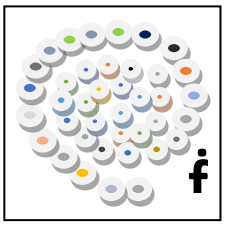

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Effects of PrEP on the HIV/AIDS dynamics with of immigration of infectives

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Abstract

In this work a six compartmental model is formulated to study the effect of PrEP and the direct inflow of HIV infective immigrants on the spread of HIV/AIDS. The positivity and the equilibrium points were analyzed; the Basic Reproduction number R_0 was generated, the local and global stability of the Disease-Free Equilibrium of the model was established and there exists a feasible region where the model is well posed, a unique Disease-Free Equilibrium point exist in the absence of HIV infective immigrants which is locally and globally asymptotically stable if $R_0 < 1$. Sensitivity index of key parameters revealed that c (number of sexual partners) makes the disease more endemic. Numerical simulation suggests that PrEP reduces the number of HIV infection despite the presence of constant inflow of infective immigrants and rigorous adherence to PrEP and treatment reduces the transmission of HIV/AIDS infection among high-risk population and can slow down the spread of infection.

1 Introduction

Human Immunodeficiency Virus (HIV) infection are spectrum of conditions caused by infection with the HIV. The late symptoms of infection are referred to as Acquired Immune Deficiency Syndrome (AIDS). The emergence of Antiretroviral (ARV), which became available in 1996 made many HIV-positive persons on treatment to have substantially lowered RNA level (viral load) enabling them to live long and healthy lives, through strict adherence to treatment regimens. Evidence does suggest that a low viral load may reduce infectiousness of HIV-positive persons receiving antiretroviral therapy (ART). Globally, 75% of people living with HIV were receiving ART as at December 2021 and 68% were virally suppressed in 2021. [11, 31, 34, 35]

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Consequently, the incidences of HIV related death have decreased considerably globally by 52% between 2010 and 2021, 650 000 death from HIV-related causes was reported and 1.5million incidences of new infections in 2021.[31] Despite the improvement in the area of treatment of HIV and the declining overall number of new HIV infections globally, across Sub-Sahara Africa the death rate are much higher and has had a major impact on the life expectancy.[14] Majorly, adolescent girls and young women (53%) are being infected at twice the rate of boys and men of same age. It is a home to two third (67%) of all people living with HIV [21].

Moreover, the link between infectious diseases and population mobility must be understood in relation to the different forms, conditions and patterns of migration, which have different influences on the distribution and spread of infectious diseases. For example, in low and middle-income countries, economic migration has played a crucial involvement in the evolution of the HIV/AIDS epidemic [10]. However, research shows that internal and cross-border migrants, particularly male migrant workers are at greater risk of HIV infection and are more likely to spread the disease when they return home. It is well known that the immigrant can either be a susceptible or infective and disease is always persistent with direct immigration of infective individual in the population. [4, 8, 12, 15, 17, 24].

In other to reduce HIV transmission and save lives of people living with HIV and their uninfected sexual partners, WHO recommended that Pre-Exposure Prophylaxis (PrEP) be offered as a prevention choice for people at substantial risk of the HIV infection as part of a combination of prevention approach. PrEP is the use of ARV by HIV negative people at substantial risk to block the acquisition of HIV infection. High quality evidences strongly supports that PrEP is effective with more than 10 randomized controlled studies among range of populations (key population groups) and their sexual partners including serodiscordant heterosexual couples where one partner is infected and other is not, high risk heterosexual couples.[33] Key population groups are people in the population who are at high risk of HIV in all countries and region, they include: men who have sex with men; people who inject drugs; people in prisons and other closed setting; sex workers and their clients; transgender people.[29, 33]. In order to reach the Fast-Track strategy to end the AIDS epidemic by 2030 globally, intervention services need to focus on key population groups and their sexual partners as they account for over 70% of HIV infections globally. In other to avoid the worst-case scenario of half a million-excess death in Sub-Sahara Africa efforts needs to be redoubled, especially among women and girls as they accounted for 50% of new infections in 2020 [31].

Currently, PrEP cannot be accessed through public programs in most countries of Sub-Sahara Africa due to slow public health response. Ideally PrEP should be offered in combination with other preventive methods especially condoms as it prevents other sexually transmitted infections (STI). South Africa became the first African country to approve the use of PrEP followed by Kenya, [28] according to PrEP watch the estimated number of people under the PrEP strategy in some African countries in 2020 is given in the table below.

Table 1: Total number of People using PrEP in some African countries at 2020

African Countries	Estimated number of People
South Africa	530 378
Uganda	269 840
Zimbabwe	89 946
Kenya	256 321
Nigeria	276 671
Zambia	273 779
Togo	100
Senegal	477
Rwanda	17 884

Ref: (http://www.prepwatch.org/)

However, in Nigeria about 1.9 million people are living with HIV and one of the countries with the largest HIV epidemic in the world [30]. Currently PrEP is not widely available in Nigeria [23]. There is the need for Nigeria to adopt the WHO recommendation on PrEP and develop guidelines to make it available in the public health sector for people at high risk of the infection. PrEP has the potential to significantly decrease new HIV infection among key populations in Nigeria. It is therefore important to consider the effect of PrEP and its awareness on the HIV dynamics of Nigeria [20]. [1] analyzed the potential impact of antiretroviral chemoprophylaxis on HIV-1 transmission in resource limited settings and concluded that PrEP could prevent 2.7 to 3.2 million new cases of HIV in sub-Saharan Africa over 10 years, if it is targeted to the highest risk groups, and disinhibition could be prevented. Then in 2016 WHO welcomed a plan by the South African ministry of health to provide immediate antiretroviral treatment to all sex workers with HIV and oral PrEP to HIV-negative sex workers to prevent them from acquiring the infection. [28].

Even though in low- and middle-income countries the cost of PrEP might be a major problem, the clinical and cost effectiveness study of antiretroviral therapy (ART) and PrEP for prevention, showed that PrEP can be cost saving if delivered to individuals at increased risk of infection and the cost of the PrEP drug is reduced [13, 27]. Mathematical models of HIV prevention measures were used to estimate the effects of early diagnosis, early treatment, on the HIV epidemic over the next 40 years, as compared with the current situation [1, 13, 16, 19, 24, 25]. Also, attention has been paid to study the effect of migration and immigration of infective [5, 8, 12, 15, 17, 24]. This study attempts to investigate the potential impact of PrEP in a population with direct flow of infective immigrants especially on the high-risk population groups.

In this study a six compartmental deterministic HIV/AIDS transmission model is develop, incorporating treatment for infected individuals and the inclusion of PrEP for HIV-negative persons at substantial risk in a population, which generalizes the model proposed by [24]. The aim is to show that PrEP, can reduce the incidence of the disease, also its potential impact on direct immigration of HIV infective.

The paper is organized as follows: section 2 is the model formulation. In section 3 the rigorous analysis of the model is presented. In section 4 sensitivity analysis, 5 the numerical simulation is carried out to and discussed in detail while section 6 bears the conclusion. The numerical study of the model is computed with the aid of the MAPLE 18 mathematical software.

2 Mathematical model formulation

There is an inflow of new members Λ and Q immigrants where the fraction $0 > \tau < 1$ is infected immigrants. The total population at time t is denoted N(t) is divided into six the susceptible class S(t), Infective class I(t) be members who are infected at primary stage, Pre-AIDS class P(t) be members in the Pre-AIDS stage, AIDS class A(t) be members with full blown Aids, Treated class T(t) are the infected members at various stage undergoing treatment and the class of susceptible members under the PrEP strategy V(t) who are assumed to be at substantial risk of acquiring the disease at time t respectively.

The following assumptions are made in the development of the model:

The population under study is heterogeneous and varies with time; it is divided into six groups: are the Susceptible (S), PrEP strategy (V), Infective (I), Pre-AIDS (P), Treatment (T) and the full blown AIDS (A) classes and $N(t)$ is the total population per unit time. $N(t) = S(t) + V(t) + I(t) + P(t) + T(t) + A(t)$.

For this study HIV is considered to be transmitted through sexual intercourse or through infection from infected needle and infected blood. Full blown AIDS are sexually inactive. There is an inflow of new members Λ, who are susceptible and Q, immigrant into the population per time where the fraction $(0 < \tau < 1)$ are infected immigrants.

Table 2

Parameters of the model
S = the susceptible class.
V = the class of susceptible individuals on the PrEP strategy.
I = the infected individuals in the primary stage.
P = the infected individuals in the pre-AIDS stage.
T = the infected individuals who are receiving treatment.
A = the infected individuals with full blown AIDS.
Λ = the constant inflow of susceptible individual into the population.
Q = the inflow of immigrants into the population.
τQ = the fraction of infected immigrants into the population.
$(1-\tau)Q$ = the fraction of uninfected immigrants into population.
ωS = the fraction of individuals under then PrEP strategy.
c = is the average number of sexual partners in a unit time.
d = the natural mortality rate of individuals in all the classes.
k = fraction of those receiving treatment who develop full blown AIDS.

$\beta_1, i = 1,2,3$ is the contact rate.
σ = the rate at which individuals taking PrEP become susceptible.
δ =the rate of movement in the infected class.
α = is the rate of movement in the pre-AIDS class.
θ = is the rate at which the AIDS patients get treatment.
μ = is the disease induced death in AIDS class.
η = fraction of the infective that get treatment.
$\gamma\delta$ =fraction of the pre-AIDS class that develop full blown AIDS.
$\varepsilon\delta$ = fraction of the infective that goes to the pre- AIDS class.

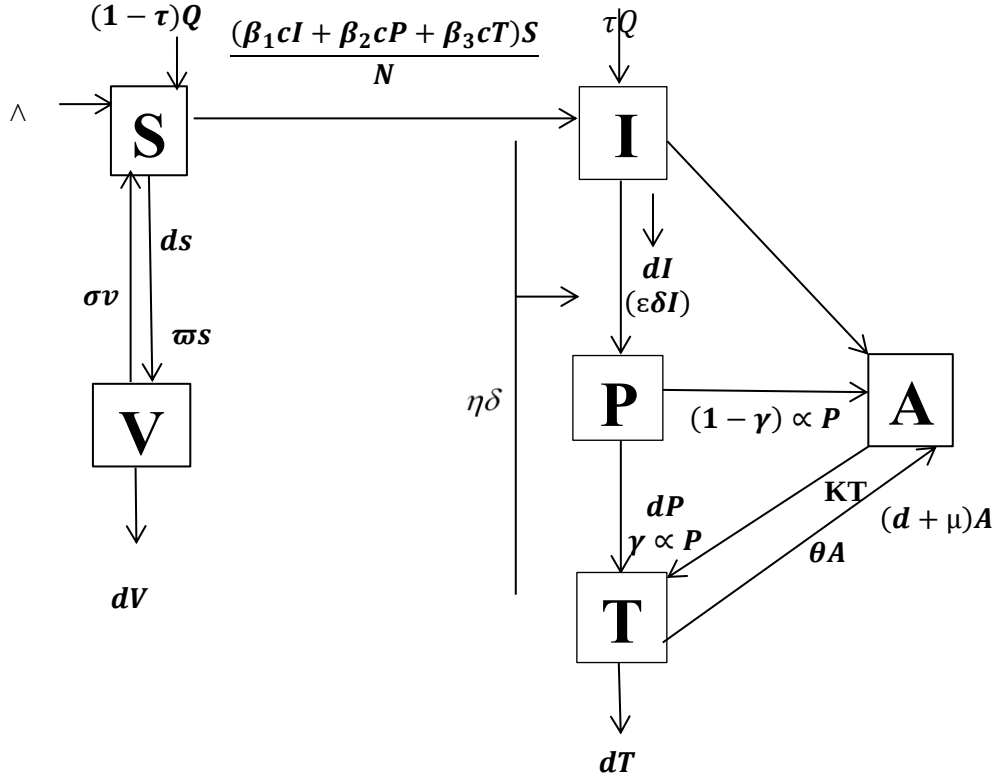

Figure 1

Table 2 and Figure 1 satisfies the model equations as shown below

$$S' = \Lambda + (1-\tau)Q - \frac{(\beta_1 cI + \beta_2 cP + \beta_3 cT)S}{N} - (\varpi + d)S + \sigma V$$

$$V' = \varpi S - (d + \sigma)V$$

$$I' = \tau Q + \frac{(\beta_1 cI + \beta_2 cP + \beta_3 cT)S}{N} - (\delta + d)I$$

$$P' = \varepsilon\delta I - (\alpha + d)P$$

$$T' = \eta\delta I + \gamma\alpha P + \theta A - (k + d)T$$

$$A' = (1-\varepsilon-\eta)\delta I + \alpha(1-\gamma)P + kT - (\theta + \mu + d)A \quad (1)$$

with the initial conditions $S \geq 0, V \geq 0, I \geq 0, P \geq 0, T \geq 0, A \geq 0$ (2)

3 Analysis of model

3.1 Positivity and boundedness of solutions

Lemma 3.1:
Let $S \geq 0, V \geq 0, I \geq 0, P \geq 0, T \geq 0, A \geq 0$. Then the solutions $\{S, V, I, P, T, A\}$ of the system (1) are non-negative for all $t \geq 0$.

Proof: It is necessary to prove that all the solution of the system (1) with positive initial data (2) will remain positive when $t \geq 0$. Considering the first equation

$$\frac{dS}{dt} = \Lambda + (1-\tau)Q - \frac{(\beta_1 cI + \beta_2 cP + \beta_3 cT)S}{N} - (\varpi + d)S + \sigma V$$

$$\frac{dS}{dt} \geq -(\varpi + d)S$$

Separating the variable $\frac{dS}{dt} \geq -(\varpi + d)S$ (3)

$$\int \frac{1}{S} dS \geq -\int (\varpi + d)dt$$

$$S(t) \geq S_0 e^{-(\varpi+d)t} \geq 0$$

Hence $S(t) \geq 0$.

The same approach can be applied to the other state variables to show that they are non-negative.

Lemma 3.2:

$$\text{Let } \Omega = \left\{ (S,V,I,P,T,A) \in R_+^6 : 0 \le S,+V+I+P+T+A \le \frac{\Lambda+Q}{d} \right\} \quad (4)$$

is positively invariant for system (1) with non-negative initial conditions (2) in all $\left(R_+^6\right)$.

Proof:

The total population size $N(t) = S(t)+V(t)+I(t)+P(t)+T(t)+A(t)$ this implies that

$$N' = S' + V' + I' + P' + T' + A' \quad (5)$$

$$N' = \Lambda + Q - dN - \mu A$$

Let $D = \Lambda + Q$. (6)

Since $\frac{dN}{dt} \le D - dN$.

A standard comparison theorem [15, 23] can then be used to show that $N(t) \le \frac{D}{d} + \left(\frac{N_0 - D}{d} \right) e^{-dt}$

Assuming $N(0) \le \frac{D}{d}$ we conclude that $N(t) \le \frac{D}{d}$. Thus, the region Ω is positively invariant.

Hence the system (1) is well posed and epidemiologically meaningful and all the feasible solutions enter the region $\Omega = \left\{ (S,V,I,P,T,A) \in R^6 : 0 \le N \le \frac{\Lambda+Q}{d} \right\}$ with non-negative initial condition. [21]

3.1 Remark

To ensure that the disease-free subspace is invariant, we assume that if the population is free of disease, then the population will remain free of disease. That is, there is no (density independent) immigration of infective. However as long as the infective immigrant are entering the population, the disease-free equilibrium will become unattainable, this is in agreement with [14, 24, 32].

3.2 Existence of equilibrium point for the model

To verify the existence of the equilibrium points, to find the Disease-Free Equilibrium (DFE), it is assumed that there are no infective immigrants by setting $Q = 0$ in and the right-hand side of the model equations in (1) is set to zero. At DFE, E_0

$$\frac{dS}{dt} = \frac{dI}{dt} = \frac{dP}{dt} = \frac{dV}{dt} = \frac{dA}{dt} = \frac{dI}{dt} = 0$$

where $S \neq 0$ and $V \neq 0$ and $I = P = A = T = 0$

Thus,

$$E^0 = (S,V,0,0,0,0) = \left(\frac{(d+\sigma)\Lambda}{d(\varpi+d+\sigma)}, \frac{\varpi\Lambda}{d(\varpi+d+\sigma)}, 0,0,0,0 \right). \tag{7}$$

Also at disease free equilibrium $N = \frac{\Lambda}{d}$ (8)

Similarly, to solve the Endemic Equilibrium Point E^* of the system (1) each of the equations is set to zero to have and substituting $S = S^*, V = V^*, I = I^*, P = P^*, T = T^*, A = A^*$. Endemic Equilibrium Point E^* of the system (1) is obtained as

$$\begin{aligned}
P^* &= \frac{\varepsilon\delta I^*}{(\alpha+d)} \\
A^* &= \frac{\left((\alpha+d)\left((k+d)(1-\varepsilon)-d\eta\right)+\varepsilon\alpha\left(k+d(1-\gamma)\right)\right)\delta I^*}{\left((\theta+\mu+d)(k+d)-\theta k\right)(\alpha+d)} \\
T^* &= \frac{\left((\alpha+d)\left(\eta(\mu+d)+\theta(1-\varepsilon)\right)+\varepsilon\alpha\left(\gamma(\mu+d)+\theta\right)\right)\delta I^*}{\left((\theta+\mu+d)(k+d)-\theta k\right)(\alpha+d)} \\
V^* &= \frac{(\Lambda+(1-\tau)Q)q\varpi N}{\left(R_0(\delta+d)I^*+Nd\right)(d+\sigma)} \\
S^* &= \frac{(\Lambda+(1-\tau)Q)qN}{\left(R_0(\delta+d)I^*+Nd\right)}
\end{aligned} \tag{9}$$

and I^* a quadratic equation:

$$C_2 I^{*2} - C_1 I^* + C_0 = 0 \tag{10}$$

where

$$C_2 = R_0(\delta+d)^2$$

$$C_1 = \left(Nd - R_0(\Lambda+Q)\right)(\delta+d)$$

$$C_0 = \tau QNd$$

By Descartes's rule of sign two change of sign means there is at most two real positive root, so there will be positive roots, this implies that $S^*, V^*, I^*, P^*, T^*, A^*$ will have positive value. Therefore, the model (1) has a positive solution.

3.3 Basic reproduction number

The basic reproduction number R_0 is defined as the effective number of secondary cases produced by a typical infected individual during the entire period of infectiousness. The next-generation matrix approach by [27] is employed. Let $x = (S,.V, I, P, T, A)^T$.

This is done by taking the largest dominant spectral radius of $R_0 = \left[\frac{\partial \mathsf{F}_i(x_0)}{\partial x_i}\right]\left[\frac{\partial \mathcal{V}_i(x_0)}{\partial x_i}\right]^{-1}$ where

F_i be the rate at which new infections appear in the compartment i

$\mathcal{V}_i^{+"}$ be the rate of transfer of individuals into of the compartment i by all other means

$\mathcal{V}_i^{-}$ be the rate of transfer of individuals out of the compartment i by all other means

And considering $\mathcal{V}_i = \mathcal{V}_i^{-} - \mathcal{V}_i^{\backslash +}$.

Then $F = \left[\frac{\partial \mathsf{F}_i(x_0)}{\partial x_i}\right]$ $V = \left[\frac{\partial \mathcal{V}_i(x_0)}{\partial x_i}\right]$ at the disease-free equilibrium point gives the following

$$F = \begin{pmatrix} \beta_1 cq & \beta_2 cq & \beta_3 cq & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{11}$$

$$V = \begin{pmatrix} (\delta + d) & 0 & 0 & 0 \\ -\varepsilon\delta & (\alpha + d) & 0 & 0 \\ -\eta\delta & -\gamma\alpha & (k + d) & -\theta \\ -(1-\varepsilon-\eta)\delta & -\alpha(1-\gamma) & -k & (\theta + \mu + d) \end{pmatrix} \tag{12}$$

where

$$K_1 = (\delta + d), K_2 = \varepsilon\delta, K_3 = (\alpha + d), K_4 = (d + k), K_5 = (1-\varepsilon-\eta)\delta\, K_6 = (1-\gamma),$$

$$K_7 = (\theta + \mu + d), K_8 = (\omega + d), K_9 = (d + \sigma),\ q = \frac{(d+\sigma)}{(\varpi + d + \sigma)} \tag{13}$$

$$V^{-1} = \begin{pmatrix} \frac{1}{K_1} & 0 & 0 & 0 \\ \frac{K_2}{K_1 K_3} & \frac{1}{K_3} & 0 & 0 \\ \frac{K_2\alpha(\gamma K_7 + \theta K_6) + K_3(\delta\eta K_7 + \theta K_5)}{K_1 K_3(K_4 K_7 - k\theta)} & \frac{\alpha(\gamma K_7 + \theta K_6)}{K_3(K_4 K_7 - k\theta)} & \frac{K_7}{(K_4 K_7 - k\theta)} & \frac{\theta}{(K_4 K_7 - k\theta)} \\ \frac{K_2\alpha(\gamma k + K_6 K_4) + K_3(\delta\eta k + K_4 K_5)}{K_1 K_3(K_4 K_7 - k\theta)} & \frac{\alpha(\gamma k + K_6 K_4)}{K_3(K_4 K_7 - k\theta)} & \frac{k}{(K_4 K_7 - k\theta)} & \frac{K_4}{(K_4 K_7 - k\theta)} \end{pmatrix}$$

$R_0 = \rho\left(FV^{-1}\right)$, that is the dominant spectral radius of the largest eigenvalues given by

$$R_0 = \text{Max}\left[\lambda_1\lambda_2\lambda_3\lambda_4\right]$$

It follows that the reproduction number R_0 for the model (1) is

$$R_0 = \frac{cq\{\beta_1 K_3\left(K_4K_7 - k\theta\right) + \beta_2 K_2\left(K_4K_7 - k\theta\right) + \beta_3 K_2\alpha\left(\left(\gamma K_7 + \theta K_6\right) + K_3\left(\delta\eta K_7 + \theta K_5\right)\right)\}}{K_1K_3\left(K_4K_7 - k\theta\right)} \tag{14}$$

3.4 Local stability of DFE

Theorem 3.4: The disease-free Equilibrium of the model (1) in the absence of infective immigrant is locally asymptotically stable if the $R_0 < 1$ and unstable if $R_0 > 1$.

Proof:

To determine the local stability of Disease-Free Equilibrium E_0, we compute the variational matrix of the linearized system (1) corresponding to the equilibrium point E_0 to have the Jacobian matrix given as:

Using the substitution in (14) to have

$$J(E_0) = \begin{pmatrix} -K_8 & \sigma & -\beta_1 cq & -\beta_2 cq & -\beta_3 cq & 0 \\ \varpi & -K_9 & 0 & 0 & 0 & 0 \\ 0 & 0 & -\left(K_1 - \beta_1 cq\right) & \beta_2 cq & \beta_3 cq & 0 \\ 0 & 0 & \varepsilon\delta & -K_3 & 0 & 0 \\ 0 & 0 & \eta\delta & \gamma\alpha & -K_4 & \theta \\ 0 & 0 & K_5 & K_6 & k & -K_7 \end{pmatrix} \tag{15}$$

The characteristics equation corresponding with (15)

$$(\lambda^2 b_0 + \lambda b_1 + b_2)(\lambda^4 a_0 + \lambda^3 a_1 + \lambda^2 a_2 + \lambda a_3 + a_4) = 0 \tag{16}$$

where

$b_0 = 1,\ b_1 = (K_8 + K_9)\,, b_2 = K_8K_9 - \omega\sigma\,,$

$a_0 = 1,\ a_1 = (K_1 + K_3 + K_4 + K_7 - cq\beta_1)$

$a_2 = K_3(K_1 + K_4 + K_7) + K_7(K_1 + K_4) + K_1K_4 - \theta k - cq(\beta_1(K_3 + K_4 + K_7) + K_2\beta_2 + \eta\delta\beta_3)$

$a_3 = K_3(K_1K_4 - k\theta) + K_7(K_1 + K_4) + K_1(K_4K_7 - k\theta) - cq((\beta_1(K_3(K_4 + K_7) + K_4K_7 - k\theta) +$

$\beta_2K_2(K_4 + K_7) + \beta_3(\eta\delta(K_7 + K_3) + \gamma\alpha K_2 + \theta K_5))$

$a_4 = K_1K_3(K_7K_4 - k\theta)(1 - R_0)\,.$

By the Routh Hurwitz criteria if $b_1 > 0, b_2 > 0$ then $b_1 b_2 > 0$ for the quadratic equation and if $a_1 > 0$, $a_2 > 0$, $a_3 > 0$, $a_4 > 0$ and $a_5 > 0$ then $a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$ for the fourth root equation. On further simplification the roots $b_j > 0$ for $j = 0,1,2$ $a_i > 0$ for $i = 0,1,2,3,4$,.

So $a_4 > 0$ to have

$$K_1 K_3 (K_7 K_4 - k\theta)(1 - R_0) > 0$$
$$(1 - R_0) > 0$$
$$\therefore R_0 < 1.$$

It follows that all the eigenvalues $J(E_0)$ have negative real parts this implies that the disease-free equilibrium is locally asymptotically stable if $R_0 < 1$.

Thus, disease free equilibrium of the model (1) is locally asymptotically stable if $R_0 < 1$.

3.5 Global stability of disease free equilibrium

To establish the global asymptotic stability (GAS) of the disease-free equilibrium (DFE) state of the model (1) the approach of [7] is employed as follows. The model is written as

$$\frac{dX}{dt} = Y(X, Z) \tag{17}$$
$$\frac{dZ}{dt} = G(X, Z), G(X^*, 0) = 0 \tag{18}$$

where $X = (S, V) \in \mathbb{R}_+^2$ denotes the number of uninfected individuals
$Z = (I, P, T, A) \in \mathbb{R}_+^4$ denotes the number of infected individuals including.

The DFE of the system is denoted $E_0 = (X^* 0)$. The two conditions H_1 and H_2 that if satisfied will guarantee the global stability

$H_1 : \frac{dX}{dt} = Y(X, 0), X^*$ is globally asymptotically stable (GAS)
$H_2 : \frac{dZ}{dt} = G(X, Z) = AY - \hat{G}(X, Z),\ \hat{G}(X, Z) \geq 0$ for $(X, Z) \in \Omega$

where $A = D_Z G(X^*, 0)$ is an M-matrix (the off diagonal elements of A are non-negative) and Ω is the region where the model makes biological sense. If the system (1) satisfies the conditions H_1 and H_2 then the following theorem 3.5 holds

Theorem 3.5
The disease-free equilibrium (DFE) point $E_0 = (X^* 0)$ of the system (1) is globally asymptotically stable provided $R_0 < 1$ then the two conditions H_1 and H_2 are satisfied.

Proof

Let $X = (S,V)$ and $Z = (I,P,T,A)$ to have two vectors valued functions

$$Y(X,Z) = \begin{pmatrix} \Lambda + (1-\tau)Q - \dfrac{(\beta_1 cI + \beta_2 cP + \beta_3 cT)S}{N} \sigma V - (w+d)S \\ wS - (d+\sigma)V \end{pmatrix} \tag{19}$$

$$G(X,Z) = \begin{pmatrix} \tau Q + \dfrac{(\beta_1 cI + \beta_2 cP + \beta_3 cT)S}{N} - (\delta + d)I \\ \varepsilon\delta I - (\alpha + d)P \\ \eta\delta I + \gamma\alpha P + \theta A - (k+d)T \\ (1-\varepsilon-\eta)\delta I + (1-\gamma)\alpha P + kT - (\theta + \mu + d)A \end{pmatrix} \tag{20}$$

Considering the reduced system $\frac{dX}{dt} = Y(X,0)$ from condition H_1

$$Y(X,0) = \begin{pmatrix} \Lambda + (1-\tau)Q + \sigma V - (w+d)S \\ wS - (d+\sigma)V \end{pmatrix} \tag{21}$$

$X^* = (S^*, V^*) = \left(\dfrac{\Lambda(d+\sigma)}{d(\omega+d+\sigma)}, \dfrac{\Lambda\omega}{d(\omega+d+\sigma)} \right)$ is a GAS equilibrium point for the reduced system (21) to show this, the second equation in (21) is solved to obtain $V(t) = \dfrac{\Lambda\omega}{d(\omega+d+\sigma)} + \left(V_0 - \dfrac{\Lambda\omega}{d(\omega+d+\sigma)} \right) e^{-(d+\sigma)t}$;it approaches zero as $\dfrac{\Lambda\omega}{d(\omega+d+\sigma)}$ as $t \to \infty$ Similarly the solution of the first equation gives $S(t) = \dfrac{\Lambda(d+\sigma)}{d(\omega+d+\sigma)} + \left(S_0 - \dfrac{\Lambda(d+\sigma)}{d(\omega+d+\sigma)} \right) e^{-(\omega+d)t}$ which approaches $\dfrac{\Lambda(d+\sigma)}{d(\omega+d+\sigma)}$ as $t \to \infty$. This asymptotic dynamic is independent of the initial condition in Ω. Thus, the convergence of the solution of the reduced system in (19) is global in Ω.

To compute $\frac{dZ}{dt} = G(W,Z) = AZ - \hat{G}(W,Z),$ and show $\hat{G}(W,Z) \geq 0$

$$A = D_z G(X^*,0) = \begin{pmatrix} \beta_1 c - (\delta + d) & \beta_2 c & \beta_3 c & 0 \\ \varepsilon\delta & -(\alpha + d) & 0 & 0 \\ \eta\delta & \gamma\alpha & -(k+d) & \theta \\ (1-\varepsilon-\eta)\delta & \alpha(1-\gamma) & k & -(\theta+\mu+d) \end{pmatrix} \tag{22}$$

$$\hat{G}(W,Z) = \begin{pmatrix} \beta_1 cI\left(1 - \frac{S}{N}\right) + \beta_2 cP\left(1 - \frac{S}{N}\right) + \beta_3 cT\left(1 - \frac{S}{N}\right) \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{23}$$

Since $1 > \frac{S}{N}$ it is clear that $\hat{G}(W,Z) \geq 0$. Hence DFE is globally asymptotically stable when $R_0 < 1$.

4 Sensitivity analysis

It is important to perform the sensitivity analysis in order to determine the relative importance of the model parameter to diseases transmission. It is therefore pertinent to know the significance of the different factors responsible for the disease transmission, to determine how best to reduce the mortality and morbidity due to HIV. The normalized forward sensitivity index using the [9]

approach of a variable to a parameter is a ratio of the relative change in the variable to the relative change in the parameter. For a differentiable variable function, the sensitivity index is defined as

$$H_m^{R_0} = \frac{m}{R_0}\frac{\partial R_0}{\partial m} \tag{24}$$

where m stands for the different parameter
We compute the numerical sensitivity indices (24) to enable us know which of the parameters have a high impact on R_0 so that it will be the target point of any control or preventive strategy.

5 Numerical simulation and discussion

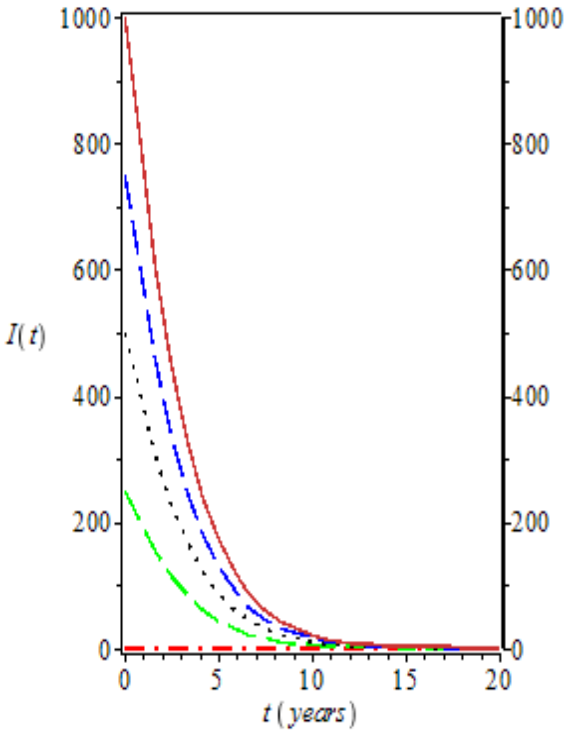

Figure 1: The global stability of the DFE at various initial values

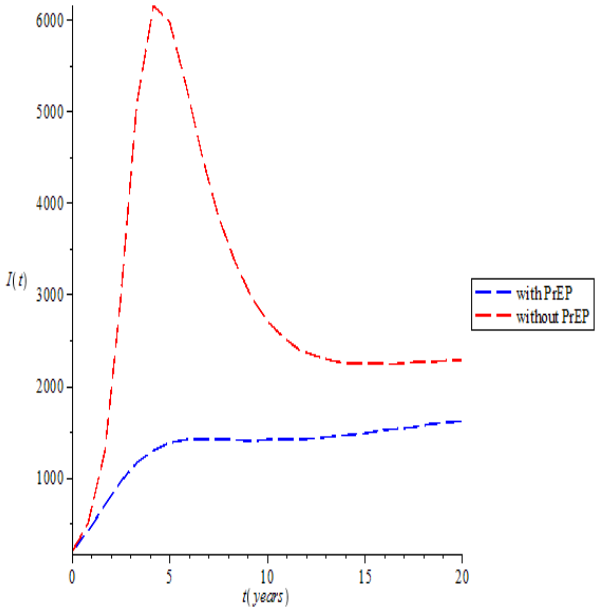

Figure 2 : The effect of PrEP on the Infective class I(t) in the absence of infected immigrants

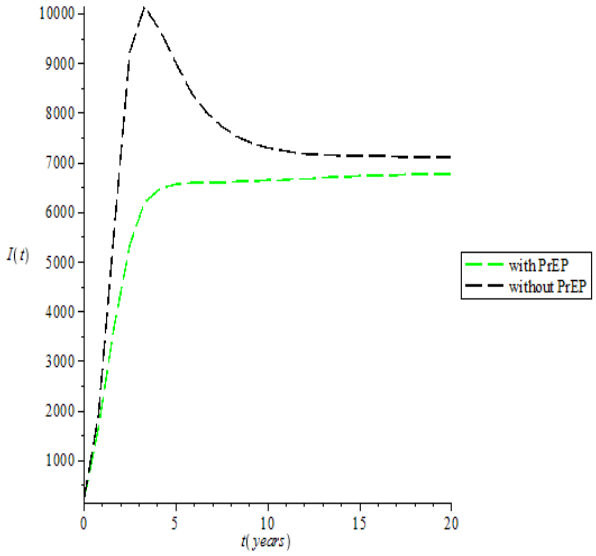

Figure 3 : The effect of PrEP on the Infective class I(t) in the presence of infected immigrants

Figure 1 demonstrates the global stability of the disease-free equilibrium point proved in the theorems 3.5. This implies that regardless of the initial size of the number of infections in the population whenever $R_0 < 1$ the infection will reduce in the population. Figure 2 shows the effect of PrEP on the infective class $I(t)$ in a population with infective immigrant.

Immigration poses a significant risk for disease dissemination; the effect may be substantial in developing countries which normally do not check the complete health status of immigrants. These immigrants place their partners in their home countries and their destination countries at risk of HIV/AIDS. It can be observed from Figure 2 that the infective population increases continuously due to the presence of infected immigrants, meaning that the presence of immigrants increases the total population initially making the infection more endemic and persistent in the population then decreases with time. It is clear that direct inflow of infected immigrants increases the numbers of infective which ultimately increase the prevalence of the disease, to check the spread of disease and prevent it from becoming endemic in the population effective immigration policies such as screening of immigrants should be taken seriously.

Figure 3 also shows that in the population where the PrEP strategy is in place, the peak of epidemic is higher in the figure 1 with presence of infected immigrants than in the absence of infected immigrants but either way it still reduces infection. Thus, PrEP can lead to reduction in the risk of sexual transmission of HIV.

Figure 4 shows the combine effect of PrEP on treatment in the population with or without the inflow of infective immigrants the result shown in Figure 4 suggests that treatment will reduce the disease prevalence in the community, it benefits can be improved when combined with the use of PrEP but their benefit can be compromised if the adherence to usage is poor and illicit sexual behavior is increased. Treatment is important to slow down the progression of HIV to AIDS due to the fact that it reduces the viral load of people living with HIV while PrEP can reduce the risk of being infected by an HIV negative person. Plot result suggest that combination of PrEP and treatment is more effective as treatment keeps people alive by rendering them much less infectious and will be on treatment for life while PrEP prevents people at risk from likely infection. PrEP and treatment can lead to decrease in new cases of infection ultimately to a substantial decline in prevalence of infection.

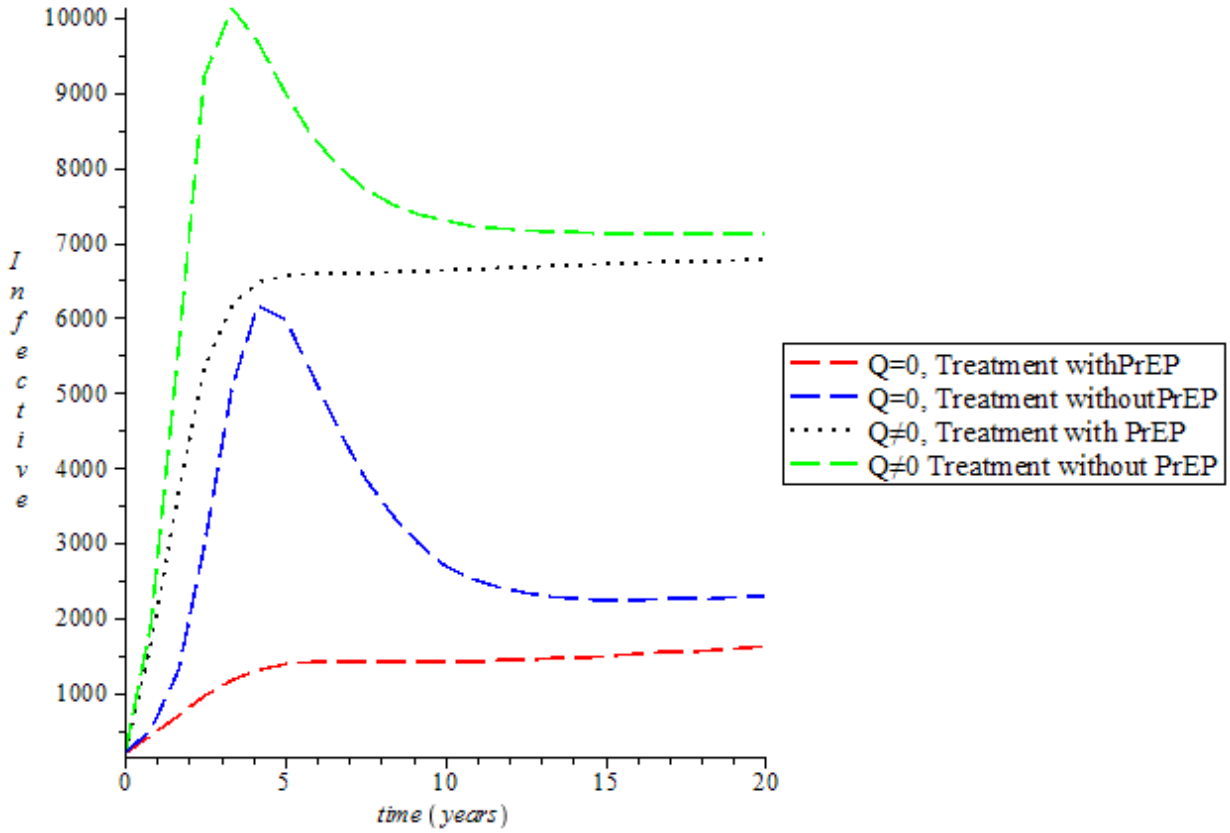

Figure 4 : The effect of PrEP on Treatment in the Infective class I(t) with or without immigration

5.1 Result of Sensitivity Index

Sensitivity analysis is used to discover parameters that have a high impact on the basic reproduction number, R_0 and should be the target of any intervention strategies. The parameter which had the greatest influence on the number of new infection caused in the primary infection (basic reproduction number R_0) was determined. Table 5.1 contains the numerical values of these parameters calculated using the approach of [9]. From Table 5.1 it can be seen that the most important parameter contributing to the infection is the number of sexual partners c also influencing the infection is the contact rate β_1 of the infective class, the number of sexual partners c and contact rates of the infective β_1 together interact to cause increased incidence of HIV and the increased prevalence of HIV. This means that while there is any increment in either c, β_1 or any of the parameters with positive values and other parameters kept constant there will be an increase in the value of R_0. The parameter with negative values means that when these values are increased while other are kept constants there is a decrease in the value R_0 .thus these parameter with positive and negative values have to be the focus or target of intervention strategies as they are crucial to the transmission and prevalence of the HIV/AIDS.

Table 5.1: Sensitivity Indices of R_0

Parameter	Sensitivity values	Value	Source
C	**+1**	**3**	**[20]**
β_1	**+0.7562310755**	**0.15**	**[20]**
ε	**+0.1369270468**	**0.6**	**[20]**
β_2	**+0.1274256821**	**0.05**	**[20]**
β_3	**+0.1163432424**	**0.05**	**[21]**
θ	**+0.0922648381**	**0.1**	**[21]**
σ	**+0.0464576074**	**0.4**	**[21]**
η	**+0.0098891756**	**0.01**	**[21]**
δ	**-0.7086120282**	**0.4**	**[20]**
ϖ	**-0.4878048780**	**0.4**	**[20]**
α	**-0.1088394479**	**0.5**	**[20]**
k	**-0.0999801506**	**0.08**	**[21]**
μ	**-0.0904557236**	**1**	**[20]**
D	**-0.0611486848**	**0.02**	**[20]**

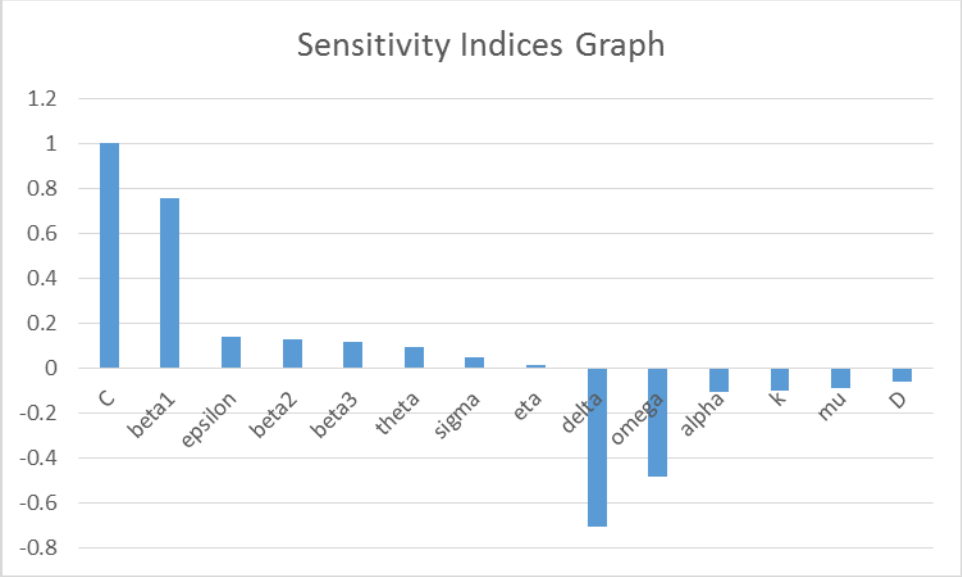

Figure 5.1: The chart of parameters

Generally, the number of sexual partner is the strongest attributor of risk of HIV acquisition; plot result also revealed that the number of new HIV infection is large due to the influence of the

increase in the number of sexual partners. Thus, to reduce the spread of the disease the number of sexual partners as well as unsafe sexual behavior and interaction with infected individuals must be restricted.

6 Conclusion

In this work, a nonlinear deterministic mathematical model was proposed and analyzed to study the effect of PrEP in the dynamics of HIV/AIDs with variable in flow of infective immigrants, and also incorporating treatment at different stage of infection using the standard incidence. Analysis of the model showed that as long as the infective immigrants are entering the population, the disease free equilibrium become unattainable and the existence and uniqueness of Disease Free Equilibrium (DFE) and Endemic Equilibrium Point (EEP) of the model without infective immigrants were proved depending on R_0 .It was established that DFE is locally asymptotically stable if $R_0 < 1$ and for $R_0 > 1$it is unstable, global stability of the DFE was proved using the Next Generation Operator method [9] and it was established that the effectiveness of PrEP is strict adherence to usage of the medication.

Numerical simulation of the effect of PrEP in the absence of immigration of infective was compared with the model without immigration, it was observed that PrEP reduces the number of new HIV incidences, however, only people who are HIV negative and are at very high risk of HIV infection should take PrEP. Productive campaign messages and awareness about PrEP in various communities needs be created that PrEP is acceptable and effective as an additional choice for the prevention of HIV infection as this in turn strengthens health education regarding HIV infection leading to AIDS. The National Health Care to HIV/AIDS should therefore seek to recommend PrEP to people at risk or have been at risk in the past as recommended by WHO also ensure that they have access to and are supported in the use of PrEP and other prevention measures regardless of social and economic status.

Sensitivity indices of the key parameter revealed that an increase in the number of sexual partner c results in the increase of the incidence of the HIV/AIDS infection. Research results suggest that reduction in the number of sexual partners, change in risky behavior as well as unsafe sexual practices and interactions are highly important for preventing subsequent transmission.

Simulation shows that when there is immigration of infected individuals then the rate of spread of the diseases will be massive as in the case where there is no protection. Effective immigration policies such as screening should be put in place to minimize the potential of infecting others by an already infected individual migrant.

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