A Mathematical Study of HIV Transmission Dynamics with Counselling and Antiretroviral Therapy

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Abstract: *In this paper, a mathematical model of HIV transmission dynamics with counseling and Antiretroviral therapy (ART) as a major means of control of infection is presented. The existence and uniqueness of solutions of the model were examined by actual solution. The stability analysis of the critical points was conducted. The results show that it is globally asymptotically stable under certain conditions. The systems of equations were solved analytically using parameter-expanding method coupled with direct integration. The results are presently graphically and discussed. It is discovered that the parameters involved play a crucial role in the dynamics of the diseases which indicate that ART and counseling could be effective methods in the control and eradication of HIV.*

Keywords: *HIV, Antiretroviral therapy, counseling, stability criteria, eradication.*

1. INTRODUCTION

A major method, apart from the use of the condom, in the control of HIV, is Antiretroviral Therapy (ART). By this approach, HIV positives are detected and placed on antiretroviral drugs. Generally, there are public awareness campaigns, which are intended to educate the general public on the spread of HIV and how to control it. Members of the public are encouraged to go for tests in order to determine their HIV status so as to benefit from ART. ART does not cure HIV infection; it only boosts the immune system of infected people against secondary infections, thereby prolonging their life span.

Mathematical models to investigate the effect of treatment and vaccination on the spread of HIV/AIDS can be found, for example, in kaosimore and Lungu [1]. Yang and Ferreira [2]. Hsu-Schmitz [3]. Swanson et al. [4]. Models for the control of HIV using the condom can be found, for example in Hsieh and Velasco-Hemandez [5]. Hsieh [6], Mastro and Limpakamjanarat [7]. Kimbir and Aboiyar [8] and Kimbir et al. [9].

This present study investigates the criteria under which the effectiveness of the public campaign and efficacy of the ART drug could lead to the stability of equilibrium point. We conducted global stability analysis of the model and provide an analytical solution via parameter-expanding method.

Following [10], the population is partitioned into three compartments of susceptible $S(t)$, infected $I(t)$ and removed $R(t)$. A susceptible is an individual that is yet to be infected, but is open to infection as he or she interacts with members of the I-class. An infected individual is one, who has contracted HIV and is at some stage of infection. A removed individual is one that is confirmed to be HIV positive, counseled and is receiving ART.

It is assumed that the recruitment into the S-class is only through birth, at a rate b and it is proportional to the total population $N(t) = S(t) + I(t) + R(t)$ at time t. Death is explicit in the model and it occurs in all classes at a constant rate μ. However, there is an additional death rate α_0 in the I and R-classes due to infection. There is a maximum period of time, T after infection, which a member in class I must leave the class through death. The death rate in the R-class is therefore, given by $\alpha = \alpha_0 e^{-KT}$, where k is the efficacy of the antiretroviral drug. The higher the value of k the smaller the value of α and vice versa. Clearly, $\alpha < \alpha_0$ and $\alpha = \alpha_0$ when $k = 0$ (i.e., no ART).

The recruitment into the $R - class$ from the I-class depends on the effectiveness of the public campaign or counseling and this is done at a rate σ. σ can also be referred to as the treatment rate.

From the assumptions made above, the following model Equations are assumed hold:

$$\frac{dS}{dt} = bN - B(t)S - \mu S \tag{1}$$

$$\frac{dI}{dt} = B(t)S - (\mu + \alpha_0 + \sigma)I \tag{2}$$

$$\frac{dR}{dt} = \sigma I - (\mu + \alpha)R \tag{3}$$

where

$$N(t) = S(t) + I(t) + R(t) \tag{4}$$

and

$$\alpha = \alpha_0 \ell^{-KT} \tag{5}$$

The incidence rate $B(t)$ at time t is given as in Hsieh [6], namely

$$B(t) = \frac{c\beta I + c'\beta' R}{N} \tag{6}$$

As initial condition, we choose

$$S(0) = S_0, \ I(0) = I_0, \ R(0) = R_0, \tag{7}$$

where, β is the probability of transmission by an individual in class I and β'

is the probability of transmission by an individual in class R, c and c' are respectively, the average number of sexual partners per unit time for individuals in class I and R. B is the reproduction rate of the population, α_0 is the population death rate of infected not receiving ART, α is the population death rate of infected receiving ART, T is the maximum lifespan after infection, k is the Efficacy of ART per unit time, β' is the probability of transmission by members of class R, σ is the proportion of infected receiving ART per unit time, b and μ are population birth rate and population death rate

2. EXISTENCE AND UNIQUENESS OF SOLUTION

Theorem 1: Let $\alpha_0 = 0$. Then the equations (1) – (3) with initial conditions (7) has a unique solution for all $t \geq 0$.

Proof: Let $\alpha_0 = 0$ and $\phi(t) = S(t) + I(t) + R(t)$, we obtain

$$\frac{d\phi}{dt} = (b - \mu)\phi, \quad \phi(0) = (S + I + R) = \phi_0 \tag{8}$$

By direct integration, we obtain the solution of problem (8) as

$$\phi(t) = \phi_0 e^{(b-\mu)t} \tag{9}$$

Then, we obtain

$$S(t) = \left(\phi_0 e^{(b-\mu)t}\right) - \left(I(t) + R(t)\right) \tag{10}$$

$$I(t) = \left(\phi_0 e^{(b-\mu)t}\right) - \left(S(t) + R(t)\right) \tag{11}$$

$$R(t) = \left(\phi_0 e^{(b-\mu)t}\right) - \left(I(t) + S(t)\right) \tag{12}$$

Hence, there exists a unique solution of problem (1) - (3). This completes the proof.

3. STABILITY ANALYSIS

Our system of equations (1) – (3) has a trivial steady state:

$$\overline{S} = \frac{b}{\mu}, \quad \overline{I} = 0, \quad \overline{R} = 0 \tag{13}$$

and a non-trivial steady state:

$$\left. \begin{array}{l} \overline{S} = \dfrac{mn}{\alpha_1 n + \alpha_2 \sigma} \\[3mm] \overline{I} = \dfrac{b(\alpha_1 n + \alpha_2 \sigma) - \mu mn}{m(\alpha_1 n + \alpha_2 \sigma)} \\[3mm] \overline{R} = \dfrac{\sigma\left(b(\alpha_1 n + \alpha_2 \sigma) - \mu mn\right)}{mn(\alpha_1 n + \alpha_2 \sigma)} \end{array} \right\} \tag{14}$$

Corresponding to clearance of infection and active disease respectively,

where $\quad m = \mu + \alpha_0 + \sigma, \quad n = \mu + \alpha, \quad \alpha_1 = c\beta, \quad \alpha_2 = c'\beta'$

Theorem 2: If $\dfrac{b}{\mu} \neq \dfrac{mn}{\alpha_1 n + \alpha_2 \sigma}$ then, there exist two equilibria

Proof: The infection-free equilibrium is given by

$$P_1 = \left(\frac{b}{\mu}, 0, 0\right)$$

If $I \neq 0$, $R \neq 0$, then $S = \dfrac{mn}{\alpha_1 n + \alpha_2 \sigma}$

Hence, the other equilibrium is

$$P_2 = \left(\frac{mn}{\alpha_1 n + \alpha_2 \sigma}, \frac{b(\alpha_1 n + \alpha_2 \sigma) - \mu mn}{m(\alpha_1 n + \alpha_2 \sigma)}, \frac{\sigma\left(b(\alpha_1 n + \alpha_2 \sigma) - \mu mn\right)}{mn(\alpha_1 n + \alpha_2 \sigma)}\right)$$

$$P_2 = \left(\phi_1, \phi_2, \phi_3\right)$$

This completes the proof.

Next, we shall conduct stability analysis of the critical points

Let

$$x = \frac{S}{N}, \quad y = \frac{I}{N}, \quad z = \frac{R}{N} \tag{15}$$

Then, the system of equations (1) – (7) reduces to

$$\frac{dx}{dt} = b - (\alpha_1 y + \alpha_2 z)x - \mu x \tag{16}$$

$$\frac{dy}{dt} = (\alpha_1 y + \alpha_2 z)x - (\mu + \alpha_0 + \sigma)y \tag{17}$$

$$\frac{dz}{dt} = \sigma y - (\mu + \alpha)z \tag{18}$$

$$x(t) + y(t) + z(t) = 1 \tag{19}$$

$$x(0) = x_0, \quad y(0) = y_0, \quad z(0) = z_0 \tag{20}$$

Then, the Jacobian matrix of our system of equations (15) – (17) is

$$Df(x, y, z) = \begin{pmatrix} -(\alpha_1 y + \alpha_2 z) - \mu & -\alpha_1 x & -\alpha_2 x \\ \alpha_1 y + \alpha_2 z & \alpha_1 x - m & \alpha_2 x \\ 0 & \sigma & -n \end{pmatrix} \tag{21}$$

The linearization of (21) at $p_1 = \left(\dfrac{b}{\mu}, 0, 0\right)$ is

$$Df(\frac{b}{\mu}, 0, 0) = \begin{pmatrix} -\mu & -q_1 & -q_2 \\ 0 & -q_3 & q_2 \\ 0 & \sigma & -n \end{pmatrix} \tag{22}$$

with eigenvalues:

$$\lambda_1 = -\mu, \text{ and } \lambda_{2,3} = \frac{-(n + q_3) \pm \sqrt{(n + q_3)^2 - 4(nq_3 - \sigma q_2)}}{2}, \tag{23}$$

where

$$q_1 = \frac{\alpha_1 b}{\mu}, \qquad q_2 = \frac{\alpha_2 b}{\mu}, \qquad q_3 = m - \frac{\alpha_1 b}{\mu}$$

By definition, all the parameters are non-negative, hence q_1, q_2 and q_3 are non-negative

if $m > \dfrac{\alpha_1 b}{\mu}$

If $nq_3 > \sigma q_2$ and $(n + q_3)^2 - 4(nq_3 - \sigma q_2) > 0,$ then eigenvalues are real, unequal and negative.

If $(n + q_3)^2 - 4(nq_3 - \sigma q_2) = 0,$ the eigenvalues are real, equal and negative.

If $nq_3 > \sigma q_2$ and $(n + q_3)^2 - 4(nq_3 - \sigma q_2) < 0$ the eigenvalues are complex with negative real part.

So in either case the disease-free equilibrium is globally asymptotically stable.

The linearization of (15) at $p_2(\phi_1, \phi_2, \phi_3)$ is

$$Df(\phi_1, \phi_2, \phi_3) = \begin{pmatrix} -r_1 & -r_2 & -r_3 \\ r_4 & -r_5 & r_3 \\ 0 & \sigma & n \end{pmatrix} \tag{24}$$

where:

$$\phi_1 = \frac{mn}{\alpha_1 n + \alpha_2 \sigma}, \phi_2 = \frac{b(\alpha_1 n + \alpha_2 \sigma) - \mu mn}{m(\alpha_1 n + \alpha_2 \sigma)}, \phi_3 = \frac{\sigma(b(\alpha_1 n + \alpha_2 \sigma) - \mu mn)}{mn(\alpha_1 n + \alpha_2 \sigma)}$$

$r_2 = \alpha_1 \phi_1, r_1 = \alpha_1 \phi_2 + \alpha_2 \phi_3 + \mu, \ r_2 = \alpha_1 \phi_1, \ r_3 = \alpha_2 \phi_1, \ r_4 = \alpha_1 \phi_2 + \alpha_2 \phi_3, \ r_5 = m - \alpha_1 \phi_1$

Thus

$$|A - \lambda \mathrm{I}| = 0 \tag{25}$$

Implies

$$\lambda_1 = -r_1$$

and

$$p(\lambda) = \lambda^3 + (r_1 + r_5 + n)\lambda^2 + (r_1 r_5 + nr_1 + nr_1 r_5 + r_2 r_4 - \sigma r_3)\lambda + (nr_5 + nr_2 r_4 + \sigma r_3 r_4 - \sigma r_1 r_3) = 0 \tag{26}$$

Theorem 3: If $r_3 = 0$. Then Equation (26) has three negative roots or one negative root and two complex roots.

Theorem 4: The infected (endemic) equilibrium is globally asymptotically stable if $r_3 = 0$

Proof of theorems

The proof of the theorems 3 and 4 involved using the

Descartes rule of signs: The number of positive zeros of a polynomial with real coefficients is either equal to the number of variations in sign of the polynomial or less than this by an even number and

Routh-Hurwitz criteria [8]: All zeros of $\lambda^3 + \alpha\lambda^2 + \beta\lambda + \gamma = 0$ have negative real parts if and only if $\alpha\beta - \gamma > 0$, therefore, all zeros of (26) have negative real parts if and only $(n + r_1 + r_5)(nr_1 + nr_5 + r_1 r_5 + r_2 r_4 - \sigma r_3) - (nr_2 r_4 + nr_1 r_5 + \sigma r_3 r_4 - \sigma r_1 r_3) > 0$

That is

$$(r_1 + r_5 + n)(r_1 r_5 + nr_1 + nr_1 r_5) + r_3(r_1 r_2 - \sigma(r_4 + r_5 + n)) + r_5(r_2 r_4 - n)$$

If $r_3 = 0$.

Proof of theorem 3

From $p(\lambda)$ in (26), we obtain

$$p(-\lambda) = -\lambda^3 + (r_1 + r_5 + n)\lambda^2 - (r_1 r_5 + nr_1 + nr_1 r_5 + r_2 r_4 - \sigma r_3)\lambda + (nr_5 + nr_2 r_4 + \sigma r_3 r_4 - \sigma r_1 r_3) = 0$$

So the number of change in sign is 3, if $r_3 = 0$. Hence by Descartes rule of signs, $p(\lambda)$ have either three negative roots or one negative root and two complex roots. This completes the proof.

Proof of theorem 4

Since the Inequality holds if $r_3 = 0$. By theorem 1 and Routh-Hurwitz criteria, (26) has

Either three negative roots or

One negative root and two complex roots whose real parts are equal and negative.

So in either case the equilibrium is globally asymptotically state. This completes the proof.

4. SOLUTION BY PARAMETER-EXPANDING METHOD

Parameter-expanding method proposed by He and was successfully applied to various engineering problems [11]. We apply parameter-expanding method to equations (15) – (17), where details can be found in [11]. Suppose the solution $x(t)$, $y(t)$, and $z(t)$ in (15) – (17) can be expressed as

$$\left.\begin{array}{l} x(t) = x_0(t) + \alpha_1 x_1(t) + \alpha_1^2 x_2(t) + h.o.t \\ y(t) = y_0(t) + \alpha_1 y_1(t) + \alpha_1^2 y(t) + h.o.t \\ z(t) = z_0(t) + \alpha_1 z_1(t) + \alpha_1^2 z(t) + h.o.t \end{array}\right\} \tag{27}$$

Let $\alpha_2 = a\alpha_1$

Where h.o.t. read ''higher order terms in α_1 and $S = x$, $I = y$, $R = z$. In our analysis, we assume α_1 is small, so we are interested only in the first two terms.

Substituting (27) into (15) – (17), and processing, we obtain:

$$\frac{dx_0}{dt} = b - \mu x_0, \qquad x_0(0) = x_0 \tag{28}$$

$$\frac{dy_0}{dt} = -my_0, \qquad y_0(0) = y_0 \tag{29}$$

$$\frac{dz_0}{dt} = \sigma y_0 - nz_0, \qquad z_0(0) = z_0 \tag{30}$$

$$\frac{dx_1}{dt} = -x_0 y_0 - ax_0 z_0 - \mu x_1, \qquad x_1(0) = 0 \tag{31}$$

$$\frac{dy_1}{dt} = x_0 y_0 + ax_0 z_0 - my_1, \qquad y_1(0) = 0 \tag{32}$$

$$\frac{dz_1}{dt} = \sigma y_1 - nz_1, \qquad z_1(0) = 0 \tag{33}$$

Solving equations (28) – (33) by direct integration, we obtain

$$x_0(t) = ce^{-\mu t} + c_1 \tag{34}$$

$$y_0(t) = y_0 e^{-mt} \tag{35}$$

$$z_0(t) = a_1 e^{-mt} + b e^{-nt} \tag{36}$$

$$x_1(t) = e^{-\mu t}\left(\frac{cy_0}{m}\left(1 - e^{-mt}\right) + \frac{c_1 y_0}{(m-n)}\left(1 - e^{-(m-\mu)t}\right) + \frac{aca_1}{m}\left(1 - e^{-mt}\right)\right) +$$

$$e^{-\mu t}\left(\frac{acb}{n}\left(1 - e^{-nt}\right) + \frac{ac_1 a_1}{(m-n)}\left(1 - e^{-(m-\mu)t}\right) + \frac{ac_1 b}{(n-\mu)}\left(1 - e^{-(n-\mu)t}\right)\right) \tag{37}$$

$$y_1(t) = p e^{-mt} - p_1 e^{-(m+\mu)t} + p_2 t e^{-mt} - p_3 e^{-(n+\mu)t} - p_4 e^{-nt} \tag{38}$$

$$z_1(1) = \sigma e^{-nt}\left(\frac{p}{(m-n)}\left(1 - e^{-(m-n)t}\right) + \frac{p_1}{(m+\mu-n)}\left(e^{-(m+\mu-n)t} - 1\right) + \frac{t}{(m-n)}e^{-(m-n)t}\right) +$$

$$\sigma e^{-nt}\left(\frac{1}{(m-n)^2}\left(1 - e^{-(m-n)t}\right) + \frac{p_3}{\mu}\left(e^{-\mu t} - 1\right) - p_4 t\right) \tag{39}$$

$$\alpha_1 = c\beta, \quad \alpha_2 = c'\beta', \quad , \quad m = \mu + \alpha_0 + \sigma, \quad n = \mu + \alpha, \quad a = \frac{\alpha_1}{\alpha_2},$$

$$c = x_0 - c_1, \quad c_1 = \frac{b}{\mu}, \quad a_1 = \frac{\sigma y_0}{n-m}, \quad b = z_0 - \frac{\sigma y_0}{n-m}$$

$$p = \frac{cy_0}{\mu} + \frac{aca_1}{\mu} + \frac{acb}{n+\mu-m} + \frac{ac_1 b}{n-m},$$

$$p_1 = \frac{cy_0}{\mu} + \frac{aca_1}{\mu}, \quad p_2 = c_1 y_0 + ac_1 a_1, \quad p_3 = \frac{acb}{n+\mu-m}, \quad p_4 = \frac{ac_1 b}{n-m}$$

The computations were done using computer symbolic algebraic package MAPLE.

5. RESULTS AND DISCUSSION

Here the existence and uniqueness of solution of our system of equations (1) – (3) is proved by actual solutions. Also, under certain conditions, we have conducted stability analysis of the disease-free and endemic equilibriums. The results showed that is globally asymptotically stable. Analytical solutions of equations (1) – (3) are achieved via parameter-expanding method and computed for the values of $c = 0$, $k = 0.2$, $b = 0.5$, $q = 0$, $\beta = 1$, $\lambda = 0.4$, $\mu = 0.1$

$T = 10$, $\alpha_0 = 0.2$, $x_0 = 4$, $y_0 = 1$ and $z_0 = 0$.

The Susceptible, Infected and Removed individuals are depicted graphically in figures 1 – 6.

From **figure 1**, we can conclude that with the increase in treatment rate (σ), the susceptible class reduces because there is no permanent cure for HIV/AIDS. This is because the removed class does not return to the susceptible class.
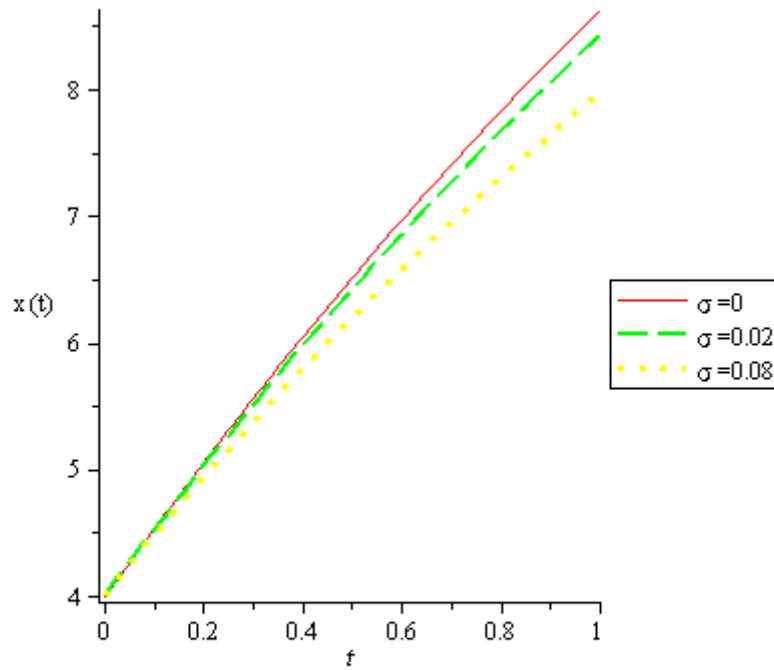
Figure 1:x(t) versus time t for various values of σ at
c=0, k=0.2, b=0.5, q=0, β=1, γ=0.4, μ=0.1, T=10,
$\alpha_0 = 0.2, x_0 = 4, y_0 = 1, z_0 = 0$

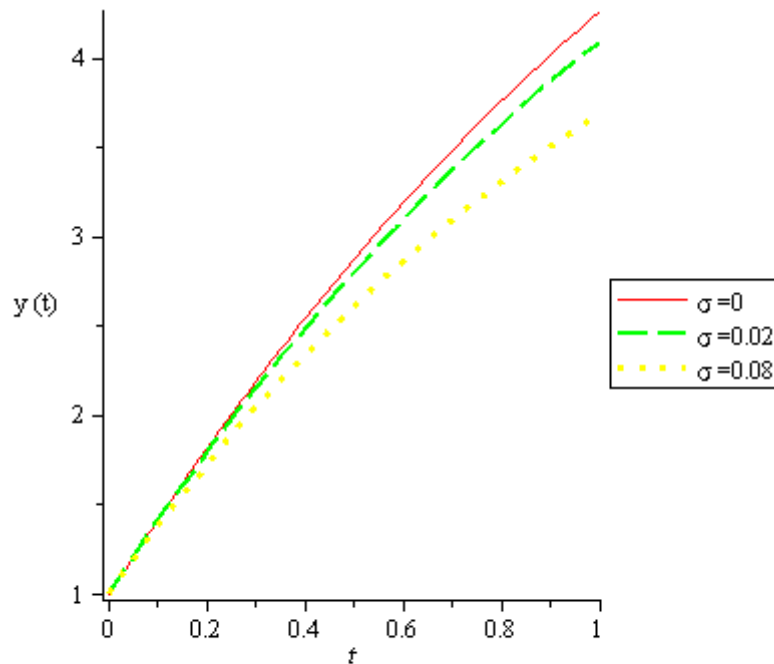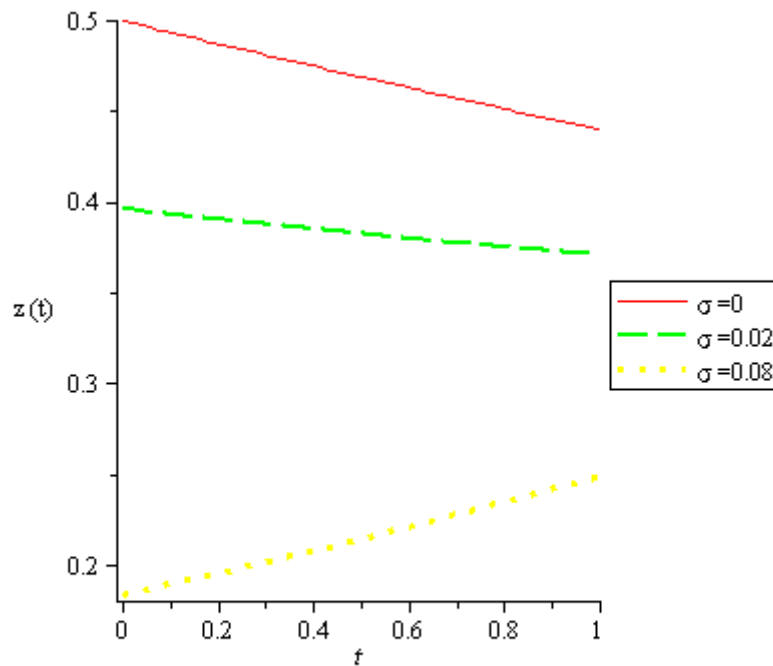From **figure 2,** we can conclude that with the increase in treatment rate(σ), the infected class reduces.

Figure 2:y(t) versus time t for various values of σ at
c=0, k=0.2, b=0.5, q=0, β=1, γ=0.4, μ=0.1, T=10,
$\alpha_0 = 0.2, x_0 = 4, y_0 = 1, z_0 = 0$

From **Figure 3**, we can conclude that with the increase in treatment rate(σ), the Removed class decreases

Figure 3:x (t) versus time t for various values of σ at
c=0, k=0.2, b=0.5, q=0, β=1, γ=0.4, μ=0.1, T=10,
$\alpha_0 = 0.2, x_0 = 4, y_0 = 1, z_0 = 0$

From **Figure 4**, we can conclude that with the increase in the efficacy of ART per unit time k, the susceptible class reduces because there is no permanent cure for HIV/AIDS.This is because the removed class does not returned to the Susceptible class.
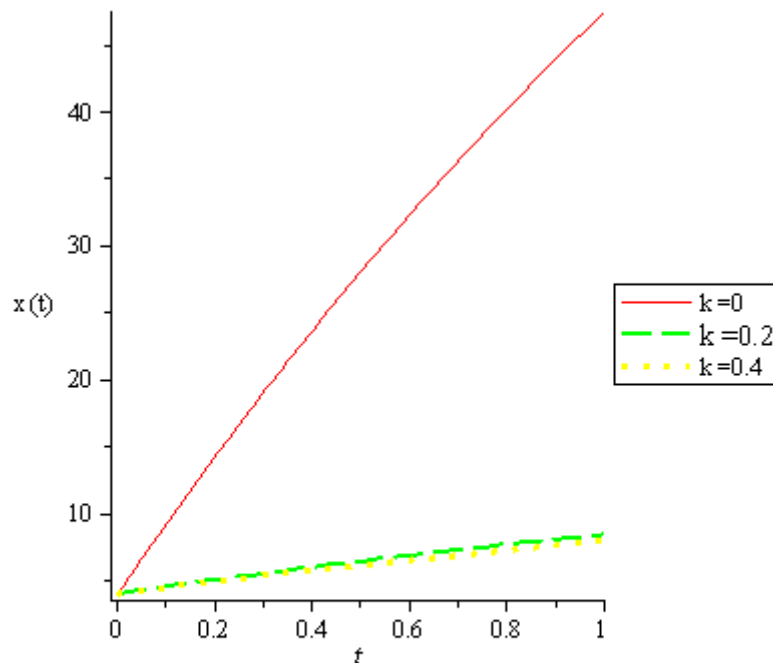

Figure 4:x (t) versus time t for various values of k at
c=0, σ =0.02, b=0.5, q=0, β=1, γ=0.4, μ=0.1, T=10,
$\alpha_0 = 0.2, x_0 = 4, y_0 = 1, z_0 = 0$

From **Figure 5,** we can conclude that with the increase in the efficacy of ART per unit time (k), the infected class decreases because with the increase in k, the graph does not change much
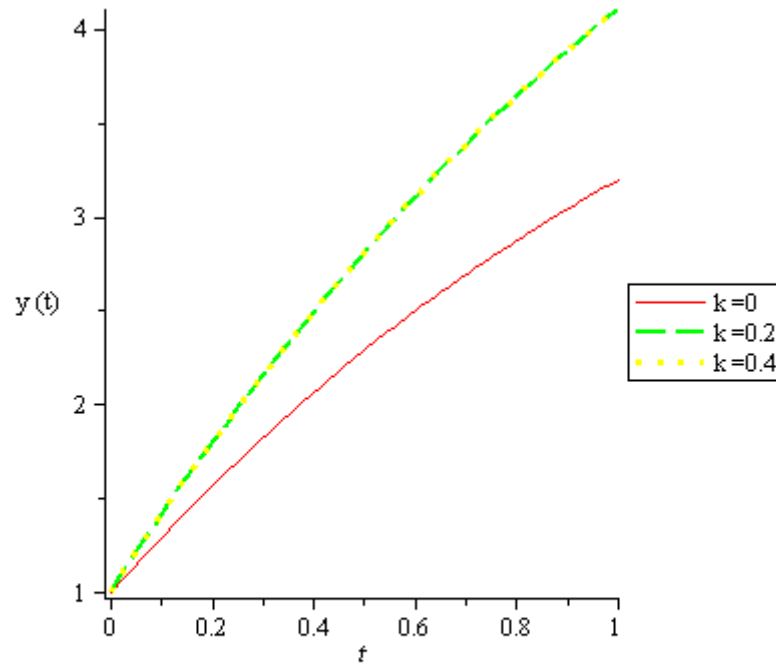
Figure 5: y (t) versus time t for various values of k at
c=0, σ =0.02, b=0.5, q=0, β=1, γ=0.4, μ=0.1, T=10,
$\alpha_0 = 0.2, x_0 = 4, y_0 = 1, z_0 = 0$

From **Figure 6**, we can conclude that with the increase in the efficacy of ART per unit time k, the Removed class increases.
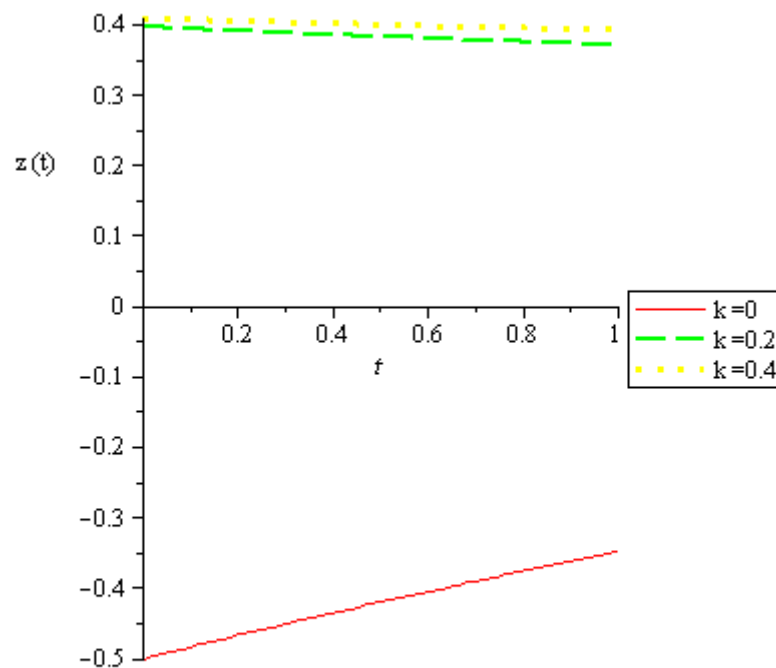

Figure 6: z (t) versus time t for various values of k at
c=0, σ =0.02, b=0.5, q=0, β=1, γ=0.4, μ=0.1, T=10,
$\alpha_0 = 0.2, x_0 = 4, y_0 = 1, z_0 = 0$

6. CONCLUSION

From the studies made on this paper we conclude that this study confirms that counseling and ART could be useful methods for the control and eradication of HIV.

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