HIV Model Enhancing UNAIDS Goal to End AIDS: Simulations in Botswana

Isack E. Kibona1,2* and Cuihong Yang1

1 School of Mathematics and Statistics, Central China Normal University, P. R. China.
2 School of Natural Science, Mbeya University of Science and Technology, United Rep. of Tanzania.

Authors’ contributions

This work was carried out in collaboration between both authors. Author IEK designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author CY was the main advisor of the study. Authors IEK and CY managed the analyses of the study. Both authors read and approved the final manuscript.

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ABSTRACT

In this paper we have modelled the spread of HIV infections enhancing UNAIDS goal to end AIDS. The goal has two dependent missions. One side of the goal is a 90-90-90 target, that by 2020, (90% of all people living with HIV (PLHIV) should know their status, 90% of whose status is known should be under ART, and 90% of patients under ART should have their viral load suppressed.

*Corresponding author: E-mail: ikibona@yahoo.com
On the other side, by 2030, UNAIDS requires to minimize up to at least 90% of both new HIV infections and AIDS-related deaths. According to the model, the goal is linked to the basic reproduction number ($R_0$). When $R_0 < 1$ the number of new HIV infections decreases.

Methodology: According to the model, we have demonstrated that HIV spread is controllable under some conditions in Botswana. For this country, $R_0 \approx 0.5051$ which is below the threshold value $R_0 = 1.6000$. Thus, suggesting her potential to achieve UNAIDS goal. According to our evaluation from the model, by 2020, 92% of PLHIV are expected to be under ART. Interestingly, in Botswana new HIV infections are mostly due to people who are not under ART. By 2030 not only that 96% of PLHIV are expected to be under ART but also both new HIV infections and AIDS related deaths are expected to decrease above 90% since their highest in 2010. Our main concern is to provide more mathematical insights for UNAIDS to keep up with progress of the goal to end AIDS by 2030.

Keywords: ART in Botswana; UNAIDS goal to end AIDS; 90-90-90 target; model simulation.

1 INTRODUCTION AND MODEL FORMULATION

1.1 Introduction

Since 1980s, a name ‘AIDS (Acquired Immune-Deficiency Syndrome)’ was initiated by Center for Disease Control (CDC) in USA. Since then, it had been a long debate as where could be the origin of AIDS [1].

It is now accepted that 1920 is a year, historically believed that transmission of Simian Immuno-deficiency Virus (SIV) to Human Immuno-deficiency Virus (HIV) took place in Kinshasa now called Democratic Republic of Congo (DRC)[2] SIV is the name of a similar virus to HIV that attacks immune system in apes and monkeys. When attacking immune system in human adapted the name HIV[3] First HIV test was in 1959 to a man from Kinshasa, the capital city of Democratic Republic of Congo (DRC). Since then, earlier cases of AIDS were pattern of death from common opportunistic infections, now known as AIDS-defining[3].

In 1982, HIV was formalized as cause of AIDS by Center for Disease Control (CDC) in USA.[1] Thus, defining AIDS as a fatal clinical condition that results from infection with HIV. HIV infections progressively damages the body’s ability to protect itself from disease causing organisms. Thus, many AIDS deaths result from pneumonia, tuberculosis or diarrhea; death is caused by one or more of these infections. [4] People with AIDS have a low number of CD4+ cells and get infections or cancers that rarely occur in healthy people. For example, Tuberculosis remains the leading cause of death among people living with HIV, accounting for around one in three AIDS-related deaths. AIDS has become a severe infectious disease in both the developed and developing nations, and is considered a world pandemic. [5] HIV transmissions among individuals is due to non-infected individual allowing blood contamination or unsafe sexual contacts with infected individuals. [6] MTCT (Mother to Child Transmission) is also a major transmission infecting many newborns especially in developing countries [7].

Since the beginning of HIV in 1981 to 2017, about 76.1 million people had been infected with HIV virus and about 35 million people have died of AIDS. Globally, about 36.7 million people were living with HIV in 2016. In June 2017, around 20.9 million (57%) PLHIV were accessing ART. This is an improvement compared to 2015 in which 46% of PLHIV had access to ART [8].

1.1.1 Some Specific Achievements

Global plan to combat AIDS by UN which was co-chaired by UNAIDS and PEPFAR in 2011, since then there has been improved results toward the plan. [9] In 2015, six priority countries (Botswana, Mozambique, Namibia, South Africa, Swaziland and Uganda) met the Global Plan target of reducing mother-to-child transmission by 90%. Outside of the priority countries, in mid-2015,
Cuba became the first country to eliminate the mother-to-child transmission of HIV in the world. In 2016, Belarus and Armenia achieved the same feat while Thailand became the first country in the Asia and Pacific region to eliminate MTCT. As PMTCT is not 100% effective, elimination is defined as a reduction of transmission to such low levels that it no longer constitutes a public health problem [10].

1.1.2 UNAIDS Goal to end AIDS by 2030

In 2014, UNAIDS proposed new goal directed to end the AIDS epidemic by 2030. Basically, there are two dependent missions in the goal. On one hand is a 90-90-90 target, requires that by 2020, 90% of all PLHIV will know their HIV status, 90% of those diagnosed with HIV infection will receive sustained combination of antiretroviral therapy (ART), and 90% of all under ART will have viral load suppression. [11, 12] On the other hand, the mission is reduction of both new infections and AIDS-related deaths by 90% from 2010 to 2030. [13] The rationale underpinning these targets is related to health benefit of ART. [14] In order to achieve the mission, funding is inevitable. For instance, at the end of 2016, US$ 19.1 billion was invested in the AIDS response in low- and middle-income countries. Recent updated UNAIDS estimates indicate that US$ 26.2 billion will be required for the AIDS response in 2020, with US$ 23.9 billion required in 2030 [8].

1.1.3 Botswana as a Case Study

Botswana has demonstrated a strong national commitment in responding to AIDS epidemic becoming an example for many in sub-Saharan Africa. It was the first country in the region to provide universal free ART in 2000s, paving a path for many other countries in the region [15]. New infections have decreased significantly, from 13,000 in 2010 to 10,000 in 2016, fig. and fig.. AIDS-related deaths have dramatically decreased.

In this study a simple HIV model is formulated and analyzed. As an example, Botswana HIV status is simulated both for 2016-2020 and 2016-2030 as typical situation in southern Africa countries. This provides some virtue information toward achieving the UNAIDS goal to end AIDS by 2030 in Botswana.

1.1.4 Mathematical Background and Objective of the Model

Mathematical models have been used extensively in research into epidemiology of HIV, so as to understand major contributing factors in the pandemic. From initial models by Anderson, RM et al. 1986 [17] and May, RM et al. 1987, [18] Various refinements have been added into modeling frameworks, and specific issues have
been addressed by researchers. [19] In recent years, more researches have been conducted to study how ART have influenced the HIV infections.

Granich, RM et al. [20] constructed the mathematical model for HIV including ART. There are four categories in each of the HIV infected class, the two classes are those under ART and those who are not. The model excludes individual under 15 years old. WHO [21, 22] in 2010 developed a paper which is about procedures required ART in children and adults. Other researchers include Cole, SR et al. [23] about “Effect of highly active antiretroviral therapy (HAART) on timing AIDS or death using marginal structure model.” Greub, G et al. 2000 [24] in Swiss HIV cohort studied the clinical progression, survival and immune recovery during ART in patients with HIV-1 and hepatitis C virus co-infection. It appears that many of the mentioned publications are about how to maintain a safer ART.

On the other hand; S. Blower et al.[25] reviewed how mathematical models have been used to evaluate potential impact of HIV epidemics both combination ART and imperfect vaccines. Most of the model based on numerical simulations. Similar review has been done by PS Rivadeira et al.[26] but is a bit different as they reviewed the potential ground-breaking impact that mathematical tools may have in the analysis and understanding of the HIV dynamics. R. H. Grey et al.[27] simulated stochastically, the impact of ART and HIV vaccines on transmission in Rakai, Uganda. They concluded that ART alone cannot control the HIV epidemic in mature epidemics such as Rakai, and persons in need of therapy will increase over time. B.G. William et al. [28] came up with a research paper titled modelling the impact of ART on the Epidemic of HIV” in 2011. Briefly, the study is embracing the ART, how would it lead to control HIV transmission in South Africa. This article is intended to link UNAIDS target to end AIDS epidemic by 2030 and model analysis. The foremost 90-90-90 target is dealt indirectly by controlling the basic reproduction number (\(R_0\)). This justifies ability to minimize new HIV infections and AIDS-related deaths. The model is formulated including several bearable assumptions. Refinements of this mathematical model start from models developed by Anderson, R. M. Anderson et al. 1986 [17] through I. E. Kibona et al. 2011 [29].

1.2 Model Formulation

A population of size \(N\) at time,\(t\) with inflow of susceptible at a rate \(\gamma N\) is considered. The population is divided into four sub-classes. There is susceptible class (\(S\)), refers to individuals not infected but are liable to infections. Infectious class (\(I\)), in which individuals have infections but not under ARV treatment. Infectious class under ART (\(T\)), one taking ARV dosage but sexually active. Removed class, \(R\), refers to individuals both under ART and not able to participate in the transmission of HIV. Both \(I\) and \(T\) classes are assumed to be infectious, meaning that they are
both sexually active, females in these classes may become pregnant and bear children. The reason is that they are taking advantage of the ART. Natural mortality rate is \( \nu \) in all classes and the disease induced death rate is \( \alpha \) in the removed class (R).

\( \beta_1 \) and \( \beta_2 \) are contact rates due to interactions that may lead to HIV transmissions from Infectious classes (I and T) to the susceptible class, S. \( c_1 \) and \( c_2 \) is the average number of partners in I and T classes respectively per individual. \( \mu \) is the rate of transfer from T individuals to R. Presumably, the susceptible S become HIV infected via unsafe contact with infectious classes (I or T) which may lead to the birth of infected newborns. It is assumed that a fraction of newborns are infected at birth, and hence are directly recruited into the R class with a rate \( \theta \). It is also assumed that some of the infectious in (I) move to join T class, depending on the viral counts, with a rate \( \sigma \delta \) and others with serious escalated viral load directly join the removed class (R) with a rate \( (1 - \sigma) \delta \), where \( 0 < \sigma < 1 \). The interaction between susceptible and infectious classes is assumed to be of standard mass action type. tab. is a summary of parameters and their definitions. The model can be expressed in a flow diagram as in fig.. Therefore, the system of equations (1.1) is the model. In this study it is considered that \( \beta_1 c_1 \gg \beta_2 c_2 \) following the assumption that PLHIV under ART are more ineffective to transmit HIV and also have lower number of partners by average.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \gamma )</td>
<td>recruitment rate per individual</td>
</tr>
<tr>
<td>( \nu )</td>
<td>Natural mortality rate</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>AIDS induced death rate</td>
</tr>
<tr>
<td>( \beta_1 )</td>
<td>effective contact rate between I and S</td>
</tr>
<tr>
<td>( c_1 )</td>
<td>Average number of partners in per individual in I</td>
</tr>
<tr>
<td>( \beta_2 )</td>
<td>effective contact rate between T and S</td>
</tr>
<tr>
<td>( c_2 )</td>
<td>Average number of partners in per individual in T</td>
</tr>
<tr>
<td>( \theta )</td>
<td>Rate of infected newborns</td>
</tr>
<tr>
<td>( \delta )</td>
<td>Rate of transfer from I to T</td>
</tr>
<tr>
<td>( \sigma )</td>
<td>Fraction of individual who remain in the T class from I</td>
</tr>
</tbody>
</table>

Fig 3: Model Flow Chart
2 ANALYSIS OF THE MODEL

2.1 Estimation of Basic Reproduction Number, \( R_0 \)

In order analytically understand the spread of an epidemic, basic reproduction number (\( R_0 \)) is the most vital quantity in mathematical modelling. \( R_0 \) is basically the average number of new infectious cases caused by single infected individual in totally susceptible population. Rearrange the model (1.1) by adding all differential equations in the system, and then coming up with another form of the model (2.1). That is simply add all equations in the model (1.1), then use the substitution \( N = S + I + T + R \), so that \( S = N - I - T - R \). At the latest, replace equation in \( S'(t) \) by one in \( N(t) \). The rest three equations remain unchanged.

\[
\begin{align*}
    S'(t) &= \gamma N - \beta_1 c_1 S \frac{T}{N} - \beta_2 c_2 S \frac{T}{N} - \nu S; \\
    I'(t) &= \beta_1 c_1 S \frac{T}{N} + \beta_2 c_2 S \frac{T}{N} - (\delta + \nu) I; \\
    T'(t) &= \sigma I - (\mu + \nu) T; \\
    R'(t) &= (1 - \sigma) I + \mu T + \theta I - (\alpha + \nu) R.
\end{align*}
\]

\( S_{t=0} = S_0, \ I_{t=0} = I_0, \ T_{t=0} = T_0, \ R_{t=0} = R_0 \)

\[ \beta_1 c_1 - (\delta + \nu) < 0 \]

\[ I = I_0 \exp[(\beta_1 c_1 - (\delta + \nu))t] \]

If \( \beta_1 c_1 - (\delta + \nu) < 0 \) then, number of individuals in \( I \) class die exponentially with time. That is there will be no infection as \( t \) approaches to infinity. So then, \( \beta_1 c_1 - (\delta + \nu) < 0 \Leftrightarrow \frac{\beta_1 c_1}{\delta + \nu} < 1 \). We estimate \( R_0 = \frac{\beta_1 c_1}{\delta + \nu} \). Define \( D = \frac{1}{\delta + \nu} \) as average life expectancy of an individual in the \( I \) class. In terms of \( D \) and \( R_0 \), \( \beta_1 c_1 - (\delta + \nu) = \frac{R_0 - 1}{D} \). Rewrite equation (2.2) as

\[ I = I_0 \exp[(R_0 - 1)\frac{1}{D}t] \]

Clearly from equation (2.3), if \( R_0 < 1 \) the epidemic dies. On the other hand, when \( R_0 > 1 \) it grows exponentially.
2.1.1 Role and Values of $R_0$

Recall equation (2.3), and assume $D = 1$, $I_0 = 4$. Substitutions of $D = 1$, $I_0 = 4$ into equation (2.3), then its graph can be plotted as shown by Fig. 2.1.1 for different values of $R_0$. Assuming that time is in years, an individual lives in 1 one year ($D = 1$) by average since infection. The population of susceptible class $S$ is considered infinitely large and induced with four infected individuals ($I_0 = 4$) initially. Basing on the nature of epidemic spread, essentially $R_0$ has two major parts. In practical terms $0 < R_0 < 1 \text{ and } R_0 > 1$. Ideally $R_0$ may assume the value of zero as the case for graph through point $A$ in fig.2.1.1, this is the situation that infected individuals are identified and strict measures to resist spread of the epidemic are 100% under control so that the disease stops in the society about time $D = 1$. Rarely as well, $R_0$ may assume the value of one, that means a single infected individual infects one person by average in her life ($D = 1$) as infectious agent. In this case the population remains with initial number of infected individuals in the whole generations, see the graph through C. On the other hand, cases for $R_0 = 0 \text{ or } 1$ acts as border to more practical situations ($0 < R_0 < 1 \text{ and } R_0 > 1$) in which most of the epidemic geometric structure are likely to fall for this model.

![Graph of $I = I_0 e^{[(R_0 - 1) D] t}$, $I_0 = 4$, $D = 1$.]

The epidemic is exponentially dying (diminishing) if $0 < R_0 < 1$, and growing (expanding) if $R_0 > 1$. Just as half-life is defined for exponential decay, there is a constant time for which the number of infected individuals remain half of the original, graph through point B fig.2.1.1 illustrates this case with $R_0 = 0.5 < 1$. It is easy to see that at point B the coordinates can be estimated as B(1.4, 2). That is after one 1.4 years (half-life of the epidemic), initial number of infected individuals is halved ($0.5 \times 4 = 2$). On the other hand, when $R_0 > 1$, as in the case for graph through point D, there is a constant time of which the epidemic doubles initial number of infected individuals, this is illustrate at point D(4.6, 8), values in approximations. That is after about 4.6 years the initial number (4) doubles to 8. It can be shown that for exact values, the half-life ($t_{1/2}$) is

$$t_{1/2} = \frac{D}{1 - R_0} \ln 2$$

and the corresponding doubling time of the epidemic ($t_2$) is
Consider half-life of the epidemic, \( t = t_2 \), substitute \( t \) in equation (2.3) so that \( l = \frac{1}{2} t_0 \). Then
\[
\frac{1}{2} l_0 = l_0 \exp\left(\frac{R_0 - 1}{D} t_2 \right) \Rightarrow \frac{1}{2} = \exp\left(\frac{R_0 - 1}{D} t_2 \right) t_2. \]
Thus, it follows that \( t_2 = \frac{D}{1 - R_0} \ln 2 \). \( \square \)

A similar approach can be used for the value of epidemic doubling time.

### 2.2 Local Stability of Equilibrium Points the Model

In order to understand the local stability of the model around equilibrium point, the Jacobean matrix, \( J \) is evaluated from the model (1.1) and used to study the local stability of disease free and endemic equilibrium. That is Jacobean matrix, \( J \) is given from the formula
\[
J = \begin{bmatrix}
\frac{\partial}{\partial S} S(t) & \frac{\partial}{\partial S} S'(t) & \frac{\partial}{\partial R} S(t) & \frac{\partial}{\partial R} S'(t) \\
\frac{\partial}{\partial I} I(t) & \frac{\partial}{\partial I} I'(t) & \frac{\partial}{\partial R} I(t) & \frac{\partial}{\partial R} I'(t) \\
\frac{\partial}{\partial T} T(t) & \frac{\partial}{\partial T} T'(t) & \frac{\partial}{\partial R} T(t) & \frac{\partial}{\partial R} T'(t) \\
\frac{\partial}{\partial E} E(t) & \frac{\partial}{\partial E} E'(t) & \frac{\partial}{\partial R} E(t) & \frac{\partial}{\partial R} E'(t)
\end{bmatrix}
\]
so that after evaluation:
\[
J = \begin{pmatrix}
(y - \nu) - (k_0 + k_1) & y + k_3 - k_2 & y + k_4 - k_5 & y + k_6 + k_7 \\
k_0 + k_1 & k_2 - [k_5 + (\delta + \nu)] & k_3 - k_4 & -(k_6 + k_7) \\
0 & \alpha \delta & -(\mu + \nu) & 0 \\
(1 - \sigma) \delta + \theta & \mu & -(\alpha + \nu)
\end{pmatrix}
\tag{2.4}
\]

of which \( k_0, k_1, k_2, k_3, k_4, k_5, k_6, k_7 \geq 0 \) by definition.

#### 2.2.1 Local Stability of the Disease Free Equilibrium Point

The DFE point, \( E^0 \) is simply evaluated from the system (1.1), by substituting \( I^0 = T^0 = R^0 = 0 \) and \( S^0 = I^0 = T^0 = R^0 = 0 \), then solve for \( S^0 \) It is found that DFE point exists when \( \gamma = \nu \) at which \( E^0(S^0 = N^0, I^0 = 0, T^0 = 0, R^0 = 0) \). Thus, the Jacobean matrix using (2.4) at DFE, \( J_{E^0} \) is
\[
J_{E^0} = \begin{pmatrix}
0 & y - \beta_1 c_1 & y - \beta_2 c_2 & 0 \\
0 & \beta_1 c_1 - (\delta + \nu) & \beta_2 c_2 & -(\mu + \nu) \\
0 & \alpha \delta & 0 & 0 \\
0 & (1 - \sigma) \delta + \theta & \mu & -(\alpha + \nu)
\end{pmatrix}
\]
Assign \( \lambda \) as eigenvalue, then characteristic polynomial, \( \chi(\lambda) \) of the Jacobean matrix is given by
\[
\chi(\lambda) = \begin{vmatrix}
-\lambda & y - \beta_1 c_1 & y - \beta_2 c_2 & y \\
0 & \beta_1 c_1 - (\delta + \nu) - \lambda & \beta_2 c_2 & 0 \\
0 & \alpha \delta & (\mu + \nu) - \lambda & 0 \\
0 & (1 - \sigma) \delta + \theta & \mu & -(\alpha + \nu) - \lambda
\end{vmatrix} = 0
\]

\[8\]
Solving $\chi(\lambda) = 0$, $\lambda_{1,2} = 0, -(\alpha + \nu)$. $\lambda_{3,4}$ are the roots of the quadratic equation

$$\lambda^2 - \lambda[(R_0 - 1)(\delta + \nu) - (\mu + \nu)] - [(R_0 - 1)(\delta + \nu)](\mu + \nu) + \beta_2 \sigma \delta].$$

From properties of roots of quadratic equation $\lambda_3 + \lambda_4 = -[(R_0 - 1)(\delta + \nu) - (\mu + \nu)]$, $\lambda_3 \cdot \lambda_4 = -[(R_0 - 1)(\delta + \nu)](\mu + \nu) + \beta_2 \sigma \delta$. $\lambda_3 \cdot \lambda_4 < 0$ if $R_0 > 1$ suggesting that $\lambda_{3,4}$ have opposite signs. In this case the DFE is asymptotically unstable.

However, when $R_0 < 1$, $\lambda_3 + \lambda_4 = -[(R_0 - 1)(\delta + \nu) - (\mu + \nu)] < 0$ and $\lambda_3 \cdot \lambda_4 = -[(R_0 - 1)(\delta + \nu)](\mu + \nu) + \beta_2 \sigma \delta > 0$. That means $\lambda_1$, $\lambda_2$, $\lambda_3$, $\lambda_4 < 0$, therefore the DFE is locally asymptotically stable when $R_0 < 1$.

### 2.2.2 Local Stability of the Endemic Equilibrium of the Model

The endemic equilibrium point, $E^*(N = N^*, I = I^*, T = T^*, R = R^*)$ is obtained by solving for $I^* \neq 0$ at the equilibrium point of the system (2.1).

$$
\begin{align*}
0 &= \gamma N - N N^* - \alpha R^* + \theta I^*; \\
0 &= \beta_1 c_1 N^* - I^* - T^* - R^* \frac{I^*}{R^*} \beta_2 c_2 (N^* - I^* - T^* - R^*) \frac{I^*}{R^*} - (\delta + \nu) I^*; \\
0 &= \sigma \delta I^* - (\mu + \nu) R^*; \\
0 &= (1 - \sigma) \delta I^* + \mu T^* + \theta I^* - (\alpha + \nu) R^*.
\end{align*}
$$

After some algebraic manipulations for the endemic equilibrium, it is found that there exists only one endemic equilibrium, $E^*(N^*, I^*, T^*, R^*)$:

$$
E^*(N^*) = \frac{k[\beta_1 c_1 + \sigma \delta c_2]}{(R_0 - 1)(\delta + \nu) + \beta_2 c_2} I^*, 
I^* = \frac{\sigma \delta}{\mu + \nu} I^*, 
R^* = \frac{(\mu + \nu(1 - \sigma)) \delta + \theta(\mu + \nu)}{(\alpha + \nu)(\mu + \nu)} I^*.
$$

Recall equation (2.5), it is observed that $k = f(I^*, T^*, R^*)$. The reason is that from equation (2.5),

$$
T^* = \frac{\alpha \delta}{\mu + \nu} \text{ and } R^* = \frac{(\mu + \nu(1 - \sigma)) \delta + \theta(\mu + \nu)}{(\alpha + \nu)(\mu + \nu)}.
$$

So that on substitution $k = 1 + \frac{T^*}{T^* + R^*}$, easy to see that $k > 0$ and defined when $I^* \neq 0$.

### 2.2.3 Existence of the Endemic Equilibrium

From equation 2.5, $I^* = 0$ if $(\delta + \nu)(R_0 - 1) + \beta_2 c_2 = 0 \iff R_0 = 1 - \frac{\beta_2 c_2}{\delta + \nu}$. $R_0 = 1 - \frac{\beta_2 c_2}{\delta + \nu}$ holds if $R_0 < 1$ of which there is no endemic.

The model (1.1) has unique endemic equilibrium point and exists when $R_0 > 1$.

**Proof.** Clearly, from equation (2.5); $k$ is unique, so is $I^*$. Endemic equilibrium exists provided that

$$
I^* = \frac{(\delta + \nu)(R_0 - 1) + \beta_2 c_2}{k[\beta_1 c_1 + \sigma \delta c_2]} > 0.
$$

The later is true provided that numerator $(\delta + \nu)(R_0 - 1) + \beta_2 c_2 > 0$.
The characteristic polynomial point of the model system is not locally stable at the endemic equilibrium for some choices of the parameters. This suggests that until we have the right choice of parameters, depending on the choice of parameters, the characteristic equation is not always Hurwitz. Therefore, there exists a unique endemic equilibrium if \( R_0 > 1 \).

### 2.2.4 Jacobean Matrix of the Endemic Equilibrium

The characteristic polynomial \( \chi(\lambda) \) obtained from Jacobean matrix, \( J_{E^*} \) at the endemic equilibrium point of the model (1.1) is given as:

\[
\chi(\lambda) = \begin{vmatrix}
(y - \nu) - (k_0^* + k_1^*) - \lambda & (y + k_3^*) - k_2^* & y + k_4^* - k_5^* & y + k_5^* + k_7^* \\
0 & \sigma \delta & 0 & 0 \\
0 & \delta + \theta & \mu & -(\mu + \nu) - \lambda \\
\end{vmatrix}
\]

(2.6)

That is \( \chi(\lambda) = \lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 = 0 \) is the characteristic equation of which \( \lambda \) is an eigenvalue.

\[
a_1 = [\alpha + \delta + \mu + 3 \nu + k_1^*] - k_2^*,
\]

\[
a_2 = [(\delta + \nu)(k_0^* + k_1^* + 1) + \sigma \delta k_4^* + (\gamma + k_3^*)(\gamma + k_5^* + \delta + \nu) - [(\alpha + \mu + 2 \nu)(\gamma + k_3^* + k_4^* + k_5^* + \delta + \nu) + \sigma \delta k_4^* + (\gamma + k_3^* + k_5^*)][(1 - \sigma) \delta + \theta] + \gamma(k_0^* + k_1^*)],
\]

\[
a_3 = \sigma \delta [k_4^*[(\gamma + \alpha)(k_0^* + k_1^*)] + (\gamma + \alpha)(k_0^* + k_1^* + k_4^* + k_5^* + \delta + \nu) + (\mu + 2 \nu + \alpha)(\gamma + \alpha)(k_0^* + k_1^* + k_4^* + k_5^* + \delta + \nu) - [(\alpha + \mu + 2 \nu)(\gamma + k_3^* + k_4^* + k_5^* + \delta + \nu) + \sigma \delta k_4^* + (\gamma + k_3^* + k_5^*)][(1 - \sigma) \delta + \theta] + \gamma(k_0^* + k_1^*)],
\]

\[
a_4 = \sigma \delta [(\gamma + \alpha)(k_0^* + k_1^* + k_4^* + k_5^* + \delta + \nu) + (\mu + 2 \nu + \alpha)(\gamma + \alpha)(k_0^* + k_1^* + k_4^* + k_5^* + \delta + \nu) - [(\alpha + \mu + 2 \nu)(\gamma + k_3^* + k_4^* + k_5^* + \delta + \nu) + \sigma \delta k_4^* + (\gamma + k_3^* + k_5^*)][(1 - \sigma) \delta + \theta] + \gamma(k_0^* + k_1^* + k_4^* + k_5^*)].
\]

Depending on the choice of parameters, the characteristic equation is not always Hurwitz. \( a_1, a_2, a_3, a_4 > 0 \) for some choices of the parameters. This suggests that until we have the right choice of parameters, the system is not locally stable at the endemic equilibrium.
3 SIMULATION AND DISCUSSION OF THE MODEL

Botswana launched the first nationwide public ART program ahead of all African countries in 2002, and ART coverage exceeded 80 percent by 2008 for patients with CD4 ≤ 200 cells/µL, according to government estimates [30]. That is over the past decade, expansion of access to ART averted millions of deaths. Thus if the proposed UN 90-90-90 Target by 2020 is reached, then will prevent additional morbidity, mortality and new HIV transmission. The tab.3 is a summary of estimated records of PLHIV in Botswana from year 2012 to 2016.[8]

Table 2: Records of PLHIV in Botswana from year 2012 to 2016

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population (N)</td>
<td>2,132,822</td>
<td>2,176,510</td>
<td>2,219,937</td>
<td>2,262,485</td>
<td>2,303,820</td>
</tr>
<tr>
<td>PLHIV (I+T+R)</td>
<td>330,000</td>
<td>340,000</td>
<td>350,000</td>
<td>350,000</td>
<td>360,000</td>
</tr>
<tr>
<td>PLHIV on ART (T)</td>
<td>61%</td>
<td>65%</td>
<td>74%</td>
<td>77%</td>
<td>83%</td>
</tr>
<tr>
<td>New HIV infections</td>
<td>13,000</td>
<td>13,000</td>
<td>12,000</td>
<td>11,000</td>
<td>10,000</td>
</tr>
<tr>
<td>Susceptible (S)</td>
<td>1,802,822</td>
<td>1,826,510</td>
<td>1,869,937</td>
<td>1,912,485</td>
<td>1,943,820</td>
</tr>
<tr>
<td>PLHIV not on ART</td>
<td>123,600</td>
<td>114,200</td>
<td>86,500</td>
<td>76,300</td>
<td>57,300</td>
</tr>
<tr>
<td>Number of deaths R</td>
<td>5100</td>
<td>4800</td>
<td>4500</td>
<td>4200</td>
<td>3900</td>
</tr>
</tbody>
</table>

In order to simulate a situation in Botswana the information in tab.3 plus some initial estimations of parameters were used with the aid of Levenberg-Marquardt algorithm to estimate the parameters of the model. The parameters were estimated as listed in tab.3

Table 3: Estimated parameters for the model in Botswana for 2012 to 2016

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>γ</td>
<td>0.0500</td>
<td>θ</td>
<td>0.00001</td>
</tr>
<tr>
<td>ν</td>
<td>0.0300</td>
<td>δ</td>
<td>3490</td>
</tr>
<tr>
<td>α</td>
<td>0.2250</td>
<td>μ</td>
<td>0.0003</td>
</tr>
<tr>
<td>β₁c₁</td>
<td>0.1900</td>
<td>σ</td>
<td>0.9750</td>
</tr>
<tr>
<td>β₂c₂</td>
<td>0.00001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PLHIV under ART (I) are clearly stated in the records as percentages, so this serves to evaluate PLHIV not under ART (I). People who are both seriously brown AIDS and hospitalized, are are assumed to neither participate in sexual relations nor care of themselves R. They are assumed to be those who died in a given year, thus it is assumed that people in the R class by average live not more than a year. Then the susceptible class S for a particular year is simply S = N − (I + T + R). This summary is given in tab. 3

The graphical simulation of the data for 2012 to 2016 for model verification is simulated, fig.3. It is observed that in both tab.2 and fig.3 the highest record of people under ART was in 2016 since 2012. In contrast, the new HIV infections have been steadily decreasing from the highest number (13000) in 2012 to lowest (10000) in 2016. Major part of the reason, is the outcome that more PLHIV are starting ART programs, fig.6(b) This is explained by comparing the two parameters $\hat{\beta}_1c_1 = 0.2250$ and $\hat{\beta}_2c_2 = 0.00001$ which are rates of infection due to individuals in T class and I class respectively. Simulation of the data suggests that PLHIV under ART compared to those who are not under treatment are practically not responsible for new infections.
This was found by comparing the values of the parameters. One of the reasons is that despite increase in the size class $T$, number of infections are decreasing yearly. Along with increasing individuals in $T$ class, PMTCT as well appears to be very effective.

The calculated $R_0 = 0.5051$ suggests that two infectious individuals only infects about one individual in their life span during infectious period. According to the simulations, HIV spread by an infectious individual by average is done before the infectious starts ART. This calls for more people to register for ART immediately after knowing their status.

### 3.1 UNAIDS Goal and Future of HIV in Botswana

Model simulation is done in order to predict and improve the vision for potentiality of UNAIDS goal to end AIDS by 2030. UNAIDS developed the Fast-Track approach that is intended to provide a road-map to the actions required to achieve this goal. In order to realize this both the Fast-Track approach (to be stabilized till 2020) and 2030 targets are simulated. The Fast-Track approach is predicted on a rapid scale-up of focused, effective prevention and treatment services over the next 3 years (starting 2017) to meet the 90-90-90 (90% of all people living with HIV knowing their status, 90% of these receiving sustained antiretroviral therapy (ART), and 90% of under ART having viral load suppression) target [11]. Believing it as a great back up to start and then maintaining implementation until 2030. Fast-Track aims to reduce new infections and AIDS-related deaths by 90% from 2010 to 2030 [13]. That the number of new infections and AIDS deaths are decreasing every year. The challenge is how should this be maintained or even make it more effective than between 2012 to 2016.

#### 3.1.1 Simulation of UNAIDS Goal to End AIDS by 2030

Gaolathe et al. [11] in 2016 found that about 83.3% of PLHIV knew their status, 87.4% of these were receiving ART and 70.2% of those under ART had viral load suppressed. These percentages were obtained by population survey. That means probably in 2017, 2018 and so forth similar research should be conducted to ensure that efforts for 90-90-90 target are on right track. However, we can avoid a tiresome activities of surveying every year by maintaining $R_0 \leq 0.5051$. We suppose that parameters estimated between 2012 and 2016 would remain constant for the next 14 years starting 2016. Fig. 7. is a simulation for the next 4 years starting 2017 to 2020.

---

**Fig 5:** $R_0 \approx 0.5051$ were evaluated and simulated for years 2012 to 2016
Fig 6: $R_0 \approx 0.5051$ between year 2012 to 2016 improved the HIV situation

Fig. 7. Simulations of $R_0 \approx 0.5051$ between year 2016 and 2020

Fig. 8. Simulations of $R_0 \approx 0.5051$ between year 2016 and 2030

Some information from fig.7 and fig.8 are recorded in tab. 4. Analysis of the data indicates that the percentage of people who knows there status are increasing on starting ART.
Table 4: Estimations of PLHIV in Botswana from year 2016 to 2030 by simulation

<table>
<thead>
<tr>
<th>Populations</th>
<th>2010</th>
<th>2016</th>
<th>2017</th>
<th>2020</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PLHIV ( (I + I + R) )</td>
<td>320,000</td>
<td>360,000</td>
<td>363,500</td>
<td>358,000</td>
<td>264,020</td>
</tr>
<tr>
<td>PLHIV on ART ( (T) )</td>
<td>50%</td>
<td>83%</td>
<td>85%</td>
<td>92%</td>
<td>96%</td>
</tr>
<tr>
<td>PLHIV not on ART ( (I) )</td>
<td>154,200</td>
<td>57,300</td>
<td>50,000</td>
<td>25,500</td>
<td>10,000</td>
</tr>
<tr>
<td>Number of deaths ( R )</td>
<td>58,000</td>
<td>3900</td>
<td>3500</td>
<td>2500</td>
<td>520</td>
</tr>
</tbody>
</table>

It is estimated that by 2020, 92% of PLHIV will be under ART. That means over 90% of people who know their status are predicted to be under ART (90-90-90 target) by 2020. It is also evident that over 90% viral load suppression because of ART has justified that new infections are due to PLHIV not under ART. On line with the 90-90-90 target, new number of PLHIV related deaths are expected to fall to about 520. This is lowest since 2010 of 5800 AIDS related deaths, therefore making it above 90% reduction in AIDS related deaths. A continuing decrease in number of PLHIV where the as its percentage is increasing suggests that new infection at the time are almost zero compared to the 2010 new HIV infections 13000. That is new HIV infections are expected to decrease above 90% between 2010 to 2030 in Botswana. It is evident therefore, that the UNAIDS target to end AIDS could be reached if Botswana can maintain or improve the current HIV infections struggle.

3.1.2 \( R_0 \) for UNAIDS Goal to End AIDS in Botswana by 2020

Simulation suggests that any \( R_0 < 0.6 \) may meet UNAIDS goal particularly for Botswana. A good example is the \( R_0 = 0.5051 \) whose results is in tab.2.2.4 and tab.2.2.4. It is possible that \( R_0 \) can be decreased by granting more PLHIV into ART programs, get more people know their status and more serious consideration for the whole nation to take precautions against unsafe sexual relations. Should it be possible that \( R_0 = 0.25 \) be reached then, more striking results are obtained, Fig.9. In this situation, by average four PLHIV infects one person in their life span of infectious period.

Fig. 9. \( R_0 \leq 0.8274 \) enhances UNAIDS goal to end AIDS by 2030 in Botswana

With \( R_0 = 0.25 \) it is expected that by 2030 above 96% of PLHIV will be under ART and no more increase of people under ART, Fig.9. The reason is that new HIV infections are expected to be lower than AIDS related deaths which are also very small at the time. This can be considered as sign to end AIDS.
3.2 $R_0 > 1$ Compromises Healthy Safety of Future Generation

Although PLHIV under ART have little contribution in the spread of HIV but when $R_0 > 1$ it is catastrophic. The seriousness of the matter only differs in length of time depending on the value of $R_0 > 1$.

![Graph](image.png)

**Fig. 10.** Any $R_0 = 1.3195 > 1$ jeopardizes biological health of future generations

The society need to understand that the health of PLHIV under ART is a compromise of a healthy person free of HIV infection. That is with $R_0 > 1$ means that PLHIV under ART are going to fill the whole world at some point in future. For example, when $R_0 = 1.3195$ the size of people under ART grows exponentially in Botswana, fig.10. The fact by simulation is that PLHIV under ART may exceed the size of susceptible population, fig.11(b)

According to simulations by this model then, the only way to save the future generation is to keep $R_0 < 1$. Nevertheless, for Southern Africa and the World at large Botswana is a good example that is keeping $R_0 = 0.5051 < 1$. Therefore, it can be observed by simulation that a small variation in the value of $R_0$ has a drastic influence in the spread of HIV, thus greatly costing the means to control the epidemic in all dimensions, economically, time, socially to mention a few.

4 CONCLUSION

Simple model of HIV spread has been formulated in order to support UNAIDS goal to end the AIDS by 2030. The UNAIDS goal is linked to the basic reproduction number ($R_0$). Among the outcomes of analyses is that when $R_0 < 1$ new HIV infections decreases. That means AIDS is controllable because there is no backward bifurcation. However, new HIV infections lead to catastrophic if $R_0 > 1$. Particularly, Botswana has been simulated to illustrate the model. Interestingly, people under ART appear to have very little impact in the transmission of HIV. New HIV infections are largely due to people who are not under ART and those who do not know their status.

According to this model Botswana has $R_0 = 0.5051$. We simulated that if $R_0 \leq 0.8274$ Botswana has potential to achieve UNAIDS goal. That means $R_0 = 0.5051$ is within the range and estimated that by 2020, 92% of PLHIV will be under ART. That means over 90% of people who know there status will be under ART (90-90-90 target). In addition, we expect at least 90% viral load suppression because simulations justified that over 95% of new HIV infections are caused by PLHIV who are not on ARV dosage. In line with UNAIDS goal, by 2030 number of AIDS related deaths are expected to fall to about 520. This is lowest since 2010 of 5800 AIDS related deaths, therefore making it above 90% reduction in AIDS related deaths. Number of new HIV infections are expected to decrease above 90% between 2010 to 2030, therefore meeting
the UNAIDS goal.

The promise from model simulations do not suggest wishful waiting for Botswana in order to achieve UNAIDS goal, but rather to remain vigilant and alert of the epidemic. That means to keep up and do more improvements. Since ART saves HIV infected individuals to remain healthier by rendering both viral load suppression and resistance to HIV transmission, then these advantages could be exploited by reducing the time an individual stays in a more infectious class $I$. Thus, infected individuals should stay less in $I$ class and longer in the $T$ class by starting ART right away when the status is known. As for people who do not know there status it is strongly urged to educate and have them tested. [31]

Researches have supported the view that early ART, in combination with other methods of control, including male circumcision, vaginal microbicide, behavior change interventions, counseling and support should reduce the incidence of HIV to low levels within ten years and the prevalence of HIV to low levels within forty years. [32] Unlike in the beginning with ART of which a lot of side effects were mentioned, now days ART is more stable, side effects are fewer, adherence is better, and resistance does not increase with earlier initiation of ART, so that many arguments for delaying treatment are no longer valid. [28]

More over, ART is not only recommended to HIV infected individuals. There are two for forms of ARV drugs that non infected individuals are advised to consider. Pre-exposure prophylaxis (PrEP) is a way for people who do not have HIV but who are at substantial risk of getting it. They can prevent HIV infection by taking a pill every day. The pill (brand name Truvada) contains two medicines (tenofovir and emtricitabine) that are used in combination with other medicines to treat HIV. When someone is exposed to HIV through sex or injection by drug use, these medicines can work to keep the virus from establishing a permanent infection. [33]

Botswana is not the first country to achieve the 90-90-90 target, Sweden is the first according to the research by Gisslem et al.,2017 [34], they took advantage of the database in hospitals to work out the study in Sweden. Another research by Tendani G et al.,2016 whose study based on population survey, as well concluded that 90-90-90 target could be possible for Botswana.[11] However, in contrast to Tendani G et al., research by Jacob L et al.,2016 did not conclude Botswana to be in the range of achieving 90-90-90 target. [35]

4.1 Future Work

Investigation of the stability of the endemic equilibrium point has not fully developed analytically. Only numerical simulation has been fully analyzed, therefore we are still working on the model including estimation of $R_0$ by other methods and compare the results. The models in this context is deterministic, considering a comparable stochastic model could provide more reliable results. Therefore, the study is open to researcher who may extend the research to a more reliable model.

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Note the acronyms from Tab 5. below are available the whole article.

Table 5: Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immune-Deficiency Syndrome</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral therapy (treatment)</td>
</tr>
<tr>
<td>ARV</td>
<td>Antiretroviral</td>
</tr>
<tr>
<td>ARVs</td>
<td>Antiretrovirals</td>
</tr>
<tr>
<td>CD4</td>
<td>Cluster of Differentiation</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention in USA</td>
</tr>
<tr>
<td>HAART</td>
<td>Highly active antiretroviral therapy</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immuno-deficiency Syndrome</td>
</tr>
<tr>
<td>MTCT</td>
<td>Mother-to-child-transmission</td>
</tr>
<tr>
<td>PEP</td>
<td>Post-Exposure Prophylaxis</td>
</tr>
<tr>
<td>PLHIV</td>
<td>People Living with HIV</td>
</tr>
<tr>
<td>PMTCT</td>
<td>Prevention of Mother-to-child-transmission</td>
</tr>
<tr>
<td>PrEP</td>
<td>Pre-exposure prophylaxis</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations Program on HIV/AIDS</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>

COMPETING INTERESTS
Authors have declared that no competing interests

References


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