# A MULTI-STATE ASSESSMENT OF THE RECOVERY PROCESS OF HIV PATIENTS UNDER ANTIRETROVIRAL THERAPY

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## ABSTRACT

The human immunodeficiency virus (HIV) remains a significant global public health challenge. This study employs multi-state models to assess the recovery process in HIV patients under antiretroviral therapy (ART). A retrospective study design with 1948 HIV patients using Secondary data. Based on probability transition matrix ( $P_{ij}$) of the Markov chain, HIV patients on antiretroviral therapy were able to transit from the unsuppressed viral load state ($S_3$) to target not detected ($S_1$) with a transition probability of 0.9059, with the lowest transition from low level viremia ($S_2$) to unsuppressed viral load ($S_3$) with a transition probability of 0.0402. The limiting distribution ($\pi_j$) of the states is 0.9079, 0.0730, and 0.0190 respectively indicating that HIV patients are likely to remain in recovery target not detected state ($S_1$) in the long run. The binary logistic regression analysis demonstrates significant factors influencing the recovery process of HIV patients under antiretroviral therapy. Specifically, Regimen1 shows a notable odds ratio with favorable outcomes compared to the reference group $with$ ($p < 0.05$). Additionally, age is a significant factor, with an odds ratio which suggest an increase in the odds of adverse outcomes for each additional year of age ($p < 0.05$). Furthermore, FirstCD4 $> 200$ is associated with a reduction in the odds of unfavorable outcomes, with an odds ratio with (p<0.05). This study employs multi-state models to evaluate HIV recovery under ART using retrospective data from 1,948 patients. Results indicate a high transition probability (0.9059) from unsuppressed viral load to undetectable status and long-term stability in recovery ($\pi_1 = 0.9079$). Logistic regression identifies regimen type, age, and initial CD4 count as significant factors influencing recovery (p<0.05), highlighting the effectiveness of multi-state models in assessing HIV treatment outcomes.

**KEYWORDS:** HIV, Antiretroviral therapy (ART), Viral load, Multi-state models.

## INTRODUCTION

Human immunodeficiency Virus (HIV) remains a significant global public health issue, with about 38.4 million people living with the virus globally in 2021. Nigeria, being the second largest HIV positive country, has 1.8 million people (Boyd *et al*., 2021). Antiretroviral Therapy (ART) is an effective treatment, targeting different stages of the HIV life cycle to suppress viral load and prevent replication (Bai *et al*., 2022). With 28.7 million people globally accessing ART, 75% of PLHIV, including 1.8 million from Nigeria, and able to live long and healthy lives (Durosinmi-Etti *et al*., 2022).

In Sub-Saharan Africa, Nigeria had an estimated 1.8 million HIV positive individuals in the year 2020 who were receiving treatment, making it the second-largest HIV-positive country in the world. South Africa had an estimated 7.5 million individuals with tested positive to HIV in the year 2021, making it the country with the greatest number of HIV-positive individuals globally. East Africa had the highest HIV prevalence rates in the year 2021, with Uganda having the highest rate and Burundi having the lowest. Investment in HIV prevention, treatment, and care programs is essential to end the epidemic (Global HIV and AIDS Statistics Factsheet, 2021).



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HIV has been a major public health challenge in Benue State, Nigeria, since the early 1980s. As of 2021, there were an estimated 184,745 people living with HIV (PLHIV) in the state, making it the state with the second highest burden of the disease in Nigeria, with a prevalence rate of 4.9%, higher than the national average of 1.4% and a viral suppression rate of 97% (Jwanle *et al*., 2023).

HIV patients' recovery process during anti-retroviral medication could be assessed by the amount of viral load in the body. HIV Viral load measures the amount of HIV virus in the blood; it is used to monitor the level of virus replication and effectiveness of the ART. The goal is to reduce the viral load copies/ml to an undetectable level less than 50 copies/ml (Mateo-Urdiales *et al*., 2019). A higher viral load indicates a higher level of HIV infection and a greater risk of transmitting the virus to others. A lower viral load indicates that the ART is working effectively to suppress the virus (Albert *et al.*, 2014). Antiretroviral therapy (ART) is used to inhibit viral replication and hence lower the risk of disease progression and transmission. Such progression could be classified into three levels namely, Target not detected, low level viremia and unsuppressed viral load copies/ml. At this point, there is need to briefly explain what you mean by target not detected, low level viremia and unsuppressed viral load. State one (target not detected) indicates optimal recovery which enables the patient to live healthy and normal life, while state two (low level viremia) indicates treatment improvement but not optimal recovery which posed some danger and may lead to opportunistic infections and even death and state three (unsuppressed viral load) indicates high viral load, amounting to treatment failure which subject the patients to high risks and sudden death, hence, state three is the worst state in the recovery of HIV patients (Gaifer and Boulassel, 2020).

Statistical models such as Kaplan-Meier survival analysis and Cox proportional hazards models have been widely used to analyze disease progression and recovery. However, these methods often fall short in capturing the complexity of health state transitions in HIV patients under ART (Andrade, 2023). To address this limitation, multi-state models have been introduced as a more comprehensive approach, enabling the representation of patients' transitions across different health states over time (Skourlis et al., 2021). Specifically, the Markov model provides a structured framework for quantifying transition probabilities between health states, while binary logistic regression helps assess the influence of patient characteristics and covariates on these transitions (Manzini et al., 2018).

This study applies a three-state Markov model to evaluate HIV disease progression and recovery, considering key transitional phases under ART. Additionally, binary logistic regression is employed to identify significant risk factors influencing these transitions. By integrating these statistical methods, the study offers a nuanced understanding of treatment effectiveness, ensuring practical insights that can guide real-world interventions. Furthermore, the parameter sensitivity analysis is presented with clear interpretations to enhance the applicability of findings in public health decision-making.



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## OBJECTIVE OF THE STUDY

The aim of this research is to assess the recovery process in HIV patients under Antiretroviral Therapy. The following are the objectives:

i. To obtain the transition probability between different states of HIV progression of PLHIV
ii. To determine the mean time of transition between states.
iii. To model the impact of various covariates and factors on the respective transitions on the Markov chain.

## LITERATURE REVIEW

Multi-state models are statistical frameworks used to analyze complex sequences of events or transitions among different states over time. These models are particularly valuable when studying processes that involve multiple stages or states, and they find applications in various fields, including epidemiology, healthcare, finance, engineering; etc. In the context of this research on assessing recovery of HIV patients undergoing Antiretroviral Therapy (ART), multi-state models offer a powerful tool to understand the intricate dynamics of disease progression and recovery, and the impact of various factors and covariates on the transitions (Manzini *et al.*, 2018).

According to (Matsena *et al*. 2019), used a multi-state Markov model to calculate bi-directional transition rates among antiretroviral therapy patients in Zimbabwe. The strongest determinant of immunological recovery was the type of healthcare facility patronized. Male patients had a 32% higher mortality risk than female patients, and their immune systems were more likely to decline. Elderly patients had higher immune deterioration rates compared to patients in the 25-34 years age group. Provincial or central hospitals had more pronounced immune recovery. Early treatment interventions may decrease mortality and improve survival outcomes when the immune system is largely gender and age neutral.

A study by Twumasi et al. (2019) used Markov Chain Modeling to study the spread of HIV, tuberculosis, and hepatitis B infections in Ghana. Conventional epidemiological models couldn't estimate critical disease metrics like the likelihood of first infection and recovery. The researchers used a discrete-time Markov chain model to address these limitations. The study found that hepatitis B was more infectious over time than tuberculosis and HIV, and individuals infected with HIV had lower life expectancies. The authors recommend using this technique for modeling disease dynamics in Ghana.

Akinyi (2022) conducted a study using Markov chains to investigate HIV progression in Homabay County. The study found that certain critical populations may transition from susceptible to infected HIV conditions or move between states, resulting in patient absorption. The data was sourced from the HIV care and treatment registry at Homabay County Referral Hospital and Key Population Size Estimates 2019. The study used the Maximum Likelihood Estimator and R code to estimate the number of individuals in each state at time t. The average period for susceptible persons to be absorbed is 264 months.

Chokobvu and Shoko's (2018) study used a Markov model to estimate HIV/AIDS-related mortality. They found that patients receiving Highly Active Antiretroviral Therapy (HAART) experienced decreased viral loads and increased CD4 cell counts. The study



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involved 320 HIV/AIDS patients from a wellness clinic in South Africa. The researchers used a time-homogeneous Markov model to forecast and explain the chance of dying from HIV/AIDS. They added a viral load principal component to explain mortality/transition components that CD4 cell counts alone couldn't. The study found that the orthogonal viral load covariate, along with CD4 baseline, gender, non-adherence to treatment, and age, had a significant effect on HIV/AIDS progression.

The study by Asena and Goshu (2019) analyzed data from September 2008 to August 2015 on the conditional probabilities of AIDS disease transitions using semi-Markov models. The results showed that the probability of a patient transitioning from a good state to a worse state increases within good states but decreases with time. The study suggests that patients should regularly monitor their CD4 count to improve survival chances and reduce death rates, and that enhanced clinical care for ART users should be reinforced.

(Melku et al., 2020) employed binary logistic regression to identify the risk factors influencing the prevalence of toxoplasmosis among HIV/AIDS patients. Significant risk factors were identified using the Wald and likelihood ratio tests. The selected model underwent diagnostic checks to evaluate its fitness through the Hosmer and Lemeshow tests, along with the Pearson and deviance goodness-of-fit tests. The findings revealed that patients living in unhygienic conditions, elderly patients, and those who were illiterate or had low levels of education were most affected by toxoplasmosis. Additionally, the prevalence was higher in urban areas compared to rural areas, likely due to the higher population density in urban regions.

A study by Kudakwashe and Mohammed (2014) conducted a hospital-based cross-sectional study using binary logistic regression to identify factors associated with immunologic status and virological suppression in HIV patients on HAART. He found that 82% of HIV patients on HAART achieved virological suppression, with factors such as CD4 cell count, age, and age playing a role. However, only 52.9% had favorable immunological status, with baseline CD4 count above 200 cells/mm3, age between 26-40 years, and urban residence. The study also found a low rate of immunological recovery, indicating the need for early HAART initiation to improve outcomes.

A study by Yunus *et al*., (2022) uses a nine-compartment model to analyze COVID-19 spread and containment in Nigeria. It uses the Caputo fractional order derivative and the Laplace-Adomian decomposition method. Simulations show recovery rates are highest at integer orders, indicating the effectiveness of interventions like vaccination and treatment. This highlights the importance of mathematical modeling in public health strategies.

Yunus and Olayiwola (2024) uses mathematical modeling to assess global malaria transmission, focusing on the effectiveness of enlightened therapy. It uses a four-compartmental approach and uses Lyapunov functions for stability analysis. The study also explores the influence of fractional-order derivatives on malaria transmission, demonstrating how increasing derivative orders affect disease control. By integrating Caputo fractional derivatives, the research enhances malaria eradication strategies and contributes to disease modeling.

**METHODOLOGY**

Markov Chain: A stochastic process $\{X_n, n = 0,1,2 \ldots\}$ that takes on countable or finite number of possible values denoted by the set of non-negative integers $\{0, 1, 2, \ldots\}$. If $X_n = i$, then the process is said to be in a state $i$ at time n. we suppose that whenever the process is in state $i$, there is a fixed probability $P_{ij}$ that it will next be in state $j$. That is



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$$P[X_k = j | X_{k-1} = i, X_{k-2,} = n \cdots X_0 = m] = P[X_k = j | X_{k-1} = i] = P_{ij} \quad (1)$$

For all the states $i_0, i_1, \ldots, i_{n-1}, i, j$ and for all $n \geq 0$. such stochastics process is known as a Markov Chain.

$P_{ij}$ = Probability that the process will, when in state $i$, next make a transition into state $j$. Since the probability are nonnegative and since the process must make a transition into state, we have that:

$P_{ij} \geq 0,\ i, j \geq 0$; where $\sum_{j=0}^{\infty} P_{ij} = 1, i = 0,1,\ldots$ (Ross, 2010)

**States of the Markov Model**

Figure 1 presents a schematic diagram of the states of the Markov process; highlighting the trajectory of the states in this model based on the viral load copies/ml. Let $X_{(t)} = \{S_1, S_2, S_3\}$ the state space of the Markov chain.

$S_1$: VL copies≤50 (Target not detected)

$S_2$: ≤51<VL copies≤999 (Low level Viremia)

$S_3$: VL copies≥1000 (Unsuppressed)

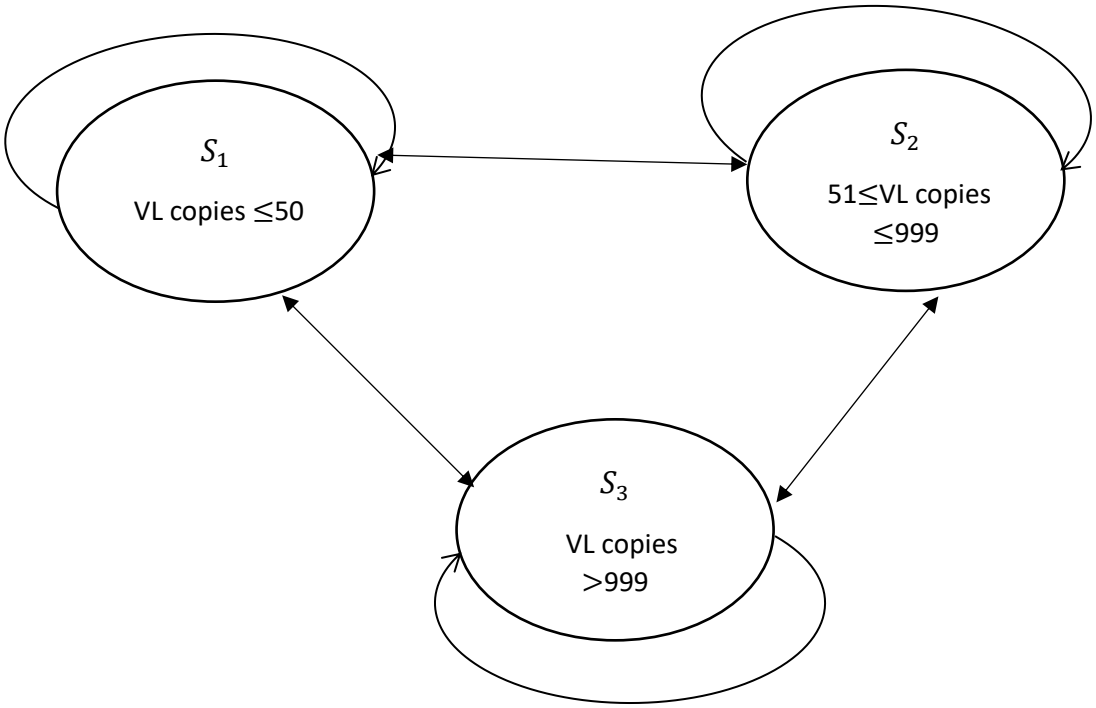


**Fig 1. Schematic Diagram of the 3 States Viral Load Trajectory**



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**Transition Probability Matrix**

The transition probability for $P_{ij}$ for $j = 1, 2, 3$ is given by the following matrix.

It is denoted by $P_{ij}$ where $j = 1, 2, 3$

$$P_{ij} = \begin{bmatrix} P_{11} & P_{12} & P_{13} \\ P_{21} & P_{22} & P_{23} \\ P_{31} & P_{32} & P_{33} \end{bmatrix} \quad (2)$$

where

$$\sum_{j=1}^{3} P_{ij} = 1 \; ; \; i = 123 \quad (3)$$

$$P_{ij} = \frac{Number\ of\ Observed\ Transitions\ from\ i\ to\ j}{Total\ Number\ of\ Observed\ Transition\ from\ i} \quad (4)$$

Limiting Distribution

Theorem. For an irreducible ergodic Markov chain $lim_{n\to\infty} P_{ij}^{(n)}$ exists and is independent of $i$. Furthermore, letting

$$\pi_j = lim_{n\to\infty} P_{ij,}^{(n)} \; j \geq 0 \quad (5)$$

Then $\pi_j$ is the unique nonnegative solution of

$$\pi_j = \sum_{i=0}^{\infty} \pi_j P_{ij\,,} \quad j \geq 0 \quad (6)$$

$$\sum_{j=0}^{\infty} \pi_j = 1 \quad \text{(Ross, 2010).} \quad (7)$$

**Binary Logistic Regression Model**

Assuming there are k explanatory variable $X = \{x_1, x_2, \dots, x_k\}$. The response variables y is a binary variable indicating whether a patient transit $(y = 1)$ or do not transit $(y = 0)$. If $\pi(x)$ is a conditional probability given the explanatory variables, then,

$$\pi(x) = p(y_i = 1 \backslash x_{i_1}, \dots, x_{i_k}) \quad (8)$$

$$1 - \pi(x) = p(y_i = 0 \backslash x_{i_1}, \dots, x_{i_k}) \quad (9)$$

A standard regression model is formulated as follows;

$$\pi(x) = \frac{exp\{\sum_{j=0}^{k} \beta_j x_{ij}\}}{1 + exp\{\sum_{j=0}^{k} \beta_j x_{ij}\}}, \quad (10)$$

and

$$1 - \pi(x) = \frac{1}{1 + \{\sum_{j=0}^{k} \beta_j x_{ij}\}} \quad (11)$$

Where $\beta = \{\beta_0, \beta_1, \dots \beta_k\}$ are unknown parameters to be estimated.

The logic transform of the equation 10 in terms of $\pi(x)$ is

$$g(x) = \beta_0 + \sum_{j=0}^{k} \beta_j \, x_{ij}. \quad (12)$$



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We use the MLE approach to estimate the explanatory variables' coefficient $(\beta_j'^s)$. For n individuals, the log-likelihood function is provided as

$$InL(\beta_0, \beta_1, \ldots \beta_k) = \sum_k \beta_i \sum_n x_{ij}\, y_i - \sum_n In\left\{exp\left(\sum_k \beta_i\, x_{ij}\right)\right\}. \quad (13)$$

Ugwuowo and Udoumoh (2011).

Log-likelihood equation differentiation with respect to $(k+1)$ $\beta_j'^s$ yields $k+1$ likelihood equations that can be solved simultaneously with special purpose software.

**Model Adequacy**

We employed the Hosmer-Lemeshow goodness of fit test to evaluate the suitability of the logistic regression model. See Hosmer and Lemeshow (1989) for details.

**RESULTS**

This study presents data analysis results, including descriptive statistics, transition trajectory, probability matrix, limiting distribution and binary logistic regression analysis. The data is presented in Tables 1, 2, 3, and 4, with matrices representing transition count, probability matrix, limiting distribution. The results are discussed in the next chapter.

**Table 1: Descriptive Statistics of Age Distribution**

| | N | Minimum | Maximum | Mean | Std. Deviation |
|---|---|---|---|---|---|
| Current Age | 1948 | 5 | 88 | 39.67 | 14.180 |

**Table 2: Frequency Distribution of Gender**

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | Female | 1415 | 72.6 | 72.6 | 72.6 |
| | Male | 533 | 27.4 | 27.4 | 100.0 |
| | Total | 1948 | 100.0 | 100.0 | |

**Table 3: Frequency Distribution of Age of Participants**

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | < 25 | 205 | 10.5 | 10.5 | 10.5 |
| | ≥ 25 | 1743 | 89.5 | 89.5 | 100.0 |



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| | | | |
|---|---|---|---|
| Total | 1948 | 100.0 | 100.0 |

The state Transition Count Matrix, $TM$ is given as

$$TM = \begin{array}{c} \\ s_1 \\ s_2 \\ s_3 \end{array} \begin{array}{c} \begin{array}{ccc} s_1 & s_2 & s_3 \end{array} \\ \begin{pmatrix} 539 & 45 & 11 \\ 311 & 14 & 8 \\ 924 & 67 & 27 \end{pmatrix} \end{array} \tag{14}$$

Transition Probability Matrix, $P_{ij}$ is presented thus:

$$P_{ij} = \begin{array}{c} \\ s_1 \\ s_2 \\ s_3 \end{array} \begin{array}{c} \begin{array}{ccc} s_1 & s_2 & s_3 \end{array} \\ \begin{pmatrix} 0.9059 & 0.0756 & 0.0184 \\ 0.9339 & 0.0420 & 0.0240 \\ 0.9059 & 0.0676 & 0.0264 \end{pmatrix} \end{array} \tag{15}$$

The Limiting distribution of the process is given as:

$$\pi_j = \begin{pmatrix} 0.9079 & 0.0730 & 0.0190 \end{pmatrix} \tag{16}$$

**Table 4: Hosmer-Lemeshow Test**

| Transitions | Chi-square | Df | Sig.Values |
|---|---|---|---|
| **1-1** | 6.907 | 8.000 | 0.547 |
| **1-2** | 12.499 | 8.000 | 0.130 |
| **1-3** | 10.436 | 8.000 | 0.236 |
| **2-1** | 6.659 | 8.000 | 0.574 |
| **2-2** | 4.417 | 8.000 | 0.818 |
| **2-3** | 5.268 | 8.000 | 0.729 |
| **3-1** | 3.632 | 8.000 | 0.889 |
| **3-2** | 6.021 | 8.000 | 0.645 |
| **3-3** | 7.418 | 8.000 | 0.492 |



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**Table 5: Logistic Regression Results for Transition (1,1)**

| Variables | B | S.E | WALD | Df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | .976 | .602 | 2.634 | 1 | .105 | 2.655 | .816 | 8.635 |
| Age | .005 | .013 | .179 | 1 | .672 | .995 | .970 | 1.020 |
| FirstCD4(1) | .257 | .379 | .461 | 1 | .497 | 1.293 | .615 | 2.719 |
| PROPHYLAXIX(1) | .208 | .736 | .080 | 1 | .777 | 1.232 | .291 | 5.209 |
| PROPHYLAXIX(2) | -17.295 | 28376.388 | .000 | 1 | 1.000 | .000 | .000 | . |
| Constant | -3.825 | .621 | 37.982 | 1 | .000 | .022 | | |

**Table 6: Binary Logistic Regression Results for Transition (1,2)**

| Variables | B | S.E | WALD | Df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | -.629 | .315 | 3.997 | 1 | .046 | .533 | .288 | .988 |
| Age | .003 | .004 | .558 | 1 | .455 | 1.003 | .995 | 1.011 |
| FirstCD4(1) | .164 | .119 | 1.902 | 1 | .168 | 1.178 | .933 | 1.486 |
| PROPHYLAXIX(1) | -.022 | .268 | .007 | 1 | .934 | .978 | .579 | 1.652 |
| PROPHYLAXIX(2) | .974 | 1.416 | .473 | 1 | .491 | 2.649 | .165 | 42.525 |
| Constant | -1.179 | .197 | 35.772 | 1 | .000 | .307 | | |

**Table 7: Binary Logistic Regression Results for Transition (1,3)**

| Variables | B | S.E | WALD | df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | -16.172 | 4176.183 | .000 | 1 | .997 | .000 | .000 | . |
| Age | -.002 | .024 | .004 | 1 | .949 | .998 | .953 | 1.046 |
| PROPHYLAXIX(1) | .972 | 1.058 | .845 | 1 | .358 | 2.644 | .332 | 21.023 |
| PROPHYLAXIX(2) | -15.909 | 28314.612 | .000 | 1 | 1.000 | .000 | .000 | . |
| FirstCD4(1) | .493 | .785 | .395 | 1 | .530 | 1.637 | .352 | 7.628 |



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| | | | | | | |
|---|---|---|---|---|---|---|
| Constant | -5.503 | 1.215 | 20.526 | 1 | .000 | .004 |

| Variables | B | S.E | WALD | df | Sig | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | 1.298 | .612 | 4.504 | 1 | .034 | .273 | .082 | .905 |
| Age | .015 | .005 | 10.311 | 1 | .001 | 1.016 | 1.006 | 1.025 |
| PROPHYLAXIX(1) | -.202 | .348 | .338 | 1 | .561 | .817 | .413 | 1.616 |
| PROPHYLAXIX(2) | 1.667 | 1.416 | 1.386 | 1 | .239 | 5.297 | .330 | 85.011 |
| FirstCD4(1) | .167 | .146 | 1.304 | 1 | .253 | 1.182 | .887 | 1.574 |
| Constant | -2.382 | .243 | 95.917 | 1 | .000 | .092 | | |

**Table 8: Binary Logistic Regression Results for Transition (2,1)**

| Variables | B | S.E | WALD | df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | -.311 | 1.229 | .064 | 1 | .800 | .733 | .066 | 8.151 |
| Age | -.022 | .023 | .961 | 1 | .327 | .978 | .935 | 1.023 |
| PROPHYLAXIX(1) | -16.230 | 4621.740 | .000 | 1 | .997 | .000 | .000 | . |
| PROPHYLAXIX(2) | -16.134 | 28078.116 | .000 | 1 | 1.000 | .000 | .000 | . |
| FirstCD4(1) | .677 | .768 | .777 | 1 | .378 | 1.967 | .437 | 8.855 |
| Constant | -4.576 | 1.123 | 16.612 | 1 | .000 | .010 | | |

**Table 9: Binary Logistic Regression Results for Transition (2,2)**

| Variables | B | S. E | WALD | df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | -14.894 | 4158.198 | .000 | 1 | .997 | .000 | .000 | . |
| Age | .023 | .026 | .781 | 1 | .377 | 1.023 | .972 | 1.077 |
| PROPHYLAXIX(1) | -15.806 | 4593.520 | .000 | 1 | .997 | .000 | .000 | . |
| PROPHYLAXIX(2) | -15.919 | 28155.022 | .000 | 1 | 1.000 | .000 | .000 | . |
| FirstCD4(1) | -.549 | .733 | .561 | 1 | .454 | .578 | .137 | 2.428 |
| Constant | -6.014 | 1.306 | 21.194 | 1 | .000 | .002 | | |

**Table 10: Binary Logistic Regression Results for Transition (2,3)**



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**Table 11: Binary Logistic Regression Results for Transitions (3,1)**

| Variables | B | S.E | WALD | df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | 0.236 | 0.246 | 0.922 | 1 | 0.037 | 1.267 | 0.782 | 2.053 |
| Age | 0.008 | 0.004 | 5.309 | 1 | 0.021 | 0.992 | 0.984 | 0.999 |
| PROPHYLAXIX(1) | -0.078 | 0.239 | 0.107 | 1 | 0.744 | 0.925 | 0.579 | 1.477 |
| PROPHYLAXIX(2) | 21.134 | 28411.24 | 0 | 1 | 0.999 | 0 | 0 | . |
| FirstCD4(1) | -0.206 | 0.105 | 3.866 | 1 | 0.049 | 0.814 | 0.663 | 0.999 |
| Constant | 0.379 | 0.177 | 4.596 | 1 | 0.032 | 1.461 | | |

**Table 12: Binary Logistic Regression Results for Transitions (3,2)**

| Variables | B | S.E | WALD | df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | 1.129 | .477 | 5.611 | 1 | .018 | 3.093 | 1.215 | 7.874 |
| Age | -.010 | .011 | .866 | 1 | .352 | .990 | .970 | 1.011 |
| PROPHYLAXIX(1) | .752 | .485 | 2.397 | 1 | .122 | 2.120 | .819 | 5.489 |
| PROPHYLAXIX(2) | -17.713 | 28407.073 | .000 | 1 | 1.000 | .000 | .000 | . |
| FirstCD4(1) | .058 | .294 | .038 | 1 | .845 | 1.059 | .595 | 1.885 |
| Constant | -3.116 | .500 | 38.858 | 1 | .000 | .044 | | |

**Table 13: Binary Logistic Regression Results for Transitions (3,3)**

| Variables | B | S. E | WALD | df | Sig. | Exp(B) | Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% C.I. for EXP(B) | |
| Regimen(1) | .087 | .894 | .009 | 1 | .923 | 1.090 | .189 | 6.290 |
| Age | -.018 | .017 | 1.204 | 1 | .272 | .982 | .950 | 1.014 |
| PROPHYLAXIX(1) | .633 | .749 | .715 | 1 | .398 | 1.883 | .434 | 8.170 |
| PROPHYLAXIX(2) | -17.026 | 28240.015 | .000 | 1 | 1.000 | .000 | .000 | . |
| FirstCD4(1) | -.888 | .394 | 5.074 | 1 | .024 | .411 | .190 | .891 |
| Constant | -3.024 | .716 | 17.866 | 1 | .000 | .049 | | |



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## DISCUSSION OF FINDINGS

The result of the analysis provided in Section 4 is significant for understanding the HIV disease progression and management and recovery process. The three states of HIV recovery process described in the analysis are commonly used to classify the severity of HIV infection and guide treatment decisions.

Discussion on Descriptive Statistics: The study included a total number of 1,948 people living with HIV (PLHIV) disease within the age range of participants spanning from 5 to 88 years; covering a wide range of age. The mean age of 39.67 years and a standard deviation of 14.180. The study population consisted of 533 males and 1,415 females, which accounts for 27.4% and 72.6% of the PLHIV (see Table 2). This gender distribution highlights a higher representation of females in the study population. Recognizing gender-specific factors is crucial in designing effective HIV treatment and prevention strategies, as the impact of the disease can vary between genders. Table 3 provides information on the age of participants in the study population. It reveals that most participants (89.5%) were adults aged 25 years or older, while only a smaller proportion (10.5%) comprised pediatric and adolescent patients below 25 years of age. This distribution emphasizes the need for tailored interventions and age-specific healthcare services to address the unique needs and challenges faced by different age groups within the PLHIV population.

Discussion on Transition Matrix (TM): From Equation (14), TM represents the number of patients that moved from one viral load state to the other. For instance, 539 patients transited from viral load not detected ($S_1$) to viral load not detected ($S_1$). This implies that 539 PLHIV who were in state $S_1$ at the beginning of the study maintained their state throughout the period under review. A total number of 45 patients out of 1948 transited from viral not detected ($S_1$) to low-level viremia ($S_2$). Eleven (11) PLHIV who were in state ($S_1$) transited to unsuppressed viral load ($S_3$) This shows that few PLHIV on ART moved from Target not detected ($S_1$) to unsuppressed viral load ($S_3$). During the study review, 311 low level viremia ($S_2$) PLHIV out of a total 1948 PLHIV moved to target not detected ($S_1$) by the end of the study indicating a positive transition, 14 PLHIV low level viremia ($S_2$) maintained their state throughout the study period under review. However, 8 PLHIV with low level viremia ($S_2$) moved to unsuppressed viral load ($S_3$). Furthermore, 924 PLHIV in unsuppressed viral load ( $S_3$) transited to target not detected ($S_1$), which shows a good recovery process. 69 PLHIV unsuppressed viral load ($S_3$) transited to low level viremia ($S_2$) while 27 PLHIV in unsuppressed viral load ($S_3$) remains in the same state.

Based on this result, more people transited from the bad state (unsuppressed state) to the good state (target not detected) and from low level viremia state to target not detected indicating improvement in the recovery process of the patients under antiretroviral therapy. Fewer people transited from the good recovery state (target not detected) to the bad states (unsuppressed viral load), which implies that, despite intervention, there is still need for continuous monitoring and intervention and proper adherence to treatment to prevent transiting to worse state from a good state. This result proves that more PLHIV patients on treatment will have suppressed viral load in-line with Chikobvu and Shoko (2018) study.

Discussion on Transition Probability Matrix ($P_{ij}$): The result in Equation (15) reveals that, a good number PLHIV on ART who were on target not detected ($S_1$) at the beginning of the study remained in the state at the end of the study, with a transition probability of 0.9059. Whereas about 7.56% target not detected ($S_1$) moved to low level viremia, ($S_2$) by the end of the study, with a transition probability of 0.0756 which reviews that few patients have chances of moving from the best recovery state to the worse state. About 1.85% of PLHIV in target not



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detected ($S_1$) transited to unsuppressed viral load ($S_3$) during the study with a transition probability of 0.0185, which also shows how effective the recovery process was, because fewer patients moved from the best state to the worst state. Amongst the PLHIV in low level viremia ($S_2$) at the beginning, 93.39% regressed to target not detected ($S_1$) at the end of the study period under review with a transition probability of 0.9339, while 4.20% of PLHIV in low level viremia ($S_2$) at the beginning of the study maintained their state ($S_2$) throughout the study period, with a transition probability of 0.0420. Only 2.40% of PLHIV in low level viremia ($S_2$) progressed to unsuppressed viral load ($S_3$) during the study period under review, with a transition probability of 0.0240, a good number of about 90.59% unsuppressed viral load patients ($S_3$) at the beginning of the study regressed to target not detected at the end of the study, with a transition probability of 0.9059. About 6.76% of PLHIV in unsuppressed viral load ($S_3$) at the beginning regressed to low level viremia by the end of the study period with a transition probability of 0.0676 and only 2.65% of unsuppressed viral load at the initiation of the study remained in that state throughout the study period, with a transition probability of 0.0265.

Based on the result of the transition probability of the Markov process, it is important to note that the transition probabilities reported in the analysis provide insights into the likelihood of PLHIV moving from one state to another over time. These probabilities can help healthcare professionals develop more targeted interventions to prevent disease progression and improve recovery outcomes. In this study, there is higher chances of recovering from the unsuppressed viral load state to target not detected state or low-level viremia to target not detected.

Discussion on Limiting Distribution ($\pi_j$): From Equation (16), the limiting distribution of the process $\pi_1 = 0.9079$, $\pi_2 = 0.0730$ and $\pi_3 = 0.0190$. This indicates that the chances of a PLHIV who is on ART will transit to target not detected in the long run is 0.9079 irrespective of the state at diagnosis. This implies that, about 90% of patients under ART will live a normal life in the long run in-line with WHO target of 90%, 90%, 90% (Sidibé et al 2016). Which means 90% of HIV patients should be tested, 90% of those tested are placed on treatment and 90% of those on treatment have viral suppression. About 7% will remain in low level viremia and 1% will remain in unsuppressed viral load in the lung-run. This suggests that the system or process is most likely to be in target not detected in the long run, with low level viremia and unsuppressed being less likely to occur.

Discussion on Binary Logistic regression: Tables 4- 13 present results of the Binary Logistic Regression analysis which is used to assess the impact of some risk factors that are associated with the recovery of PLHIV who were enrolled on ART for all pairs of transitions $(i,j); i,j = 1,2,3$. The Hosmer and Lemeshow test in Table 4 is a goodness of fit test that is used to test the null hypothesis that the predicted model does not significantly differ from the observed for all pair of transitions $(i,j); i,j = 1,2,3$. Since the significant values {(1,1) = 0.547, (1,2) = 0.130, (1,3) = 0.2366, (2,1) = 0.574, (2,2) = 0.818, (2,3) = 0.729, (3,1) = 0.889, (3,2) = 0.645, (3,3) = 0.492} in Table 4 are all greater than $\alpha = 0.05$, the null hypothesis is accepted; indicating that the predicted models are not significantly different from the observed models.

Table 5 presents the Binary Logistic Regression Analysis results of factors that are associated with the transition of HIV patients on ART remaining at state 1 (target not detected) throughout the period of study. From the results, Regimen (1) is significant with Significant -value = 0.046 , $B = -0.629$, Wald Statistic = 3.997, Significant-value = 0.046, $Exp(B)$ (odds ratio) = 0.533. This implies that Regimen (1) has significant effect on HIV patients who were in state 1 (target not detected) at the commencement of ART remaining at the same state at the



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end of the study period. The coefficient for Regimen (1) indicates a negative relationship with the log-odds of the outcome. The odds ratio suggests that being in Regimen 1 (TDF-3TC-DTG) is associated with a 73% reduction in the odds of the outcome compared to the reference category.

Table 6 presents the Binary Logistic Regression Analysis results of factors that are associated with the transition of HIV patients from state 1 (target not detected) to state 2 (low level viremia). From the results, there is not a significant risk factor at the pair of transition (1,2). Table 7 presents the Binary Logistic Regression Analysis results of factors that are associated with the transition of HIV patients from state 1 (target not detected) to state 3 (unsuppressed viral load). The results show that there are no significant risk factors at the pair of transition (1,3).

Table 8 presents the Binary Logistic Regression results of factors which are associated with the transition of HIV patients on ART from State 2 (Low level viremia) to State 1 (target not detected). From the results Regimen (1) is significant with $B = 1.298$, Wald Statistic = 4.504, Significant value = 0.034, $Exp(B)$ (odds ratio) = 0.273. This is an indication that Regimen (1) has a significant effect on the transition of HIV patients from State 2 (Low level viremia) to state 1 (target not detected). The coefficient for Regimen (1) indicates a positive relationship with the log-odds of the outcome. The odds ratio indicates that, in comparison to the reference group, being in Regimen 1 is linked to a 73% decrease in the probabilities of the outcome. Wald Statistic = 10.311, significant value = 0.001, and odds ratio = 1.016 indicate that age is also significant. According to the age coefficient, the log-odds of the outcome slightly increase for every unit rise in age. With every incremental year of age, the probabilities of the outcome appear to increase by 1.6%, according to the odds ratio of 1.016.

Table 9 presents the Binary Logistic Regression Analysis results of factors that are associated with the transition of HIV patients on ART from State 2 (low level viremia) to State 2 (low level viremia). From the results, there are no significant risk factors at the pair of transition (2,2). Table 10 presents the Binary Logistic Regression Analysis results of factors that are associated with the transition of HIV patients on ART from State 3 (unsuppressed viral load) to State 1 (target not detected). The results indicate that there are no significant risk factors at the pair of transition (2,3).

Table 11 presents the Binary Logistic Regression Analysis results of factors which are associated with the transition of HIV patients who were on ART from State 3 (Unsuppressed viral load) to State 1 (target not detected). From the results in Table 11, Regimen is significant with $B = 0.236$, Wald Statistic = 0.922, Significant value = 0.033, $Exp(B)$ (odds ratio) = 1.267. The coefficient for Regimen (1) indicates a positive relationship with the log-odds of the transitions. The result is statistically significant (p-value = 0.033), indicating that Regimen (1) has a significant effect on the recovery process of HIV patients.
Age is also significant with $B = 0.008$, Wald Statistic = 5.309, Signficant-value = 0.021, $Exp(B)$ (odds ratio) = 0.992. The coefficient for Age indicates that for every one-unit increase in age, the log-odds of the outcome increase slightly. The odds ratio of 0.992 suggests a 0.8% reduction in the odds of the outcome for each additional year of age. This effect is statistically significant (p-value = 0.021), meaning that age significantly affects the transitions. FirstCD4 (1) is significant with $B = 0.105$, Wald Statistic = 1.000, p-value = 0.049, $Exp(B)$ (odds ratio) = 0.814. The coefficient for FisrtCD4(1) indicates a positive relationship with the log-odds of the transitions. The odds ratio suggests that being in FirstCD4 >200 is associated with a 10.5% reduction in the odds of the outcome compared to the reference category. The result is



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statistically significant (significant value = 0.049), indicating that FisrtCD4(1) has a significant effect on the recovery process of HIV patients.

Table 12 presents the Binary Logistic Regression Analysis results to assess the factors which are associated with the transition of HIV patients who were on ART from State 3 (Unsuppressed viral load) to State 2 (Low level viremia). Table 12 shows that Regimen (1) is significant with $B = 1.129$, Wald Statistic = 5.611, p-value 0.018, $Exp(B)$ (odds ratio) = 3.093. The coefficient for Regimen (1) indicates a positive relationship with the log-odds of the transitions. The odds ratio is 3.093, meaning that for individuals on this regimen, the odds of the outcome are approximately 3 times higher compared to the reference category. The result is statistically significant (significant value = 0.033), indicating that Regimen (1) has a significant effect on the recovery process of HIV patients.

Table 13 presents the Binary Logistic Regression Analysis results to assess the factors which are associated with the transition of HIV patients who were on ART from State 3 (Unsuppressed viral load) to State 3 (Unsuppressed viral load). The results show that FirstCD4 is significant with $B = 0.888$, Wald Statistic = 5.074, Significant value = 0.024, $Exp(B)$ (odds ratio) = 0.411 The regression analysis shows that FirstCD4 has a statistically significant effect on the transition or persistence of HIV patients in State 3 (unsuppressed viral load). Specifically, higher FirstCD4 counts are associated with a 58.9% reduction in the odds of remaining in the unsuppressed viral load state, indicating that patients with better initial immune status (as measured by CD4 count) are more likely to progress toward viral suppression. This is a statistically significant result, as indicated by the p-value of 0.024, demonstrating a meaningful impact of the initial CD4 count on viral load outcomes.

## CONCLUSION

The study provided valuable insights into HIV disease progression and recovery. The classification of HIV progression into three states is relevant for guiding treatment decisions and assessing the severity of infection. The study had a substantial sample size (1,948 individuals), representing a diverse range of ages (5 to 88 years). Understanding the age distribution of the study population is crucial for tailoring interventions and healthcare services to meet the specific needs of different age groups. The gender distribution in the study population shows a higher representation of females (72.6%) compared to males (27.4%). This emphasizes the importance of considering gender-specific factors in HIV treatment and prevention strategies.

The transition probabilities between different states of HIV progression highlight the effectiveness of antiretroviral therapy. The majority of PLHIV in the study remained at target not detected throughout the study period, which shows the effectiveness of antiretroviral therapy in the management of HIV cases. However, a significant few proportions progressed to low level viremia, indicating the need for continuous monitoring and sensitization. The limiting distribution of the Markov Process suggests that the system is most likely to remain in state 1 in the long run, followed by state two and State three. The binary logistic regression model reveals that regimen, age, and baseline CD4 >200 are the dominant risk factors influencing HIV patient recovery.

## RECOMMENDATIONS

Based on the result of the research work, the following recommendations were made:



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1. It is recommended that healthcare professionals focus on diagnosis and initiation of antiretroviral therapy for people living with HIV (PLHIV) to prevent disease progression.
2. Ongoing monitoring and management are crucial, particularly for PLHIV in unsuppressed and low-level viremia patients to enable them attain target not detected
3. Healthcare professionals should also pay close attention to PLHIV in unsuppressed patients, who have a high probability of remaining in this state and develop appropriate interventions to manage their condition effectively.
4. Since the study found that age, regimen, and baseline CD4 count were statistically significant factors influencing transitions between recovery states, interventions targeted towards these specific factors will be more effective in managing the disease and improving patient recovery outcomes.

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