St. Xavier's College (Autonomous), Kolkata

DETERMINISTIC EPIDEMIC MODELLING

HIV/AIDS

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I affirm that I have identified all my sources and that no part of my dissertation paper uses unacknowledged materials.

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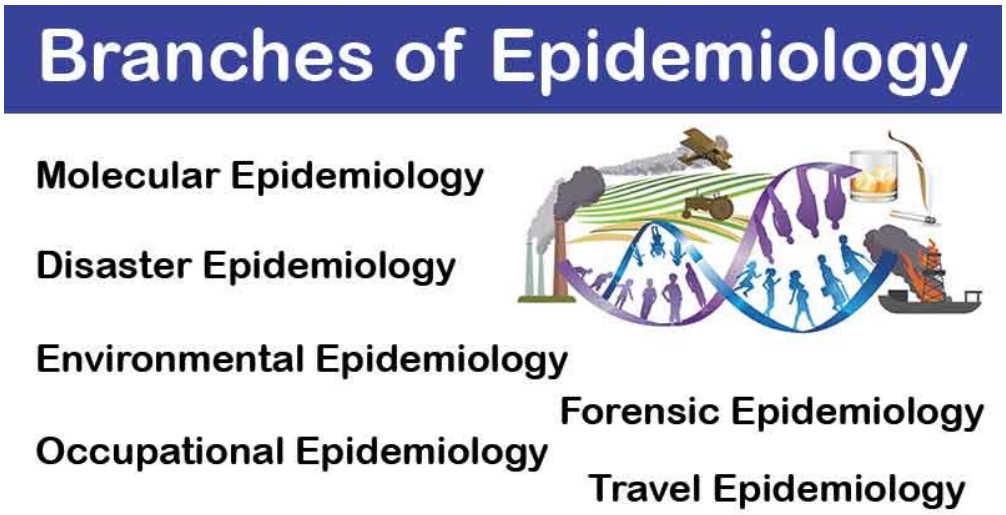
INTRODUCTION

The spread of infectious diseases has always been of concerns and a threat to public health. It has caused serious problems for the survival of human beings and other species, and for the economic and social development of the human society. In the early 1500s, smallpox was introduced into the Caribbean by the Spanish armies led by Cortez, from where it spread to Mexico, Peru, and Brazil. It is probable that smallpox was one of the factors that resulted in widespread deaths among the Incas. The population of Mexico was reduced from up to 30 million to less than 2 million during a period of 50 years after the Spanish invasion, smallpox being the principal cause of death.

The fighting with infectious diseases has had a long history, and great progresses had been achieved, especially during the 20th century. John Snow is famous for his investigations into the causes of the 19th-century cholera epidemics, and is also known as the father of (modern) epidemiology. He began with noticing the significantly higher death rates in two areas supplied by Southwark Company. His identification of the Broad Street pump as the cause of the Soho epidemic is considered the classic example of epidemiology. Snow used chlorine in an attempt to clean the water and removed the handle; this ended the outbreak. In 1991, World Health Assembly passed a resolution to eliminate leprosy as a public health problem by the year 2000, where elimination of leprosy as a public health problem is defined as a prevalence rate of less than one case per 10,000 persons. The target was achieved on time. Poliomyelitis (polio) is a highly infectious viral disease, which mainly affects young children. When the Global Polio Eradication Initiative was launched in 1988, wild poliovirus was

endemic in more than 125 countries on five continents, paralyzing more than 1000 children every day. As a result of the Global Polio Eradication Initiative — the single largest, internationally coordinated public health project to date — by the end of 2006, only four countries remained which had never interrupted endemic transmission of wild poliovirus (Nigeria, India, Pakistan, and Afghanistan). In 2006, less than 2000 cases were reported.

In the early 20th century, mathematical methods were introduced into epidemiology by Ronald Ross, Janet Lane-Claypon, Anderson Gray McKendrick, and others. In a parallel development during the 1920s, German-Swiss pathologist Max Askanazy and others founded the International Society for Geographical Pathology to systematically investigate the geographical pathology of cancer and other non-infectious diseases across populations in different regions. After World War II, Richard Doll and other non-pathologists joined the field and advanced methods to study cancer, a disease with patterns and mode of occurrences that could not be suitably studied with the methods developed for epidemics of infectious diseases. Geography pathology eventually combined with infectious disease epidemiology to make the field that is epidemiology today.



To prevent and to control infectious diseases more effectively, it is important to first fully understand the mechanism of the spread and the transmission dynamics of the diseases, and then provide useful predictions and guidance so that better strategies can be established. The research in infectious diseases can be basically classified as descriptive, analytic, experimental, and theoretic. Epidemic dynamics study is an important theoretic approach to investigate the transmission dynamics of infectious diseases. It formulates mathematical models to describe the mechanisms of disease transmissions and dynamics of infectious agents.

The mathematical models are based on population dynamics, behaviour of disease transmissions, features of the infectious agents, and the connections with other social and physiologic factors. Through quantitative and qualitative analysis, sensitivity analysis, and numeric simulations, mathematical models can give us good understanding of how infectious diseases spread, discover general principles governing the transmission dynamics of the diseases, and identify more important and sensitive parameters, to make reliable predictions and provide useful prevention and control strategies and guidance.

The major areas of epidemic modelling include disease causation, transmission, outbreak, investigation, disease surveillance, screening, biomonitoring, and comparisons of treatment effects such as in clinical trials. Epidemiologists rely on other scientific disciplines like biology to better understand disease processes, statistics to make efficient use of the data and draw appropriate conclusions, social sciences to better understand proximate and distal causes, and engineering for exposure assessment.

While mathematical modelling of infectious diseases can be traced back to 1760 when Bernoulli used mathematical models for smallpox the research on infectious diseases, using deterministic mathematical models, actually began in the 20th century. Hamer formulated a discrete-time model for the spread of measles in 1906. A physician, Dr. Ross, used a differential equation model to describe the transmissions of malaria between human beings and mosquitoes in 1911, and determined that there exists a threshold of the size of mosquitoes below which the spread of malaria can be controlled. More developments and progresses have been particularly made during the past 100 years. Massive mathematical models have been formulated and developed to study various infectious diseases, ranging from more theoretic, general ones to more specific ones especially for measles, malaria, tuberculosis, sexually transmitted diseases (STD), or AID/HIV.

From the perspective of transmission mechanisms, those models have included a variety of factors. For example, contact, vertical, and vector transmissions have been considered. Models incorporating incubation or latent periods, isolations, quarantines, vaccination with or without immunity loss, and infection within groups or between groups, or different population dynamics that epidemic modelling bases on have been formulated. More sophisticated models with age structure, infection-age structure, or spatial structure have also been studied. From the perspective of mathematical structures of the models, while most deterministic models are based on ordinary differential equations, first- and second-order

partial differential equations and delayed differential equations have been used for age-structured, spatial-structured, or reaction–diffusion models, and models with latent or incubation periods, respectively. Impulse differential systems have also been applied to evolution processes with a short-term perturbation.

Mathematical models can also be categorized, based on the described diseases, populations, and environments, as linear, nonlinear, autonomous, or nonautonomous models. There exist, moreover, modelling variations in each category.

EPIDEMIC MODELS:

1. Susceptible-Infective Model (SI):

This is the most basic epidemic model that's consist of only susceptible and infective classes. The susceptible person gets infected by an infective person and they get add to the infective group.

Let a population consist of (n+1) persons of which n persons are susceptible and only one is infected. So

$$S(t) + I(t) = n + 1, \;\; S(0) = n, \;\; I(0) = 1$$

A susceptible person gets infected when he encounters an infected one and mathematically, we can say that the rate of increase of the infected class is proportional to the product of the susceptible and infected persons. Hence, the susceptible class also decreases at the same rate. The system of differential equations governing this model is

$$\frac{dS}{dt} = -\alpha SI$$

$$\frac{dI}{dt} = \alpha SI \;\; (\alpha > 0)$$

$$\Rightarrow \frac{dS}{dt} = -\alpha S(n + 1 - S) \;\; \& \;\; \frac{dI}{dt} = \alpha I(n + 1 - I)$$

$$\frac{dS}{dt} = -\alpha S(n+1-S)$$

we take $\frac{1}{s} = z$.

$$\therefore -\frac{1}{S^2}\frac{dS}{dt} = \frac{\alpha(n+1)}{S} - \alpha$$

$$\Longrightarrow \frac{dz}{dt} - \alpha(n+1)z = -\alpha$$

$$\therefore\ I = e^{-\alpha(n+1)\int dt}$$

$$= e^{-\alpha(n+1)t}$$

$$\Longrightarrow \frac{d}{dt}\left(ze^{-\alpha(n+1)t}\right) = -\alpha e^{-\alpha(n+1)t}$$

$$\Longrightarrow ze^{-\alpha(n+1)t} = \frac{e^{-\alpha(n+1)t}}{(n+1)} + c$$

$$\Longrightarrow z = \frac{1}{n+1} + ce^{\alpha(n+1)t}$$

At t = 0, s = n. $\Longrightarrow z = \frac{1}{n}$

$$\therefore c = \frac{1}{n(n+1)}$$

$$\Longrightarrow \frac{1}{s} = \frac{1}{n+1}\left(1 + \frac{e^{\alpha(n+1)t}}{n}\right)$$

$$\Longrightarrow s(t) = \frac{n(n+1)}{n + e^{(n+1)\alpha t}}$$

Similarly, we get I(t). Therefore,

$$S(t) = \frac{n(n+1)}{n+e^{(n+1)\alpha t}} \quad \& \quad I(t) = \frac{(n+1)}{1+ne^{-(n+1)\alpha t}}$$

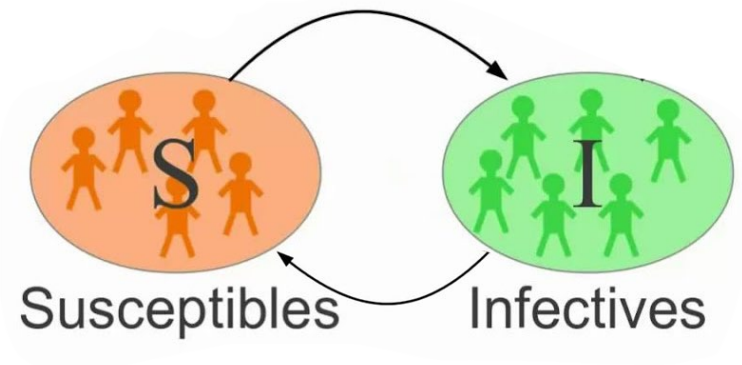
And as $t \to \infty$, $S(t) \to 0$ $and\ I(t) \to n+1$

Therefore, we conclude that as time increases, all the susceptible persons will become infected.

2. Susceptible-Infective-Susceptible Model (SIS) :

This is the modified version of SI model. In this model when an infective person gets cured, they again join the susceptible class. We assume that the infected person has the ability to recover and move to the susceptible class at a rate β (say). So, we get the SIS model as,

$$\frac{dS}{dt} = -\alpha SI + \beta I \;\; \& \;\; \frac{dI}{dt} = \alpha SI - \beta I$$



Since S(t) + I(t) = n + 1 we get,

$$\frac{dS}{dt} = \alpha S^2 - S\{\beta + \alpha(n+1)\} + \beta(n+1)$$

$$\frac{dI}{dt} = I\{\alpha(n+1) - \beta - \alpha I\}$$

taking $\gamma = \alpha(n+1) - \beta$,

$$\frac{dI}{dt} = I\gamma - \alpha I^2$$

$$\Longrightarrow -\frac{1}{I^2}\frac{dI}{dt} + \gamma\frac{1}{I} = -\alpha$$

taking $\frac{1}{I} = z$,

$$\Longrightarrow \frac{dz}{dt} + \gamma z = -\alpha$$

$$\Longrightarrow \frac{d}{dt}(ze^{\gamma t}) = -\alpha e^{\gamma t}$$

$$\Longrightarrow ze^{\gamma t} = \frac{\alpha e^{\gamma t}}{\gamma} + c$$

$$\Longrightarrow z = \frac{\alpha}{\gamma} + ce^{-\gamma t}$$

at initial contd. $c = (1 - \frac{\alpha}{\gamma})$

$$\therefore \frac{1}{I} = \frac{\alpha}{\gamma} + \left(1 - \frac{\alpha}{\gamma}\right) e^{-\gamma t}$$

$$\Longrightarrow I(t) = \frac{1}{\frac{\alpha}{\gamma} + \left(1 - \frac{\alpha}{\gamma}\right) e^{-\gamma t}} = \frac{\gamma}{\alpha + (\gamma - \alpha) e^{-\gamma t}}$$

Similarly, solving for S we get,

$$I(t) = \frac{\gamma}{\alpha + (\gamma - \alpha) e^{-\gamma t}} \quad and \quad S(t) = \frac{\beta + (n\gamma - \beta) e^{-\gamma t}}{\alpha + (\gamma - \alpha) e^{-\gamma t}}$$

$$So\ as\ t \to \infty \quad I(t) \to \frac{\gamma}{\alpha} = n + 1 - \frac{\beta}{\alpha} \quad and \quad S(t) \to \frac{\beta}{\alpha} \quad provided\ \gamma > 0$$

Hence, in this case, a Continuous Models Using Ordinary Differential Equations fraction of susceptible persons will be there, which have not been infected or an infected person has recovered and become susceptible again.

3. Susceptible-Infective-Recovered Model (SIR):

In 1927, Kermack, McKendrick created a model in which they considered a fixed population with only three compartments: susceptible, *S(t),* Infected, *I(t)* and recovered, *R(t)*.

- S(t) is used to represent the individuals not yet infected with the disease at time t or those susceptible to the disease.
- I(t) represents the individuals of the population who have been infected with the disease and are capable of spreading the disease to others (susceptible).
- R(t) represents the individuals of the population who have been infected and then removed from the disease, either due to death or due to immunization.

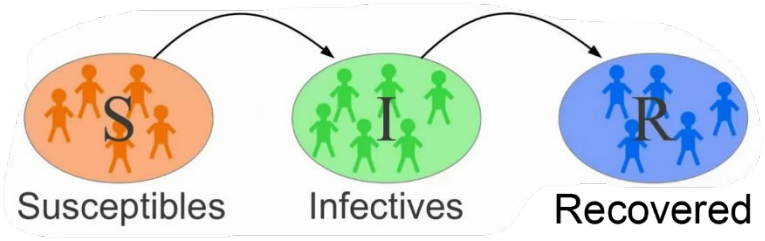
Let β and γ are transmission rate and recovery rate respectively i.e., rate of increase of infected person proportional to encounter of a susceptible, an infected person and recovery rate is a portion of infected person. So we can write,

$$\frac{dS}{dt} = -\beta SI \qquad \ldots\ldots\ldots (i)$$

$$\frac{dI}{dt} = \beta SI - \gamma I \qquad \ldots\ldots\ldots (ii) \qquad \& \quad \frac{dR}{dt} = \gamma I \qquad \ldots\ldots\ldots (iii)$$

With, $S(0) = S_0$, $I(0) = I_0$, $R(0) = R_0$ and $S(t) + I(t) + R(t) = N$.

$$\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$$



3.1 Solution:

Dividing (ii) by (i) we get,

$$\frac{dI}{dS} = -1 + \frac{\gamma}{\beta S} \quad \Rightarrow dI = \left(-1 + \frac{\gamma}{\beta S}\right) dS$$

$I(t) = -S + \rho log S + c$, $\rho = \frac{\gamma}{\beta}$ *and* c is arbitrary constant

at $t = 0$, $I(0) = -S_0 + \rho log S_0 + c$

$$\therefore I(t) = I_0 + S_0 - S(t) + \rho log \frac{S(t)}{S_0}$$

Now at $t = 0$, $S_0 + I_0 = N$.

$$\Rightarrow I(t) = N - S(t) + \rho log \frac{S(t)}{S_0}$$

Therefore, $I_\infty = N - S_\infty + \rho log \frac{S_\infty}{S_0}$, assuming as $t \to \infty$, $I(t) \to I_\infty$ *and* $S(t) \to S_\infty$

Again dividing (i) by (iii) we get,

$$\frac{dS}{dR} = \frac{\beta}{\gamma} S \quad \Rightarrow \frac{dS}{S} = \frac{\beta}{\gamma} dI$$

$$\Rightarrow logS = -\frac{R}{\rho} + c$$

at $t = 0,\ c = logS_0$. Therefore,

$$S = S_0 e^{-\frac{R}{\rho}}$$

3.2 Basic Reproductive Rate (R_0):

This is average number of cases caused by a single infected person in a completely susceptible population. Epidemic will not get started unless the initial number of susceptible exceeds certain threshold for which $R_0 > 1$. If $R_0 \geq 1$ then infection will spread in a susceptible population, on the other hand if $R_0 < 1$ the infection will die out in a susceptible population.

So, if R_0 >1, =1, < 1; it is Epidemic, Endemic and Disease Die Out respectively. So, for disease to spread we have,

$$\frac{dI}{dt} \geq 0 \quad \Rightarrow \beta SI - \gamma I \geq 0 \quad \Rightarrow \frac{\beta S}{\gamma} \geq 1$$

taking $R_0 = \frac{\beta S}{\gamma}$, if S_0 is the threshold then $R_0 = \frac{\beta S_0}{\gamma}$.

If the whole population is susceptible then $N = S_0 \Rightarrow R_0 = \frac{\beta N}{\gamma}$.

3.3 Final Size Relation:

Adding (i) and (ii) we get,

$\frac{d}{dt}(S + I) = -\gamma I$, at time t = M integrating we get,

$$\int_0^M d(S + I) = -\gamma \int_0^M I\, dt$$

$$\Rightarrow S(M) + I(M) - S(0) - I(0) = -\gamma \int_0^M I\, dt \quad \ldots\ldots\ldots (iv)$$

Now as, M $\rightarrow \infty$, the epidemic ends. So,

$$\lim_{t\to\infty} S(t) = S_\infty \ and \ \lim_{t\to\infty} I(t) = I_\infty = 0\,.$$

Taking the limit at (iv),

$$S_\infty - N = -\gamma \lim_{M\to\infty} \int_0^M I(t)dt \qquad as\ I(0) + S(0) = N$$

$$\Rightarrow \frac{N - S_\infty}{\gamma} = \lim_{M\to\infty} \int_0^M I(t)dt \quad \ldots\ldots\ldots (v)$$

Again from (i),

$$\frac{dS}{S} = -\beta I dt$$

$$\Rightarrow \lim_{M\to\infty} \int_0^S \frac{dS}{S} = -\beta \lim_{M\to\infty} \int_0^M I(t)dt$$

$$\Rightarrow \frac{logS_\infty - logS_0}{-\beta} = \lim_{M\to\infty} \int_0^M I(t)dt$$

So, from (v),

$$\log\left(\frac{S_0}{S_\infty}\right) = \frac{\beta}{\gamma}(N - S_\infty)$$

$$\Rightarrow \log\left(\frac{S_0}{S_\infty}\right) = \frac{R_0}{N}(N - S_\infty)$$

$$\Rightarrow \log\left(\frac{S_0}{S_\infty}\right) = R_0\left(1 - \frac{S_\infty}{N}\right) \quad \ldots\ldots\ldots (vi)$$

This is known as the final size reaction.

3.4 Herd Immunity:

Anderson and May (1978) assumed that the effect of immunisation transfer the member of population from susceptible class to recovered class and thus reducing the initial number of susceptible members S_0.

Let p be the proportion of population who have received vaccine whose aim is to reduce $R_0 < 1$. So reduced S_0 is $(1-p)S_0$. Hence,

$$R_0 = \frac{\beta(1-p)S_0}{\gamma} < 1 \quad \Rightarrow (1-p) < \frac{\gamma}{\beta S_0}$$

$$\Rightarrow p > 1 - \frac{1}{R_0}$$

So at least $\left(1-\frac{1}{R_0}\right)$x100% needs to be immunised to attained herd immunity.

Note:

(1) We consider that once a person recover can't be infected again.

(2) Quarantine will reduce the susceptible class.

(3) Finding value of the parameter is a problem as this may not be constant throughout the epidemic time and vary from one country to another.

4. SEIR Model:

In many infectious diseases there is an exposed period after the infection from susceptible to potentially infected member before developed symptoms and can transmit infection. We incorporate mean exposed period $\frac{1}{k}$ into SIR model to get SEIR model.

Let, α = birth rate, β = transmission rate, γ = recovery rate, κ = exposed rate, μ = death rate

$$\frac{dS}{dt} = \alpha N - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \kappa E - \mu E$$

$$\frac{dI}{dt} = \kappa E - \gamma I - \mu I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$

taking $s(t) = \frac{S(t)}{N}$, $e(t) = \frac{E(t)}{N}$, $i(t) = \frac{I(t)}{N}$, $r(t) = \frac{R(t)}{N}$, we get,

$$\frac{ds}{dt} = \alpha - \beta si - \mu s$$

$$\frac{de}{dt} = \beta si - \kappa e - \mu e$$

$$\frac{di}{dt} = \kappa e - \gamma i - \mu i$$

$$\frac{dr}{dt} = \gamma i - \mu r$$

Adding we get,

$$\frac{ds}{dt} + \frac{de}{dt} + \frac{di}{dt} + \frac{dr}{dt} = \alpha - \mu = 0\,, \quad \text{if birth rate and death rate are equal}$$

and hence constant population.

Basic Reproductive Rate (R_0):

We make the variables S, E, I, R into two category disease class $\mathcal{F}$ and non-disease class $\mathcal{V}$ where $\mathcal{F}$ contains only secondary infection rate (β). Then we obtain a matrix F which is the partial derivative of disease class with respect to the original dependent variables. Similarly, V can be obtained from non-disease class. Then we find FV^{-1} and its dominant eigenvalue which gives R_0. Here in SEIR model equation containing Disease class is,

$$\frac{de}{dt} = \beta si - \kappa e - \mu e$$

$$\frac{di}{dt} = \kappa e - \gamma i - \mu i$$

So,

$$\mathcal{F}(X,Y) = \begin{pmatrix} \beta si \\ 0 \end{pmatrix} \quad , \quad \mathcal{V}(X,Y) = \begin{pmatrix} \kappa e + \mu e \\ -\kappa e + \mu i + \gamma i \end{pmatrix}.$$

$$X = (e,i) \;\; and \;\; Y = (s,r) \;\; and \; \frac{dX}{dt} = \mathcal{F}(X,Y) - \mathcal{V}(X,Y)$$

at t = 0, e = 0, i = 0, s = $\frac{S}{N}$ = 1

$$\therefore \;\; F = \begin{pmatrix} \frac{\partial f_1}{\partial e} & \frac{\partial f_1}{\partial i} \\ \frac{\partial f_2}{\partial e} & \frac{\partial f_2}{\partial i} \end{pmatrix} = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} \frac{\partial v_1}{\partial e} & \frac{\partial v_1}{\partial i} \\ \frac{\partial v_2}{\partial e} & \frac{\partial v_2}{\partial i} \end{pmatrix} = \begin{pmatrix} \kappa + \mu & 0 \\ -\kappa & \gamma + \mu \end{pmatrix}$$

$$K = FV^{-1} = \frac{1}{(\kappa+\mu)(\gamma+\mu)}\begin{pmatrix}0 & \beta\\ 0 & 0\end{pmatrix}\begin{pmatrix}\gamma+\mu & 0\\ \kappa & \kappa+\mu\end{pmatrix}$$

$$= \frac{1}{(\kappa+\mu)(\gamma+\mu)}\begin{pmatrix}\beta\kappa & \beta(\kappa+\mu)\\ 0 & 0\end{pmatrix}$$

K_{12} is expected number of secondary infections produced in compartment E by an individual in compartment I and K_{11} is the expected number of secondary infections produced in compartment E by an infected individual originally in E. So, the numerically largest eigenvalue is given by,

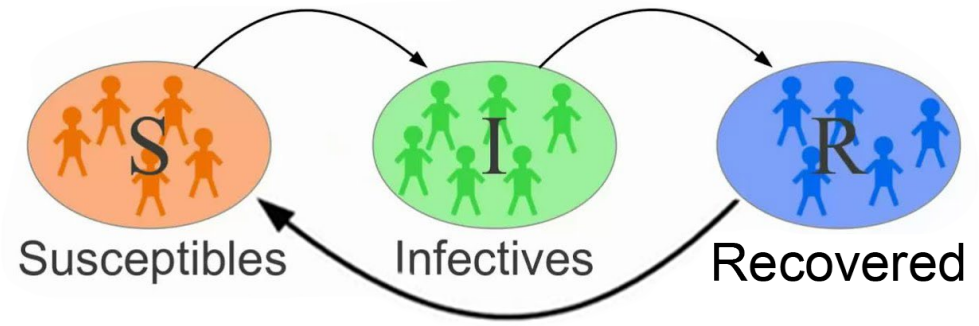
$$R_0 = \frac{\beta\kappa}{(\kappa+\mu)(\gamma+\mu)}$$

5. SIRS Model:

In this model we consider temporal immunity. Therefore, recovered person after sometime move back to susceptible class. So, if δ be the immunity loss by recovered then scaled equations are,

$$\frac{ds}{dt} = -\beta si + \delta r$$
$$\frac{di}{dt} = \beta si - \gamma i$$
$$\frac{dr}{dt} = \gamma i - \delta r$$

where, $s + i + r = 1$.



(1) Putting, i = 0 in the second equation,

$s = \frac{\beta}{\gamma}$. $s + r = 1$

So, from the first equation, $r = 0$. So, $s = 1$.

Therefore, the non-disease fixed point is = (1,0,0).

(2) From the third equation $i = \frac{\delta r}{\gamma}$, $s = \frac{\gamma}{\beta}$ $\Rightarrow r = 1 - s - i$

$$\Rightarrow r\left(1 + \frac{\delta}{\gamma}\right) = 1 - \frac{\gamma}{\beta}$$

$$\Rightarrow r = \frac{(\beta-\gamma)\gamma}{\beta(\delta+\gamma)}$$

Therefore, the equilibrium point is = $\left(\frac{\gamma}{\beta}, \frac{\delta r}{\gamma}, \frac{(\beta-\gamma)\gamma}{\beta(\delta+\gamma)}\right)$.

Basic Reproduction Rate (R_0):

In this model if $R_0 > 1, = 1, < 1$; it is Epidemic, Endemic and Disease Die Out respectively. So, for disease to spread we have,

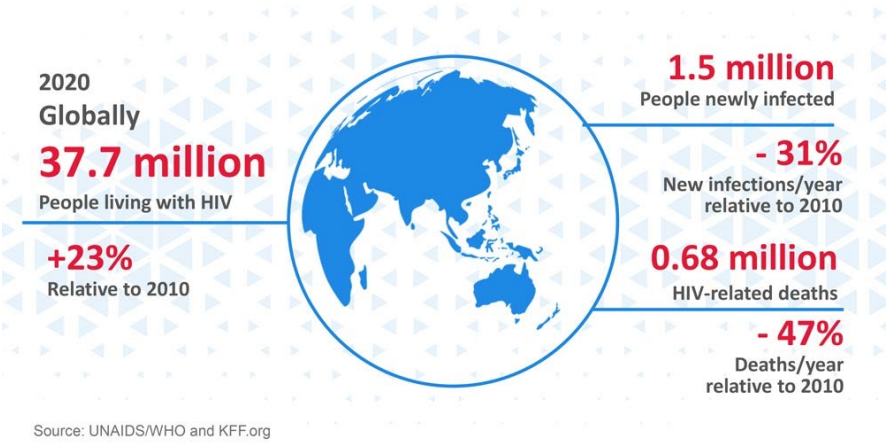
$$\frac{di}{dt} \geq 0 \quad \Rightarrow \beta si - \gamma i \geq 0 \quad \Rightarrow \frac{\beta}{\gamma} \geq 1$$

We take $R_0 = \frac{\beta}{\gamma}$.

Deterministic Epidemic Modelling of HIV/AIDS

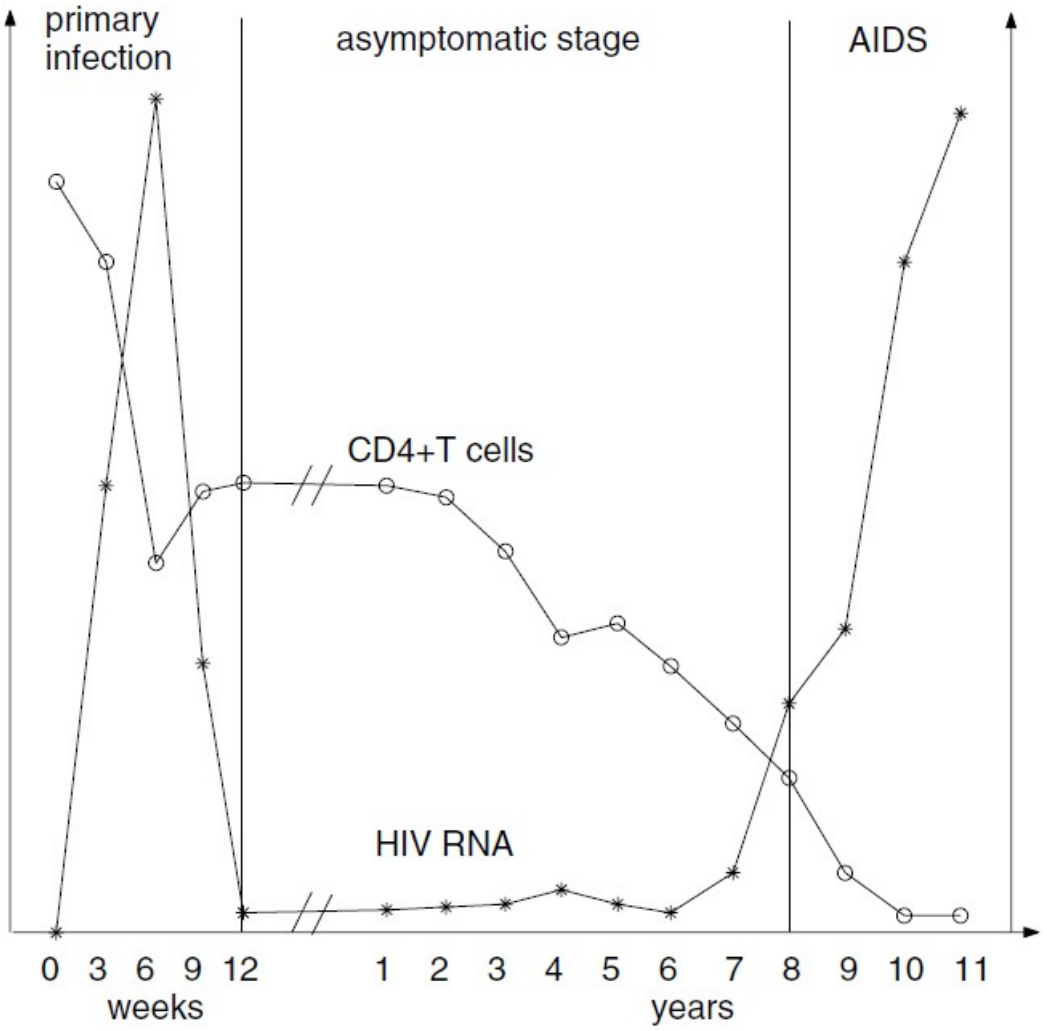
1. Introduction:

Since the diagnosis of the first AIDS case in 1981 in Los Angeles, California, the AIDS epidemic has grown by dangerous proportions. In 1983 HIV was identified at the causative agent for AIDS. The mean time from HIV infection to AIDS is approximately 10 years. There is no effective medicine to cure it and the infected individuals do not recover, they continue to be infectious throughout their lives. According to the World Health Organization (WHO), since the beginning of the epidemic, almost 78 million people have been infected with the HIV virus and about 39 million people have died of HIV. In 2020, about 37 million people worldwide were living with HIV and 680,000 deaths had occurred in that year. An estimated 20.6 million of these live in eastern and southern Africa. HIV infections in women is increasing, which has additional implications for mother-to-child transmission. Women now make up about 42% of those infected worldwide. HIV/AIDS is considered a pandemic, a disease outbreak which is present over a large area and is actively spreading. HIV/AIDS has had a large impact on society, both as an illness and as a source of discrimination. The disease also has large economic impacts. There are many misconceptions about HIV/AIDS, such as the belief that it can be transmitted by casual non-sexual contact. The disease has become subject to many controversies involving religion, including the Catholic Church's position not to support condom use as prevention. It has attracted international medical and political attention as well as large-scale funding since it was identified in the 1980s.



The three known modes of transmission of HIV are sexual contact, significant exposure with HIV-infected blood fluids or tissues, and perinatal/vertical transmission from an infected mother to child during pregnancy, delivery, or breastfeeding. There is no risk of acquiring HIV if exposed to feces, nasal secretions, saliva, sputum, sweat, tears, urine, or vomit unless these are contaminated with blood. It is also possible to be co-infected by more than one strain of HIV—a condition known as HIV superinfection. South Africa remains the epicentre of the pandemic and continues to have high rates of new HIV infections. Outside of sub-Saharan Africa, a third of all HIV infections are acquired through injecting drug use, most of which are in Eastern Europe and Central and Southeast Asia.

Typical course of HIV infection is defined by three stages: primary infection and first viremia, asymptomatic stage, and AIDS. The viral load and the CD4 count change as the disease progressing. The primary infection is characterized by a spike viremia and a migration into lymphatic tissue. The first viremia is characterized by an array of month-long clinical symptoms, including fever, diarrhoea, rash, headache, and lethargy. The immune response reduces HIV replication to a set-point equilibrium that for the most part lasts during the asymptomatic stage until a second viremia induces the onset of AIDS.



Without treatment, HIV infection gradually destroys the immune system. Standard HIV treatment (also called antiretroviral therapy or ART) involves taking a combination of HIV medicines from at least two different HIV drugs classes every day. ART is highly effective at preventing HIV from multiplying. Having less HIV in the body protects the immune system and prevents HIV from advancing to AIDS. ART also reduces the risk of HIV drug resistance.

There are three main approaches to modelling HIV/AIDS transmission. The first and most direct approach to predicting AIDS cases is the extrapolation. This method is to fit an assumed form of AIDS incidence curve to an AIDS incidence data in recent years and then to extent this curve for several years as a prediction of AIDS cases in the future. This method assumed that the current trends will continue at least

for a few years in the future. Often separate curves and extrapolations are done for various risk groups. Advantages of extrapolation are its simplicity and ease to use. The second approach is the back calculation. The total number of AIDS cases at time t is the summation up to time t of the product of the HIV incidence at time τ and the probability of developing AIDS within $t-\tau$ years after infection. The third approach is to use HIV transmission dynamic models. Those models often have the population divide into compartments consisting of those who are susceptible, in each of the infectious stages, or in the AIDS phase.

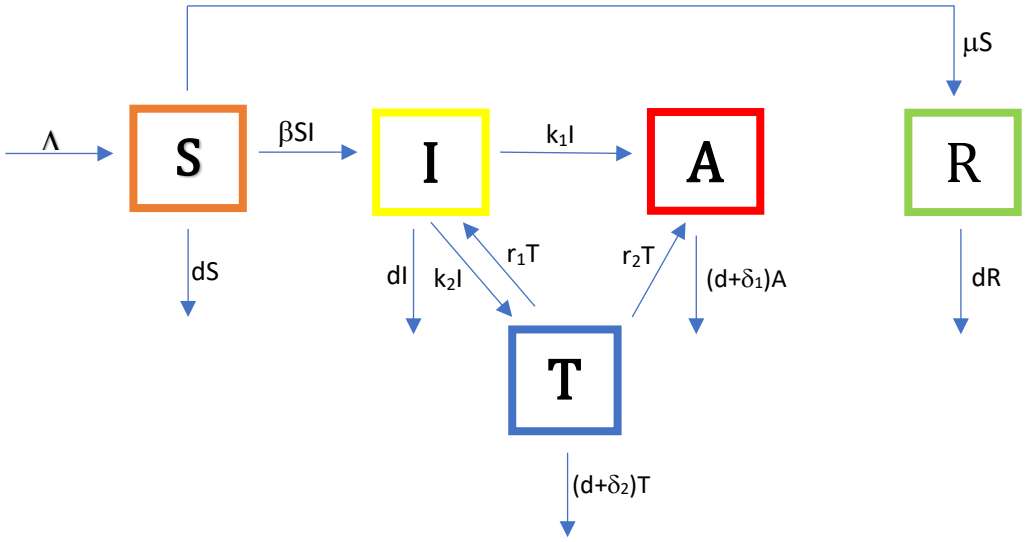
In recent years there has been tremendous number of modelling papers. Here we've derived a model and presented some numerical simulations.

2. Formulation of the Model:

N(t) denotes the total sexually active population at time t. The Population N(t) is divided into five mutually exclusive compartments, namely, S(t), the number of susceptible individuals, I(t), the number of HIV-positive individuals in the stage of HIV infection, T(t), the number of individuals being treated, A(t), the number of individuals with full blown AIDS, R(t), the number of susceptible individuals who are immune to HIV infection by sexual contact. R(t) class are people who take up safe sexual habits and maintain the habits for the rest of their lives.
So, the total population N(t) is given by:

$$\boldsymbol{N(t) = S(t) + I(t) + T(t) + A(t) + R(t)}$$

The following figure is the transfer diagram of the model:



So, the model dynamics is given by the following system of differential equations,

$$\begin{aligned}
\frac{dS}{dt} &= \boldsymbol{\Lambda} - \boldsymbol{\beta SI} - (\boldsymbol{\mu} + \boldsymbol{d})\boldsymbol{S} \\
\frac{dI}{dt} &= \boldsymbol{\beta SI} + \boldsymbol{r_1 T} - (\boldsymbol{d} + \boldsymbol{k_1} + \boldsymbol{k_2})\boldsymbol{I} \\
\frac{dT}{dt} &= \boldsymbol{k_2 I} - (\boldsymbol{r_1} + \boldsymbol{d} + \boldsymbol{\delta_2} + \boldsymbol{r_2})\boldsymbol{T} \\
\frac{dA}{dt} &= \boldsymbol{k_1 I} + \boldsymbol{r_2 T} - (\boldsymbol{\delta_1} + \boldsymbol{d})\boldsymbol{A} \\
\frac{dR}{dt} &= \boldsymbol{\mu S} - \boldsymbol{dR}
\end{aligned} \qquad \textbf{(1)}$$

where,

Table 1. Description of the Parameters

Parameters	**Description**
Λ	Recruitment rate of the population
β	Transmission coefficient of the infection stage
k_1	Progression rate to *A* from *I*
k_2	Progression rate to *T* from *I*
r_1	Proportion of successful treatment
r_2	Proportion of treatment failure
d	Natural death rate
μ	The rate of susceptible individuals who changed their habits
δ_1	Disease-related death rate of the AIDS

δ_2	Disease-related death rate of being treated

3. Basic Properties:

3.1 Positivity of Solution:

A viable mathematical model for epidemiology must ensure that the solutions of the model under consideration remain non-negative once started from an interior point of the positive cone and remains bounded at all future time.

Statement: The solutions S(t), I(t), T(t), A(t), R(t) of system (1) are positive for all t > 0.

Proof:

From the first equation of the system (1),

$$\frac{dS}{dt} = \Lambda - \beta SI - (\mu + d)S \geq -(\mu + d)S$$

$$\Rightarrow S(t) \geq S(0)e^{-(\mu + d)t} > 0$$

From the second equation of the system (1),

$$\frac{dI}{dt} = \beta SI + r_1 T - (d + k_1 + k_2)I \geq -(d + k_1 + k_2)I$$

$$\Rightarrow I(t) \geq I(0)e^{-(d + k_1 + k_2)I} > 0$$

Similarly from the last three equations we get,

$$T(t) > 0, \quad A(t) > 0, \quad R(t) > 0$$

3.2 Invariant Region:

Statement: The feasible region defined by,

$$\boldsymbol{\Omega} = \left\{ \left(\boldsymbol{S(t), I(t), A(t), T(t), R(t)}\right) \in \mathbb{R}_+^5 \mid \boldsymbol{0 \leq S(t) + I(t) + R(t) + T(t) + A(t) \leq \frac{\Lambda}{d}} \right\}$$

as $t \to \infty$.

Proof:

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

differentiating both sides with respect to t we get,

$$\frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dI(t)}{dt} + \frac{dT(t)}{dt} + \frac{dA(t)}{dt} + \frac{dR(t)}{dt}$$

Substituting from the system of equation (1),

$$\frac{dN(t)}{dt} = \Lambda - dN - \delta_1 A - \delta_2 T \leq \Lambda - dN$$

$$\Rightarrow \frac{dN(t)}{dt} + dN \leq \Lambda$$

$$\Rightarrow \frac{d}{dt}(N(t)e^{dt}) \leq \Lambda e^{dt}$$

$$\Rightarrow N(t)e^{dt} \leq \frac{\Lambda}{d}e^{dt} + c$$

$$\Rightarrow N(t) \leq \frac{\Lambda}{d} + ce^{-dt}$$

At $t = 0,\ c = N(0)$.

So we get,

$$0 \leq N(t) \leq \frac{\Lambda}{d} + N(0)e^{-dt}$$

So as $t \to \infty$, $\frac{\Lambda}{d} + N(0)e^{-dt} \to \frac{\Lambda}{d}$

Therefore, we have,

$$\Omega = \left\{\left(S(t), I(t), A(t), T(t), R(t)\right) \in \mathbb{R}_+^5 \mid 0 \leq S(t) + I(t) + R(t) + T(t) + A(t) \leq \frac{\Lambda}{d}\right\}$$

as $t \to \infty$.

4. Disease free equilibrium and the Basic Reproduction Number:

The **D**isease **F**ree **E**quilibrium (DFE) is acquired by setting I = 0, A = 0, T = 0.

$$0 = \Lambda - (\mu + d)S \qquad 0 = \mu S - dR$$

$$\Rightarrow S = \frac{\Lambda}{(\mu + d)} \qquad \Rightarrow R = \frac{\mu S}{d} = \frac{\mu \Lambda}{d(\mu + d)}$$

Therefore, the DFE is given by,

$$E_0 = \left(\frac{\Lambda}{(\mu + d)}, 0, 0, 0, \frac{\mu \Lambda}{d(\mu + d)} \right)$$

The **B**asic **R**eproduction **N**umber (BRN) is a number which is defined as the new infective formed by solitary infective individual for the duration of their effectual infectious epoch when introduced into an utterly susceptible populace at equilibrium.

To find the BRN of our proposed model structure (1), we use the next generation matrix method formula.

Let, y = (I, A, T, S, R)^T

Then the system (1) can be written as,

$$\frac{dy}{dt} = \mathcal{F}(y) - \nu(y)$$

where,

$$\mathcal{F}(y) = \begin{pmatrix} \beta SI \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \quad \text{and} \quad \nu(y) = \begin{pmatrix} (d + k_1 + k_2)I - r_1 T \\ (\delta_1 + d)A - k_1 I - r_2 T \\ (r_1 + d + \delta_2 + r_2)T - k_2 I \\ \beta SI + (\mu + d)S - \Lambda \\ dR - \mu S \end{pmatrix}$$

$\mathcal{F}$ is known the transmission part which, articulates the production of new infection and ν is known as transition part, which explain the alter in state.

The Jacobian matrices of $\mathcal{F}$(y)and ν(y) at the DFE E_0 is given by,

$$D\mathcal{F}(E_0) = \begin{pmatrix} F_{3x3} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, \qquad D\nu(E_0) = \begin{pmatrix} V_{3x3} & & & 0 \\ \beta \frac{\Lambda}{\mu + d} & 0 & 0 & 0 \\ 0 & 0 & 0 & d \end{pmatrix}$$

where,

$$F_{3x3} = \begin{pmatrix} \beta\frac{\Lambda}{\mu+d} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}. \quad V_{3x3} = \begin{pmatrix} k_1+k_2+d & 0 & -r_1 \\ -k_1 & \delta_1+d & -r_2 \\ -k_2 & 0 & \delta_2+d+r_1+r_2 \end{pmatrix}$$

Next Generation Matrix:

In 1990, Diekmann and Hesterbeck introduced a method to find R_0 or Basic Reproductive Number (BRN) by using NGM which is now the most popular method. In population dynamics it is used to compute the basic reproduction number for structured population models. It is also used in multi-type branching models for analogous computations.

So, FV^{-1} is the **N**ext **G**eneration **M**atrix (NGM) of the model structure (1). Thus, the MRN, R_0, is given by:

$$R_0 = \rho(FV^{-1}) = \frac{\beta(d+\delta_2+r_1+r_2)\Lambda}{(k_1+k_2+d)(\delta_2+r_1+d+r_2)(\mu+d)-r_1k_2(\mu+d)}$$

$$= \frac{\beta\Lambda}{(k_1+k_2+d)(\mu+d)-\frac{r_1k_2(\mu+d)}{(\delta_2+r_1+d+r_2)}} \qquad \textbf{(2)}$$

5. Stability Analysis of Disease-Free Equilibrium:

The sensitivity analysis for the endemic threshold (the controlled reproduction number R_0) tells us how important each parameter is to disease transmission. It is used to understand parameters that have a high impact on the threshold R_0 and should be targeted by intervention strategies. More precisely, sensitivity indices allow us to measure the relative change in a variable when a parameter changes.

5.1 **Statement:** The diseases-free equilibrium E_0 is locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$.

Proof:

The Jacobian of the system (1) at DFE $E_0\left(\frac{\Lambda}{(\mu+d)}, 0, 0, 0, \frac{\mu\Lambda}{d(\mu+d)}\right)$ is given by,

$$J_{E_0} =$$

$$\begin{pmatrix} -(\mu + d) & -\frac{\beta\Lambda}{(\mu+d)} & 0 & 0 & 0 \\ 0 & \frac{\beta\Lambda}{(\mu+d)} - (d + k_1 + k_2) & 0 & r_1 & 0 \\ 0 & k_1 & -\delta_1 + d & r_2 & 0 \\ 0 & k_2 & 0 & -(\delta_2 + r_1 + d + r_2) & 0 \\ \mu & 0 & 0 & 0 & -d \end{pmatrix}$$

The characteristic equation of the matrix is given by,

$$\det(J_{E_0} - \lambda I) = 0$$

where λ is an eigen value of the matrix J_{E_0}.

Therefore,

$$(\lambda + d)(\lambda + (\mu + d))(\lambda - (d - \delta_1))(\lambda + (r_1 + \delta_2 + d))(\lambda - r_1 k_2 - (\delta_2 + r_1 + d + r_2)\left(\frac{\beta\Lambda}{(\mu + d)} - (d + k_1 + k_2)\right) = 0$$

So, the eigen values are,

$$\lambda_1 = -d < 0$$

$$\lambda_2 = -(\mu + d) < 0$$

$$\lambda_3 = -(\delta_1 - d) < 0$$

$$\lambda_4 = -(r_1 + \delta_2 + d) < 0$$

$$\lambda_5 = (\delta_2 + r_1 + d + r_2)\left(\frac{\beta\Lambda}{(\mu + d)} - (d + k_1 + k_2)\right) + r_1 k_2$$

Therefore, the system is locally asymptotically at the DFE $E_0\left(\frac{\Lambda}{(\mu + d)}, 0, 0, 0, \frac{\mu\Lambda}{d(\mu + d)}\right)$ if $\lambda_5 < 0$

This implies,

$$(\delta_2 + r_1 + d + r_2)\left(\frac{\beta\Lambda}{(\mu + d)} - (d + k_1 + k_2)\right) + r_1 k_2 < 0$$

$$\Rightarrow (\delta_2 + r_1 + d + r_2)\left(\beta\Lambda - (d + k_1 + k_2)(\mu + d)\right) + r_1 k_2(\mu + d) < 0$$

$$\Rightarrow (\delta_2 + r_1 + d + r_2)\beta\Lambda < (\delta_2 + r_1 + d + r_2)(d + k_1 + k_2)(\mu + d) - r_1 k_2(\mu + d)$$

$$\Rightarrow \frac{\beta\Lambda}{(k_1 + k_2 + d)(\mu + d) - \frac{r_1 k_2(\mu + d)}{(\delta_2 + r_1 + d + r_2)}} < 1$$

$$\Rightarrow R_0 < 1$$

Hence, the DFE $E_0\left(\frac{\Lambda}{(\mu + d)}, 0, 0, 0, \frac{\mu\Lambda}{d(\mu + d)}\right)$ is locally asymptotically stable under the condition $R_0 < 1$ and becomes unstable if $R_0 > 1$.

5.2 **Statement:** The Disease-Free Equilibrium E_0 of model (1) is globally asymptotically stable if $R_0 < 1$.

Proof:

We introduce the Lyapunov Candidate Function,

$$V(t) = I + mT \; ; m > 0$$

Differentiating both sides with respect to t we get,

$$\frac{dV}{dt} = \frac{dI}{dt} + m\frac{dT}{dt}$$

Substituting $\frac{dI}{dt}$ and $\frac{dT}{dt}$ using the equations in system (1) we get,

$$\frac{dV}{dt} = \beta SI + r_1 T - (d + k_1 + k_2)I + m(k_2 I - (r_1 + d + \delta_2 + r_2)T)$$

Now $S_0 = \frac{\Lambda}{(\mu + d)}$, we have,

$$\frac{dV}{dt} \leq \left(\frac{\beta\Lambda}{(\mu + d)} - (d + k_1 + k_2) + mk_2\right)I + \left(r_1 - m(r_1 + d + \delta_2 + r_2)\right)T$$

Putting m = $\frac{r_1}{(r_1 + d + \delta_2 + r_2)}$, we get

$$\frac{dV}{dt} \leq \left(\frac{\beta\Lambda}{(\mu+d)} - (d+k_1+k_2) + \frac{r_1}{(r_1+d+\delta_2+r_2)}k_2\right) I$$

$$= \frac{\beta\Lambda(r_1+d+\delta_2+r_2)-(d+k_1+k_2)(r_1+d+\delta_2+r_2)(\mu+d)+(\mu+d)r_1k_2}{(\mu+d)(r_1+d+\delta_2+r_2)} I$$

Now,

$$R_0 - 1 = \frac{\beta\Lambda(r_1+d+\delta_2+r_2)-(d+k_1+k_2)(r_1+d+\delta_2+r_2)(\mu+d)+(\mu+d)r_1k_2}{(\mu+d)(r_1+d+\delta_2+r_2)(\boldsymbol{d+k_1+k_2-r_1k_2})}$$

$$\frac{dV}{dt} \leq \frac{(R_0-1)[(d+k_1+k_2)(r_1+d+\delta_2+r_2)(\mu+d)-(\mu+d)r_1k_2]}{(\mu+d)(r_1+d+\delta_2+r_2)} I$$

$$= \frac{(R_0-1)[(d+k_1+k_2)(r_1+d+\delta_2+r_2)-r_1k_2]}{(r_1+d+\delta_2+r_2)} I \leq 0$$

At $\frac{dV}{dt} = 0$, I = T = 0.

So, we get, as $t \to \infty$ $S \to \frac{\Lambda}{(\mu+d)}$, $A \to 0$, $R \to \frac{\mu\Lambda}{d(\mu+d)}$

Thus the disease-free equilibrium is globally asymptotically stable if $R_0 < 1$.

6. Existence of Endemic Equilibrium Point and its Stability:

6.1 **Statement:** If $R_0 > 1$, then the model has unique endemic equilibrium $E^*(S^*,I^*,A^*,T^*,R^*)$

Proof:

We have, $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dT}{dt} = \frac{dA}{dt} = \frac{dR}{dt} = 0$

$\therefore$ $S^* = \frac{\Lambda}{\beta I^* + \mu + d}$

$$A^* = \frac{k_1 I^* + r_2 T^*}{d+\delta_1}$$

$$T^* = \frac{k_2 I^*}{r_1+d+\delta_2+r_2}$$

$$R^* = \frac{\mu}{d} S^* = \frac{\mu\Lambda}{d(\beta I^* + \mu + d)} \quad \textbf{(3)}$$

$$\text{And} \quad I^* = \frac{r_1 T}{\beta S - (d+k_1+k_2)} = \frac{\frac{(d+k_1+k_2)}{\beta} - \frac{r_1 k_2}{\beta(r_1+d+\delta_2+r_2)} - \frac{\Lambda}{(\mu+d)}}{\frac{r_1 k_2 - d - k_1 - k_2}{(\mu+d)}}$$

$$= \frac{\Lambda - \frac{(d+k_1+k_2)(\mu+d)}{\beta} + \frac{(\mu+d)}{(r_1+d+\delta_2+r_2)\beta} r_1 k_2}{(d+k_1+k_2-r_1 k_2)}$$

$$= \frac{\beta\Lambda(r_1+d+\delta_2+r_2) - (d+k_1+k_2)(r_1+d+\delta_2+r_2)(\mu+d) + (\mu+d) r_1 k_2}{\beta(d+k_1+k_2-r_1 k_2)(r_1+d+\delta_2+r_2)}$$

Now,

$$R_0 - 1 = \frac{\beta\Lambda(r_1+d+\delta_2+r_2) - (d+k_1+k_2)(r_1+d+\delta_2+r_2)(\mu+d) + (\mu+d) r_1 k_2}{(\mu+d)(r_1+d+\delta_2+r_2)(d+k_1+k_2-r_1 k_2)}$$

$$\Rightarrow R_0 - 1 = \frac{\beta\Lambda(r_1+d+\delta_2+r_2) - (d+k_1+k_2)(r_1+d+\delta_2+r_2)(\mu+d) + (\mu+d) r_1 k_2}{\beta(r_1+d+\delta_2+r_2)(d+k_1+k_2-r_1 k_2)} \frac{\beta}{(\mu+d)}$$

$$= I^* \frac{\beta}{(\mu+d)}$$

$$\therefore \quad I^* = \frac{(R_0-1)(\mu+d)}{\beta}.$$

6.2 **Statement:** If $R_0 > 1$, the endemic equilibrium E^* of this model is globally asymptotically stable.

Proof:

We use the *Lyapunov function* V as follows:

$$V = S - S^* lnS + B(I - I^* lnI) + D(T - T^* lnT)$$

Differentiating with respect to t we get,

$$\frac{dV}{dt} = \frac{dS}{dt}\left(1 - \frac{S^*}{S}\right) + B\frac{dI}{dt}\left(1 - \frac{I^*}{I}\right) + D\frac{dT}{dt}\left(1 - \frac{T^*}{T}\right)$$

$$= (\Lambda - \beta SI - (\mu+d)S)\left(1 - \frac{S^*}{S}\right) + B(\beta SI + r_1 T - (d + k_1 + k_2)I)\left(1 - \frac{I^*}{I}\right) + D(k_2 I - (r_1 + d + \delta_2 + r_2)T)\left(1 - \frac{T^*}{T}\right)$$

$$= (\beta S^* I^* + (\mu+d)S^* - \beta SI - (\mu+d)S)\left(1 - \frac{S^*}{S}\right) + B\left(\beta SI + r_1 T - \frac{\beta S^* I^* + r_1 T^*}{I^*} I\right)\left(1 - \frac{I^*}{I}\right) + D\left(k_2 I - \frac{k_2 I^*}{T^*} T\right)\left(1 - \frac{T^*}{T}\right)$$

take $\frac{S}{S^*} = x, \quad \frac{I}{I^*} = y, \quad \frac{T}{T^*} = z$ **(4)**

$$\frac{dV}{dt} = (\beta S^* I^* + (\mu + d)S^* - \beta S^* I^* xy - (\mu + d)S^* x)\left(1 - \frac{1}{x}\right) + B\left(\beta S^* I^* xy + r_1 T^* z - \frac{\beta S^* I^* + r_1 T^*}{I^*} I^* y\right)\left(1 - \frac{1}{y}\right) + D\left(k_2 I^* y - \frac{k_2 I^*}{T^*} T^* z\right)\left(1 - \frac{1}{z}\right)$$

$$= \left(1 - \frac{1}{x}\right)[\beta S^* I^*(1 - xy) + (\mu + d)S^*(1 - x)] + B\left(1 - \frac{1}{y}\right)[\beta S^* I^*(xy - y) + r_1 T^*(z - y)] + D\left(1 - \frac{1}{z}\right) k_2 I^*(y - z)$$

$$= \beta S^* I^*\left(1 - xy - \frac{1}{x} + y\right) - (\mu + d)S^* \frac{(1-x)^2}{x} + B\beta S^* I^*(xy - y - x + 1) + Br_1 T^*(z - y - \frac{z}{y} + 1) + Dk_2 I^*(y - z - \frac{y}{z} + 1)$$

$$= (\beta S^* I^* + B\beta S^* I^* + Br_1 T^* + Dk_2 I^*) + (-\beta S^* I^* + B\beta S^* I^*)xy + (\beta S^* I^* - B\beta S^* I^* - Br_1 T^* + Dk_2 I^*)y + (Br_1 T^* - Dk_2 I^*)z - (\mu + d)S^* \frac{(1-x)^2}{x} - \frac{\beta S^* I^*}{x} - B\beta S^* I^* x - Br_1 T^* \frac{z}{y} - Dk_2 I^* \frac{y}{z}$$

Here the coefficients of xy, z are positive. So, we make the coefficients of these terms to be zero.

$$-\beta S^* I^* + B\beta S^* I^* = 0 \quad \Rightarrow \quad B = 1$$

$$Br_1 T^* - Dk_2 I^* = 0 \quad \Rightarrow \quad D = \frac{r_1 T^*}{k_2 I^*}$$

Therefore,

$$\frac{dV}{dt} = (2\beta S^* I^* + 2r_1 T^*) - (\mu + d)S^* \frac{(1-x)^2}{x} - \frac{\beta S^* I^*}{x} - \beta S^* I^* x - r_1 T^*\left(\frac{z}{y} + \frac{y}{z}\right)$$

$$= \beta S^* I^*\left(2 - x - \frac{1}{x}\right) - (\mu + d)S^* \frac{(1-x)^2}{x} + r_1 T^*\left(2 - \frac{z}{y} - \frac{y}{z}\right)$$

now,

$$\frac{x + \frac{1}{x}}{2} \geq \left(x * \frac{1}{x}\right)^{\frac{1}{2}} \qquad [AM \geq GM]$$

$$\Rightarrow x + \frac{1}{x} - 2 \geq 0 \quad \& \, equality \; holds \; for \; x = 1$$

Similarly,

$$\Rightarrow \frac{z}{y}+\frac{y}{z}-2 \geq 0 \quad \& \, equality \; holds \; for \; y = z$$

Now,

$$S^* = \frac{\Lambda}{\beta I^* + \mu + d}, \quad \mu = -\beta I^*$$

$$\Rightarrow d = \frac{\Lambda}{S^*}$$

Therefore, from system (1) and (4),

$$\frac{d(xS^*)}{dt} = \Lambda - \beta S^* I^* xy - (\mu + d)S^* x$$

$$\Rightarrow S^* \frac{dx}{dt} = \Lambda - \beta S^* I^* xy - \left(-\beta I^* + \frac{\Lambda}{S^*}\right) S^* x$$

$$\Rightarrow \frac{dx}{dt} = \frac{\Lambda}{S^*} - \beta I^* xy + \beta I^* x - \frac{\Lambda}{S^*} x$$

$$\Rightarrow \frac{dx}{dt} = \left[\frac{\Lambda}{S^*}\left(\frac{1}{x} - 1\right) + \beta I^*(1-y)\right] x$$

Putting x = 1,

$$0 = \beta I^*(1-y)$$

$$\Rightarrow y = 1$$

So, y = z = 1. The maximum invariant set of system **(1)** on the set $\{(x,y,z) \mid \frac{dV}{dt} = 0\}$ is the singleton (1,1,1). Thus by LaSalle Invariance Principle, the Endemic Equilibrium of system (1) is globally asymptotically stable if $R_0 > 1$

7. Numerical Verification and Discussions:

To fit our proposed HIV/ AIDS model system (1) to the yearly new cases we perform numerical simulations. Data are collected from the official website of World Health Organization (**WHO**). We first estimate the values of different parameters of the model given in table 2.

Table 2. Values of parameter of model

Parameters	Description	Values
Λ	Recruitment rate of the population	0.61 $year^{-1}$
β	Transmission coefficient of the infection stage	0.028 $year^{-1}$
k_1	Progression rate to *A* from *I*	0.15 $year^{-1}$
k_2	Progression rate to *T* from *I*	0.35 $year^{-1}$
r_1	Proportion of successful treatment	Variable
r_2	Proportion of treatment failure	Variable
d	Natural death rate	0.0195 $year^{-1}$
μ	The rate of susceptible individuals who changed their habits	0.055
δ_1	Disease-related death rate of the AIDS	0.0807 $year^{-1}$
δ_2	Disease-related death rate of being treated	0.0657 $year^{-1}$

The values of r_1 and r_2 are taken as variables. So, we aspire to see the effect on the disease spreading. For different values of r_1 and r_2, the values of R_0 are presented in the following table.

Table 3. Values of R_0 for different r_1 and r_2

r_1	**0.08**	**0.8**	**0.45**
r_2	0.03	0.001	0.005
R_0	0.60965	1.12635	1

We've formulated a non-linear mathematical model. The sufficient conditions are given ensuring the local and global stability of the **D**isease-**F**ree **E**quilibrium Point and unique **E**ndemic **E**quilibrium **P**oint. The **D**isease-**F**ree **E**quilibrium Point E_0 is shown locally

asymptotically stable when the basic reproduction number R_0 is less than unity. The global stability is also investigated. Finally, we have shown that the model has a unique **E**ndemic **E**quilibrium **P**oint which is locally asymptotically stable.

```
import matplotlib.pyplot as plt
import numpy as np
from scipy.integrate import odeint

'''
S˙ = A − βIS − μS − dS,
I˙ = βIS + r1T − dI − k1I − k2I,
A˙ = k1I − (δ1 + d)A + r2T,
T˙ = k2I − r1T − (d + δ2 + r2)T,
R˙ = μS − dR.
'''


def f(l, t):
    a = 0.61
    b = 0.028
    u = 0.055
    d = 0.0195
    k1 = 0.15
    k2 = 0.35
    r1 = 0.08       # variable
    r2 = 0.03       # variable
    d1 = 0.0807
    d2 = 0.0657
    s = l[0]
    i = l[1]
    a_ = l[2]
    z = l[3]

    ds_dt = a - b*i*s - u*s - d*s
    di_dt = b*i*s + r1*z - d*i - k1*i - k2*i
    da_dt = k1*i - (d1+d)*a_ + r2*z
    dz_dt = k2*i - r1*z - (d+d2+r2)*z
    return [ds_dt, di_dt, da_dt, dz_dt]


t = np.linspace(0, 200)
s0 = [37.7, 25, 15, 10]

s = odeint(f, s0, t)

plt.plot(t, s[:, 0], "b-", lw=0.5)
plt.plot(t, s[:, 1], "g-", lw=0.5)
plt.plot(t, s[:, 2], "r-", lw=0.5)
plt.plot(t, s[:, 3], "m-", lw=0.5)
plt.xlabel("Time")
plt.ylabel("Population Size")
plt.margins(0)
plt.legend(["S", "I", "A", "T"])
plt.show()
```

Note: The program is done on pycharm.

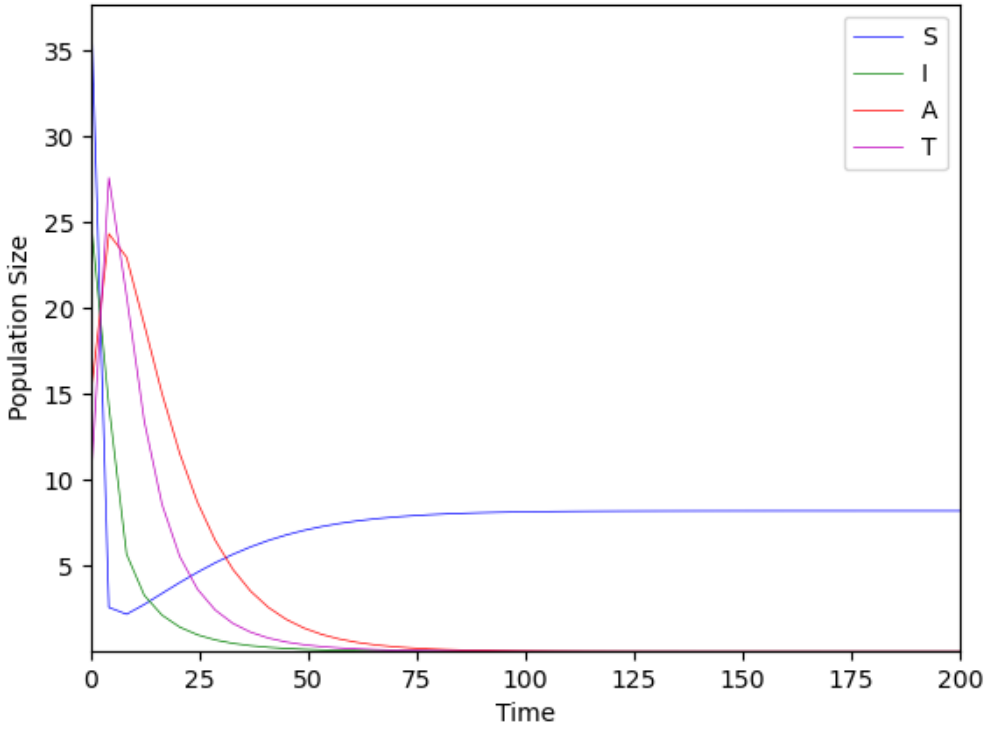


Fig. 2. $r_1 = 0.08$, $r_2 = 0.03$, $R_0 = 0.60965 < 1$, the disease-free equilibrium E_0 is globally asymptotically stable.

Here $R_0 < 1$, the **D**isease-**F**ree **E**quilibrium Point E_0 is globally asymptotically stable. At first the individuals with AIDS are increasing. After treatment, the people suffering from AIDS eventually reduced to almost zero.

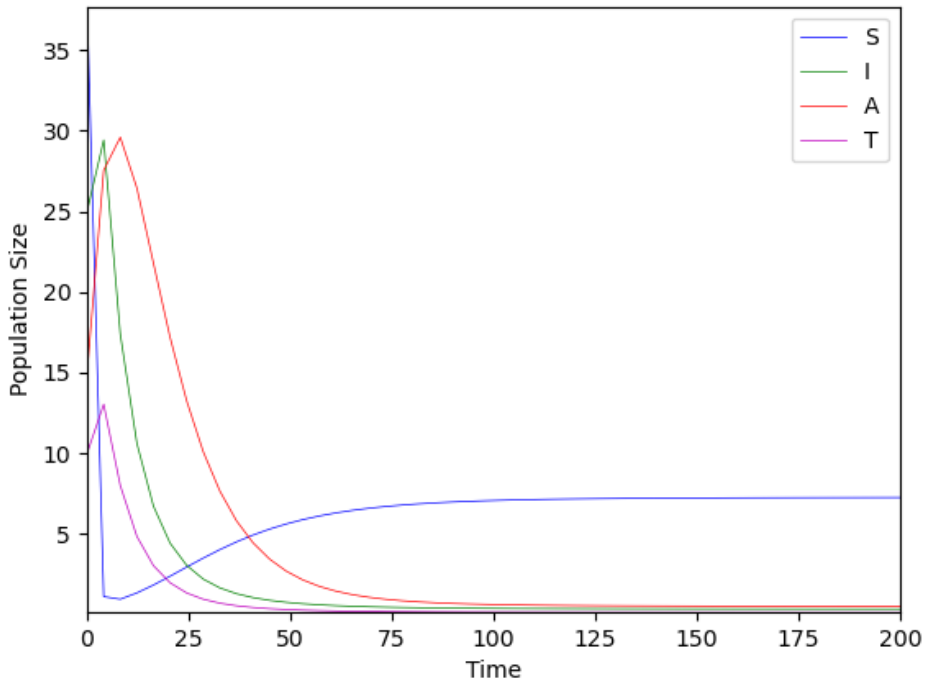


Fig. 3. $r_1 = 0.8$, $r_2 = 0.001$, $R_0 = 1.12635 > 1$, the endemic equilibrium E^* is globally asymptotically stable.

Here $R_0 > 1$, the endemic equilibrium E^* is globally asymptotically stable. As time goes the number of people finally tends to constant but never reaches 0.

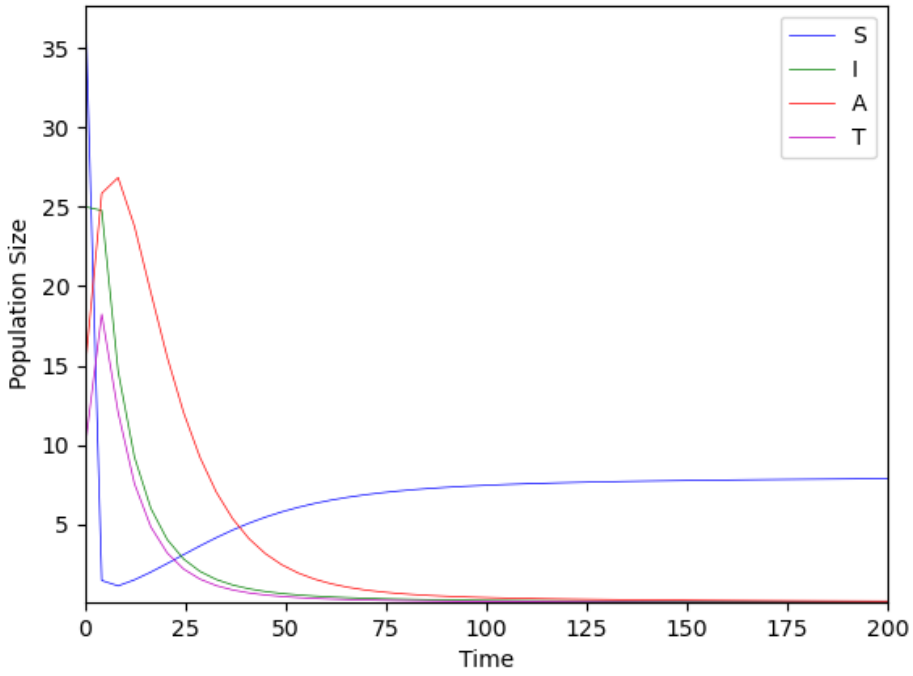


Fig. 4. $r_1 = 0.45$, $r_2 = 0.005$, $R_0 = 1$, the disease-free equilibrium E_0 is globally asymptotically stable.

Here $R_0 = 1$. So, the **D**isease-**F**ree **E**quilibrium Point E_0 is globally asymptotically stable.

CONCLUSION

In this paper we have formulated and studied an epidemic model of HIV/AIDS which is transferred from human to human. So far, the daily confirmed HIV/AIDS cases are increasing day by day. Therefore, prediction about infected individual is very much important for health concern arrangement of the citizens. It is also important to control spread rate of the HIV/AIDS virus with restricted supply.

We construct an epidemic model to figure out the most effective way to lower the incidence rate of the susceptible population. To fulfil our aim, we perform a detailed numerical simulation of our proposed model. We first simulate HIV/AIDS situation and thereafter predicted numerically through graphical approach using python3. We estimated the values of the parameter and the initial condition taken as per the information accessible on 2021. With the help of the next generation matrix method, we obtain the basic reproduction number R_0 and derive the global dynamics of the model. When the basic reproduction number R_0 is less than unity, the disease-free equilibrium is globally asymptotically stable, that means that the disease will be extinct. When the basic reproduction number R_0 is greater than unity, the endemic equilibrium is globally asymptotically stable, that means that the disease will be permanent. Our results show that we can control the disease by controlling the effective contact rate of the infected population. Also, the early treatment of AIDS is necessary to reduce the threat on lives.

Just like HIV/AIDS there are many different epidemics like SARS, Ebola virus outbreak, recurring influenza outbreak which have been suppressed in the past using various others epidemic models. Brian J Coburn, Bradley G Wagner & Sally Blower (1919) proposed a model to provide insights of influenza A (H1N1) variant. By modifying the pre-existing SEIR model Muhammad Rafiq, Waheed Ahmad & Dumitru Baleanu proposed a new model for Ebola outbreak. Most of these models explains the mechanism of transmission dynamics of the infections, the sudden spread and influence of outside factors such as genetics, climate, natural resources and how they affect each other. From our model it's most obvious that except the depending factors the main essence of the model i.e., the way it deals with the epidemic and provide insights to lower the spread is almost identical. So just like HIV/AIDS if one can control the spread of disease by taking proper steps beforehand one can easily decrease the rate of spread of the following disease. Awareness between the public is an absolute necessity. The

method is to control the spread until preventive measures can be taken like using vaccination or a cure comes out. In the SEQIR model proposed by D. Pal, D. Ghosh, P.K. Santra, G.S. Mahapatra they've introduced a quarantined class to control the spread of the disease to susceptible class by isolating the infected individuals for a certain period of time. By taking these preventive measures one can possibly push the epidemic to go extinct.

In this paper we've proposed a model to analyse the epidemic HIV/AIDS. Now though it may seem like that the fit was more or less good with the actual data, the model has quite a few restrictions when working in the real-life scenario. The epidemic models depend on the parameters you're working with as well as the model that is introduced. So, the accuracy changes when the model changes. Also depending on the time, climate and place the parameters also varies. We're trying to oversimplify a vague system with only a few parameters. So total accuracy can never be achieved. So, the model has to be flexible with certain conditions as well as it needs to evolve as time progresses. This is one of the downsides or restrictions of epidemic modelling.

Finally, we conclude that if everyone takes proper step time to time then the infected number of populations will be differed from our predicted number as time progress, and we can surely decrease the infected persons and the victims. The public awareness is absolutely necessary to fight against the dangerous HIV/AIDS as per the proposed model.

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