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# Treatment Discontinuation in Adult HIV-Infected Patients on First-Line Antiretroviral Therapy in Nigeria

**OO Agbaji**[1], **IO Abah**[*,2], **KD Falang**[3], **AO Ebonyi**[4], **J Musa**[5], **P Ugoagwu**[6], **PA Agaba**[7], **AS Sagay**[5], **T Jolayemi**[8], **P Okonkwo**[8], **JA Idoko**[9], **Phyllis Kanki**[10]

[1]Department of Medicine, University of Jos/Jos University Teaching Hospital, Jos, Nigeria.

[2]Pharmacy Department, Jos University Teaching Hospital, Jos, Nigeria.

[3]Department of Pharmacology, Faculty of Pharmaceutical Sciences, University of Jos, Nigeria.

[4]Department of Paediatrics, University of Jos/Jos University Teaching Hospital, Jos, Nigeria.

[5]Department of Obstetrics and Gynaecology, University of Jos/Jos University Teaching Hospital, Jos, Nigeria.

[6]Jos University Teaching Hospital, AIDS Prevention Initiative in Nigeria (APIN) Ltd./Gte.-Supported HIV Centre, Jos, Nigeria.

[7]Department of Family Medicine, University of Jos/Jos University Teaching Hospital, Jos, Nigeria.

[8]AIDS Prevention Initiative in Nigeria (APIN) Ltd./Gte., Abuja, Nigeria.

[9]National Agency for the control of AIDS (NACA), Abuja, Nigeria.

[10]Harvard School of Public Health, Boston, MA, USA.

## Abstract

**Background:** Retention in care and treatment services is critical to health outcomes of individuals diagnosed and living with HIV. We evaluated the incidence of and risk factors for treatment discontinuation (TD) in a large adult HIV population on ART in Nigeria.

**Method:** A retrospective cohort study of adult HIV patients initiated on first-line ART between 2004 and 2011 at the Jos University Teaching Hospital (JUTH) in Nigeria. Follow up information of participants was retrieved from various sources (patient visit database, pharmacy data and patients charts) up to the end of 2012.The primary study endpoint was TD, defined as discontinuation of ART for any reason, including death or loss to follow-up (lack of pharmacy pick-up for periods ≥12 months). The Incidence and hazard for TD were estimated by Kaplan-Meier and Cox proportional regression analysis, respectively.

**Result:** Overall, 3,362 (28%) patients discontinued treatment during 49,436 person-years (py) of follow-up (incidence rate (IR) 6.8 TD per 100 py). The hazard of treatment discontinuation decreased with increasing age (adjusted hazard ratio (aHR 0.99; 95% CI 0.98 – 0.99). Other independent risk factor for treatment discontinuation were: being unmarried (aHR 1.24; 95% CI: 1.12–1.38), having primary or secondary level of education as compared to tertiary level education

[*]Corresponding: Isaac Abah: isaacabah@gmail.com, Phone: +234 803 703 5932.

(aHR 1.24; 95% CI: 1.12–1.40) and average percent adherence to drug refill visits <95% (adjusted hazard ratio (aHR) 2.13; 95% CI: 1.9–2.40). Compared to tenofovir, greater hazard of TD was noted in patients initiated on ART containing didanosine (aHR) 1.73; 95% CI: 1.03–2.91), but lower in those initiated on zidovudine containing regimen (aHR 0.77; 95% CI: 0.69–0.86).

**Conclusion:** Long-term treatment discontinuation rate in this study was comparable to estimates in resource-rich countries. Younger patients, as well as patients with lower educational levels and those with poor adherence had significant hazards for treatment discontinuation and should be the target of interventions to reduce treatment discontinuation and improve retention, especially within the first year of ART.

### Keywords

Treatment discontinuation; Loss to follow-up; HIV; ART; Nigeria

## Introduction

Global efforts in scaling up antiretroviral therapy (ART) services have resulted in a dramatic increase in the number of people accessing treatment in sub-Saharan Africa (SSA), with about 7.5 million people on treatment by 2012.[1]Retention in care and treatment services is critical to health outcomes of individuals diagnosed and living with HIV.[2]

The benefits of ART are well documented, including reduction in morbidity and mortality, improved life expectancy, and reduction in HIV transmission.[3–6]Once life-long ART is initiated, a sustained high level of adherence is required to maximize the life-extending benefits of ART.[7–8] Upon interruption for any reason, the benefits of ART are rapidly reversed, resulting in poorer health outcomes, increased HIV transmission, and emergence of drug resistance, with consequent treatment failure and need for more expensive and difficult-to-implement second-line regimens.[9–10] Discontinuation of treatment may constitute wastage of scarce treatment resources and negates much of the benefit sought by implementing treatment programs.

Discontinuation of ART or attrition from antiretroviral treatment programs may be attributed to different causes including: death of the patient, “loss to follow-up”; a general category for patients who miss scheduled clinic appointments or medication pickups for a specified period of time stopping antiretroviral medication while remaining in care, and transfer to other facilities to continue on ART.[11]

The magnitude and determinants of treatment discontinuation varies substantially across programs and settings. Understanding the magnitude of the problem can help programs to evaluate the effectiveness of ART services and identify opportunities for improvement. Retention on ART potentially takes on an even more important role in Africa than in industrialized settings as the vast majority of HIV-infected people live in SSA where there has been a rapid scaling up of ART services over the past decade.[1]

This study assessed the incidence of and hazard for treatment discontinuation in a large adult HIV cohort receiving ART in Jos, Nigeria.

## Method

### Study design

A retrospective cohort study using one of the largest clinical HIV treatment databases in Nigeria, which includes demographic, clinical, and laboratory data on over 14,000 patients initiated on ART collected as part of routine HIV care. Patients enrolled on ART between 2004 and 2011, were considered eligible for this study. Follow-up was until December 31, 2012 to ensure at least 1-year of follow-up time for evaluation. ART experienced patients and those initiated on triple nucleos(t)ide reverse transcriptase (NRTI) ART were excluded from the analysis. The clinical protocol and use of clinical data for research was approved by the ethical committee at JUTH and the institutional review board (IRB) at Harvard School of Public Health (HSPH), Boston, USA. All patients included in the study provided written informed consent for the use of their data for research.

### Setting and study population

The comprehensive HIV treatment and support program at JUTH, located in North Central Nigeria started in 2002 as part of the Government of Nigeria (GoN) ART initiative. However, in 2004, the collaboration between AIDS Prevention Initiative in Nigeria (APIN) Lte./Gte., HSPH, the University of Jos and JUTH, with support from a United States President's Emergency Plan for AIDS Relief (PEPFAR) grant, led to rapid scale-up of ART services. The JUTH HIV clinic provides comprehensive HIV care services for the city of Jos and serves as a referral centre for health facilities in Plateau State and other states in the region.

### Patient's eligibility and standard of care

Patients included in the study were HIV-1 infected, treatment naïve, adults (15 years and above), initiated on first-line non-nucleoside reverse transcriptase inhibitor (NNRTI)-based ART (an NNRTI plus two NRTIs) between January 2004 and December 2011.The NNRTIs included efavirenz (EFV) and nevirapine (NVP), and NRTIs included abacavir (ABC), zidovudine (AZT), stavudine (d4T), tenofovir (TDF) and didanosine (DDI). Data were extracted from an electronic database (FileMaker Pro, FileMaker, Inc. USA) utilized in the clinic for patient care. ART dispensing occurred monthly and at scheduled clinical visits, and pharmacy pick-up data were documented in the pharmacy database developed for this purpose. Adherence was determined using pharmacy dispensing records over the duration of ARV therapy for each patient. Drug refill adherence which had been previously described [12] was calculated as the total number of days behind schedule for drug refill divided by total number of days the patient was assumed to be exposed to ART given the dispensed number of pills multiplied by 100. Patient tracking was well established in the study setting and employs strategies, such as home visits, telephone calls and support groups.

### Study end points

The primary study endpoint was treatment discontinuation, defined as discontinuation of ART for any reason, including death, loss to follow-up; lack of pharmacy pick-up for periods ≥12 months or no pharmacy pick-up in the calendar year 2012 with efforts at

tracking being done, and self-withdrawal (SW) from ART. Transfer to another ART facility was not regarded as treatment discontinuation; patients who transferred were assumed to still be in care.

### Statistical analysis

All of the analyses were performed using SPSS for windows version 20 (SPSS Inc, Chicago, Illinois, USA). Descriptive analyses included median [interquartile range (IQR)] for continuous variables, and frequencies and proportions for categorical variables. Bi-variate associations of each independent variable with treatment discontinuation were examined using the Pearson's chi-squared test. The medians and interquartile ranges of continuous variables were compared using the Mann Whitney U-test. All tests were two-sided and a p-value of 0.05 was considered significant.

Kaplan-Meier survival analysis was performed using months as the time unit in order to assess the probability of treatment discontinuation among all patients. Observation commenced at first ARV pick-up and observations were censored at the last follow-up date (date of last ARV pick-up or at transfer out to other ART facilities) or at the end of the observation period, which was pre-defined as December 31, 2012. Total time of observation contributed by each patient was summed to obtain total person-years of observation. Variables associated with treatment discontinuation in bi-variate analysis ($p<0.1$) were included in the Cox regression analysis to adjust for factors associated with treatment discontinuation. To evaluate the contribution of cumulative adherence to treatment discontinuation; given the different time exposure to ART, the multivariate Cox analysis for predictors of treatment discontinuation was performed using separate models with or without the adherence covariate.

## Results

A total of 14,040 adults were enrolled on ART within the study period. Of these patients, a total of 2027 patients consisting of 1820 ART experienced at enrollment and 207 initiated on triple nucleoside reverse transcriptase ART were excluded from the analysis. In all 12,013 eligible patients, with median (IQR) duration on ART of 50 (17–78) months were analyzed (Figure 1). The patients contributed a total of 49,436 person-years (py) of follow-up. Table 1 summarizes patient demographics, and baseline clinical characteristics. The study population was made up of mostly (66%) females, had a median (IQR) age and CD4 cell count of 35 (30–42) years and 145 (72–241) cells/$mm^3$, respectively, at ART initiation.

### Treatment discontinuation:

A total of 3362 patients out of 12013 (28.1%) discontinued treatment [incidence rate (IR) 6.8 treatment discontinuations per 100 person-years (py)]. Treatment discontinuation occurred after a median (IQR) of 12 (4–27) months post ART initiation. The cumulative probability of treatment discontinuation is shown in Figure 2. A total of 1674 patients discontinued treatment within the first year (50% of total discontinuation), giving the first year crude cumulative incidence of 14% for treatment discontinuation. Incidence

of treatment discontinuation showed a steep increase within the first two years of ART initiation compared to subsequent years.

Overall, 25.3% (n= 3038) patients were loss to follow-up (LTFU) (Incidence Rate (IR) 6.1 LTFU per 100 py). LTFU accounted for 90% of the total treatment attrition, while 294 (2.4%) deaths were reported, contributing 8.7% attrition (IR 0.6 deaths per 100 py), and 0.2% (n=33) self-withdrew (SW) from treatment (IR 0.06 SW per 100 py). A total of 1590 (13.2%) patients were transferred to other ART facilities (IR 3.2 transfers per 100 py).

### Predictors of treatment discontinuation:

A bi-variate analysis to evaluate the relationship between baseline demographic and clinical characteristics (Table 1) showed that patients who discontinued treatment had lower median (IQR) age compared to those retained on treatment [34 (29–41) versus 35 (30–42) years, ($p$ =0.03)]. Other factors significantly associated with treatment discontinuation were sex, level of education, marital status, and ART regimen. Patients who initiated treatment between June 2004 and December 2005 had a significantly higher retention on ART (72%) compared to those who initiated treatment between 2006 and 2007 (66 and 68% respectively). However a marked improvement in retention was observed from year 2008 upwards, with retention rate up to 92%. Additionally, we found that initial ART regimen was significantly associated with treatment discontinuation. It was higher in patient initiated on EFV compared to NVP ($P$= 0.001), and lowest in AZT containing regimen compared to ABC, d4T, ddi and TDF ($P$=0.001). After adjusting for confounding variables in the Cox regression analysis (Table 3); unmarried patients had about 24% increased hazard of discontinuing treatment compared to the married. Similarly, compared to those with tertiary education, patients with primary or no formal education, and those with secondary education had 24% higher hazard of treatment discontinuation. The hazard of treatment discontinuation decreased by 1% with every year increase in age. Compared to tenofovir, greater hazard of treatment discontinuation was noted in patients initiated on ART containing didanosine (aHR) 1.73; 95% CI: 1.03–2.91), but lower in those initiated on zidovudine containing regimen (aHR) 0.77; 95% CI: 0.69–0.86).

### Adherence and treatment discontinuation:

Retention on ART increased proportionately with increased adherence to drug refill visits for the entire duration of ART. However the greatest difference was observed at adherence levels ≥95% (Figure 3). When adherence was included in the final multivariate Cox regression model, there was a 2-fold increase in the hazard of treatment discontinuation in patients' with <95% adherence to pharmacy refill visits compared with those with ≥ 95% adherence.

## Discussion

The purpose of this study was to estimate the incidence of and risk factors for treatment discontinuation to ART in our adult HIV treatment program. During the 8.5-year study period about 72% of our initial cohort were retained on ART, suggesting high patient retention in ART programs in our setting. Age, marital status, education, NRTI

backbone and adherence to pharmacy drug refill were significant predictors of treatment discontinuation in our setting.

Our analysis showed a one and two years treatment discontinuation incidence of 14% and 20% respectively comparable to that reported in US cohorts, [13–16] and lower than percentages in other cohorts in SSA where on average of up to 40% discontinuation from treatment have been reported after two years of treatment initiation.[17] Interestingly, over half of the treatment discontinuation in this study occurred within the first year of ART, and by the third year up to 90% of the treatment discontinuation had accrued. Our finding is suggestive of improved retention on ART over time. This finding corroborates with a recent study by Meloni *et al*,[18] which reported that the majority of loss occurs within the first 12–18 months of treatment in the Harvard/APIN PEPFAR program in Nigeria. Other findings from Vietnam, [19] and other African countries,[20–21] have also observed similar trends. The improved retention over time in our program may be due to the robust adherence counseling and overall improvement in HIV care and treatment services instituted as a result of support enjoyed from PEPFAR. Other quality improvement initiatives that might have contributed to improved retention in our program include simplification of patients appointment system, use of electronic database to track and flag missed appointments, enhanced patient tracking through a tracking team, health education, patient tracking, formation of support groups of people living with HIV, and improved laboratory monitoring to identify patients at risk of treatment failure

Of concern in this study is the disposition of patients who discontinued treatment. While mortality accounted for less than 10% of the treatment attrition, the majority of treatment discontinuation was due to loss to follow-up. The findings reported here highlight the importance of further evaluating and improving patient tracking strategies in the program, especially within the first two years of treatment initiation. More efficient and active patient tracking systems are critically needed within ART programs in Nigeria.

Consistent with a number of studies in Western, Eastern, and Southern Africa, [18, 22–23] we observed increased hazard of treatment discontinuation with younger age. Increased risk of treatment discontinuation in younger persons; who constitute the majority of people living with HIV in Nigeria, [1] and those who would have the longest life expectancy on successful ART, underscores the need to urgently identify risk factors for treatment discontinuation in this population. This will help the development of targeted interventions to increase treatment retention among young people.

Lower educational levels were associated with greater risk of treatment discontinuation in our study. Our findings are consistent with reports from Uganda, [23] whereas a study from Kenya found no association between educational status and loss to follow-up.[24] While the causal relationship is not clear, it is expected that more educated people have better understanding of HIV disease process which could reflect on their attitude to care and potentially more resources to facilitate care. Education and counseling intensification are useful strategies that could improve retention in care in our setting, since the majority of our patients have a low level of education.

An important finding in this study is the variability in risk of treatment discontinuation according to NRTI backbone. Surprisingly, the risk of discontinuing treatment was higher in patients who initiated treatment with TDF containing regimen compared to AZT. There is a shift towards the use of TDF in combination with lamivudine in the more recent WHO guideline for treatment and prevention of HIV in adults and adolescents.[25] Other studies [18] have reported similar risk of lost to follow-up with use of TDF and therefore merits further investigation.

Consistent with established evidence linking poor adherence to poor health outcomes in patients on ART, [18, 26–28] our analysis found that patients with poor adherence to pharmacy drug pick up visits were at greater risk of treatment discontinuation. The adherence threshold of greatest impact was average percent adherence ≥ 95%. Since adherence is a modifiable risk factor, adherence interventions could improve retention in care in our setting.

A major strength of this study is the large sample of our cohort and the length of follow up. We analyzed one of the largest databases in a single centre providing ART in Nigeria, with longitudinal data of up to 8.5years, the longest so far of the published studies on patient retention in an African setting.[17–18, 20–23] Using carefully collected clinical data; we learnt that interventions to improve retention on ART should include enhanced counseling for younger patients, the unmarried and those with lower levels of education. ART regimen should be carefully selected at treatment initiation with preference to simplified regimens to achieve maximal adherence and ease of usage at all levels of health care. In addition, a system to track patient's adherence to treatment should be put in place to enable early identification of patients at risk of treatment discontinuation.This study had a few notable limitations. First, this was a single institutional, retrospective study; hence the generalization of the study results should be done cautiously. Secondly, there was little or no information on the disposition of patients lost to follow up. A number of these patients might have died without notification to the clinic, hence underestimating the true mortality rate in our patient cohort. Thirdly, patients transferred to other ART facilities are presumed to be retained in care without adequate linkage information between our treatment facility and other ART facilities to ensure that these patients are in care. Fourthly, the association of patients geographic location with treatment discontinuation; which would have been interesting to consider in decentralizing HIV/AIDS treatment services was not investigated. Finally, though our analysis revealed a trend in treatment discontinuation with changing levels of adherence to drug refill visits, our determination of average percent adherence did not consider the different duration of therapy and might be a bit biased towards those on treatment for longer period.

## Conclusion

About 7 out of 100 adults initiated on ART in our setting discontinued treatment per year. The rate of treatment discontinuation was comparable to estimates in resource rich countries. More efficient interventions are needed, particularly within the first year of ART, to reduce the incidence of treatment discontinuation and improve retention in antiretroviral programs, with a special focus on younger patients, those with lower educational status and poor adherence.

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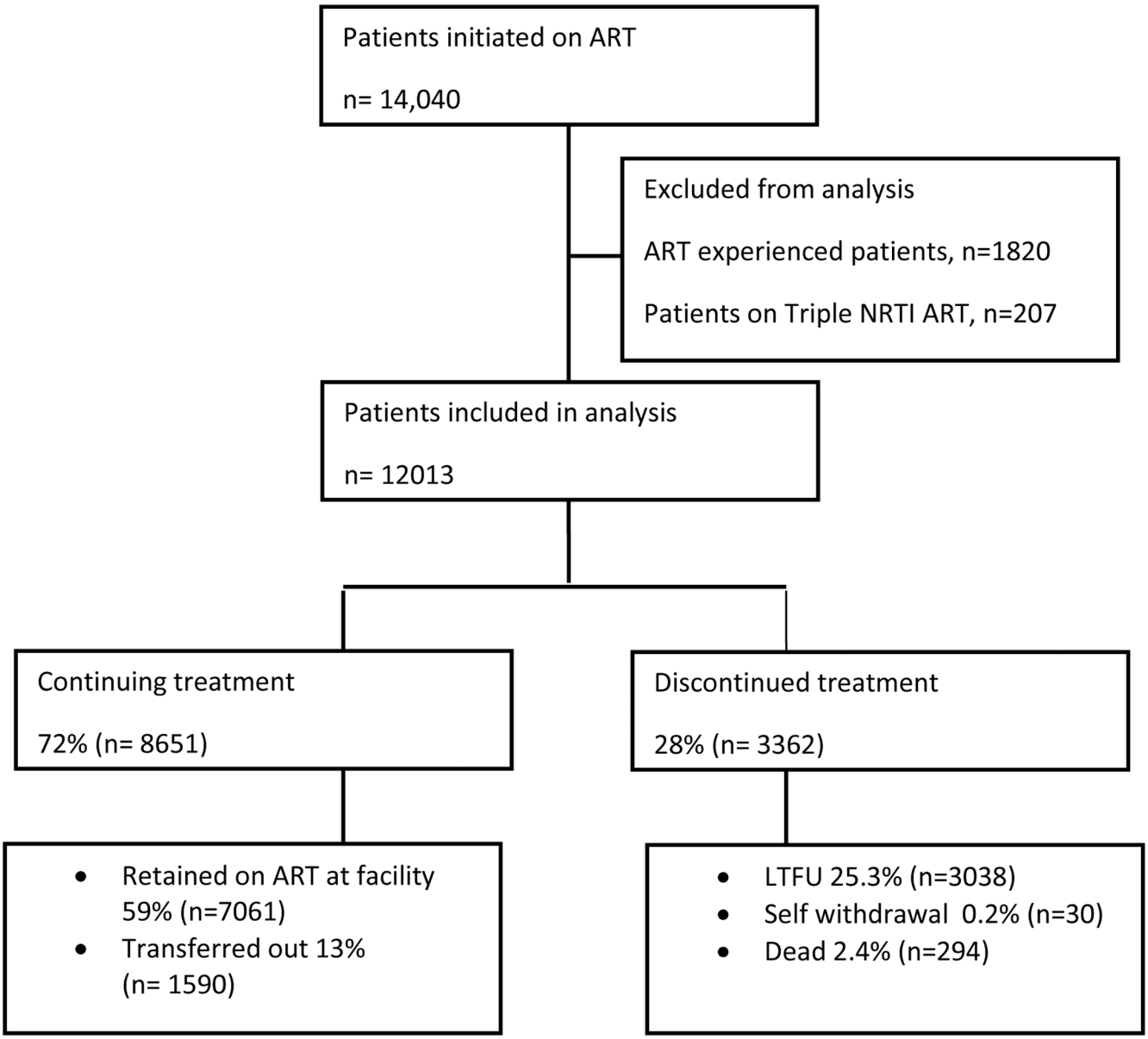
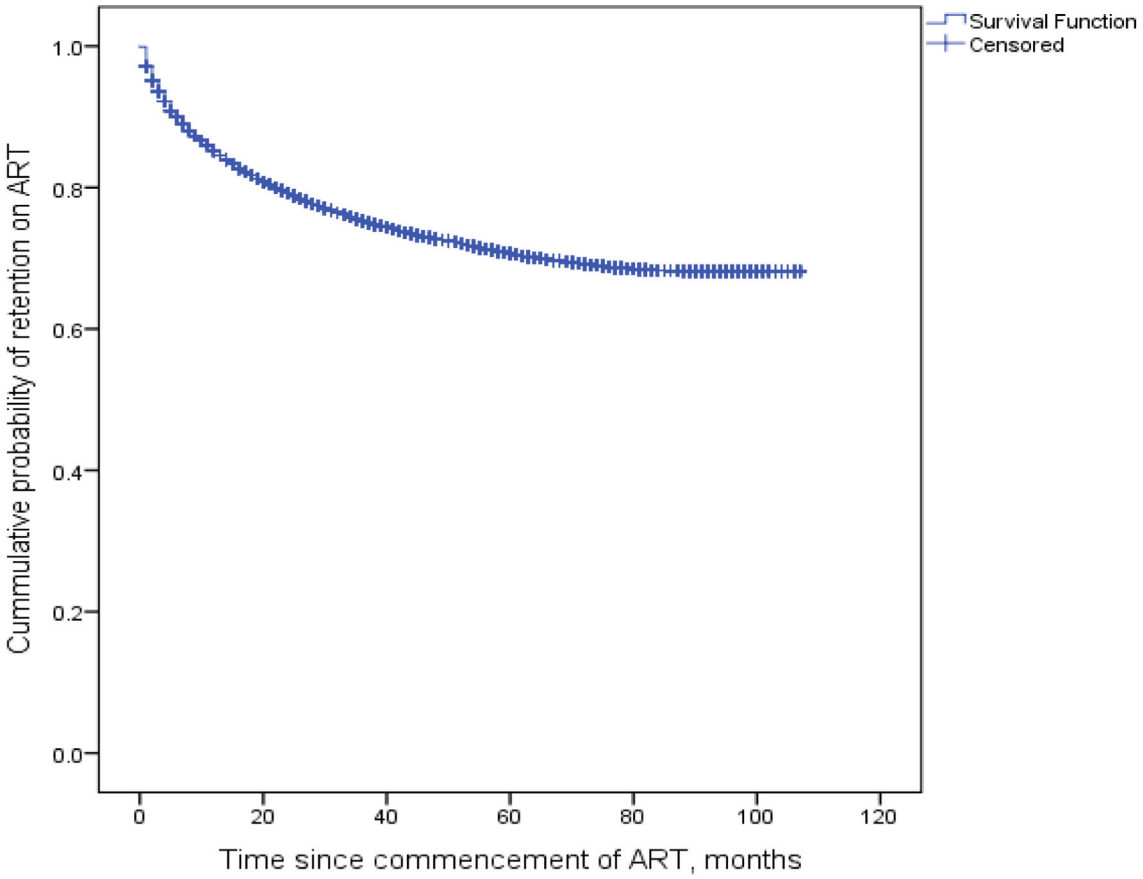



**Figure 1:**
Disposition of 14,040 patients initiated on ART in Jos University Teaching Hospital, June 2004 to December 2011.




| Time (months) | 12 | 24 | 36 | 48 | 60 | 72 | 84 | 96 |
|---|---|---|---|---|---|---|---|---|
| Cumulative probability of TD | 0.14 | 0.20 | 0.25 | 0.27 | 0.29 | 0.31 | 0.32 | 0.32 |
| Number of events | 1674 | 2394 | 2810 | 3053 | 3229 | 3320 | 3359 | 3362 |
| Number remaining | 9997 | 8510 | 7285 | 6251 | 4902 | 3608 | 2402 | 1028 |
| Cumulative % of total TD | 49.79 | 71.21 | 83.58 | 90.81 | 96.04 | 98.75 | 99.91 | 100 |

**Figure 2:**
Kaplan-Meier estimates of time to treatment discontinuation of patients (n=12013) on first-line ART in Jos, Nigeria.

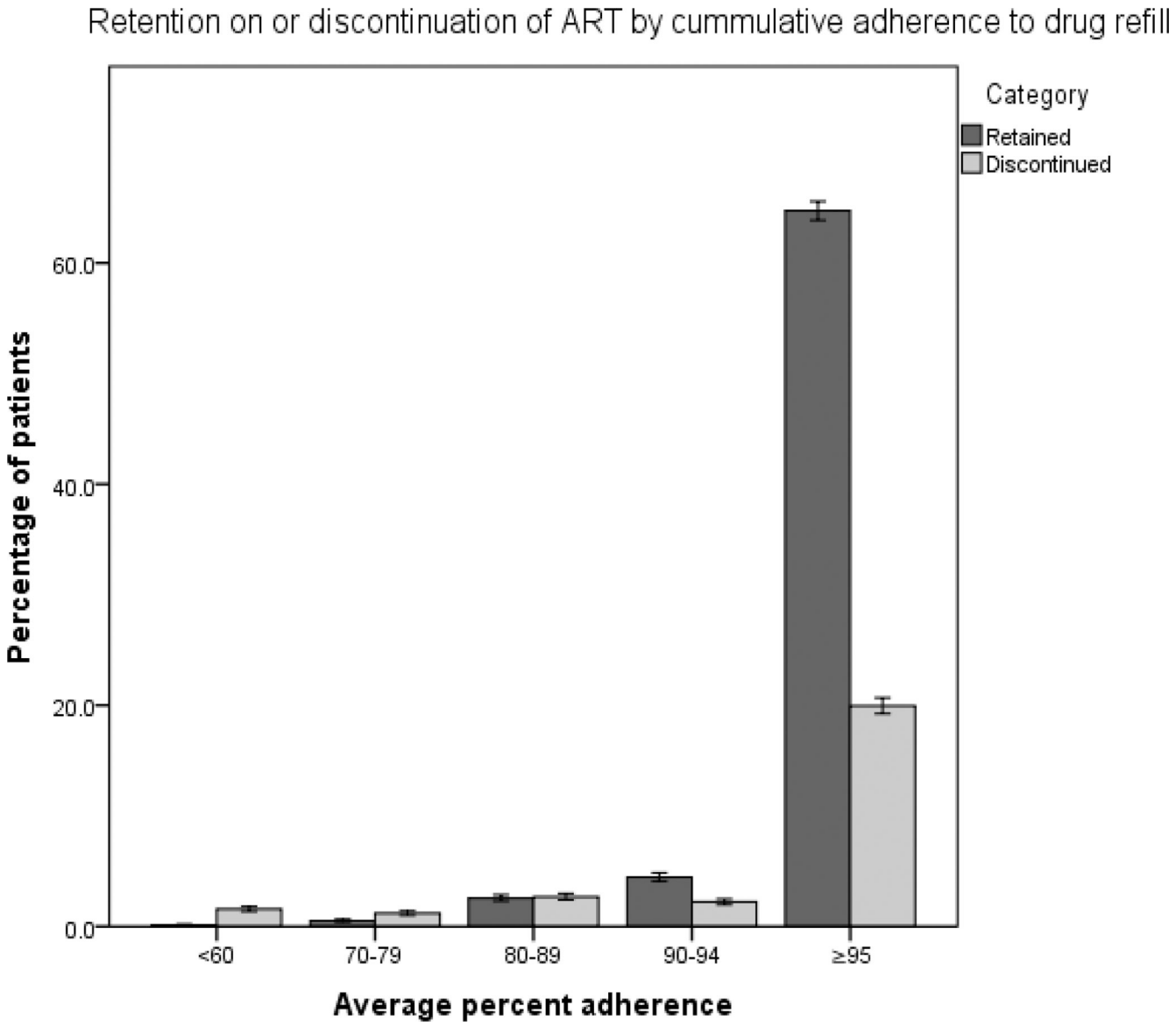



**Figure 3:**
Association between cumulative percent adherence to drug refill retention on or discontinuation of ART

**Table 1:**

Baseline demographic and clinical characteristics of patients on ART in Jos and bi-variate association with treatment discontinuation

| Characteristics | All patients | Retained on ART | Discontinued ART | *P*-value |
|---|---|---|---|---|
| N | 12013 | 8651 (72) | 3362 (28) | |
| **Time in months on ART**, median (IQR) | 50 (19 – 78) | 64 (39 – 85) | 12 (4 – 27) | |
| **Age in years**, median (IQR) | 35 (30 – 42) | 35 (30 – 42) | 34 (29 – 41) | **0.027** |
| **Sex**, n (%) | | | | |
| Male | 4008 (33.4) | 2772 (69.2) | 1236 (30.8) | **<0.001** |
| Female | 8005 (66.) | 5879 (73.4) | 2126 (26.6) | |
| **Education**, n (%) | | | | |
| Primary / NFE | 4123 (35.2) | 2874 (69.6) | 125 (30.4) | **<0.001** |
| Secondary | 3589 (30.6) | 2573 (71.7) | 1016 (28.3) | |
| Tertiary | 4019 (34.2) | 3000 (74.6) | 1019 (25.4) | |
| Missing data | 277 | | | |
| **Marital status**, n (%) | | | | |
| Married | 6454 (55) | 4786 (74.2) | 1668 (25.8) | **<0.001** |
| Single | 2342 (20) | 1603 (68.4) | 739 (31.6) | |
| Divorced/separated | 956 (8.1) | 643 (67.3) | 313 (32.7) | |
| Widowed | 1984 (16.9) | 1415 (72) | 569 (28.7) | |
| Missing data | 277 | | | |
| **Employment status**, n (%) | | | | |
| Employed | 8648 (72) | 6237 (72.1) | 2411 (27.9) | 0.67 |
| Unemployed | 3365 (28) | 2414 (71.7) | 951 (28.3) | |
| Missing data | 277 | | | |
| **HIV transmission risk**, n (%) | | | | |
| Heterosexual | 11179 (96) | 8048 (72) | 3131 (28) | 0.5 |
| Transfusion | 312 (2.7) | 224 (71.8) | 88 (28.2) | |
| Others | 148 (1.3) | 113 (1) | 35 (23.6) | |
| Missing data | 374 | | | |
| **HBV status at baseline**, n (%) | | | | |
| Negative | 8269 (79.4) | 5974 (72.2) | 2295 (27.8) | 0.21 |
| Positive | 2146 (20.6) | 1521 (70.9) | 625 (29.1) | |
| Missing data | 1598 | | | |
| **WHO disease stage**, n (%) | | | | |
| 1 | 3759 (35) | 2738 (72.8) | 1021 (27.2) | 0.142 |
| 2 | 3367 (31.4) | 2377 (70.6) | 990 (29.4) | |
| 3 | 2923 (27.2) | 2110 (72.2) | 813 (27.8) | |
| 4 | 691 (6.4) | 508 (73.5) | 183 (26.5) | |
| Missing data | 1273 | | | |
| **CD4 cell count**, cells/mm3, n (%) | | | | |
| ≤50 | 2037 (17.1) | 1433 (70.3) | 604 (29.7) | 0.07 |

| Characteristics | All patients | Retained on ART | Discontinued ART | *P*-value |
|---|---|---|---|---|
| 51 – 100 | 2159 (18.1) | 1550 (71.8) | 609 (28.2) | |
| 101 – 200 | 3677 (30.9) | 2702 (73.5) | 975 (26.5) | |
| >200 | 4027 (33.8) | 2885 (71.6) | 1142 (28.4) | |
| Missing data | 113 | | | |
| **Viral load**, copies/mL, n (%) | | | | |
| <1000 | 842 (14.2) | 672 (79.8) | 170 (20.2) | **0.001** |
| 1000 – 9 999 | 1044 (17.6) | 757 (72.5) | 287 (27.5) | |
| 10 000 – 99 999 | 2207 (37.1) | 1659 (75.2) | 548 (24.8) | |
| ≥100 000 | 1851 (31.1) | 1363 (73.6) | 488 (26.4) | |
| Missing data | 6069 | | | |
| **Year of ART initiation** | | | | |
| June 2004 – Dec 2005 | 2953 (24.5) | 2110 (71.5) | 843 (28.5) | **<0.001** |
| 2006 | 2562 (21.3) | 1696 (66.2) | 866 (33.8) | |
| 2007 | 2055 (17.1) | 1393 (67.8) | 662 (32.2) | |
| 2008 | 1793 (14.9) | 1317 (73.5) | 476 (26.5) | |
| 2009 | 1130 (9.4) | 830 (73.5) | 300 (26.5) | |
| 2010 | 747 (6.2) | 591 (79.1) | 156 (20.9) | |
| 2011 | 773 (6.4) | 714 (92.4) | 59 (7.6) | |
| **NNRTI backbone at ART initiation** | | | | |
| efavirenz | 2459 (20.5) | 1702 (69.2) | 757 (30.8) | **0.001** |
| nevirapine | 9554 (79.5) | 6949 (72.7) | 2605 (27.3) | |
| **NRTI backbone at ART initiation** * | | | | |
| Abacavir + 3TC | 268 (2.3) | 180 (67.2) | 88 (32.8) | **<0.001** |
| Zidovudine + 3TC | 5652 (47.5) | 4187 (74.1) | 1465 (25.9) | |
| Stavudine + 3TC | 1978 (16.6) | 1424 (72) | 554 (28) | |
| Didanosine + 3TC | 237 (2) | 134 (56.5) | 103 (43.5) | |
| tenofovir+ 3TC | 3758 (31.6) | 2644 (70.4) | 1114 (29.6) | |

Missing data were excluded from the analysis. Abbreviations: ART: antiretroviral therapy, IQR: Interquartile range, NFE: No formal education, TB: tuberculosis, HBV: hepatitis B virus, WHO: World Health Organization, NNRTI: nucleoside reverse transcriptase inhibitor, NRTI: nucleos(t)ide reverse transcriptase inhibitor, 3TC: lamivudine,

*120 patients on abacavir/zidovudine NTRI excluded

**Table 3:**

Multivariate Cox regression analysis of hazards for treatment discontinuation in patients on first-line ART in Jos, Nigeria (n=12,013)

| Variable | Unadjusted Cox analysis | | | Adjusted Cox model A | | | Adjusted Cox model B | | |
|---|---|---|---|---|---|---|---|---|---|
| | HR | 95% CI | *p* value | aHR | 95% CI | *p* value | aHR | 95% CI | *p* value |
| Sex | | | | | | | | | |
| Male | 1.18 | 1.10–1.26 | <0.001 | 1.16 | 1.00–1.35 | 0.06 | 1.12 | 0.96–1.30 | 0.15 |
| Female | Ref | | | Ref | | | Ref | | |
| Age, years | 0.99 | 0.99–1.0 | 0.09 | .990 | 0.98–0.99 | 0.01 | .99 | 0.98–0.99 | 0.02 |
| Marital status | | | | | | | | | |
| Unmarried | 1.22 | 1.13–1.30 | <0.001 | 1.28 | 1.16–1.42 | <0.001 | 1.24 | 1.12–1.38 | <0.001 |
| Married | Ref | | | Ref | | | Ref | | |
| Highest Education | | | | | | | | | |
| Primary/Secondary | 1.23 | 1.14–1.32 | <0.001 | 1.30 | 1.16–1.46 | <0.001 | 1.24 | 1.12–1.40 | <0.001 |
| Tertiary | Ref | | | Ref | | | Ref | | |
| Viral load, copies/mL | | | | | | | | | |
| <1000 | 0.72 | 0.81–0.86 | <0.001 | 0.76 | 0.64–0.92 | <0.001 | .77 | 0.64–0.92 | <0.001 |
| 1000 – 9 999 | 1.03 | 0.89–1.20 | 0.66 | 1.08 | 0.93–1.26 | 0.32 | 1.10 | 0.95–1.28 | 0.21 |
| 10 000 – 99 999 | 0.94 | 0.83–1.06 | 0.31 | 1.00 | 0.88–1.13 | 0.98 | 1.02 | 0.90–1.15 | 0.77 |
| ≥100 000 | Ref | | | Ref | | | Ref | | |
| NNRTI backbone | | | | | | | | | |
| Nevirapine | 0.79 | 0.73–0.86 | <0.001 | 0.86 | 0.73–1.01 | 0.071 | 0.89 | 0.76–1.05 | 0.18 |
| Efavirenz | Ref | | | Ref | | | Ref | | |
| NRTI backbone | | | | | | | | | |
| abacavir + 3TC | 0.94 | 0.76–1.17 | 0.62 | 0.96 | 0.51–1.83 | 0.91 | 0.97 | 0.52–1.84 | 0.94 |
| zidovudine + 3TC | 0.78 | 0.73–0.85 | <0.001 | 0.77 | 0.69–0.87 | <0.001 | 0.77 | 0.69–0.86 | <0.001 |
| stavudine + 3TC | 0.73 | 0.66–0.81 | <0.001 | 0.97 | 0.74–1.27 | 0.82 | 0.92 | 0.70–1.20 | 0.54 |
| didanosine + 3TC | 1.37 | 1.11–1.68 | <0.001 | 1.76 | 1.04–2.97 | 0.04 | 1.73 | 1.03–2.91 | 0.04 |
| tenofovir + 3TC | Ref | | | Ref | | | Ref | | |
| Year of ART initiation | | | | | | | | | |
| Jun 2004 – Dec 2005 | Ref | | | Ref | | | Ref | | |
| 2006 | 1.31 | 1.20–1.45 | <0.001 | 0.86 | 0.65–1.15 | 0.32 | 0.82 | 0.61–1.09 | 0.18 |

| Variable | Unadjusted Cox analysis | | | Adjusted Cox model A | | | Adjusted Cox model B | | |
|---|---|---|---|---|---|---|---|---|---|
| | HR | 95% CI | *p* value | aHR | 95% CI | *p* value | aHR | 95% CI | *p* value |
| 2007 | 1.35 | 1.22–1.49 | <0.001 | 1.24 | 1.02–1.50 | 0.03 | 1.26 | 1.04–1.53 | 0.02 |
| 2008 | 1.12 | 0.99–1.25 | 0.05 | 1.03 | 0.85–1.24 | 0.77 | 1.07 | 0.89–1.29 | 0.47 |
| 2009 | 1.24 | 1.09–1.42 | 0.001 | 1.05 | 0.85–1.29 | 0.66 | 1.05 | 0.56–1.29 | 0.62 |
| 2010 | 1.06 | 0.89–1.26 | 0.52 | 0.91 | 0.72–1.16 | 0.46 | 0.90 | 0.71–1.14 | 0.38 |
| 2011 | 0.45 | 0.34–0.59 | <0.001 | 0.35 | 0.25–0.50 | <0.001 | 0.35 | 0.25–0.50 | <0.001 |
| average % adherence | | | | | | | | | |
| <95% | 2.82 | 2.62–3.04 | <0.001 | - | - | - | 2.13 | 1.90–2.40 | <0.001 |
| ≥ 95% | Ref | | | | | | Ref | | |

Model B; average % adherence included as covariate, HR: hazard ratio, aHR: adjusted hazard ratio, CI: confidence interval, NNRTI: non-nucleoside reverse transcriptase inhibitor, NRTI: nucleos(t)ide reverse transcriptase inhibitor, 3TC: lamivudine, ART: antiretroviral therapy