

Statistical Modelling of Disease Progression among HIV-Infected Patients on Antiretroviral Therapy at Howard Opportunistic Infection Clinic

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ABSTRACT

Background: Sustaining high rates of adherence to antiretroviral therapy (ART) is critical to suppressing HIV viral replication, delaying disease progression, and improving survival. While prior research indicates that treatment adherence and mortality patterns vary across demographic factors such as marital status, the specific differential trajectories of immunologic indicators and clinical disease progression between married and non-married patients remain under-investigated in sub-Saharan Africa. This study evaluated patterns of change in immunologic markers (CD4+ T-cell count) and clinical parameters (haemoglobin and weight) over time according to marital status among HIV-infected adults initiating ART.

Methods: A retrospective cohort study was conducted utilizing longitudinal clinical records from 143 adult HIV-infected patients (each with at least 3 longitudinal waves of data across baseline, 3, 6, and 12 months) initiating ART at Howard Mission Hospital Opportunistic Infection (OI) Clinic in Mashonaland Central, Zimbabwe. Independent sample t-tests and Wilcoxon rank-sum tests were used for baseline group comparisons. Longitudinal trajectory modelling was conducted using Multilevel Random Effects Models and Hierarchical Linear Models (HLM) to evaluate within-individual and between-group changes in CD4 counts. Model selection was guided by the minimum Akaike Information Criterion (AIC).

Results: At ART initiation, 77.6% (n=111) of participants presented with severe immunosuppression (CD4 <200 cells/ μ L). All male patients (100%) and 57.2% of female patients presented with subnormal haemoglobin levels. Baseline median CD4 count was significantly higher among non-married patients compared to married patients (119 cells/ μ L vs. 82 cells/ μ L, $p=0.006$). Both groups exhibited significant immune reconstitution over 12 months, with median CD4 count increases exceeding 50 cells/ μ L at 6 months and 150 cells/ μ L at 12 months ($p<0.001$). However, trajectory modelling demonstrated that the rate of CD4 recovery was significantly higher among non-married individuals compared to married individuals. The random effects model provided superior goodness-of-fit (AIC = 7 509.29 vs. 7 510.38). In the random effects specification, non-married patients achieved an expected monthly CD4 count increase of 116.09 cells/ μ L over baseline (slope = +116.09, $p<0.001$), whereas married status was associated with a negative relative coefficient adjustment (-153.74 cells/ μ L, $p<0.001$).

Conclusion: Significant immunologic recovery occurs following ART initiation, but trajectories differ markedly by marital status. Non-married patients demonstrated superior CD4 T-cell recovery compared to married patients. These findings highlight the necessity of integrating psychosocial and marital dynamics into ART monitoring frameworks, targeted counselling, and adherence support interventions to optimize long-term clinical outcomes.

Keywords: Antiretroviral Therapy (ART); CD4 Lymphocyte Trajectory; Statistical Modelling; Random Effects Model; Hierarchical Linear Model; Marital Status; HIV Disease Progression; Zimbabwe.

Background

Acquired Immune Deficiency Syndrome (AIDS), caused by the Human Immunodeficiency Virus (HIV), remains a global public health challenge, with sub-Saharan Africa carrying two-thirds of the global burden. The pathogenesis of HIV infection is defined by the progressive depletion of cluster of differentiation 4 (CD4)-positive T-helper lymphocytes, leading to severe immunodeficiency, heightened vulnerability to opportunistic infections (OIs), and accelerated mortality. The primary goals of Antiretroviral Therapy (ART) are to suppress viral replication, facilitate quantitative and qualitative immunological reconstitution, reduce morbidity, and prolong survival.

In Zimbabwe, national scale-up of ART began in 2004 across public and mission health facilities. Clinical monitoring of ART response relies heavily on surrogate markers, including absolute CD4⁺ T-cell count, haemoglobin levels, and body weight dynamics. On average, successful ART initiation in treatment-naïve patients yields an expected CD4 T-cell increase of approximately 50 cells/ μ L within the first 6 months and at least 150 cells/ μ L by 12 months. Failure to achieve these thresholds signifies immunological failure and heightened disease progression risk.

While the clinical efficacy of ART regimens is well established, long-term therapeutic success depends strictly on high medication adherence (typically $\geq 95\%$). Previous epidemiological studies present conflicting observations regarding the influence of demographic factors—specifically marital status—on HIV outcomes. Certain behavioral studies have reported higher ART adherence rates among single, divorced, or widowed individuals compared to married or cohabiting couples (OR = 1.79, $p = 0.028$)^[5,7]. Conversely, epidemiological survival analyses frequently document lower overall mortality rates among married individuals compared to non-married counterparts^[6].

Despite these conflicting observations regarding adherence and mortality, there is a critical gap in longitudinal research evaluating whether actual patterns of immunologic recovery (CD4 trajectories) and clinical indicator changes over time differ significantly by marital status. Understanding these longitudinal trajectories is vital for tailoring clinical monitoring, adherence support, and psychosocial care. Therefore, this study aimed to model and compare the longitudinal change in CD4 T-cell counts and clinical parameters among HIV-infected patients initiating ART at Howard Mission Hospital OI Clinic in Zimbabwe using Multilevel Random Effects and Hierarchical Linear Modelling (HLM) techniques.

METHODS

Study Design and Setting

A retrospective longitudinal cohort study was conducted using secondary clinical records from the Salvation Army Howard Mission Hospital Opportunistic Infection (OI) Clinic, situated in Mazowe District, Mashonaland Central Province, Zimbabwe. Howard Hospital serves a catchment population across 30 rural wards and commercial farming estates, providing comprehensive HIV care, cotrimoxazole prophylaxis, and ART services.

Study Population and Eligibility Criteria

The study population comprised adult HIV-infected patients (aged ≥ 15 years) who were initiated on first-line ART at Howard OI Clinic between January 2007 and December 2008. To enable longitudinal trajectory analysis, inclusion was restricted to patients who had completed at least three longitudinal waves of clinical and immunologic measurements across four scheduled observation points: baseline (ART initiation), 3 months, 6 months, and 12 months follow-up. Out of 991 patients initiated on ART during the study timeframe, 143 met all eligibility criteria and were included in the final analytical sample.

Variables and Measurement

The primary dependent variable was the absolute CD4⁺ T-helper lymphocyte count (cells/ μ L), measured at baseline and follow-up intervals. Secondary clinical outcomes included haemoglobin level (g/dL) and body weight (kg). The main predictor variable was marital status, categorized as married vs. non-married

(encompassing single, divorced, and widowed individuals). Key demographic and clinical covariates included age, sex, World Health Organization (WHO) clinical stage (Stages I–IV), and time since ART initiation (measured in months).

Statistical Analysis

Data management and statistical analyses were performed using SPSS, STATA, and HLM v6.08 software. Continuous baseline parameters were summarized using means, standard deviations (SD), medians, and interquartile ranges (IQRs). Between-group baseline comparisons across marital status and sex were conducted using independent sample t-tests and Wilcoxon rank-sum tests for continuous variables, and Pearson's chi-square tests for categorical variables. Immunologic response over time was evaluated by computing median CD4 count changes at 6 and 12 months.

Longitudinal Trajectory Modelling: To model longitudinal trajectories of CD4 count and account for repeated measures nested within individual patients, two multilevel modelling approaches were specified:

1. Hierarchical Linear Model (HLM): a two-level linear model where Level-1 captured within-individual repeated measurements over time, and Level-2 evaluated inter-individual differences in growth trajectories as a function of marital status.
2. Multilevel Random Effects Model: a random-intercept and fixed-slope/covariate model accounting for variance components and within-subject auto-correlation.

Model goodness-of-fit was assessed using the deviance statistic (–2 restricted log-likelihood), Akaike Information Criterion (AIC), and Bayesian Information Criterion (BIC), where the minimum AIC indicated the optimal empirical fit. Model diagnostics were conducted by evaluating Level-1 and Level-2 residuals using box-and-whisker distribution plots and residual-versus-predicted scatter plots to assess normality, linearity, and homoscedasticity assumptions.

Ethical Considerations

Institutional permission to utilize anonymised clinical database records was granted by the Chief Medical Officer of Howard Hospital (Dr Paul Thistle). Confidentiality was strictly maintained by anonymising all personal identification details and utilizing unique OI/ART registration codes.

RESULTS

Baseline Demographic and Clinical Characteristics

Among the 143 analyzed patients, 63.6% (n=91) were female and 36.4% (n=52) were male. Overall, 40.6% of participants were married and 59.4% were non-married (including 11.2% divorced and widowed). Among male participants, 59.6% were married, compared to only 29.7% of female participants (p<0.05). At ART initiation, 70.3% of female participants belonged to the non-married category.

Table 1. Baseline clinical and immunologic characteristics of the study cohort (N = 143)

Variable	Category	N (%)
Haemoglobin, females (n=91)	<12.0 g/dL (low)	52 (57.2%)
	12.0–16.0 g/dL (normal)	17 (18.7%)
	>16.0 g/dL (high)	22 (24.2%)
Haemoglobin, males (n=46*)	<14.0 g/dL (low)	46 (100.0%)
	14.0–18.0 g/dL (normal)	0 (0.0%)
	>18.0 g/dL (high)	0 (0.0%)

Baseline CD4+ cell count (n=143)	<200 cells/ μ L (severe risk)	111 (77.6%)
	200–500 cells/ μ L (moderate risk)	24 (16.8%)
	>500–600 cells/ μ L (low risk)	8 (5.6%)
	>600–1200 cells/ μ L (normal range)	5 (3.5%)
WHO clinical stage (n=143)	Stage I	49 (34.3%)
	Stage II	30 (21.0%)
	Stage III	51 (35.8%)
	Stage IV	13 (8.9%)
Median baseline CD4 count	Overall cohort	104 cells/ μ L (IQR: 53–168)
Median baseline haemoglobin	Overall cohort	11.0 g/dL (IQR: 10.0–12.2)
Median baseline body weight	Overall cohort	54.0 kg (IQR: 45.0–63.0)

* Six male participants had missing baseline haemoglobin records (n=46 of 52 with data). † Author to verify: the four baseline CD4 categories reported (111 + 24 + 8 + 5 = 148) sum to more than N = 143; please confirm the correct category boundaries and frequencies before submission.

As shown in Table 1, 77.6% (n=111) of patients presented with CD4 counts below 200 cells/ μ L at ART start, and only 3.5% (n=5) initiated ART with normal CD4 counts (>600–1200 cells/ μ L). Anaemia was highly prevalent at baseline: 100% of males had haemoglobin levels below 14.0 g/dL, while 57.2% of females presented with haemoglobin below 12.0 g/dL.

Baseline Comparisons by Marital Status and Sex

Table 2 presents the cross-tabulation and mean/median comparisons of baseline clinical parameters stratified by marital status.

Table 2. Baseline clinical and immunologic parameter comparisons by marital status

Parameter	Married (n=58)	Non-married (n=85)	p-value
CD4 <200 cells/ μ L, n (%)	49 (84.5%)	62 (72.9%)	0.122
CD4 >500 cells/ μ L, n (%)	0 (0.0%)	8 (9.4%)	0.016*
Median baseline CD4 count (IQR)	82 cells/ μ L (42–133)	119 cells/ μ L (68–217)	0.006*
Median baseline haemoglobin (IQR)	10.8 g/dL (10.5–12.1)	11.1 g/dL (9.9–12.3)	0.617
Median baseline weight (IQR)	56.0 kg (52.0–63.5)	50.0 kg (32.0–60.0)	<0.001*

* Statistically significant at $p < 0.05$.

Non-married patients presented with significantly higher baseline median CD4 counts compared to married patients (119 vs. 82 cells/ μ L, $p = 0.006$). Additionally, 9.4% of non-married patients presented with CD4 >500 cells/ μ L compared to 0% of married patients ($p = 0.016$). Conversely, married patients exhibited significantly higher baseline body weight (56.0 kg vs. 50.0 kg, $p < 0.001$). Baseline haemoglobin levels did not differ significantly by marital status. Comparisons across sex revealed no statistically significant baseline differences in CD4 count ($p = 0.163$), haemoglobin ($p = 0.242$), or weight ($p = 0.599$).

Immunologic Response to Treatment Over 12 Months

Immunologic recovery was evaluated by changes in median CD4 count from baseline to 6 and 12 months follow-up.

Table 3. Longitudinal CD4 T-cell count response at 6 and 12 months by marital status

Marital status	Baseline median CD4 (IQR)	6-month median CD4 (IQR)	12-month median CD4 (IQR)
Non-married	119 cells/ μ L (68–217)	229.5 cells/ μ L (106–396)*	288.0 cells/ μ L (168–474)*
Married	82 cells/ μ L (47–133)	150.0 cells/ μ L (73–292)*	207.0 cells/ μ L (144–439)*

* Statistically significant increase from baseline ($p < 0.001$).

Both marital groups achieved statistically significant CD4 count increases exceeding 50 cells/ μ L at 6 months and 150 cells/ μ L at 12 months ($p < 0.001$). However, absolute CD4 reconstitution was consistently higher among non-married patients, reaching a median of 288.0 cells/ μ L at 12 months, compared to 207.0 cells/ μ L among married patients (Table 3).

Statistical Trajectory Modelling and Model Comparison

To compare individual CD4 trajectories over time by marital status, Hierarchical Linear Models and Multilevel Random Effects Models were fitted.

Table 4. Statistical model parameter estimates and goodness-of-fit comparison

Model component / variable	HLM	Multilevel random effects model	p-value
Intercept (base non-married CD4)	129.38 (SE: 36.00)	157.74 (SE: 50.31)	<0.005*
Time coefficient (per wave/month)	+112.28 (SE: 9.05)	+116.09 (SE: 13.23)	<0.001*
Marital status (married vs. non-married)	−136.76 (SE: 45.41)	−153.74 (SE: 29.86)	<0.005*
Level-1 residual variance, $\text{Var}(e_{ij})$	324.10 (SE: 10.04)	322.54 (SE: 10.02)	—
Level-2 random intercept, $\text{Var}(u_{0j})$	—	48.81	—
Intraclass correlation (ICC)	0.478 (47.8%)	—	—
Model R-squared	11.5%	—	—
Log-likelihood	−3 757.19	−3 750.65	—
LR test chi-square	101.39	96.16	<0.001*
Akaike Information Criterion (AIC)	7 510.38	7 509.29 (min AIC)	Best fit
Bayesian Information Criterion (BIC)	7 527.41	7 526.31	Best fit

* Statistically significant at $p < 0.05$.

Model comparison (Table 4) based on the minimum AIC criterion established the Multilevel Random Effects Model as the optimal fitting model (AIC = 7 509.29 vs. 7 510.38 for HLM). Under the random effects model, the mathematical trajectory equation for CD4 cell count is specified as:

$$\text{CD4}(t) = 157.74 - 153.74 \times (\text{Marital Status}) + 116.09 \times (\text{Time})$$

In this model, non-married status serves as the reference group, exhibiting an expected baseline CD4 count of 157.74 cells/ μ L and a positive monthly slope of +116.09 cells/ μ L per time unit. Being married was associated with a statistically significant negative relative shift (−153.74 cells/ μ L, $p < 0.001$), indicating that married patients experienced a substantially suppressed rate of CD4 count recovery over time compared to non-married patients.

Model Diagnostics

Model diagnostic evaluation of Level-1 residuals for the random effects model via box-and-whisker plots demonstrated an approximately symmetric, normal residual distribution with minor right-skewness attributable

to a subset of patients achieving high CD4 recovery (>600 – 1200 cells/ μ L). Scatter plots of Level-1 predicted values against residuals showed random scatter without systemic curvature, confirming satisfactory compliance with linear mixed-modelling assumptions.

DISCUSSION

This longitudinal study evaluated clinical parameters and CD4 T-cell recovery trajectories over 12 months of ART among HIV-infected adults in rural Zimbabwe. The key empirical finding is that while both married and non-married patients achieve statistically significant immunologic reconstitution following ART initiation, non-married patients demonstrate a significantly higher rate of CD4 recovery over time compared to married patients.

At ART initiation, 77.6% of patients presented with severe immunodeficiency ($CD4 < 200$ cells/ μ L), reflecting delayed presentation and clinical entry into care typical of sub-Saharan African settings during the early ART expansion era. Furthermore, baseline anaemia was universal among male patients (100%) and highly prevalent among females (57.2%). Lower baseline CD4 count and low haemoglobin are established independent predictors of mortality and opportunistic disease progression.

The observed superior CD4 recovery trajectory among non-married patients aligns with previous behavioral literature reporting higher ART adherence rates among single, divorced, or widowed individuals^[5, 7]. In rural settings, non-married individuals who disclose their status and enter care may experience greater personal autonomy over medication schedules, fewer obstacles related to intra-spousal stigma, and direct engagement with health services. Conversely, married individuals—particularly women—may face complex partner dynamics, fear of status disclosure, gender power imbalances, and economic dependency that hinder consistent daily adherence.

However, these findings stand in contrast to epidemiological survival studies that report lower overall mortality rates among married adults^[6]. This apparent paradox between immunological recovery rate and overall survival may stem from misclassification of non-HIV causes of death in general population mortality studies, or residual social support benefits in married households that protect against non-disease clinical decline despite lower CD4 recovery slopes.

Study Limitations

Several limitations should be considered. First, this study relied on secondary retrospective clinical records, leading to missing data for secondary markers (such as viral load and serial haemoglobin). Second, inclusion was restricted to patients with at least three longitudinal waves of data, which may introduce survivor bias by excluding individuals who died or were lost to follow-up within the first 3 months of ART initiation. Third, specific behavioral metrics such as self-reported adherence scores and household income were not systematically recorded in the primary clinical database.

CONCLUSIONS

In conclusion, longitudinal trajectory modelling demonstrates that HIV-infected patients initiating ART achieve substantial immunologic recovery, but the rate of CD4 T-cell recovery is significantly higher among non-married patients compared to married patients. Multilevel random effects modelling provided superior empirical fit for capturing these longitudinal trajectory differences. These results emphasize the need for clinical HIV programmes to integrate psychosocial assessment and household dynamics into routine ART care. Interventions should include targeted couple counselling, strategies for safe spousal disclosure, and structured adherence support for married individuals to eliminate disparities in immunologic recovery and optimize long-term clinical outcomes.

Declarations

Ethics Considerations and Consent to Participate: Not applicable. Secondary analysis of fully anonymised, routine clinical registry data.

Consent for Publication: Not applicable. The manuscript contains no individual person's identifiable data or images.

Data Availability and Materials: The datasets analyzed during the current study are available from the corresponding author upon reasonable request and with permission of Howard Mission Hospital.

Conflict of Interest: The authors declare no conflicts of interest.

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Author Contributions: RM conceptualised the study, managed the data, performed statistical trajectory modelling, interpreted the results, and drafted the manuscript. PM Data Curation, Validation, Writing – review & editing. All authors contributed to the article and approved the submitted version.

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