

A Stochastic Model for Assessing the Efficacy of Antiretroviral Therapy (ART) on Farmers Living with HIV/AIDS

***Agada, P.O¹., Apeagee, B.B²., and Ogwuche, I.O³**

¹ Department of Mathematics/Statistics/Computer Science,
University of Agriculture Makurdi,

^{2, 3} Department of Mathematics and Computer Science,
Benue State University, Makurdi

Abstract

The Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) remains one of the greatest public health challenges still facing Nigeria and the entire world as it has become drug resistant in some patients. Hence, treatment failure and spread of drug resistant HIV/AIDS results. In view of this, it becomes imperative to assess the efficacy of the Antiretroviral Therapy (ART) treatment and hence the life expectancy of the HIV/AIDS patients. This was achieved in this study via a stochastic model based on the Markov chain modelling methodology. The CD4 cell counts of a sample of 28,582 patients (farmers) receiving treatment every six (6) months at the HIV counselling and Testing (HCT) unit of the Federal Medical Centre Makurdi, Benue State was used in the modelling process. The CD4 cell count states were developed based on the United States Centres for Disease Control and Prevention (CDC) classification system as follows; State 1: CD4 cell counts ≥ 500 cells/ μL , State 2: CD4 cell count in the range of 200 – 499 cells/ μL , and State 3: CD4 cell count < 200 cells/ μL . They represent the Good, Moderate and Poor health states of the patients respectively. The HIV/AIDS progression in the study was investigated using The N-Step transition probability Matrix of the Markov Chain while, the efficacy of the ART was examined from one CD4 cell count state to another using the Steady State probabilities of the Markov Chain as well as the Mean Recurrence Time of each CD4 count state. The study result shows that; the initial probabilities that a patient will stay in the good, moderate, and poor health states in the first six (6) months of the ART are; 0.834, 0.333 and 0.280 respectively. The overall efficacy of the ART showed a 78%, 19%, and 3.3% chances that a patient will be in the Good, Moderate and Poor health states respectively with respective mean recurrence times of 0.64, 2.69 and 14.99 years. Further results shows that the total life expectancy of patients in the good and moderate health states are 20.425 and 19.275 years respectively. The study recommends that the methodology be applied to a cohort study to further validate study these results.

Key words: Stochastic, Model, Efficacy, ART, Farmers, HIV/AIDS, CD4

Introduction

The human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) is becoming drug resistant in some patients. This is posing a great challenge as some HIV patients do well for some extended period of time with low CD4 cell count, while some patients with very high CD4 cell counts deteriorate more rapidly. As a result, this lead to treatment failure and spread of drug resistant HIV/AIDS result. This compromises the effectiveness of the limited therapeutic options like the antiretroviral therapy (ART). Therefore, it becomes imperative to assess the efficacy of the ART treatment as well as predict the life expectancy of HIV-infected persons.

However, recent studies using Markov Chain have been carried out in classifying the dynamics and natural history of HIV/AIDS, determining markers of disease progression, but fails to include the assessment of the ART efficacy. The focus of this work is to improve the work of Agada *et al* (2018). The Markov Chain Model of Agada *et al* (2018) was able to bridge this gap but failed to include the determination of the life expectancy of patients. This created another gap which this study intends to bridge.

HIV/AIDS reduces the rate of growth particularly in countries most seriously affected with the disease. The effect of HIV/AIDS on agricultural production can be linked to labour and productivity as well as increase in post-harvest losses. A strong supporter of this view is Parker *et al* (2009). They noted that HIV/AIDS affects not only the health of infected individuals, but also the socio-economic status of the individuals, their families and broader community. In recognition of the various impacts of HIV/AIDS to postharvest losses, Asenso-Okyere *et al* (2010) stated that poor health due to AIDS brings hardships to households including debilitation, substantial monetary expenditures, loss of labour and eventually death.

Review of Related works

According to Joint United Nations Programme on HIV/AIDS (UNAIDS, 2014), an estimated 36.9 million people were living with HIV worldwide of which 3.2 million were estimated to be in Nigeria, the second largest burden in the world after South Africa. However,

only an estimated 1.1 million of these know their status accounting for just 30%. Although, 88% of those who know their status are on treatment and 81% of those infected with the virus have achieved viral suppression. This seems worse when considered the total number of people living with HIV, indicating that only 30% of people living with HIV in Nigeria are on treatment. A global scale-up of antiretroviral therapy (ART) have been known to be the major contributing factor that accounts for 48% decline in HIV-related deaths worldwide from a peak of 1.9 million in 2015. Around mid-2017, there were approximately 20.9 million people receiving ART which accounted for only 53% of people living with HIV at the end of 2016 (World Health Organization, WHO, 2018).

Owing to the constant challenges posed by HIV/AIDS, (Agada *et al.*, 2018) developed a Markov Chain Model to assess the progress and predicts the efficacy of antiretroviral therapy (ART) using the CD4 counts of HIV/AIDS patients. They concluded that the difference in the chances of the health state of patients might be due to antiretroviral drug resistance among other factors. They recommended that these factors should be identified and considered when administering ART to ensure very high chances of the good, moderate and poor health states.

HIV infection progressively weakens the immune system by reducing the CD4 cell counts, thus making the patients vulnerable to various opportunistic infections (Grover *et al.*, 2013). The CD4 cell counts provide a marker for characterizing the clinical stages of HIV patients. A part from being a leading marker of disease progression, CD4 cell counts have also been used as an indicator of Antiretroviral Therapy (ART) initiation . They are also used for disease progression, deciding when to commence therapy, staging the disease, determining treatment failure, and defining the risk for mother-to-child transmission (Agada *et al.*, 2018).

The hallmark of the HIV infection is the progressive depletion of a class of lymphocytes named CD4+ which plays a pivotal regulatory role in the immune response to infections and tumours (Dessie, 2014). Mathematical models of HIV transmission that incorporate the dynamics of disease progression can estimate the potential

impact of adjunctive strategies to antiretroviral therapy (ART) for HIV treatment and prevention (Ross *et al.*, 2016).

A great deal has been accomplished over the past few years in elucidating the natural history of HIV infection and also developing treatments for HIV patients. To this end, Tarylee (2011) applied multistate Markov Model to HIV progression using CD4 count intervals with ARV initiation as an absorbing state. He analysed HIV progression using CD4 counts intervals of six months since enrolment on ART with the objective of investigating the probabilities of transitions to lower CD4 counts and estimating the average stay in the CD4 count states. Also, in modelling the progress of HIV/AIDS epidemic, Adeniyi (2014) applied Discrete-Time Markov process to modelled HIV/AIDS disease progression. The study concluded that the rate at which susceptible becomes infective and the rate at which infective becomes AIDS are crucial parameters which when kept low, the epidemic will be kept under control.

Another research work on Markov Chain Modelling analysis of HIV/AIDS progression was a race-based forecast in the United States that investigated the most vulnerable racial minority population (the African Americans) in the United States and the second least affected (the Caucasians) in order to predict the trends of the epidemic (Lee *et al.*, 2014). The results revealed discrepancy in HIV infection, AIDS diagnosis and deaths due to HIV/AIDS among the African Americans and the Caucasians races. They stated that there is need for interventions focusing on HIV/AIDS prevention and management, optimum resource allocation and development of ANTI-AIDS campaigns to reduce the infection rate.

The effects of Highly Active Antiretroviral Therapy (HAART) of *stavudine*, *lamivudine* and *nevirapine* on the CD4 lymphocyte count of HIV-infected Africans was also studied (Erhabor *et al.*, 2006; Rotich, 2016). In this study, changes in CD4 counts in the HAART treated subjects and the untreated controls were assessed based on starting baseline CD4 count; < 200 cells/ μ L, $200-350$ cells/ μ L and > 350 cells/ μ L. They concluded that it is important to access the CD4 lymphocyte count of HIV infected patients before the initiation of

HAART, which is used as a prognostic marker in predicting the initial response to HAART and in determining the optimal time to initiate therapy.

A determination of the life expectancy of HIV/AIDS patients in Anambra State using stationary and smoothed non-stationary Markov Chain Models is another research relevant to the study (Nwosu, 2015). The result of the study showed that the smoothed Non stationary Markov Chain Model is conceptually better than the stationary Markov Chain in determining the life expectancies of patients. Similarly, a multistate model to study the generation of mean transition time in transient state of HIV disease progression in Kenya using a four state Markov Model with reversible transitions was also considered (Mwambura and Karoki, 2017). The study concluded that CD4 cell count is a good indicator for gauging the strength of the immune system and determining whether a person is at risk of infection with certain organisms.

Materials and Methods

Sample Size/Study Population

The study population consists of the CD4 counts of 28,582 HIV/AIDS patients enrolled for care at the ART Centre of the HIV counselling and Testing (HCT) unit of the Federal Medical Centre (FMC) Makurdi, from January, 2008-July, 2018. It is of importance to this study that over 70% of the patients were farmers.

Data description and Transformation

The data details for this study include the CD4 counts of the HIV/AIDS patients, Date of visits and patients identification number. The patients present for treatment every six (6) months at the HIV counselling and Testing (HCT) unit of FMC Makurdi, Benue State. These parameters assisted the researcher in tracking the progress of treatment of each patient. The CD4 cell counts of the HIV/AIDS patients were carefully organized to reflect the transition among health states. The states were defined as; CD4 cell count equal or greater than 500 cells/ μ L, CD4 cell count between 200-499 cells/ μ L, and CD4 cell count less than 200 cells/ μ L. This study largely adopted the revised United States (U.S) Centres for Disease Control and Prevention (CDC, 1993) classification system for HIV infection and Expanded Surveillance Case

Definition for AIDS among Adolescents and Adults. In view of the aforementioned, the health states were classified as states I, II, and III, representing the Good, Moderate and Poor health states of the patients respectively.

Method of Data Analysis

A three (3) state Markov Chain Model was used in the analysis of the transformed data. The mathematical details of the model is provided as follows.

Basic mathematical concepts of the markov chain model

Markov chain

A Markov Chain is a sequence or chain of discrete states in time or space with fixed probabilities for the transition from one state to a given state in the next step in the chain. If a stochastic process $\{X(n); n \geq 0\}$ is the series of transition from one state to another such that the probabilities associated with each transition depend only on the immediate past state of the process and not on how the process reached that state. Then the process is said to be markov dependent. That is if

$$P(X_n|X_0, X_1, \dots, X_{n-1}) = P(X_n|X_{n-1}) \quad 1$$

A stochastic process that is markov dependent is said to possess the markovian property. This property is equivalent to the statement that the conditional probability of any future state $(X_{n+1} = j)$, given any past states $(X_0 = i_0, X_1 = i_1, \dots, X_{n-1} = i_{n-1})$, and the present state (X_n) , is independent of the past states. The markov property asserts that the process is memory-less. (Udom, 2010).

Transition probability matrix

Every Markov Chain has associated with it transition probabilities; the probabilities of moving from one state of the chain to another. (Udom, 2010). Transition probabilities are usually based on frequency distribution of the number of transition from one state to another in the system under consideration (using historic data). The frequencies are converted to estimates of the probabilities by dividing each row by its total.

Consider a finite Markov Chain with r possible states, x_1, x_2, \dots, x_r . Let p_{ij} be the conditional probability that the process will be in

state x_j given that it was in state x_i at the preceding observation time. The transition probability matrix of the Markov Chain is defined to be the $r \times r$ matrix P with elements p_{ij} . Thus,

$$P = \begin{pmatrix} p_{11} & p_{12} & \dots & p_{1r} \\ p_{21} & p_{22} & \dots & p_{2r} \\ \dots & \dots & \dots & \dots \\ p_{r1} & p_{r2} & \dots & p_{rr} \end{pmatrix} \quad 2$$

These elements p_{ij} are also called stationary probabilities. They are defined as

$$P(X_r = j|X_{r-1} = i) = P_{ij} \quad 3$$

N-Step transition probability matrix

For any value of n ($n = 2, 3, \dots$), the n^{th} power P^n of the matrix P in equation (2) above which specify the probability P_{ij}^n that the chain will be in state j after n -steps given that it begins in state i is called the n -step probability matrix.

In general, the n -step transition probability matrix

$$P^{(n)} = P_n = P^{n-1}P, n \geq 1.$$

Steady state probability of a markov chain.

Consider a Markov Chain with r -states and the row vector

$$\pi = (\pi_1, \pi_2, \dots, \pi_r)$$

Such that

- (i) $\pi_i \geq 0$
- (ii) $\sum_{i=1}^r \pi_i = 1$
- (iii) $\pi_j = \lim_{n \rightarrow \infty} \pi_{ij}^n$ Where P_{ij} is defined in

equation (2) above, then $(\pi_1, \pi_2, \dots, \pi_r)$ is called the steady state vector of the Markov Chain. This means that as $n \rightarrow \infty$, the probability that the chain will transit from state x_i to a state x_j is independent of the initial state x_i . π can be obtained by solving the relation

$$\pi = \pi P$$

The steady state probability matrix is shown below

$$\pi = \begin{pmatrix} \pi_1 & \pi_2 & \dots & \pi_r \\ \pi_1 & \pi_2 & \dots & \pi_r \\ \dots & \dots & \dots & \dots \\ \pi_1 & \pi_2 & \dots & \pi_r \end{pmatrix} \quad 4$$

It was used in this study to predict the long run (steady state) probabilities of patients when forecasting the efficacy of the ART.

Mean recurrence time

Assume that a process starts in state *i*. Consider the length of time before it returns to *i* for the first time. It is clear that, it must return, since it either stays at *i* the first step or go to some other state *j*, and from any other state *j*, it will eventually reach *i* because the chain is ergodic (Udom, 2010). Hence, we find the mean return time from the stationary distribution using the equation below.

$$\mu_r = \frac{1}{\pi_r} \tag{5}$$

It was used in this study to compute the expected number of steps or expected time a patient returns to state *i* having started and transitioned from state *i* to state *j*.

Absorbing State of a Markov Chain

Definition. A state *s_i* of a Markov Chain is called absorbing if it is impossible to leave it (i.e., *P_{ii}* = 1 and *P_{ij}* = 0). A Markov Chain is absorbing if it has at least one absorbing state, and if from every state it is possible to go to an absorbing state (not necessarily in one step).

Canonical form of an absorbing markov chain

Consider a finite Markov Chain with transition probability matrix *p*. If there are *r* absorbing states and *t* transient states, the transition matrix will have the following canonical form

$$P = \begin{matrix} & \begin{matrix} \text{TR.} & \text{ABS.} \end{matrix} \\ \begin{matrix} \text{TR.} \\ \text{ABS.} \end{matrix} & \left(\begin{array}{c|c} Q & R \\ \hline 0 & I \end{array} \right) \end{matrix} \tag{6}$$

Where, I is an *r*-by-*r* identity matrix, 0 is an *r*-by-*t* zero matrix, R is a nonzero *t*-by-*r* matrix, and Q is a *t*-by-*t* matrix. The first *t* states are transient and the last *r* states are absorbing. As earlier mentioned, we noted that the entry *P_{ij}⁽ⁿ⁾* of the matrix *Pⁿ* is the probability of being in the state *s_j* after *n* steps, when the chain is started in states_{*i*}. A standard matrix algebra shows that *Pⁿ* is of the form;

$$\begin{matrix} \text{TR.} \\ \text{ABS.} \end{matrix} \left(\begin{array}{c|c} \text{TR.} & \text{ABS.} \\ \hline & \end{array} \right)$$

$$P^n = \begin{matrix} & Q^n & R \\ & 0 & I \end{matrix} \tag{7}$$

Where R is the *t*-by-*r* matrix in the upper right-hand corner of *Pⁿ*. The form of *Pⁿ* shows that the entries of *Qⁿ* gives the probabilities for being in each of the transient states after *n* steps for each possible transient starting state. It was used in the work to segregate the number of patients that may fall out of the system and those expected to continue with the ART.

Fundamental matrix

The computation of (I-Q)⁻¹ is called the fundamental matrix where I is an identity matrix. It was used in this study to determine the expected length of time a patient spends in the transient state *j*, having started from the transient state *i*. Thus, this model was used to calculate the life expectancy of patients in state *j* who entered the ART initiation in state *i*. The assumption here is that, life expectancy is a random stochastic variable prevailing in the HIV/AIDS dynamics (Nwosu, 2015). The fundamental matrix is denoted by;

$$(I - Q)^{-1} = \begin{bmatrix} F_{11} & \cdots & F_{1N} \\ \vdots & \ddots & \vdots \\ F_{N1} & \cdots & F_{NN} \end{bmatrix} \tag{8}$$

Where I is an identity matrix and Q is the initial probability matrix

Use of Statistical Software

The Microsoft Excel (MS Excel, 2013) Package was employed in transforming the CD4 counts of HIV/AIDS patients into states (I, II, and III), while a Pascal program (Turbo Pascal version 1.5) was used in computing powers of transition probability matrices as well as the steady state probability matrix.

Results

Assessing the Efficacy of ART to Patients without Absorption

The CD4 cell counts of the 28,582 HIV/AIDS patients were carefully organized and managed to reflect the transition among the states I, II and III representing the Good, Moderate and Poor health states of patients respectively for every six (6) months during the period under review. This is captured in (table 1) below.

Table 1: CD4 Transition counts of the HIV/AIDS patients

	I	II	III	Total
I	13003	2337	246	15586
II	5921	3263	604	9788
III	1673	637	898	3208
Total	20597	6237	1748	28582

The initial transition probability matrix (P^1) was obtained from table 1 above, by dividing the elements of each row by their corresponding row totals. This is shown in Figure 1 and represented in figure 2 by a transition diagram. This matrix shows the initial probabilities that a patient will transit from one health state to another in the first six (6) months of the ART initiation. The diagonal elements from the matrix

indicates that there are 83%, 33% and 28% chances that a patient will stay in Good, Moderate and Poor health states respectively. While the off-diagonal elements shows the chances of a patient transiting between the three health states respectively. The matrix below therefore, provides progress information on patient's responses to the ART from the Good, Moderate and Poor health states in the first six (6) months of the ART initiation.

$$P^1 = \begin{matrix} & \begin{matrix} \text{I} & \text{II} & \text{III} \end{matrix} \\ \begin{matrix} \text{I} \\ \text{II} \\ \text{III} \end{matrix} & \begin{pmatrix} 0.834 & 0.150 & 0.016 \\ 0.605 & 0.333 & 0.062 \\ 0.521 & 0.199 & 0.280 \end{pmatrix} \end{matrix}$$

Figure 1: Initial Transition probability Matrix in the first six (6) month

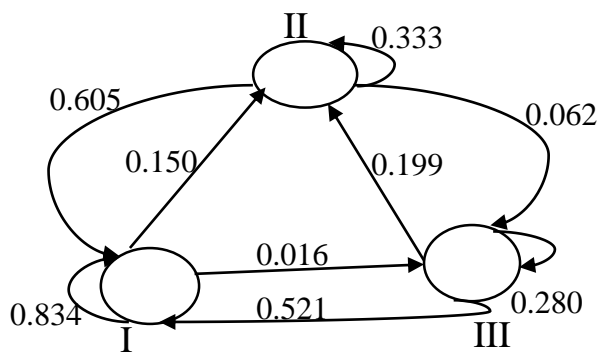


Figure 2: Transition Diagram of patients between health states.

N-Step Transition Probabilities

However, for the remaining six (6) months interval appointments, the N-Step transition probability matrix was used and these were obtained by finding powers of the initial transition matrix (p^1). The resulting matrices for $p^2, P^3, P^4, \dots, P^{12}$ showing the chances of patients transiting between the three health states at the 2nd, 3rd, ..., 12th six (6) months interval appointments are depicted in (tables 2). Thus, P^{12}

shows the steady state probability matrix of patient's response to the ART. The diagonal elements of each matrix presented below indicates the chances that a patient will stay or maintain in Good, Moderate and Poor health states, while the off-diagonal elements shows the chances of a patient transiting between the three health states respectively as can be seen in (tables 2) below.

Table 2: N-Step Transition probabilities

N th Six Month interval appointments	Previous State	Transition Probability Actual State		
		I	II	III
2 nd	I	0.794642	0.178234	0.027124
	II	0.738337	0.213977	0.047686
	III	0.700789	0.200137	0.099074
3 rd	I	0.784695	0.183946	0.031360
	II	0.770074	0.191494	0.038432
	III	0.757158	0.191480	0.051362
4 th	I	0.782061	0.185199	0.032740
	II	0.778119	0.186927	0.034955
	III	0.774075	0.187558	0.038368
5 th	I	0.781342	0.185496	0.033163
	II	0.780253	0.185920	0.033827
	III	0.779040	0.186203	0.034757
6 th	I	0.781142	0.185571	0.033288
	II	0.780836	0.185681	0.033483
	III	0.780481	0.185778	0.033741
7 th	I	0.781085	0.185591	0.033324
	II	0.780999	0.185620	0.033381
	III	0.780896	0.185651	0.033453
8 th	I	0.781069	0.185596	0.033335
	II	0.781045	0.185604	0.033351
	III	0.781015	0.185613	0.033372
9 th	I	0.781065	0.185597	0.033338
	II	0.781058	0.185600	0.033342
	III	0.781049	0.185602	0.033348
10 th	I	0.781063	0.185598	0.033339
	II	0.781061	0.185599	0.033340
	III	0.781059	0.185599	0.033342
11 th	I	0.781063	0.185598	0.033339
	II	0.781063	0.185598	0.033339
	III	0.781062	0.185598	0.033340
12 th	I	0.781063	0.185598	0.033339
	II	0.781063	0.185598	0.033339
	III	0.781063	0.185598	0.033339

The proceeding figures (3-5) were obtained from the table 2 above with view to better explain the progress of patients' response to the ART. Figure 3 indicates the transition probabilities from states I, II, III to I after the first six (6) months of the appointment. The probability that a patient will stay or maintain in state I is 0.794642 (79%) chance while the chances that he/she will transit from states II, III

to state I are 0.738337 (74%) and 0.700789 (70%) respectively for the second six (6) months appointment or period. This shows an erratic decline chance of the patient's health improving from moderate and poor health states to the Good health state in the second six (6) months period under review. These chances decrease continually over the rest of the appointments and becomes constant or stable at the 12th appointment given a

steady state value at 0.781 explaining a 78% chance that a patient will be in Good health state at the long run.

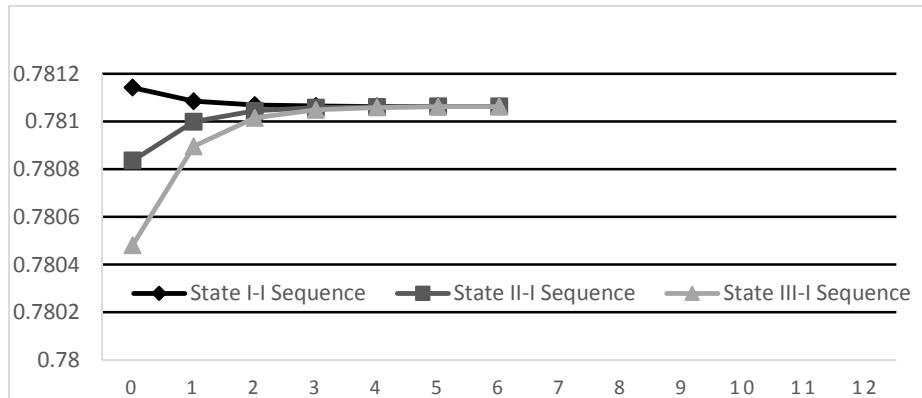


Figure 3. Transition probabilities of patients from states I, II, III to I

The transition probabilities of patients from states I, II, III to state II is depicted in Figure 4 below. In this situation, the probabilities that a patient will remain or stay in the Moderate health state is 0.213977 (21%) after the second six (6) months period or appointment. The chances of transition from the Good and poor health states to

the moderate health state are 0.178234 (18%) and 0.200137 (20%) respectively. However, these chances continue to change over the rest of the appointments and became steady during the 12th appointment which stood at a value 0.185598 (19%). This indicates a 19% chance that a patient will be in the moderate health state at the long run.

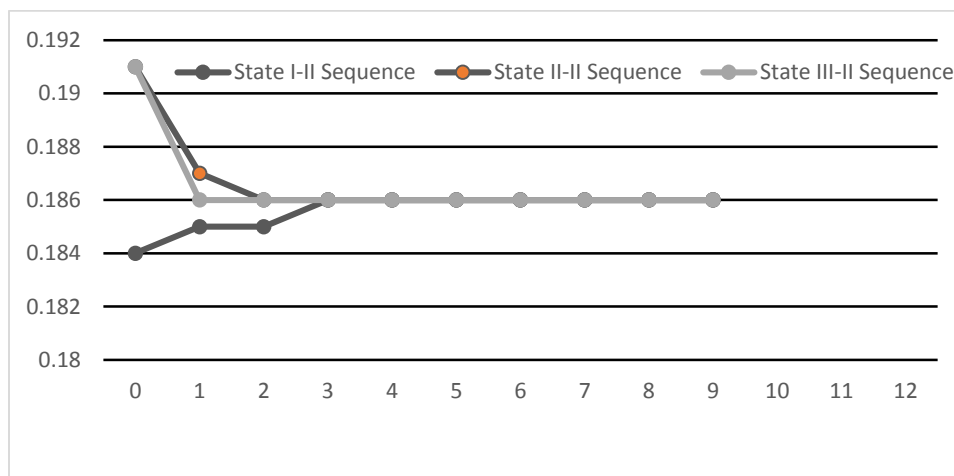


Figure 4. Transition probabilities of patients from states I, II, III to II

Figure 5 below illustrates the transition probabilities of patients from states I, II, III to III. Here, the probability that a patient will remain in the poor health state is 0.099074 (9.9%) after the second six (6) months appointment. The chances of transiting from the Good and Moderate health states to the poor health state are 0.027124 (2.71) and 0.047686 (4.77%) respectively.

Here also, the chances continued to mutate over the rest of the appointment and became steady during the 12th appointment at a value of 0.033339 (3.3%). This result shows that, there is a 3.3% chance that a patient will remain in the poor health state at the long run.

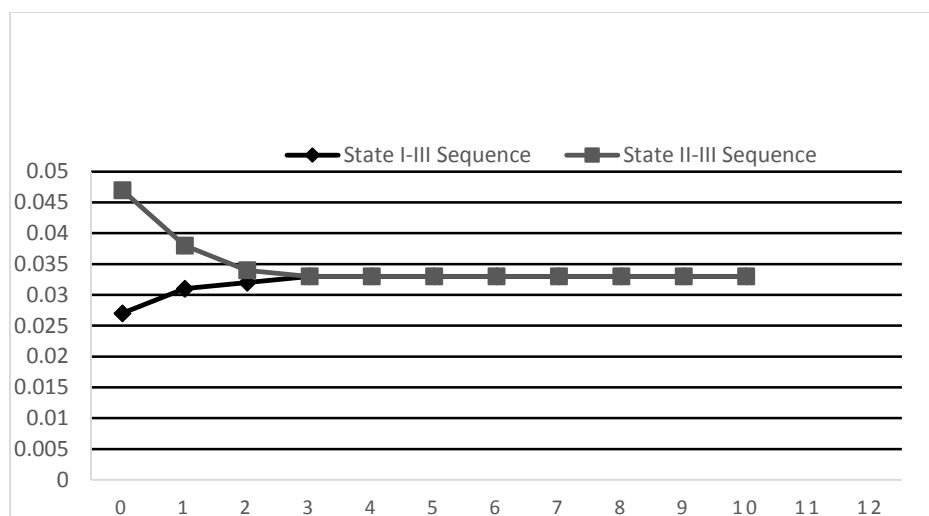


Figure 5: Transition Probabilities of patients from states I, II, III to III

Mean Recurrence Times of Patients Health States

The long run probabilities or steady state of patients in their respective health state were

obtained from the chances of their respective states shown in (table 2) during the 12th appointment. This is shown in the matrix (P¹) below represented as Figure 6.

$$P^{12} = \begin{matrix} & \begin{matrix} \text{I} & \text{II} & \text{III} \end{matrix} \\ \begin{matrix} \text{I} \\ \text{II} \\ \text{III} \end{matrix} & \begin{bmatrix} 0.781063 & 0.185598 & 0.033339 \\ 0.781063 & 0.185598 & 0.033339 \\ 0.781063 & 0.185598 & 0.033339 \end{bmatrix} \end{matrix}$$

Figure 6: The long run probabilities or Steady state of patients Health States

As earlier noted, this shows a 78%, 19%, and 3.3% chances that a patient will be in the Good, Moderate and Poor health states respectively. Mean recurrence time (years) for each state was computed by finding the reciprocal of their respective steady state probabilities and the resulting recurrence mean time for each state exhibited the following values as 0.64, 2.69 and 14.99 respectively.

such that a patient will be in the Good health state 78% of the time, 19% of the time in Moderate health state and 3.3% of the time in poor health state with mean recurrence times of 0.64, 2.69 and 14.99 years respectively.

Forecasting the Efficacy of ART

The efficacy of a treatment or therapy is a measure of maximum response of patients to treatments (Agada *et al.*, 2018). However, efficacy as used in this context or study is referred to as the long run ability of the ART to produce desired effects on the patients. Therefore, in forecasting the efficacy of the ART, we make use of the long run probabilities or steady state probabilities of patient’s health states.

Life Expectancy of the HIV/AIDS Patients

When death is taken into account, we further modified the transition matrix for the three health states in Figure 1 and determine a new transition matrix (P*) for an absorbing Markov Chain. To do this, patients in the state III (CD4 count < 200) were considered to die out of the system. As earlier explained, the fundamental matrix is a model required for the computation of the life expectancy of the HIV/AIDS patients.

Hence, this information enable us to predict the long run (steady state) chances of patients being in a given health state. To this end, we stated that the overall efficacy of the ART is

The computation (I-P*)⁻¹ is called the fundamental matrix where I is an identity matrix and P* is as defined above. It was used in this work to determine the expected length of time a patient spends in the transient state *j*, having started from the transient state *i*. This implies the

life expectancy of patients in state j who entered the ART initiation in state i .

In order to compute the elements of the fundamental matrix, it is required to first

determine the Canonical form of the original transition probability matrix (P) as this will help determine P^* . The details is as follows.

Let the Canonical form of matrix P be denoted as P_{can} . Then,

$$P_{can} = \begin{matrix} & \begin{matrix} \text{I} & \text{II} & \text{III} \end{matrix} \\ \begin{matrix} \text{I} \\ \text{II} \\ \text{III} \end{matrix} & \left(\begin{array}{ccc|c} 0.834 & 0.150 & & 0.016 \\ 0.605 & 0.333 & & 0.062 \\ 0.000 & 0.000 & & 1.000 \end{array} \right) \end{matrix}$$

Hence,

$$P^* = \begin{matrix} & \begin{matrix} \text{I} & \text{II} \end{matrix} \\ \begin{matrix} \text{I} \\ \text{II} \end{matrix} & \left(\begin{array}{cc} 0.834 & 0.150 \\ 0.605 & 0.333 \end{array} \right) \end{matrix}$$

And the fundamental matrix is now obtained by finding the inverse of the $(I-P^*)$

$$(I-P^*)^{-1} = \left(\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} - \begin{pmatrix} 0.834 & 0.150 \\ 0.605 & 0.333 \end{pmatrix} \right)^{-1}$$

$$= \begin{pmatrix} 33.350 & 7.500 \\ 30.250 & 8.300 \end{pmatrix}$$

Adding the row elements we have;

$$= \begin{pmatrix} 40.85 \\ 38.55 \end{pmatrix}$$

From the result of the fundamental matrix above, the life expectancies of patients in each health state before been absorbed is clearly shown as elements of the fundamental matrix. From this matrix, the total life expectancy of patients in the good and moderate health states were 20.425 and 19.275 years respectively. Observe that the life expectancies are close. It is pertinent to note at this point that, the life expectancies of the patients are not 100%. This can be shown from their respective elements of the fundamental matrix. The differences in the life expectancies of the patients in states I and II might be the leading cause of death of patients in state III.

Study Implication

The results of the study implied that, HIV infected farmers will be strong all year round by the continuous use of ART as they carry out their farming activities during and after harvest. This

will reduce HIV-related deaths and increase labour and productivity with decline in postharvest losses.

Conclusion

The following conclusions were made from the study.

- i. The initial probabilities that a patient will stay in the Good, Moderate, and Poor health states in the first six (6) months of the ART initiation were 0.834, 0.333, and 0.280 chances respectively.
- ii. The overall efficacy of the ART is such that a patient will be in the Good health state 78% of the time, 19% of the time in Moderate health state and 3.3% of the time in Poor health state.
- iii. The mean recurrence times (years) of the Good, Moderate and Poor health states were 0.64, 2.69 and 14.99 respectively.

- iv. The patients' health were assessed at each appointment to be transiting between the Good, Moderate and Poor health states at defined chances.
- v. The total life expectancy of patients in the good and moderate health states were 20.425 and 19.275 respectively.

Recommendations

The following recommendations were drawn from the study

- (i) The Markov Chain model should be used in assessing the efficacy of ART of HIV/AIDS patients.
- (ii) The methodology of this study should be applied to a cohort study to further validate study results.

References

- Adeniyi, O.O. (2014). On the use of discrete time markov process for HIV/AIDS epidemic modelling. *Internal Journal of Modern Mathematical Sciences*, 9(2):82-95
- Agada, P.O., Eneh, J.E., & Ikughur, J.A. (2018). A model for assessing the progress and predicting the efficacy of antiretroviral therapy (ART). *FUW Trends in Science and Technology Journal*, 3(2), 12-26
- Asenso-Okyere, K., Aragon, C., Thangata, P., Andam, K., & Mekonmen, D.A. (2010). HIV and AIDS and farm labor productivity: A review of recent evidence in Africa. *Journal of Development and Agricultural Economics*, 2(12), 406-415
- CDC (1993). Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *MMWR Recomm Rep* 1992, 41(RR-17), 1-19
- Chunling, C., & Tsokos, C. (2009). Markov Modelling of breast cancer. *Journal of Modern Applied Statistical Methods*, 8(2), 626-631.
- Dessie, Z.G. (2014). Modelling of HIV/AIDS dynamic evolution using non-homogeneous semi-markov process. *Springer Plus*, 3:537. Retrieved from <http://www.springerplus.com/content/3/1/537>
- Erhabor, O., Ejele, O.A., & Nwauche, C.A. (2006). The Effects of Highly Active Antiretroviral Therapy (HAART) of Stavudine, Lamivudine and Nevirapine on the CD4 Lymphocyte Count of HIV-Infected Africans: The Nigerian Experience. *Nigerian Journal of Clinical Practice*, 9 (2), 128-133.
- Grover, G., Gadpayle, A. K., Swain, P.K., & Dekka, B. (2013). A Multistate Markov Model Based on CD4 Cell Count for HIV/AIDS Patients on Antiretroviral Therapy (ART). *International Journal of Statistics in Medical Research*, 2:144-151.
- Lee, S., Ko, J., Tan, X., Petel, I., Balkrishnan, R., & Chang, J. (2014). Markov Chain Modelling analysis of HIV/AIDS progression. A Race-based forecast in the United States. *Indian Journal of Pharmaceutical Studies*, 76(2), 167-115.
- Mwambura, S.K., & Karoki, S. (2017). Generation of Mean (Sojourn) Time in Transient State of HIV Disease Progression in Kenya. *International Journal of Social Science and Humanities Research*, 5(2), 734-739.
- Nwosu, C.A (2015). Determining the life expectancy of HIV/AIDS patients in Anambra using stationary and smoothed non-stationary Markov Chain Models. *ABACUS*, 42(2), 93-107.
- Parker, D.C., Jacobsen, K.H., & Komwa, M.K. (2009). A qualitative study of the impact of HIV/AIDS on agricultural households in South-eastern Uganda. *International Journal of Environmental Research and Public Health*, 6: 2113-2138.
- Ross, J.M., Ying, R., Celum, C.L., Baeten, J.M., Thomas, K.K., Murnane, P.M. *et al.*, (2016). Modelling HIV disease progression and transmission at population level: the potential impact of modifying disease progression in HIV treatment programs. Retrieved from <https://doi.org/10.1101/097337>.
- Rotich, K. T. (2016). Mathematical modelling of the spread of HIV/AIDS by markov chin process. *American Journal of applied Mathematics*, 4(5), 235-246.
- Tarylee, R. (2011). Application of Multistate Markov Models to HIV disease

- progression. (Master's published thesis)
University of KwaZulu-Natal, South-Africa
- Udom, A. U. (2010). *Elements of Applied Mathematical Statistics*. Akwa-Ibom, Nigeria: ICIR.
- UNAIDS (2014) Global AIDS Response Progress Reporting
- WHO (2018). Monitoring Health for the SDGs, Sustainable Development Goals