of new infection rates and $\mathcal{V}(Y, A)$ is the vector of all other rates such as recovery rates and death rates. We can see from our model that:

$$\mathcal{F} = \begin{pmatrix} \lambda cX \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} (v + \mu)Y \\ -pvY + (d + \mu)A \end{pmatrix}$$

Now, we find the Jacobian of both these vectors, first starting with $\mathcal{F}$:
Let $g = \lambda cX = \frac{\beta Y}{N} cX$ and $h = 0$. Now, we define the Jacobian, F, of $\mathcal{F}$ as:

$$\begin{aligned} F &= \begin{bmatrix} \frac{\partial g}{\partial Y} & \frac{\partial g}{\partial A} \\ \frac{\partial h}{\partial Y} & \frac{\partial h}{\partial A} \end{bmatrix} \\ &= \begin{bmatrix} \beta cX & 0 \\ 0 & 0 \end{bmatrix} \end{aligned}$$

Evaluating F at the DFE gives:

$$F(DFE) = \begin{bmatrix} \beta c & 0 \\ 0 & 0 \end{bmatrix}$$

Now, doing the same for $\mathcal{V}$: Let $g = (\upsilon + \mu)Y$ and $h = -p\upsilon Y + (d+\mu)A$. We define the Jacobian, V, of $\mathcal{V}$ as:

$$\begin{aligned} V &= \begin{bmatrix} \frac{\partial g}{\partial Y} & \frac{\partial g}{\partial A} \\ \frac{\partial h}{\partial Y} & \frac{\partial h}{\partial A} \end{bmatrix} \\ &= \begin{bmatrix} \beta\upsilon + \mu & 0 \\ -p\upsilon & d+\mu \end{bmatrix} = V(DFE) \end{aligned}$$

We wish to calculate FV^{-1} which is called the next generation matrix, in order to calculate this V must be non-singular. The spectral radius of FV^{-1} gives us $\mathcal{R}_0$, which is given to be the maximum eigenvalue of FV^{-1}. To find the inverse we use:

$$A^{-1} = \frac{1}{ad-bc}\begin{bmatrix} d & -b \\ -c & a \end{bmatrix}$$

Giving:

$$\begin{aligned} V^{-1} &= \frac{1}{(\upsilon+\mu)(d+\mu)}\begin{bmatrix} d+\mu & p\upsilon \\ 0 & \frac{1}{d+\mu} \end{bmatrix} \\ &= \begin{bmatrix} \frac{1}{\upsilon+\mu} & \frac{p\upsilon}{(\upsilon+\mu)(d+\mu)} \\ 0 & \frac{1}{d+\mu} \end{bmatrix} \end{aligned}$$

Now calculating the Next Generational Matrix FV^{-1}:

$$\begin{aligned} FV^{-1} &= \begin{bmatrix} \beta c & 0 \\ 0 & 0 \end{bmatrix}\begin{bmatrix} \frac{1}{\upsilon+\mu} & \frac{p\upsilon}{(\upsilon+\mu)(d+\mu)} \\ 0 & \frac{1}{d+\mu} \end{bmatrix} \\ &= \begin{bmatrix} \frac{\beta c}{\upsilon+\mu} & \frac{\beta c p\upsilon}{(\upsilon+\mu)(d+\mu)} \\ 0 & 0 \end{bmatrix} \end{aligned}$$

The next step is to find the eigenvalues of the next generation matrix:

$$\begin{aligned} \left|FV^{-1} - eI_2\right| &= 0 \\ \begin{vmatrix} \frac{\beta c}{\upsilon+\mu} - e_1 & \frac{\beta c p\upsilon}{(\upsilon+\mu)(d+\mu)} \\ 0 & 0 - e_2 \end{vmatrix} &= 0 \\ \left(\frac{\beta c}{\upsilon+\mu} - e_1\right)(0 - e_2) &= 0 \\ e_1 = \frac{\beta c}{\upsilon+\mu}, \qquad e_2 &= 0 \end{aligned}$$

To find the spectral radius, we choose the largest (dominant) eigenvalue, e_1, which implies:

$$\mathcal{R}_0 = \frac{\beta c}{\upsilon+\mu}$$

3.3 Plotting estimates of $\mathcal{R}_0$

In this section we will use parameter estimates from to estimate values of $\mathcal{R}_0$, this will allow us to see how the $\mathcal{R}_0$ number will affect the outbreak. We will keep the parameters for all of our estimates the same except one of them, the average number of sexual partners (c). We will see that in our model, c will affect the $\mathcal{R}_0$ number and greatly affect the epidemic outcome. The parameters we will be using are as follows: $\beta = 0.3$, $p = 0.2$, $d = 0.5$, $v = 0.7$, the initial number of susceptibles, $X(0) = 20000$ and the initial number of men infected with HIV, $Y(0) = 5$.

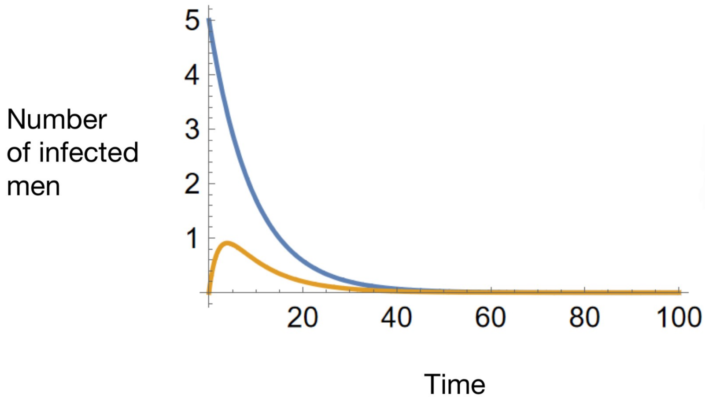

Figure 3.2: Here $\mathcal{R}_0 = 0.849$, number of sexual partners: $c = 2$, the blue line represents the number of infected men with HIV and the orange lines represents the number of men who developed AIDS. We see that no outbreak occurs.

Looking at 3.2 we see no outbreak has occurred, we see an exponential decrease of HIV cases which tends to zero as time increases. The number of AIDS cases initially increases, and peaks at 1 and then decreases toward zero. This initial increase is due to the progression of HIV to AIDS in the initial infected population and those they infected. This is the expected outcome of such a scenario as $\mathcal{R}_0 < 0$. Note that the number of men infected with HIV never goes higher than the initial number of those infected by HIV $Y(0) = 5$.

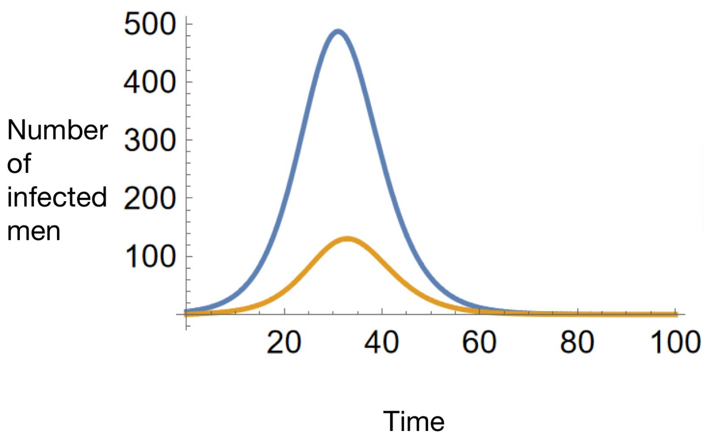

Figure 3.3: Here $\mathcal{R}_0 = 1.273$, number of sexual partners: $c = 3$, the blue line represents the number of infected men with HIV and the orange lines represents the number of men who developed AIDS. We see that an outbreak occurs.

From 3.3 we observe that an outbreak does occur, we see an exponential increase of HIV infections which reaches a peak of 500, (2.5% of the population infected at peak), then the number of HIV infections decreases and approaches zero as time increases. The same trend is observed with the AIDS cases which peaks at 100 cases (0.5% of the population at peak). The curve we see corresponding to the AIDS cases is slightly shifted to the right relative to the curve corresponding to the HIV infections, this is due to the fact that HIV takes time to develop into AIDS and so the peak number of cases of HIV and AIDS do not occur at the same time. The scenario we observe in 3.3 is expected as $\mathcal{R}_0 > 0$.

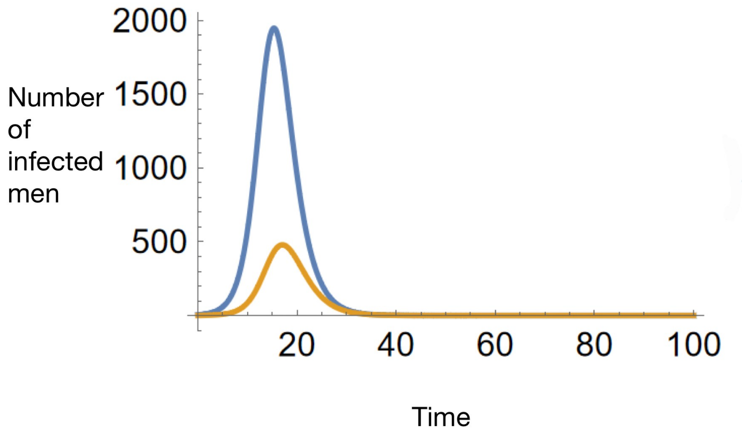

Figure 3.4: Here $\mathcal{R}_0 = 1.697$, number of sexual partners: $c = 4$, the blue line represents the number of infected men with HIV and the orange lines represents the number of men who developed AIDS. We see that an even bigger outbreak occurs.

In 3.4 we observe an outbreak which is larger, the same trends occur as aforementioned in the previous paragraph, how ever, the number of HIV infections reaches a peak of 2000 (10% of the population infected at peak) and the number of AIDS cases reaches a peak of 500 (2.5% of the population at peak). It's important to note how much a small increase in $\mathcal{R}_0$ causes a large increase in the peak number of cases for HIV/AIDS; the difference between the $\mathcal{R}_0$ number in 3.3 and the $\mathcal{R}_0$ number in 3.4 increased by 0.424 in comparison to the $\mathcal{R}_0$ number in 3.3, causing an increase of 1500 and 400 in HIV and AIDS cases respectively.

Overall, in the context in which and when this model is used, the knowledge of how HIV spreads and how to prevent transmission was perhaps unknown or at least not widely known, thus perhaps we have used a low value of transmission probability (β); as well as this, the average number of sexual partners was almost likely higher than 2. Studies such as [Hal12] have shown that discrimination and homophobia fuel the HIV epidemic in homosexual populations, in mind of this it's likely that the $\mathcal{R}_0$ number was much higher than 1.7. The figures above help us imagine the devastating scale of the HIV/AIDS epidemic in the homosexual populations in the 70s and 80s.

Why is an outbreak occurring when $\mathcal{R}_0 > 1$? When looking at the epidemic at an early stage we already know that the number of susceptibles is approximately the number in the total population that is $X \simeq N$, thus the solution of the equation which estimates the growth of the infectious HIV men (Y-class) has the solution:

$$Y(t) = Y(0)e^{\upsilon(\mathcal{R}_0 - 1)t}$$

It's easy to see that in order for the exponential function to increase then we must have $\mathcal{R}_0 > 1$. As a result of this, the number of infections increases exponentially, causing an outbreak (or an epidemic). This is the core idea behind the basic reproduction number.

Chapter 4

Epidemic Model for HIV Infection in two Heterosexual Age Groups in Kenya

4.1 The model

In this section we look at a more complex model to help us understand the dynamics of HIV within and between two different age group in Kenya (taken from [OL19]). In this model we have taken it to be that HIV transmission is mainly in heterosexual populations. The male and female populations are divided into young adults (aged 15-24) and adult (age 25 and over) sub-populations with each sub-population divided into susceptible individuals (S), infected individuals (I) and those who have been enrolled into a treatment programme (T). Unlike the previous model, here we have not taken into account the AIDS compartment as full blown AIDS patients are usually hospitalized and/or sexually inactive as such it is assumed that they are not able to engage in HIV transmission activities hence do not contribute to HIV infection. The total variable population at time t is described by:

$$N(t) = N_m(t) + N_f(t)$$

where the subscripts m and f denote male and female and the individual sex oriented population described by

$$N_m(t) = S_{dm} + S_{am} + I_{dm} + I_{am} + T_{dm} + T_{am}$$
$$N_f(t) = S_{df} + S_{af} + I_{df} + I_{af} + T_{df} + T_{af}$$

It can also be shown that:

$$N_m = \frac{\mu_a(\mu_d + \alpha)}{\Pi\tau(\alpha + \mu_a)}$$
$$N_f = \frac{\mu_a(\mu_d + \alpha)}{\Pi(1-\tau)(\alpha + \mu_a)}$$

Here we have that d and a represent the young adults and the adults, respectively. Following the SIR model concept [Wei13] individuals move from one compartment to the other as their status evolves with respect to the infection. The population of the susceptible young adults is generated at the rate Π via maturation into adulthood or immigration of which a proportion τ are assumed to be males and $(1-\tau)$ are assumed to be females. We also have that the population is reduced by young adults maturing into adult hood at the rate α and by a natural death rate μ_d. The infection rate of the young adults in both males and females is respectively, given by

$$\lambda_{dm} = \frac{\beta_1\gamma_1\left(I_{df} + \theta_1 I_{af} + \theta_2 T_{df} + \theta_3 T_{af}\right)}{N_m} \text{ and } \lambda_{df} = \frac{\beta_2\gamma_2(I_{dm} + \theta_4 I_{am} + \theta_5 T_{dm} + \theta_6 T_{am})}{N_f}.$$

β_1 and β_2 are the probabilities of HIV infection through contacts with individuals in I_{ij} and T_{ij} where i and j refers to young adults and adults, respectively. Also $\theta_{1,2,3,4,5,6}$ are modification factors in transmission probabilities. The infected young adults for both males and females are connected to treatment and care at the rates ϕ_1 and δ_1, respectively. The male and female adults infections are generated at the rates given by

$$\lambda_{am} = \frac{\beta_3\gamma_3\left(I_{df} + \eta_1 I_{af} + \eta_2 T_{df} + \eta_3 T_{af}\right)}{N_m} \text{ and } \lambda_{af} = \frac{\beta_4\gamma_4(I_{dm} + \eta_4 I_{am} + \eta_5 T_{dm} + \eta_6 T_{am})}{N_f},$$

respectively. β_3 and β_4 are the probabilities of HIV infection through contacts with individuals in I_{ij} and T_{ij} where i and j refers to young adults and adults respectively. The parameter $\eta_{1,2,3,4,5,6}$ are modification factors in transmission probabilities as before. Similar to the young adults, the infected male and female adults are connected to treatment and care at the respective rates given by ϕ_2 and δ_2. The adult populations are reduced at a natural death rate of μ_a. The parameters γ_k, for $k = 1, ..4$, are the rate at which individuals in each age category acquire sexual partners. These compartments have been illustrated as a flow chart in 4.1. Given the above descriptions and assumptions, the dynamics of HIV in the population is given by the following deterministic system of non-linear differential equations

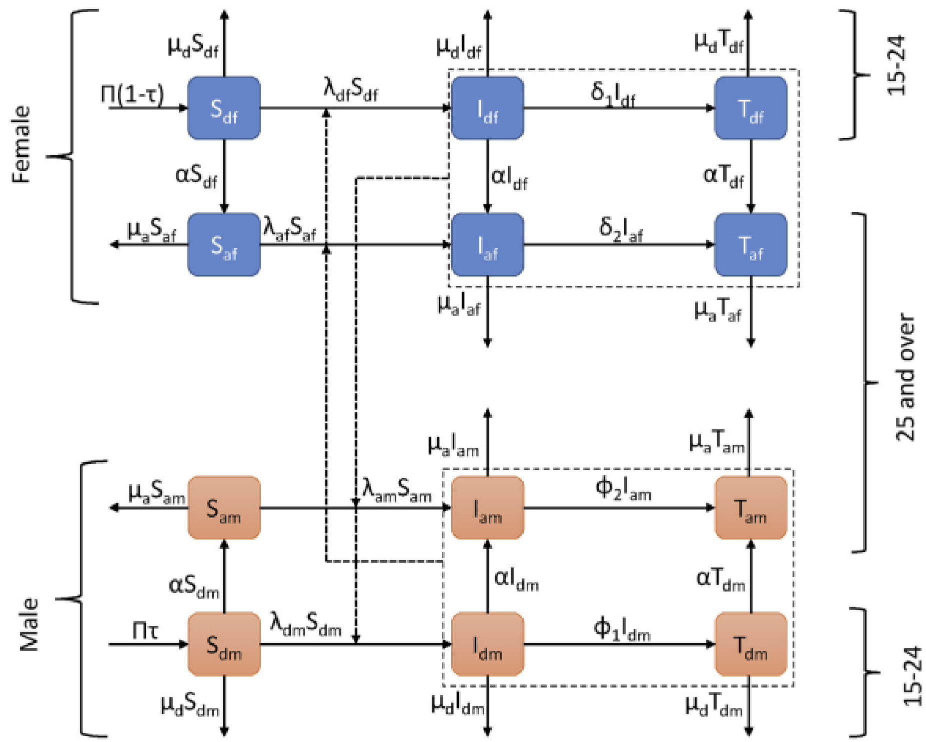

Figure 4.1: Flow chart for HIV infection in model 2 for which we will be using to create our model system.

$$\frac{dS_{dm}}{dt} = \Pi\tau - \lambda_{dm}S_{dm} - (\mu_d + \alpha)S_{dm}, \qquad \frac{dS_{df}}{dt} = \Pi(1-\tau) - \lambda_{df}S_{df} - (\mu_d + \alpha)S_{df},$$
$$\frac{dI_{dm}}{dt} = \lambda_{dm}S_{dm} - (\phi_1 + \alpha + \mu_d)I_{dm}, \qquad \frac{dI_{df}}{dt} = \lambda_{df}S_{df} - (\alpha + \delta_1 + \mu_d)I_{df},$$
$$\frac{dT_{dm}}{dt} = \phi_1 I_{dm} - (\alpha + \mu_d)T_{dm}, \qquad \frac{dT_{df}}{dt} = \delta_1 I_{df} - (\alpha + \mu_d)T_{df},$$
$$\frac{dS_{am}}{dt} = \alpha S_{dm} - \lambda_{am}S_{am} - \mu_a S_{am}, \qquad \frac{dS_{af}}{dt} = \alpha S_{df} - \lambda_{af}S_{af} - \mu_a S_{af},$$
$$\frac{dI_{am}}{dt} = \lambda_{am}S_{am} + \alpha I_{dm} - (\phi_2 + \mu_a)I_{am}, \qquad \frac{dI_{af}}{dt} = \lambda_{af}S_{af} + \alpha I_{df} - (\delta_2 + \mu_a)I_{af},$$
$$\frac{dT_{am}}{dt} = \phi_2 I_{am} + \alpha T_{dm} - \mu_a T_{am}, \qquad \frac{dT_{af}}{dt} = \delta_2 I_{af} + \alpha T_{df} - \mu_a T_{af},$$

Which are dependent on the following conditions:

$$S_{ijm}(0) \geq 0, I_{ijm}(0) \geq 0, T_{ijm}(0) \geq 0, S_{ijf}(0) \geq 0, I_{ijf}(0) \geq 0, T_{ijf}(0) \geq 0, \text{ for } i,j = d,a.$$

4.2 Calculating $\mathcal{R}_0$ values

First we will look at the disease-free equilibrium for the model, this can be calculated using the same method found in Section 3.2. In this model we have 4 different sub-populations namely S_{dm}, S_{am}, S_{df} and S_{af} - when looking at the DFE, all of their respective infected and treatment variables are 0. On top of this, the rates of change of the sub-populations is 0, using this information we can look at the DFE for the young adult male population:

$$\Pi\tau - \lambda_{dm}S_{dm} - (\mu_d + \alpha)S_{dm} = 0$$
$$\textbf{(N.B } \lambda_{dm} = \textbf{0 due to DFE conditions)}$$
$$\Pi\tau - (\mu_d + \alpha)S_{dm} = 0$$
$$S_{dm} = \frac{\Pi\tau}{\mu_d + \alpha}$$

Thus, the DFE for the young adult male population is:

$$DFE = (\frac{\Pi\tau}{\mu_d + \alpha}, 0, 0)^T$$

Next, calculating the DFE for the young adult female population:

$$\Pi(1-\tau) - \lambda_{df}S_{df} - (\mu_d + \alpha)S_{df} = 0$$
$$\textbf{(N.B } \lambda_{df} = \textbf{0 due to DFE conditions)}$$
$$\Pi(1-\tau) - (\mu_d + \alpha)S_{df} = 0$$
$$S_{df} = \frac{\Pi(1-\tau)}{\mu_d + \alpha}$$

Thus, the DFE for the young adult female population is:

$$DFE = (\frac{\Pi(1-\tau)}{\mu_d + \alpha}, 0, 0)^T$$

Moving onto the adult sub-populations, beginning with the adult male population:

$$\alpha S_{dm} - \lambda_{am} S_{am} - \mu_a S_{am} = 0$$
$$\textbf{(N.B } \lambda_{am} \textbf{ = 0 due to DFE conditions)}$$
$$\alpha S_{dm} - \mu_a S_{am} = 0$$
$$S_{am} = \frac{\alpha S_{dm}}{\mu_a}$$
$$\textbf{From the young male adult population we know } S_{df} = \frac{\Pi\tau}{\mu_d + \alpha}$$
$$\textbf{Thus, the DFE for the adult male population is:}$$
$$DFE = (\frac{\alpha\Pi\tau}{\mu_a(\mu_d + \alpha)}, 0, 0)^T$$

Next, the adult female population:

$$\alpha S_{df} - \lambda_{af} S_{af} - \mu_a S_{af} = 0$$
$$\textbf{(N.B } \lambda_{af} \textbf{ = 0 due to DFE conditions)}$$
$$\alpha S_{df} - \mu_a S_{af} = 0$$
$$S_{af} = \frac{\alpha S_{df}}{\mu_a}$$
$$\textbf{From the young female adult population we know } S_{df} = \frac{\Pi(1-\tau)}{\mu_d + \alpha}$$
$$\textbf{Thus, the DFE for the adult female population is:}$$
$$DFE = (\frac{\alpha\Pi(1-\tau)}{\mu_a(\mu_d + \alpha)}, 0, 0)^T$$

We are able to combine these vectors into one for the whole population of the model, which gives:

$$DFE = (\frac{\Pi\tau}{\mu_d + \alpha}, 0, 0, \frac{\alpha\Pi\tau}{\mu_a(\mu_d + \alpha)}, 0, 0, \frac{\Pi(1-\tau)}{\mu_d + \alpha}, 0, 0, \frac{\alpha\Pi(1-\tau)}{\mu_a(\mu_d + \alpha)}, 0, 0)^T$$

In light of the mathematical intractability, we are unable to explicitly express the basic reproduction number for the entire system of differential equations, as a result of this we must split the model to cover within and between age groups, this is possible as the model allows for free mixing of individuals from the different age groups.

4.2.1 Basic reproduction number, $\mathcal{R}_{0d}$, between young adults

Now, Let f be vector of infected classes, thus

$$\frac{df}{dt} = \mathcal{F}(I_{dm}, T_{dm}, I_{df}, T_{df})^T - \mathcal{V}(I_{dm}, T_{dm}, I_{df}, T_{df})^T$$

Where $\mathcal{F}(I_{dm}, T_{dm}, I_{df}, T_{df})^T$ is the vector of new infection rates and $\mathcal{V}(I_{dm}, T_{dm}, I_{df}, T_{df})^T$ is the vector of all other rates such as recovery rates and death rates. We can see from our model that:

$$\mathcal{F} = \begin{pmatrix} \lambda_{dm} S_{dm} \\ 0 \\ \lambda_{df} S_{df} \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} (\mu_d + \alpha + \phi_1) I_{dm} \\ (\mu_d + \alpha) T_{dm} - \phi_1 I_{dm} \\ (\mu_d + \alpha + \delta_1) I_{df} \\ (\mu_d + \alpha) T_{df} - \delta_1 I_{dm} \end{pmatrix}$$

Now, we find the Jacobian of both these vectors, first starting with $\mathcal{F}$:
Let $g_1 = \lambda_{dm} S_{dm}$, $h_1 = 0$, $g_2 = \lambda_{df} S_{df}$ and $h_2 = 0$. Now, we define the Jacobian, F, of $\mathcal{F}$ as:

$$F = \begin{bmatrix} \frac{\partial g_1}{\partial I_{dm}} & \frac{\partial g_1}{\partial T_{dm}} & \frac{\partial g_1}{\partial I_{df}} & \frac{\partial g_1}{\partial T_{df}} \\ \frac{\partial h_1}{\partial I_{dm}} & \frac{\partial h_1}{\partial T_{dm}} & \frac{\partial h_1}{\partial I_{df}} & \frac{\partial h_1}{\partial I_{df}} \\ \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{df}} & \frac{\partial g_2}{\partial T_{df}} \\ \frac{\partial h_2}{\partial I_{dm}} & \frac{\partial h_2}{\partial T_{dm}} & \frac{\partial h_2}{\partial I_{df}} & \frac{\partial h_2}{\partial T_{df}} \end{bmatrix}$$
$$= \begin{bmatrix} 0 & 0 & \frac{\beta_1 \gamma_1 S_{dm}}{N_m} & \frac{\beta_1 \gamma_1 \theta_2 S_{dm}}{N_m} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_2 \gamma_2 S_{df}}{N_f} & \frac{\beta_2 \gamma_2 \theta_5 S_{df}}{N_f} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Evaluating F at the DFE for the young adult population $= (\frac{\Pi\tau}{\mu_d}, 0, 0, \frac{\Pi(1-\tau)}{\mu_d}, 0, 0)^T$ (α not included as $\mathcal{R}_{0d}$ does not take into account the maturation of young adults into adults and the natural death rate of adults) gives:

$$F(DFE) = \begin{bmatrix} 0 & 0 & \beta_1\gamma_1 & \beta_1\gamma_1\theta_2 \\ 0 & 0 & 0 & 0 \\ \beta_2\gamma_2 & \beta_2\gamma_2\theta_5 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$
$$\textbf{As for DFE } S_{dm} = \frac{\Pi\tau}{\mu_d} = N_m \textbf{ and } S_{df} = \frac{\Pi(1-\tau)}{\mu_d} = N_f$$

Now, doing the same for $\mathcal{V}$: Let $g_1 = (\phi_1 + \mu_d)I_{dm}$, $h_1 = -\phi_1 I_{dm} + \mu_d T_{dm}$, $g_2 = (\delta_1 + \mu_d)I_{df}$ and $h_2 = -\delta_1 I_{df} - \mu_d T_{df}$. We define the Jacobian, V, of $\mathcal{V}$ as:

$$V = \begin{bmatrix} \frac{\partial g_1}{\partial I_{dm}} & \frac{\partial g_1}{\partial T_{dm}} & \frac{\partial g_1}{\partial I_{df}} & \frac{\partial g_1}{\partial T_{df}} \\ \frac{\partial h_1}{\partial I_{dm}} & \frac{\partial h_1}{\partial T_{dm}} & \frac{\partial h_1}{\partial I_{df}} & \frac{\partial h_1}{\partial I_{df}} \\ \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{df}} & \frac{\partial g_2}{\partial T_{df}} \\ \frac{\partial h_2}{\partial I_{dm}} & \frac{\partial h_2}{\partial T_{dm}} & \frac{\partial h_2}{\partial I_{df}} & \frac{\partial h_2}{\partial T_{df}} \end{bmatrix}$$
$$= \begin{bmatrix} \mu_d + \phi_1 & 0 & 0 & 0 \\ -\phi_1 & \mu_d & 0 & 0 \\ 0 & 0 & \delta_1 + \mu_d & 0 \\ 0 & 0 & \delta_1 & \mu_d \end{bmatrix} = V(DFE)$$

We wish to calculate FV^{-1} which is called the next generation matrix. The spectral radius of FV^{-1} gives us $\mathcal{R}_0$, which is given to be the maximum eigenvalue of FV^{-1}. To find the inverse we use the fact that our matrix, V, has zeros in the top right and bottom left quadrants. This allows us to split the matrix into two 2x2 matrices (the top left and bottom right quadrants) of which we find the inverse of both and then combine them and use the original 4x4 form with the 2 quadrants with zeros in the bottom left and top right:

$$V(DFE) = \begin{bmatrix} \mu_d + \phi_1 & 0 & 0 & 0 \\ -\phi_1 & \mu_d & 0 & 0 \\ 0 & 0 & \delta_1 + \mu_d & 0 \\ 0 & 0 & \delta_1 & \mu_d \end{bmatrix}$$
$$V^{-1} = \begin{pmatrix} \begin{bmatrix} \mu_d + \phi_1 & 0 \\ -\phi_1 & \mu_d \end{bmatrix}^{-1} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \mu_d + \delta_1 & 0 \\ -\delta_1 & \mu_d \end{bmatrix}^{-1} \end{pmatrix}$$

Giving:

$$V^{-1} = \begin{pmatrix} \frac{1}{\mu_d(\mu_d+\phi_1)}\begin{bmatrix} \mu_d & 0 \\ \phi_1 & \mu_d+\phi_1 \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \frac{1}{\mu_d(\mu_d+\delta_1)}\begin{bmatrix} \mu_d & 0 \\ \delta_1 & \mu_d+\delta_1 \end{bmatrix} \end{pmatrix}$$

$$= \begin{pmatrix} \begin{bmatrix} \frac{1}{\mu_d+\phi_1} & 0 \\ \frac{\phi_1}{\mu_d(\phi_1+\mu_d)} & \frac{1}{\mu_d} \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \frac{1}{\mu_d+\delta_1} & 0 \\ \frac{\delta_1}{\mu_d(\delta_1+\mu_d)} & \frac{1}{\mu_d} \end{bmatrix} \end{pmatrix} = \begin{bmatrix} \frac{1}{\mu_d+\phi_1} & 0 & 0 & 0 \\ \frac{\phi_1}{\mu_d(\phi_1+\mu_d)} & \frac{1}{\mu_d} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_d+\delta_1} & 0 \\ 0 & 0 & \frac{\delta_1}{\mu_d(\delta_1+\mu_d)} & \frac{1}{\mu_d} \end{bmatrix}$$

Now calculating the Next Generational Matrix FV^{-1}:

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \beta_1\gamma_1 & \beta_1\gamma_1\theta_2 \\ 0 & 0 & 0 & 0 \\ \beta_2\gamma_2 & \beta_2\gamma_2\theta_5 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\mu_d+\phi_1} & 0 & 0 & 0 \\ \frac{\phi_1}{\mu_d(\phi_1+\mu_d)} & \frac{1}{\mu_d} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_d+\delta_1} & 0 \\ 0 & 0 & \frac{\delta_1}{\mu_d(\delta_1+\mu_d)} & \frac{1}{\mu_d} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\beta_1\gamma_1}{\mu_d+\delta_1} + \frac{\beta_1\gamma_1\theta_2\delta_1}{\mu_d(\mu_d+\delta_1)} & \frac{\beta_1\gamma_1\theta_2}{\mu_d} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_2\gamma_2}{\mu_d+\phi_1} + \frac{\beta_2\gamma_2\theta_5\phi_1}{\mu_d(\mu_d+\phi_1)} & \frac{\beta_2\gamma_2\theta_5}{\mu_d} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The next step is to find the eigenvalues of the next generation matrix:

$$\left|FV^{-1} - \lambda I_4\right| = 0$$

Which gives us the characteristic polynomial:

$$\lambda^2(\lambda^2 - (\frac{\beta_2\theta_5\phi_1\gamma_2}{\mu_d(\phi_1+\mu_d)} + \frac{\beta_2\gamma_2}{\phi_1+\mu_d})(\frac{\beta_1\delta_1\theta_2\gamma_1}{\mu_d(\delta_1+\mu_d)} + \frac{\beta_1\gamma_1}{\delta_1+\mu_d})) = 0$$

That is:

$$\lambda^2 = 0$$

$$\lambda^2 - \left[(\frac{\beta_2\theta_5\phi_1\gamma_2 + \beta_2\gamma_2\mu_d}{\mu_d(\phi_1+\mu_d)})(\frac{\beta_1\theta_2\delta_1\gamma_1 + \beta_1\gamma_1\mu_d}{\mu_d(\delta_1+\mu_d)})\right] = 0$$

Thus the eigenvalues of FV^-1 are:

$$\lambda_{1,2} = 0$$

$$\lambda_3 = -\sqrt{\left[\frac{\beta_1\gamma_1(\delta_1\theta_2+\mu_d)}{\mu_d(\mu_d+\delta_1)}\right]\left[\frac{\beta_2\gamma_2(\mu_d+\theta_5\phi_1)}{\mu_d(\mu_d+\phi_1)}\right]}$$

$$\lambda_4 = \sqrt{\left[\frac{\beta_1\gamma_1(\delta_1\theta_2+\mu_d)}{\mu_d(\mu_d+\delta_1)}\right]\left[\frac{\beta_2\gamma_2(\mu_d+\theta_5\phi_1)}{\mu_d(\mu_d+\phi_1)}\right]}$$

To find the spectral radius, we choose the largest (dominant) eigenvalue $= \lambda_4$, which implies:

$$\mathcal{R}_{0d} = \sqrt{\left[\frac{\beta_1\gamma_1(\delta_1\theta_2+\mu_d)}{\mu_d(\mu_d+\delta_1)}\right]\left[\frac{\beta_2\gamma_2(\mu_d+\theta_5\phi_1)}{\mu_d(\mu_d+\phi_1)}\right]}$$

4.2.2 Basic reproduction number, $\mathcal{R}_{0a}$, between adults

Now, Let f be vector of infected classes, thus

$$\frac{df}{dt} = \mathcal{F}(I_{am}, T_{am}, I_{af}, T_{af})^T - \mathcal{V}(I_{am}, T_{am}, I_{af}, T_{af})^T$$

Where $\mathcal{F}(I_{am}, T_{am}, I_{af}, T_{af})^T$ is the vector of new infection rates and $\mathcal{V}(I_{am}, T_{am}, I_{af}, T_{af})^T$ is the vector of all other rates such as recovery rates and death rates. We can see from our model that:

$$\mathcal{F} = \begin{pmatrix} \lambda_{am} S_{am} \\ 0 \\ \lambda_{af} S_{af} \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} -\alpha I_{dm} + (\mu_a + \phi_2) I_{am} \\ -\phi_2 I_{am} - \alpha T_{dm} + \mu_a T_a m \\ -\alpha I_{af} + (\delta_2 + \mu_a) I_{af} \\ -\delta_2 I_{af} - \alpha T_{df} + \mu_a T_{af} \end{pmatrix}$$

Now, we find the Jacobian of both these vectors, first starting with $\mathcal{F}$:
Let $g_1 = \lambda_{am} S_{am}$, $h_1 = 0$, $g_2 = \lambda_{af} S_{af}$ and $h_2 = 0$. Now, we define the Jacobian, F, of $\mathcal{F}$ as:

$$F = \begin{bmatrix} \frac{\partial g_1}{\partial I_{am}} & \frac{\partial g_1}{\partial T_{am}} & \frac{\partial g_1}{\partial I_{af}} & \frac{\partial g_1}{\partial T_{af}} \\ \frac{\partial h_1}{\partial I_{am}} & \frac{\partial h_1}{\partial T_{am}} & \frac{\partial h_1}{\partial I_{af}} & \frac{\partial h_1}{\partial I_{af}} \\ \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{af}} & \frac{\partial g_2}{\partial T_{af}} \\ \frac{\partial h_2}{\partial I_{am}} & \frac{\partial h_2}{\partial T_{am}} & \frac{\partial h_2}{\partial I_{af}} & \frac{\partial h_2}{\partial T_{af}} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\beta_3 \gamma_3 \eta_1 S_{am}}{N_{am}} & \frac{\beta_3 \gamma_3 \eta_3 S_{am}}{N_{am}} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_4 \gamma_4 \eta_4 S_{af}}{N_{af}} & \frac{\beta_4 \gamma_4 \eta_6 S_{af}}{N_{af}} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Evaluating F at the DFE for the adult population $= (\frac{\Pi\tau}{\mu_a}, 0, 0, \frac{\Pi(1-\tau)}{\mu_a}, 0, 0)^T$ (α and μ_d not included as $\mathcal{R}_{0a}$ does not take into account the maturation of young adults into adults and the natural death rate of young adults) gives:

$$F(DFE) = \begin{bmatrix} 0 & 0 & \beta_3\gamma_3\eta_1 & \beta_3\gamma_3\eta_3 \\ 0 & 0 & 0 & 0 \\ \beta_4\gamma_4\eta_4 & \beta_4\gamma_4\eta_6 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\textbf{As for DFE } S_{am} = \frac{\Pi\tau}{\mu_a} = N_{am} \textbf{ and } S_{af} = \frac{\Pi(1-\tau)}{\mu_a} = N_{af}$$

Now, doing the same for $\mathcal{V}$: Let $g_1 = -\alpha I_{dm} + (\mu_a + \phi_2) I_{am}$, $h_1 = -\phi_2 I_{am} - \alpha T_{dm} + \mu_a T_a m$, $g_2 = -\alpha I_{af} + (\delta_2 + \mu_a) I_{af}$
and $h_2 = -\delta_2 I_{af} - \alpha T_{df} + \mu_a T_{af}$. We define the Jacobian, V, of $\mathcal{V}$ as:

$$V = \begin{bmatrix} \frac{\partial g_1}{\partial I_{am}} & \frac{\partial g_1}{\partial T_{am}} & \frac{\partial g_1}{\partial I_{af}} & \frac{\partial g_1}{\partial T_{af}} \\ \frac{\partial h_1}{\partial I_{am}} & \frac{\partial h_1}{\partial T_{am}} & \frac{\partial h_1}{\partial I_{af}} & \frac{\partial h_1}{\partial I_{af}} \\ \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{af}} & \frac{\partial g_2}{\partial T_{af}} \\ \frac{\partial h_2}{\partial I_{am}} & \frac{\partial h_2}{\partial T_{am}} & \frac{\partial h_2}{\partial I_{af}} & \frac{\partial h_2}{\partial T_{af}} \end{bmatrix}$$

$$= \begin{bmatrix} \mu_a + \phi_2 & 0 & 0 & 0 \\ -\phi_2 & \mu_a & 0 & 0 \\ 0 & 0 & \delta_2 + \mu_a & 0 \\ 0 & 0 & \delta_2 & \mu_a \end{bmatrix} = V(DFE)$$

We wish to calculate FV^{-1} which is called the next generation matrix. The spectral radius of FV^{-1} gives us $\mathcal{R}_0$, which is given to be the maximum eigenvalue of FV^{-1}. To find the inverse we use the fact that our matrix, V, has zeros in the top right and bottom left quadrants. This allows us to split the matrix into two 2x2 matrices (the top left and bottom right quadrants) of which we find the inverse of both and then combine them and use the original 4x4 form with the 2 quadrants with zeros in the bottom left and top right:

$$V(DFE) = \begin{bmatrix} \mu_a + \phi_2 & 0 & 0 & 0 \\ -\phi_2 & \mu_a & 0 & 0 \\ 0 & 0 & \delta_2 + \mu_a & 0 \\ 0 & 0 & \delta_2 & \mu_a \end{bmatrix}$$

$$V^{-1} = \begin{pmatrix} \begin{bmatrix} \mu_a + \phi_2 & 0 \\ -\phi_2 & \mu_a \end{bmatrix}^{-1} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \mu_a + \delta_2 & 0 \\ -\delta_2 & \mu_a \end{bmatrix}^{-1} \end{pmatrix}$$

Giving:

$$V^{-1} = \begin{pmatrix} \frac{1}{\mu_a(\mu_a+\phi_2)}\begin{bmatrix} \mu_a & 0 \\ \phi_2 & \mu_a+\phi_2 \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \frac{1}{\mu_a(\mu_a+\delta_2)}\begin{bmatrix} \mu_a & 0 \\ \delta_2 & \mu_a+\delta_2 \end{bmatrix} \end{pmatrix}$$

$$= \begin{pmatrix} \begin{bmatrix} \frac{1}{\mu_a+\phi_2} & 0 \\ \frac{\phi_2}{\mu_a(\phi_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \frac{1}{\mu_a+\delta_2} & 0 \\ \frac{\delta_2}{\mu_a(\delta_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix} \end{pmatrix} = \begin{bmatrix} \frac{1}{\mu_a+\phi_2} & 0 & 0 & 0 \\ \frac{\phi_2}{\mu_a(\phi_2+\mu_a)} & \frac{1}{\mu_a} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_a+\delta_2} & 0 \\ 0 & 0 & \frac{\delta_2}{\mu_a(\delta_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix}$$

Now calculating the Next Generational Matrix FV^{-1}:

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \beta_3\gamma_3\eta_1 & \beta_3\gamma_3\eta_3 \\ 0 & 0 & 0 & 0 \\ \beta_4\gamma_4\eta_4 & \beta_4\gamma_4\eta_6 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\mu_a+\phi_2} & 0 & 0 & 0 \\ \frac{\phi_2}{\mu_a(\phi_2+\mu_a)} & \frac{1}{\mu_a} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_a+\delta_2} & 0 \\ 0 & 0 & \frac{\delta_2}{\mu_a(\delta_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\beta_3\gamma_3\eta_1}{\mu_a+\delta_2} + \frac{\beta_3\gamma_3\eta_3\delta_2}{\mu_a(\mu_a+\delta_2)} & \frac{\beta_3\gamma_3\eta_3}{\mu_a} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_4\gamma_4\eta_4}{\mu_a+\phi_2} + \frac{\beta_4\gamma_4\eta_6\phi_2}{\mu_a(\mu_a+\phi_2)} & \frac{\beta_4\gamma_4\eta_6}{\mu_a} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The next step is to find the eigenvalues of the next generation matrix:

$$\left|FV^{-1} - \lambda I_4\right| = 0$$

Which gives us the characteristic polynomial:

$$\lambda^2(\lambda^2 - (\frac{\beta_4\eta_6\phi_2\gamma_4}{\mu_a(\phi_2+\mu_a)} + \frac{\beta_4\gamma_4\eta_4}{\phi_2+\mu_a})(\frac{\beta_3\delta_2\eta_3\gamma_3}{\mu_a(\delta_2+\mu_a)} + \frac{\beta_3\gamma_3\eta_1}{\delta_2+\mu_a})) = 0$$

That is:

$$\lambda^2 = 0$$

$$\lambda^2 - \left[(\frac{\beta_4\eta_6\phi_2\gamma_4 + \beta_4\gamma_4\eta_4\mu_a}{\mu_a(\phi_2+\mu_a)})(\frac{\beta_3\eta_3\delta_2\gamma_3 + \beta_3\gamma_3\mu_a\eta_1}{\mu_a(\delta_1+\mu_d)})\right] = 0$$

Thus the eigenvalues of FV^-1 are:

$$\lambda_{1,2} = 0$$

$$\lambda_3 = -\sqrt{\left[\frac{\beta_3\gamma_3(\delta_2\eta_3+\eta_1\mu_a)}{\mu_a(\mu_a+\delta_2)}\right]\left[\frac{\beta_4\gamma_4(\eta_4\mu_a+\eta_6\phi_2)}{\mu_a(\mu_a+\phi_2)}\right]}$$

$$\lambda_4 = \sqrt{\left[\frac{\beta_3\gamma_3(\delta_2\eta_3+\eta_1\mu_a)}{\mu_a(\mu_a+\delta_2)}\right]\left[\frac{\beta_4\gamma_4(\eta_4\mu_a+\eta_6\phi_2)}{\mu_a(\mu_a+\phi_2)}\right]}$$

To find the spectral radius, we choose the largest (dominant) eigenvalue $= \lambda_4$, which implies:

$$\mathcal{R}_{0a} = \sqrt{\left[\frac{\beta_3\gamma_3(\delta_2\eta_3+\eta_1\mu_a)}{\mu_a(\mu_a+\delta_2)}\right]\left[\frac{\beta_4\gamma_4(\eta_4\mu_a+\eta_6\phi_2)}{\mu_a(\mu_a+\phi_2)}\right]}$$

4.2.3 Basic reproduction number, $\mathcal{R}_{0mdfa}$, between young male adults and female adults

Now, Let f be vector of infected classes, thus

$$\frac{df}{dt} = \mathcal{F}(I_{dm}, T_{dm}, I_{af}, T_{af})^T - \mathcal{V}(I_{dm}, T_{dm}, I_{af}, T_{af})^T$$

Where $\mathcal{F}(I_{dm}, T_{dm}, I_{af}, T_{af})^T$ is the vector of new infection rates and $\mathcal{V}(I_{dm}, T_{dm}, I_{af}, T_{af})^T$ is the vector of all other rates such as recovery rates and death rates. We can see from our model that:

$$\mathcal{F} = \begin{pmatrix} \lambda_{dm} S_{dm} \\ 0 \\ \lambda_{af} S_{af} \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} (\mu_d + \alpha + \phi_1) I_{dm} \\ -\phi_1 I_{dm} + (\alpha + \mu_a) T_d m \\ -\alpha I_{df} + (\delta_2 + \mu_a) I_{af} \\ -\delta_2 I_{af} - \alpha T_{df} + \mu_a T_{af} \end{pmatrix}$$

Now, we find the Jacobian of both these vectors, first starting with $\mathcal{F}$:
Let $g_1 = \lambda_{dm} S_{dm}$, $h_1 = 0$, $g_2 = \lambda_{af} S_{af}$ and $h_2 = 0$. Now, we define the Jacobian, F, of $\mathcal{F}$ as:

$$F = \begin{bmatrix} \frac{\partial g_1}{\partial I_{dm}} & \frac{\partial g_1}{\partial T_{dm}} & \frac{\partial g_1}{\partial I_{af}} & \frac{\partial g_1}{\partial T_{af}} \\ \frac{\partial h_1}{\partial I_{dm}} & \frac{\partial h_1}{\partial T_{dm}} & \frac{\partial h_1}{\partial I_{af}} & \frac{\partial h_1}{\partial I_{af}} \\ \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{af}} & \frac{\partial g_2}{\partial T_{af}} \\ \frac{\partial h_2}{\partial I_{dm}} & \frac{\partial h_2}{\partial T_{dm}} & \frac{\partial h_2}{\partial I_{af}} & \frac{\partial h_2}{\partial T_{af}} \end{bmatrix}$$
$$= \begin{bmatrix} 0 & 0 & \frac{\beta_1 \gamma_1 \theta_1 S_{dm}}{N_{dm}} & \frac{\beta_1 \gamma_1 \theta_3 S_{dm}}{N_{dm}} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_4 \gamma_4 S_{af}}{N_{af}} & \frac{\beta_4 \gamma_4 \eta_5 S_{af}}{N_{af}} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Evaluating F at the DFE for the young male adult and female adult sub-populations, $= (\frac{\Pi\tau}{\mu_d+\alpha}, 0, 0, \frac{\Pi(1-\tau)}{\mu_a(\mu_d+\alpha)}, 0, 0)^T$ (Note this time α and μ_d is included as $\mathcal{R}_{0mdfa}$ takes into account the maturation of young adults into adults and the natural death rate of young adults) gives:

$$F(DFE) = \begin{bmatrix} 0 & 0 & \frac{\beta_1 \gamma_1 \theta_1 \mu_a}{\alpha+\mu_a} & \frac{\beta_1 \gamma_1 \theta_3 \mu_a}{\alpha+\mu_a} \\ 0 & 0 & 0 & 0 \\ \frac{\alpha \beta_4 \gamma_4}{\alpha+\mu_a} & \frac{\alpha \beta_4 \gamma_4 \eta_5}{\alpha+\mu_a} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

As for DFE $\frac{S_{dm}}{N_m} = (\frac{\Pi\tau}{\mu_d + \alpha})(\frac{\mu_a(\mu_d + \alpha)}{\Pi\tau(\alpha + \mu_a)}) = \frac{\alpha}{\alpha + \mu_a}$ **and** $\frac{S_{af}}{N_f} = (\frac{\alpha\Pi(1-\tau)}{(\mu_a(\mu_d + \alpha)})(\frac{\mu_a(\mu_d + \alpha)}{\Pi(1-\tau)(\alpha + \mu_a)}) = \frac{1}{\alpha + \mu_a}$

Now, doing the same for $\mathcal{V}$: Let $g_1 = (\phi_1 + \alpha + \mu_d) I_{dm}$, $h_1 = -\phi_1 I_{dm} + (\alpha + \mu_d) T_{dm} + \mu_a T_a m$, $g_2 = -\alpha I_{df} + (\delta_2 + \mu_a) I_{af}$ and $h_2 = -\delta_2 I_{af} - \alpha T_{df} + \mu_a T_{af}$. We define the Jacobian, V, of $\mathcal{V}$ as:

$$V = \begin{bmatrix} \frac{\partial g_1}{\partial I_{dm}} & \frac{\partial g_1}{\partial T_{dm}} & \frac{\partial g_1}{\partial I_{af}} & \frac{\partial g_1}{\partial T_{af}} \\ \frac{\partial h_1}{\partial I_{dm}} & \frac{\partial h_1}{\partial T_{dm}} & \frac{\partial h_1}{\partial I_{af}} & \frac{\partial h_1}{\partial I_{af}} \\ \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{dm}} & \frac{\partial g_2}{\partial I_{af}} & \frac{\partial g_2}{\partial T_{af}} \\ \frac{\partial h_2}{\partial I_{dm}} & \frac{\partial h_2}{\partial T_{dm}} & \frac{\partial h_2}{\partial I_{af}} & \frac{\partial h_2}{\partial T_{af}} \end{bmatrix}$$
$$= \begin{bmatrix} \mu_a + \phi_1 + \alpha & 0 & 0 & 0 \\ -\phi_1 & \alpha + \mu_d & 0 & 0 \\ 0 & 0 & \delta_2 + \mu_a & 0 \\ 0 & 0 & -\delta_2 & \mu_a \end{bmatrix} = V(DFE)$$

We wish to calculate FV^{-1} which is called the next generation matrix. The spectral radius of FV^{-1} gives us $\mathcal{R}_0$, which is given to be the maximum eigenvalue of FV^{-1}. To find the inverse we use the fact that our matrix, V, has zeros in the top right and bottom left quadrants. This allows us to split the matrix into two 2x2 matrices (the top left and bottom right quadrants) of which we find the inverse of both and then combine them and use the original 4x4 form with the 2 quadrants with zeros in the bottom left and top right:

$$V(DFE) = \begin{bmatrix} \mu_a + \phi_1 + \alpha & 0 & 0 & 0 \\ -\phi_1 & \alpha + \mu_d & 0 & 0 \\ 0 & 0 & \delta_2 + \mu_a & 0 \\ 0 & 0 & -\delta_2 & \mu_a \end{bmatrix}$$

$$V^{-1} = \begin{pmatrix} \begin{bmatrix} \mu_a + \phi_1 + \alpha & 0 \\ -\phi_1 & \alpha + \mu_d \end{bmatrix}^{-1} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \mu_a + \delta_2 & 0 \\ -\delta_2 & \mu_a \end{bmatrix}^{-1} \end{pmatrix}$$

Giving:

$$V^{-1} = \begin{pmatrix} \frac{1}{(\mu_d+\alpha)(\mu_d+\phi_1+\alpha)} \begin{bmatrix} \mu_d+\alpha & 0 \\ \phi_1 & \mu_d+\phi_1+\alpha \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \frac{1}{\mu_a(\mu_a+\delta_2)} \begin{bmatrix} \mu_a & 0 \\ \delta_2 & \mu_a+\delta_2 \end{bmatrix} \end{pmatrix}$$

$$= \begin{pmatrix} \begin{bmatrix} \frac{1}{\mu_d+\phi_1+\alpha} & 0 \\ \frac{\phi_1}{(\mu_d+\alpha)(\phi_1+\mu_d+\alpha)} & \frac{1}{\alpha+\mu_d} \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \frac{1}{\mu_a+\delta_2} & 0 \\ \frac{\delta_2}{\mu_a(\delta_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix} \end{pmatrix} = \begin{bmatrix} \frac{1}{\mu_a+\phi_2+\alpha} & 0 & 0 & 0 \\ \frac{\phi_1}{(\mu_d+\alpha)(\phi_1+\mu_d+\alpha)} & \frac{1}{\mu_a+\alpha} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_a+\delta_2} & 0 \\ 0 & 0 & \frac{\delta_2}{\mu_a(\delta_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix}$$

Now calculating the Next Generational Matrix FV^{-1}:

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{\beta_1\gamma_1\theta_1\mu_a}{\alpha+\mu_a} & \frac{\beta_1\gamma_1\theta_3\mu_a}{\alpha+\mu_a} \\ 0 & 0 & 0 & 0 \\ \frac{\alpha\beta_4\gamma_4}{\alpha+\mu_a} & \frac{\alpha\beta_4\gamma_4\eta_5}{\alpha+\mu_a} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\mu_a+\phi_2+\alpha} & 0 & 0 & 0 \\ \frac{\phi_1}{(\mu_d+\alpha)(\phi_1+\mu_d+\alpha)} & \frac{1}{\mu_a+\alpha} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_a+\delta_2} & 0 \\ 0 & 0 & \frac{\delta_2}{\mu_a(\delta_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\beta_1\gamma_1\delta_2\theta_3}{(\mu_a+\alpha)(\delta_2+\mu_a)} + \frac{\beta_1\gamma_1\theta_1}{(\alpha+\mu_a)(\mu_a+\delta_2)} & \frac{\beta_1\gamma_1\theta_3}{\alpha+\mu_a} \\ 0 & 0 & 0 & 0 \\ \frac{\alpha\beta_4\gamma_4\eta_5\phi_1}{(\alpha+\mu_d+\phi_1)(\alpha+\mu_a)(\alpha+\mu_d)} + \frac{\alpha\beta_4\gamma_4}{(\alpha+\mu_a)(\mu_d+\phi_1+\alpha)} & \frac{\alpha\beta_4\gamma_4\eta_5}{(\mu_a+\alpha)(\alpha+\mu_d)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The next step is to find the eigenvalues of the next generation matrix:

$$\left|FV^{-1} - \lambda I_4\right| = 0$$

Which gives us the characteristic polynomial:

$$\lambda^2(\lambda^2 - (\frac{\alpha\beta_1\beta_4\gamma_1\gamma_4(\alpha+\eta_5\phi_1+\mu_a)(\delta_2\theta_1+\theta_3\mu_a)}{(\mu_d+\alpha)(\mu_a+\alpha)^2(\delta_2+\mu_a)(\alpha+\phi_1+\mu_d)} = 0$$

That is:

$$\lambda^2 = 0$$

$$\lambda^2 - \left[\frac{\alpha\beta_4\gamma_4(\eta_5\phi_1+\alpha+\mu_d)}{(\mu_d+\alpha)(\mu_d+\phi_1+\alpha)(\mu_a+\alpha)}\right]\left[\frac{\beta_1\gamma_1(\theta_1\mu_a+\delta_2\theta_3)}{(\delta_2+\mu_a)(\mu_a+\alpha)}\right] = 0$$

Thus the eigenvalues of $FV^{-}1$ are:

$$\lambda_{1,2} = 0$$

$$\lambda_3 = -\sqrt{\left[\frac{\alpha\beta_4\gamma_4(\eta_5\phi_1+\alpha+\mu_d)}{(\mu_d+\alpha)(\mu_d+\phi_1+\alpha)(\mu_a+\alpha)}\right]\left[\frac{\beta_1\gamma_1(\theta_1\mu_a+\delta_2\theta_3)}{(\delta_2+\mu_a)(\mu_a+\alpha)}\right]}$$

$$\lambda_4 = \sqrt{\left[\frac{\alpha\beta_4\gamma_4(\eta_5\phi_1+\alpha+\mu_d)}{(\mu_d+\alpha)(\mu_d+\phi_1+\alpha)(\mu_a+\alpha)}\right]\left[\frac{\beta_1\gamma_1(\theta_1\mu_a+\delta_2\theta_3)}{(\delta_2+\mu_a)(\mu_a+\alpha)}\right]}$$

To find the spectral radius, we choose the largest (dominant) eigenvalue $= \lambda_4$, which implies:

$$\mathcal{R}_{0mdfa} = \sqrt{\left[\frac{\alpha\beta_4\gamma_4(\eta_5\phi_1+\alpha+\mu_d)}{(\mu_d+\alpha)(\mu_d+\phi_1+\alpha)(\mu_a+\alpha)}\right]\left[\frac{\beta_1\gamma_1(\theta_1\mu_a+\delta_2\theta_3)}{(\delta_2+\mu_a)(\mu_a+\alpha)}\right]}$$

4.2.4 Basic reproduction number, $\mathcal{R}_{0fdma}$, between young female adults and male adults

Now, Let f be vector of infected classes, thus

$$\frac{df}{dt} = \mathcal{F}(I_{am}, T_{am}, I_{df}, T_{df})^T - \mathcal{V}(I_{am}, T_{am}, I_{df}, T_{df})^T$$

Where $\mathcal{F}(I_{am}, T_{am}, I_{df}, T_{df})^T$ is the vector of new infection rates and $\mathcal{V}(I_{am}, T_{am}, I_{df}, T_{df})^T$ is the vector of all other rates such as recovery rates and death rates. We can see from our model that:

$$\mathcal{F} = \begin{pmatrix} \lambda_{am} S_{am} \\ 0 \\ \lambda_{df} S_{df} \\ 0 \end{pmatrix}, \qquad \mathcal{V} = \begin{pmatrix} -\alpha I_{dm} + (\phi_2 + \mu_a) I_{am} \\ -\phi_2 I_{am} - \alpha T_{dm} + \mu_a T_{am} \\ (\alpha + \delta_1 + \mu_d) I_{df} \\ -\delta_1 I_{df} + (\alpha + \mu_d) T_{df} \end{pmatrix}$$

Now, we find the Jacobian of both these vectors, first starting with $\mathcal{F}$:
Let $g_1 = \lambda_{am} S_{am}$, $h_1 = 0$, $g_2 = \lambda_{df} S_{df}$ and $h_2 = 0$. Now, we define the Jacobian, F, of $\mathcal{F}$ as:

$$F = \begin{bmatrix} \frac{\partial g_1}{\partial I_{am}} & \frac{\partial g_1}{\partial T_{am}} & \frac{\partial g_1}{\partial I_{df}} & \frac{\partial g_1}{\partial T_{df}} \\ \frac{\partial h_1}{\partial I_{am}} & \frac{\partial h_1}{\partial T_{am}} & \frac{\partial h_1}{\partial I_{df}} & \frac{\partial h_1}{\partial I_{df}} \\ \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{df}} & \frac{\partial g_2}{\partial T_{df}} \\ \frac{\partial h_2}{\partial I_{am}} & \frac{\partial h_2}{\partial T_{am}} & \frac{\partial h_2}{\partial I_{df}} & \frac{\partial h_2}{\partial T_{df}} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\beta_3 \gamma_3 S_{am}}{N_m} & \frac{\beta_3 \gamma_3 \eta_2 S_{am}}{N_m} \\ 0 & 0 & 0 & 0 \\ \frac{\beta_2 \gamma_2 \theta_4 S_{df}}{N_f} & \frac{\beta_2 \gamma_2 \theta_6 S_{df}}{N_f} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

Evaluating F at the DFE for the young male adult and female adult sub-populations, $= (\frac{\alpha \Pi \tau}{\mu_a(\mu_d + \alpha)}, 0, 0, \frac{\Pi(1-\tau)}{\mu_d + \alpha}, 0, 0)^T$ (Note this time α and μ_d is included as $\mathcal{R}_{0fdma}$ takes into account the maturation of young adults into adults and the natural death rate of young adults) gives:

$$F(DFE) = \begin{bmatrix} 0 & 0 & \frac{\alpha \beta_3 \gamma_3}{\alpha + \mu_a} & \frac{\alpha \beta_3 \gamma_3 \eta_2}{\alpha + \mu_a} \\ 0 & 0 & 0 & 0 \\ \frac{\mu_a \beta_2 \gamma_2 \theta_4}{\alpha + \mu_a} & \frac{\mu_a \beta_2 \gamma_2 \theta_6}{\alpha + \mu_a} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

As for DFE $\frac{S_{am}}{N_m} = (\frac{\alpha \Pi \tau}{\mu_a(\mu_d + \alpha)})(\frac{\mu_a(\mu_d + \alpha)}{\Pi \tau (\alpha + \mu_a)}) = \frac{\alpha}{\alpha + \mu_a}$ **and** $\frac{S_{df}}{N_f} = (\frac{\Pi(1-\tau)}{\mu_d + \alpha})(\frac{\mu_a(\mu_d + \alpha)}{\Pi(1-\tau)(\alpha + \mu_a)}) = \frac{\mu_a}{\alpha + \mu_a}$

Now, doing the same for $\mathcal{V}$: Let $g_1 = -\alpha I_{dm}(\phi_2 + \mu_a) I_{am}$, $h_1 = -\phi_2 I_{am} - \alpha T_{dm} + \mu_a T_{am}$, $g_2 = (\alpha + \delta_1 + \mu_d) I_{df}$ and $h_2 = -\delta_1 I_{df} + (\alpha + \mu_d) T_{df}$. We define the Jacobian, V, of $\mathcal{V}$ as:

$$V = \begin{bmatrix} \frac{\partial g_1}{\partial I_{am}} & \frac{\partial g_1}{\partial T_{am}} & \frac{\partial g_1}{\partial I_{df}} & \frac{\partial g_1}{\partial T_{df}} \\ \frac{\partial h_1}{\partial I_{am}} & \frac{\partial h_1}{\partial T_{am}} & \frac{\partial h_1}{\partial I_{df}} & \frac{\partial h_1}{\partial I_{df}} \\ \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{am}} & \frac{\partial g_2}{\partial I_{df}} & \frac{\partial g_2}{\partial T_{df}} \\ \frac{\partial h_2}{\partial I_{am}} & \frac{\partial h_2}{\partial T_{am}} & \frac{\partial h_2}{\partial I_{df}} & \frac{\partial h_2}{\partial T_{df}} \end{bmatrix}$$

$$= \begin{bmatrix} \mu_a + \phi_2 & 0 & 0 & 0 \\ -\phi_2 & \mu_a & 0 & 0 \\ 0 & 0 & \delta_1 + \mu_d + \alpha & 0 \\ 0 & 0 & -\delta_1 & \mu_d + \alpha \end{bmatrix} = V(DFE)$$

We wish to calculate FV^{-1} which is called the next generation matrix. The spectral radius of FV^{-1} gives us $\mathcal{R}_0$, which is given to be the maximum eigenvalue of FV^{-1}. To find the inverse we use the fact that our matrix, V, has zeros in the top right and bottom left quadrants. This allows us to split the matrix into two 2x2 matrices (the top left and bottom right quadrants) of which we find the inverse of both and then combine them and use the original 4x4 form with the 2 quadrants with zeros in the bottom left and top right:

$$V(DFE) = \begin{bmatrix} \mu_a + \phi_2 & 0 & 0 & 0 \\ -\phi_2 & \mu_a & 0 & 0 \\ 0 & 0 & \delta_1 + \mu_d + \alpha & 0 \\ 0 & 0 & -\delta_1 & \mu_d + \alpha \end{bmatrix}$$

$$V^{-1} = \begin{pmatrix} \begin{bmatrix} \mu_a + \phi_2 & 0 \\ -\phi_2 & \mu_a \end{bmatrix}^{-1} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \mu_d + \delta_1 + \alpha & 0 \\ -\delta_1 & \mu_d + \alpha \end{bmatrix}^{-1} \end{pmatrix}$$

Giving:

$$V^{-1} = \begin{pmatrix} \frac{1}{\mu_a(\mu_a+\phi_2)}\begin{bmatrix} \mu_a & 0 \\ \phi_2 & \mu_a+\phi_2 \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \frac{1}{(\mu_d+\alpha)(\mu_d+\delta_1+\alpha)}\begin{bmatrix} \mu_d+\alpha & 0 \\ \delta_1 & \mu_d+\delta_1+\alpha \end{bmatrix} \end{pmatrix}$$

$$= \begin{pmatrix} \begin{bmatrix} \frac{1}{\phi_2+\mu_a} & 0 \\ \frac{\phi_2}{\mu_a(\phi_2+\mu_a)} & \frac{1}{\mu_a} \end{bmatrix} & \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \\ \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} & \begin{bmatrix} \frac{1}{\mu_d+\delta_1+\alpha} & 0 \\ \frac{\delta_1}{(\mu_d+\alpha)(\mu_d+\delta_1+\alpha)} & \frac{1}{\mu_d+\alpha} \end{bmatrix} \end{pmatrix} = \begin{bmatrix} \frac{1}{\mu_a+\phi_2} & 0 & 0 & 0 \\ \frac{\phi_2}{\mu_a(\phi_2+\mu_a)} & \frac{1}{\mu_a} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_d+\delta_1+\alpha} & 0 \\ 0 & 0 & \frac{\delta_1}{(\mu_d+\alpha)(\delta_1+\mu_d+\alpha)} & \frac{1}{\mu_d+\alpha} \end{bmatrix}$$

Now calculating the Next Generational Matrix FV^{-1}:

$$FV^{-1} = \begin{bmatrix} 0 & 0 & \frac{\alpha\beta_3\gamma_3}{\alpha+\mu_a} & \frac{\alpha\beta_3\gamma_3\eta_2}{\alpha+\mu_a} \\ 0 & 0 & 0 & 0 \\ \frac{\mu_a\beta_2\gamma_2\theta_4}{\alpha+\mu_a} & \frac{\mu_a\beta_2\gamma_2\theta_6}{\alpha+\mu_a} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\mu_a+\phi_2} & 0 & 0 & 0 \\ \frac{\phi_2}{\mu_a(\phi_2+\mu_a)} & \frac{1}{\mu_a} & 0 & 0 \\ 0 & 0 & \frac{1}{\mu_d+\delta_1+\alpha} & 0 \\ 0 & 0 & \frac{\delta_1}{(\mu_d+\alpha)(\delta_1+\mu_d+\alpha)} & \frac{1}{\mu_d+\alpha} \end{bmatrix}$$

$$= \begin{bmatrix} 0 & 0 & \frac{\alpha\beta_3\gamma_3}{(\mu_a+\alpha)(\delta_1+\mu_d+\alpha)} + \frac{\alpha\beta_3\gamma_3\eta_2\delta_1}{(\alpha+\mu_a)(\mu_d+\alpha)(\mu_d+\delta_1+\alpha)} & \frac{\alpha\beta_3\gamma_3\eta_2}{\alpha+\mu_d} \\ 0 & 0 & 0 & 0 \\ \frac{\mu_a\beta_2\gamma_2\theta_4}{(\alpha+\mu_a)(\phi_2+\mu_a)} + \frac{\beta_2\gamma_2\theta_6\phi_2}{(\alpha+\mu_a)(\mu_a+\phi_2)} & \frac{\beta_2\gamma_2\theta_6}{(\mu_a+\alpha)} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}$$

The next step is to find the eigenvalues of the next generation matrix:

$$\left|FV^{-1} - \lambda I_4\right| = 0$$

Which gives us the characteristic polynomial:

$$\lambda^2(\lambda^2 - (\frac{\alpha\beta_2\beta_3\gamma_2\gamma_3(\alpha+\eta_2\delta_1+\mu_d)(\mu_a\theta_4+\theta_6\phi_2)}{(\mu_d+\alpha)(\mu_a+\alpha)^2(\phi_2+\mu_a)(\alpha+\delta_1+\mu_d)} = 0$$

That is:

$$\lambda^2 = 0$$

$$\lambda^2 - \left[\frac{\beta_2\gamma_3(\theta_4\mu_a+\theta_6\phi_2)}{(\mu_a+\alpha)(\mu_a+\phi_2)}\right]\left[\frac{\alpha\beta_3\gamma_3(\alpha+\delta_1\eta_2+\mu_d)}{(\delta_1+\mu_d+\alpha)(\mu_a+\alpha)(\alpha+\mu_d)}\right] = 0$$

Thus the eigenvalues of $FV^{-}1$ are:

$$\lambda_{1,2} = 0$$

$$\lambda_3 = -\sqrt{\left[\frac{\beta_2\gamma_3(\theta_4\mu_a+\theta_6\phi_2)}{(\mu_a+\alpha)(\mu_a+\phi_2)}\right]\left[\frac{\alpha\beta_3\gamma_3(\alpha+\delta_1\eta_2+\mu_d)}{(\delta_1+\mu_d+\alpha)(\mu_a+\alpha)(\alpha+\mu_d)}\right]}$$

$$\lambda_4 = \sqrt{\left[\frac{\beta_2\gamma_3(\theta_4\mu_a+\theta_6\phi_2)}{(\mu_a+\alpha)(\mu_a+\phi_2)}\right]\left[\frac{\alpha\beta_3\gamma_3(\alpha+\delta_1\eta_2+\mu_d)}{(\delta_1+\mu_d+\alpha)(\mu_a+\alpha)(\alpha+\mu_d)}\right]}$$

To find the spectral radius, we choose the largest (dominant) eigenvalue $= \lambda_4$, which implies:

$$\mathcal{R}_{0fdma} = \sqrt{\left[\frac{\beta_2\gamma_3(\theta_4\mu_a+\theta_6\phi_2)}{(\mu_a+\alpha)(\mu_a+\phi_2)}\right]\left[\frac{\alpha\beta_3\gamma_3(\alpha+\delta_1\eta_2+\mu_d)}{(\delta_1+\mu_d+\alpha)(\mu_a+\alpha)(\alpha+\mu_d)}\right]}$$

It's also important to note that the $\mathcal{R}_0$ value is between the two age groups is given to be $\mathcal{R}_0 = max\{\mathcal{R}_{0fdma}, \mathcal{R}_{0mdfa}\}$ as the maximum basic reproduction number will give the worst case scenario which is what we want to prevent.

Chapter 5

Conclusion

5.0.1 Discussion

The HIV/AIDS epidemic has been on going for many years now, firstly concentrated in homosexual populations in the outset, but now it is mostly prevalent in heterosexual populations in Sub-Saharan Africa. Fortunately, treatments for HIV been developed and there is ongoing research into developing mRNA vaccines for HIV, but this has proved to be immensely difficult [MHC21], sadly, no cure has been found yet. Despite on going education and awareness about HIV, the HIV epidemic in Sub-Saharan Africa is still devastating, estimates for the $\mathcal{R}_0$ have been estimated to be as high as 17 in Uganda [NWMS14]. In mind of this, this project has shown how to calculate the $\mathcal{R}_0$ value for any given SIR based model, this work can be applied onto different diseases such as COVID-19 using the same methods.

5.0.2 Further work

In this project we used the estimates of the basic reproduction value to simulate an outbreak of HIV in a completely susceptible population in the model from [Mur02]. An avenue of further work and investigation would be doing the same for the model from [OL19]; this will be much more difficult. In this model, we have 24 parameters all of which need to be estimated from a real world study of HIV infection in Sub-Saharan Africa; 12 of these parameters are modification factors in transmission probabilities, these may be much harder to estimate due to the variance in sexual behaviour - this may give a less accurate $\mathcal{R}_0$ value. For both models we could perform statistical analyses on them such as the goodness-of-fit of the model helping us understand furthermore the usefulness of these models.

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