Sensitivity Analysis of Effect of Screening and HIV Therapy on the Dynamics of Spread of HIV

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Abstract

This paper examines the effect of screening and HIV therapy on the dynamics of the spread of HIV in a population. In modeling of the dynamics of HIV, the population is divided into five subpopulations: susceptible, unaware infectives, screened infectives, therapy infectives, and AIDS patients. The effective reproduction numbers are calculated using the next generation matrix method. A sensitivity analysis discovers parameters that have a high impact on effective reproduction number and should be targeted by intervention strategies. Sensitivity indices are used to measure the relative change in the effective reproduction number if a parameter change. The results shows that the disease-free equilibrium point is asymptotically stable when the effective reproduction number is less than one and unstable when the effective reproduction number is greater than one. According to the analysis, screening of unaware infectives and therapy of screened HIV infectives have the effect of reducing the transmission of the disease. Finally, numerical simulation of the model shows that the most sensitive parameter is contact rate of unaware infectives with susceptibles, allowed by the rate of progression of unaware infectives to screened infectives.

Keywords: HIV/AIDS, Screening of HIV, HIV therapy, Effective reproduction number, Disease-free equilibrium point, Sensitivity analysis
1. Introduction

HIV (Human Immunodeficiency) and AIDS (Acquired Immune Deficiency Syndrome) is one of the health problems. Recently, there is no country that is free of HIV/AIDS and HIV/AIDS has led to a multidimensional crisis, especially in the health field. One of the programs in order to minimize the prevalence of HIV/AIDS is the HIV screening and HIV therapy for people who tested HIV positive.

Until now, many studies have been developed to analyze mathematically the impact of the screening of unaware infectives on the spread of HIV infections, for example Tripathi et al. [1] presented a theoretical framework for transmission of HIV/AIDS with screening of unaware infectives. Shabani et al. [2] analyzed a mathematical model of the effect of screening the HIV infection in a homogeneous population with infective immigrants. Naresh et al. [3] presented modelling the effect of risky sexual behavior on the spread of HIV/AIDS. Modelling the effect of screening and treatment on transmission of HIV/AIDS infection in a population can be found in Safiel et al. [4].

Sensitivity analysis allows to investigate how uncertainty in the input variables affect the model outputs and which input variables tend to drive variation in the outputs. Sensitivity of the effective reproduction number for a HIV/AIDS model can be found in Safiel et al. [4]. In this paper will focus on the sensitivity analysis of the effective reproduction number and numerical simulation models are implemented to account for the model parameters that influence the spread of HIV/AIDS. We study a nonlinear mathematical model of the effect of screening and therapy on the spread of HIV infection in a population. It is refer to Safiel et al. [4] but this model incorporates the assumption that the recruitment rate into the susceptibles is constant and only screened infectives can be treated with ARV therapy.

2. Model with Screening and HIV Therapy

In modelling the disease dynamics, the population \( N \) is divided into five subclass: susceptibles or HIV negative \( (S) \), unaware infectives or HIV positive that do not know they are infected \( (I_1) \), screened infectives or HIV positive that know they are infected after a screening method \( (I_2) \), therapy infectives or HIV positive and accept HIV therapy after being screened \( (T) \), and AIDS patient or full blown AIDS \( (A) \).

The model assumed that: transmission rate \( (\lambda) \) proportional to the susceptibles, and the ratio between the number of infected population and the total population; unaware infectives can be screened infectives at rate \( \theta \); only screened infectives can be therapy infectives at rate \( \delta \); unaware infectives, screened infectives and therapy infectives move to full blown AIDS at different
rates \( \sigma_1, \sigma_2 \) and \( \sigma \) respectively \( (\sigma < \sigma_2 < \sigma_1) \); unaware infectives, screened infectives and therapy infectives can infect susceptibles at different rates \( \beta_1, \beta_2 \) dan \( \beta_3 \) respectively \( (\beta_3 < \beta_2 < \beta_1) \); the recruitment rate into susceptible \( \Lambda \); the AIDS related dead rate \( \gamma \) and the natural mortality rate \( \mu \).

Taking into account the above considerations, we have system of nonlinear differential equations:

\[
\begin{align*}
\frac{dS}{dt} &= \Lambda - \lambda S - \mu S \\
\frac{dI_1}{dt} &= \lambda S - (\theta + \sigma_1 + \mu)I_1 \\
\frac{dI_2}{dt} &= \theta I_1 - (\delta + \sigma_2 + \mu)I_2 \\
\frac{dT}{dt} &= \delta I_1 - (\sigma + \mu)T \\
\frac{dA}{dt} &= \sigma_1 I_1 + \sigma_2 I_2 + \sigma T - (\gamma + \mu)A
\end{align*}
\]

where

\[
\lambda = \frac{c_1 \beta_1 I_1 + c_2 \beta_2 I_2 + c_3 \beta_3 T}{N}; \quad N = S + I_1 + I_2 + T + A
\]

with initial conditions

\[
S(0) = S_0, I_1(0) = I_{10}, I_2(0) = I_{20}, T(0) = T_0, A(0) = A_0.
\]

The meaning of the parameters of the model, together with the baseline values used in numerical analysis, are given in Table 1.
Table 1 Parameters used in the HIV model with screening and HIV therapy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
<th>Values</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1$</td>
<td>per capita contact rate for susceptible individuals with unaware infective</td>
<td>0.86</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\beta_2$</td>
<td>per capita contact rate for susceptible individuals with screened infective</td>
<td>0.15</td>
<td>Tripathi et al. [1]</td>
</tr>
<tr>
<td>$\beta_3$</td>
<td>per capita contact rate for susceptible individuals with therapy infective</td>
<td>0.1</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\theta$</td>
<td>the rate at which unaware infective are detected by screened method to become screened infective</td>
<td>0.6</td>
<td>Shabani et al. [2]</td>
</tr>
<tr>
<td>$\delta$</td>
<td>the rate at which screened infectives are therapy</td>
<td>0.99</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\sigma_1$</td>
<td>the rate at which unaware infective develop full blown AIDS</td>
<td>0.2</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\sigma_2$</td>
<td>the rate at which screened infective develop full blown AIDS</td>
<td>0.01</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>the rate at which therapy infective develop full blown AIDS</td>
<td>0.001</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\mu$</td>
<td>natural mortality rate</td>
<td>0.1</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>AIDS related death rate</td>
<td>1</td>
<td>Tripathi et al. [1]</td>
</tr>
<tr>
<td>$c_1$</td>
<td>average number of sexual partners per unit time for unaware infective</td>
<td>1</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$c_2$</td>
<td>average number of sexual partners per unit time for screened infective</td>
<td>2</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$c_3$</td>
<td>average number of sexual partners per unit time for therapy infective</td>
<td>3</td>
<td>Safiel et al. [3]</td>
</tr>
<tr>
<td>$\Lambda$</td>
<td>the recruitment rate into the susceptible class</td>
<td>700</td>
<td>Estimated</td>
</tr>
</tbody>
</table>

3. Effective Reproduction Number

Due to biological reasons, only nonnegative solutions of the initial value problem (1) - (3) are acceptable. Hence all feasible solution of system (1) subject to given initial conditions (3) enter region

$$\Gamma = \left\{(S_1, I_1, I_2, T, A) \in \mathbb{R}_+^5 \mid S_1 + I_1 + I_2 + T + A = N \leq \frac{\Lambda}{\mu}\right\}. $$

It can be verified that $\Gamma$ is a positively invariant set with respect to (1).

The disease-free equilibrium point of the model (1) was given by

$$E_0 = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right), \mu > 0.$$ (4)
The local stability of $E_0$ was established by using the next generation matrix method on the system (1). The basic reproduction number is defined as the effective number of secondary infections caused by typical infected individual during his entire period of infectiousness (Diekmann et al. [5]). This definition is given for the models that represent the spreading of infection in a population.

An important measure of transmissibility of the disease is the epidemiological concept of basic (effective) reproduction number. It provides an invasion criterion for the initial spread of the virus in a susceptible population. The effective reproduction number which is given by the largest eigen value for the normalised model system (1) with screening and HIV therapy denoted by $R_e$ was obtained by using the next generation matrix method and is given by (Marsudi et al. [7]),

$$R_e = \frac{c_1\beta_1(\delta + \sigma_1 + \mu)(\delta + \mu) + c_2\beta_2\theta(\delta + \mu) + c_3\beta_3\delta\theta}{(\theta + \sigma_1 + \mu)(\delta + \sigma_2 + \mu)(\delta + \mu)}.$$  \hfill (5)

The effective reproduction number shows the average number of new infections caused by a single HIV infected individual in a population which screening and HIV therapy program is used to control strategies.

Using Theorem 2 van den Driessche and Watmough [6], the disease-free equilibrium of the HIV model system (1) is locally asymptotically stable if $R_e < 1$ and unstable if $R_e > 1$. In order to assess the contribution of $I_1, I_2$ and $T$ in terms $\beta_1, \beta_2, \beta_3$ from equation (5), we let

$$R_{e_1} = \frac{c_1\beta_1}{\theta + \sigma_1 + \mu}$$ \hfill (6)

$$R_{e_2} = \frac{c_2\beta_2\theta}{(\theta + \sigma_1 + \mu)(\delta + \sigma_2 + \mu)}$$ \hfill (7)

$$R_{e_T} = \frac{c_3\beta_3\delta\theta}{(\theta + \sigma_1 + \mu)(\delta + \sigma_2 + \mu)(\delta + \mu)}$$ \hfill (8)

then

$$R_e = R_{e_1} + R_{e_2} + R_{e_T}.$$ \hfill (9)

From the equations (6)-(8) above, it is clear that $R_{e_1} > R_{e_2} > R_{e_T}$ which implies that unaware infectives ($I_1$) have a significant contribution on the transmission of the HIV/AIDS infection followed by screened infectives ($I_2$) and keeping the disease endemic in the population via $c_1\beta_1$ and $c_2\beta_2$ respectively compared to therapy infectives ($T$) via $c_3\beta_3$. In the absence of infection, the population size approaches a steady state $\Lambda \mu$. Further, analyzed the four epidemiological situations in population:

(i) We consider the model with screening and HIV therapy when therapy infectives do not transmit the infection in population ($\delta \neq 0$ and $\beta_1 = 0$), we have the basic reproduction number given by
\[ R_{90} = \frac{c_i \beta_i (\delta + \sigma_2 + \mu) + c_i \beta_i \theta}{(\theta + \sigma_i + \mu)(\delta + \sigma_2 + \mu)}. \] (10)

It is clear that \( R_{90} < R_9 \) and \( R_9 \rightarrow R_{90} \) as \( \beta_1 \rightarrow 0 \). Thus, the endemicity of the infection is reduced when the therapy infectives present a positive attitude towards preventive measures and do not take part in the transmission of the disease.

(ii) We consider the model with screening and HIV therapy when both screened and therapy infectives respectively do not transmit the infection in population (\( \theta \neq 0, \beta_2 = 0, \delta \neq 0 \) and \( \beta_3 = 0 \)), we have the basic reproduction number given by

\[ R_{92} = \frac{c_i \beta_i}{\theta + \sigma_i + \mu}. \] (11)

It is clear that \( R_{92} < R_{90} < R_9 \) and \( R_9 \rightarrow R_{92} \) as \( \beta_2 \rightarrow 0 \) and \( \beta_3 \rightarrow 0 \). Thus, the endemicity of the infection is reduced when the screened and therapy infectives both reflect a positive attitude towards preventive measures and do not take part in the transmission of the disease.

(iii) We consider the model in the absence of HIV therapy (screening only and \( \delta = 0 \)). If there is no therapy (\( \delta = 0 \)), then \( T \rightarrow 0 \) and we have the basic reproduction number given by

\[ R_{93} = \frac{c_i \beta_i (\sigma_2 + \mu)}{(\theta + \sigma_i + \mu)(\sigma_2 + \mu)}. \] (12)

It is clear that \( R_9 < R_{93} \) and \( R_9 \rightarrow R_{93} \) as \( \delta \rightarrow 0 \). Thus, the endemicity of the infection increases in the absence of therapy with ARV for the screened infectives.

(iv) We consider the model in the absence of screening (\( \theta = 0 \)). If there is not screening of unaware infectives (\( \theta = 0 \)), then \( I_2 \rightarrow 0 \) and \( T \rightarrow 0 \) in this case we have the basic reproduction number given by

\[ R_{94} = \frac{c_i \beta_i}{\sigma_i + \mu}. \] (13)

It is clear that \( R_9 < R_{93} < R_{94} \) and \( R_{93} \rightarrow R_{94} \) as \( \theta \rightarrow 0 \). Thus, the endemicity of the infection increases in the absence of detection of unaware infectives by screening.
By analyzing the four epidemiological situations discussed above, it may be concluded that the endemicity of the disease is reduced by screening of unaware HIV infectives and therapy of the screened HIV infectives in the population.

4. Sensitivity Analysis

We perform sensitivity analysis in order to determine the relative importance of model parameters to disease transmission. In determining how best to reduce human mortality and morbidity due to AIDS, the sensitivity indices of $R_e$ to the parameters in the model was calculated using approach of Chitnis et al. [8]. Sensitivity analysis is used to discover parameters that have a high impact on $R_e$ and should be targeted by intervention strategies.

Sensitivity indices allow us to measure the relative change in a variable when a parameter changes. These indices tell us how crucial each parameter is to disease transmission and prevalence and discover parameters that have a high impact on and should be targeted by intervention strategies. The normalized forward sensitivity indices of a variable with respect to a parameter is a ratio of the relative change in the variable to the relative change in the parameter. When a variable is a differentiable function of the parameter, the sensitivity indices may be alternatively defined using partial derivatives.

The normalized forward sensitivity indices of $R_e$ that depends differentiably on a parameter $p_i$ is defined by

$$I_{p_i}^{R_e} = \frac{\partial R_e}{\partial p_i} \frac{p_i}{R_e}.$$  \hspace{1cm} (14)

Given the explicit formula (4) for $R_e$, we derive an analytical expression for the sensitivity of $R_e$ with respect to each parameter that comprise it. For example, using the parameter values from Table 1, the sensitivity indices of $R_e$ with respect to $\beta_1$ and $\theta$ are given by

$$I_{\beta_1}^{R_e} = \frac{\partial R_e}{\partial \beta_1} \frac{\beta_1}{R_e} = 0.9237 \quad \text{and} \quad I_{\theta}^{R_e} = \frac{\partial R_e}{\partial \theta} \frac{\theta}{R_e} = -0.5904$$  \hspace{1cm} (15)

respectively. Table 2 shows the sensitivity indices of other parameters with respect to $R_e$.

From Table 2, it shows that $\beta_1, \beta_2, \beta_3, c_1, c_2$ and $c_3$ have positive sensitivity indices, meaning that when the parameters $\beta_1, \beta_2, \beta_3, c_1, c_2$ and $c_3$ increase while the other parameters remain constant they increase the value of $R_e$. While the parameters $\theta, \sigma_1, \sigma_2, \mu$ and $\delta$ have negative sensitivity indices, meaning that when the parameters $\theta, \sigma_1, \sigma_2, \mu$ and $\delta$ increase while the other parameters remain constant they decrease the value of $R_e$. 

Table 2 shows the parameters are ordered from most sensitive to the least sensitive. The most sensitive parameter is the contact rate of unaware HIV infective $\beta_1$ with susceptible. This is followed by the rate at which unaware infectives are detected by screened method to become screened infective $\theta$, followed by the rate at which unaware infective develop full blown AIDS $\sigma_1$ and natural mortality rate $\mu$. The least sensitive parameter is the rate at which screened infective develop full blown AIDS $\sigma_2$.

### Table 2  Sensitivity indices of $R_e$ for the HIV model with screening and therapy

<table>
<thead>
<tr>
<th>Parameter symbol</th>
<th>Sensitivity indices</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\beta_1$ and $c_1$</td>
<td>0.9237</td>
</tr>
<tr>
<td>$\theta$</td>
<td>-0.5904</td>
</tr>
<tr>
<td>$\sigma_1$</td>
<td>-0.2222</td>
</tr>
<tr>
<td>$\mu$</td>
<td>-0.1197</td>
</tr>
<tr>
<td>$\delta$</td>
<td>-0.0671</td>
</tr>
<tr>
<td>$\beta_2$ and $c_2$</td>
<td>0.0586</td>
</tr>
<tr>
<td>$\beta_3$ and $c_3$</td>
<td>0.0177</td>
</tr>
<tr>
<td>$\sigma_2$</td>
<td>-0.0007</td>
</tr>
</tbody>
</table>

5. Numerical Analysis

Numerical simulation of model system (1) are carried out using the set of estimated parameters values and following values for the initial conditions (3):

\[
S_0 = 20,000,000,000, \quad I_{10} = 2,000,000, \quad I_{20} = 250,000, \\
T_0 = 50,000 \quad \text{and} \quad A_0 = 20,000.
\] (16)

The final time was $t_f = 10$ years. Computations were run in Matlab with ode45 routine. This function implements a Runge-Kutta method with a variable time step for efficient computation.

Figure 1 shows the numeric solutions to system (1) for the initial conditions (3) with the baseline parameter values given in Table 1 for susceptibles, unaware infectives, screened infectives, therapy infectives and AIDS patient.
Sensitivity analysis of effect of screening and HIV therapy

Figure 1 shows that the proportion of susceptible population decrease with time who are under therapy with ARV increases, and then reaches its equilibrium position. Initially proportion of unaware infectives increases but due to the increase in screening and therapy, the rates $\theta$ and $\delta$ respectively, decreases then reaches its equilibrium position. This ultimately leads to the decrease of the proportion of AIDS patients.

Figure 2 shows behaviour of the effective reproduction number ($R_e$) if the transmission (the contact rate) for susceptible with unaware infectives, screened infectives and therapy infectives can infect susceptibles at rates $\beta_1$, $\beta_2$ and $\beta_3$ respectively. It is seen that if $\beta_1$, $\beta_2$ or $\beta_3$ increases, then the effective reproduction number also increases. Therefore the rate of contact with the infected population has a direct impact on the dynamics of the disease.

Figure 3 presents the variation of proportions of susceptible, unaware, screened and therapy HIV infective populations and proportion of AIDS patient population for different values of $\theta$. From Figure 3 (a), it is seen that $\theta$ increases, the proportion of susceptible population increases. Figure 3 (b) shows that the unaware HIV infectives become aware of their infection which results in the decrease of the proportion of unaware infectives population and increase in the
proportions of screened and therapy HIV infectives (Figure 3 (c) and (d)) respectively. This ultimately leads to decrease of the proportion of AIDS patient as shown in Figure 3 (e). In general, it shows increases in \( \theta \), reduces the effective reproduction number, \( R_e \). This show the screening of unaware HIV infectives have the effect of reducing the transmission of the disease.

Figure 3. Proportion of population for different values of \( \theta \)

Figure 4 below show the variation of proportions of susceptible, unaware, screened and treated HIV infective populations and proportion of AIDS patient population for different values of \( \delta \). From Figure 4 (c), it is seen that \( \delta \) increases, the proportion of screened infectives decreases, but the proportion of
Sensitivity analysis of effect of screening and HIV therapy (Figure 4). If \( \delta \) increases, the proportion of susceptibles and unaware infectives relatively unchanged (Figure 4 (a) and (b)). This ultimately leads to decrease of the proportion of AIDS patient as shown in Figure 4 (e). In general, it shows increases in \( \delta \), reduces the effective reproduction number, \( R_e \). This shows therapy of screened HIV infectives have the effect of reducing the transmission of HIV.

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Figure 4. Proportion of population for different values of \( \delta \)

Figure 5 below show the variation of proportions of all infectives classes (unaware infectives, screened infectives, therapy infectives and AIDS patient) for different values of \( \beta_i \). It seen that the contact rate of unaware HIV infectives(\( \beta_i \))
increased, proportion of all infectives classes populations ($I_1$, $I_2$, $T$ and $A$) increases (Figure 5 (a)-(c)). In general, it shows increases in $\beta_1$, increases the effective reproduction number, $R_e$.

![Graphs showing variation of proportions](image)

(a) Effect on $I_1$ of the variation of $\beta_1$  
(b) Effect on $I_2$ of the variation of $\beta_1$

(c) Effect on $T$ of the variation of $\beta_1$  
(d) Effect on $A$ of the variation of $\beta_1$

Figure 5. Proportion of population for different values of $\beta_1$

Figure 6 below show the variation of proportions of unaware infectives and proportion of AIDS patient population for different values of $\beta_2$. When $\beta_2 = 0$ and the proportion of unaware infectives decreases leading to the decrease of proportion of AIDS patients. It is also seen that in the absence of screening of unaware infectives, the higher proportion of unaware and screened infectives respectively leads to increase of the proportion of AIDS patients. Thus screened infectives should be abstain from sexual interaction and therefore reducing the transmission of HIV and the AIDS epidemics. It also accurs in the proportion of unaware infectives and AIDS patient for different values of $\beta_3$ (Figure 7).

![Graphs showing variation of proportions](image)

(a) Effect on $I_1$ of the variation of $\beta_2$  
(b) Effect on $A$ of the variation of $\beta_2$

Figure 6. Proportion of unaware infectives and AIDS patient for different values of $\beta_2$
Sensitivity analysis of effect of screening and HIV therapy

Figure 7. Proportion of unaware infectives and AIDS patient for different values of $\beta_3$

Figure 8 below show the variation of proportions of all infective classes (unaware infectives, screened infectives, therapy infectives and AIDS patient) for different values of the progression rates ($\sigma_1$, $\sigma_2$ and $\sigma$). It shows that when $\sigma_1$, $\sigma_2$ and $\sigma$ increase, proportions of unaware infectives, screened infectives, therapy infectives and AIDS patient decreases (Figure 8 (a), (b) and (c)) but the proportion of AIDS patient increase (Figure 8 (d)). In general, it shows increases in $\sigma_1$, $\sigma_2$ and $\sigma$, reduces the effective reproduction number, $R_e$.

Figure 8. Proportion of unaware infectives and AIDS patient for different values of $\beta_3$
6. Conclusions

In this study a nonlinear mathematical model has been used to numerically assess effect of screening interventions on unaware infectives and HIV therapy on infectives screened in the spread of HIV in the population. The next generation matrix has been used to calculate the effective reproduction number (threshold quantity) as well as to investigate the local stability of the disease-free equilibrium point. The disease-free equilibrium point is shown to be locally asymptotically stable when the effective reproduction number less than unity and unstable when the effective reproduction number rather than unity.

Numerically based on the values of parameters and initial population is given, the effective reproduction number is equal to 3.1035. A sensitivity analysis shows that by decreasing the parameters, $\beta_i, c_1, \beta_2, c_2, \beta_3$ and $c_3$, the effective reproduction number decrease. By increasing the key parameters, $\theta, \sigma_1, \mu, \delta$ and $\sigma_2$, there is a point where by the threshold quantity becomes less than unity. Thus, from the simulations part it can be concluded that the screening of unaware infectives and therapy of screened infectives have the effect of reducing the transmission of HIV/AIDS.

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