Background: The effectiveness of the first regimen of antiretroviral therapy (ART) is a major key to long-term success and sustainability of HIV treatment program. Aims: The objectives of this study were to determine the incidence rate, reasons, and factors associated with modification of initial ART regimen. Methods: A total of 502 patient files were reviewed. Modification of ART regimen was defined as either substitution or switch of a single drug in the regimen. Results: The total duration of follow-up was 629.8 person-years (PYs) over a median follow-up period of 37 months. About 92 (18.2%) of patients had their initial ART regimen modified, with a resulting incidence rate of modification at 14.6/100 PYs. Drug unavailability 49 (53.3%), drug toxicity 16 (17.4%), treatment failure 10 (10.9%), nonadherence 7 (7.6%), and concomitant condition 7 (7.6%) were common reasons for ART modifications. In the adjusted multivariate Cox proportional hazard model, the type of initial ART regimen (zidovudine/lamivudine (3TC)/efavirenz vs. tenofovir/3TC/nevirapine (NVP), aHR 4.78, 95% confidence interval [CI] [1.42, 16.12], P = 0.012), and duration on regimen (≤1 year vs. >3 years, aHR 4.11, 95% CI [1.02–9.22], P = 0.0001) were significantly associated with modification of initial ART regimen. Conclusion: Our findings indicate that the incidence rate of initial ART regimen modification was high. Hence, implementing better health systems to ensure a steady supply of drugs as well as early HIV diagnosis and ART initiation will reduce the rate of regimen change.

Keywords: Antiretroviral therapy regimen modification, Cameroon, incidence, survival analysis

Introduction

For over 30 years since its discovery, HIV remains a global challenge with little success of possible eradication having been achieved thus far. Sub-Saharan Africa has been worst affected with over 69.9% of the total HIV cases being reported from this region including Cameroon. Antiretroviral therapy (ART) has been beneficial in subduing this scourge of HIV/AIDS. The goal of ART is to produce virologic suppression and immunologic reconstitution. There are several ART regimens that achieve this goal.[2] Change in ART regimen is necessary because of both acute and chronic toxicities, as well as concomitant clinical conditions.[1] However, these changes can also result in poor viral control as well as cross-resistance between different alternative drugs,[4,5] hence, limiting the success of ART.

The incidence of ART change varies greatly between countries, with most reports from Western countries and fewer from low- and middle-income settings.[6] Similar studies done in Brazil had an incidence rate of 28.3/100 person-years (PYs)[7] and Mali 16.2/100 PYs.[8] Drug toxicity is the most frequently reported reason for ART regimen change;[9,10] however, other reasons include treatment failure,[11] drug unavailability,[12] and nonadherence.[13] Reported factors predictive of regimen change are baseline CD4,[13,14] the WHO stage,[9] initial ART regimen,[11,15] and body weight.[9]
Cameroon, like many other countries in sub-Saharan Africa, has been greatly affected by HIV/AIDS scourge with the current nationwide prevalence at 4.3%. The lack of resources further limits the availability of treatment options in cases where ART modification is required. In the wake of these financial constraints as well as limited supply of a wide array of drugs, there is an increased need to sustain patients on a potent regimen for as long as possible while ensuring minimal toxicity and continuous efficacy of the drugs. This, therefore, calls for a need to understand the reasons and factors associated with ART regimen change so that efforts can be targeted at preventing initial regimen change.

Methods

Study area and period

This study was conducted from January to March 2016 in the Buea and Limbe regional hospitals’ (LRHs) HIV/AIDS treatment centers in the Southwest region of Cameroon. HIV/AIDS treatment Center of the Buea Regional Hospital (BRH) runs from Mondays to Fridays except Wednesdays meanwhile that for the LRH runs from Mondays to Fridays without exceptions.

HIV/AIDs treatment centers of the BRH and LRH were initiated in 2001. Over 9000 patients have been enrolled to these treatment centers since then. In these treatment centers, the patients have a regular monthly follow-up for medication refill, and all patients who have been diagnosed to be HIV positive are eligible for treatment. The above treatment criteria were according to the recent WHO recommendation, which is to treat all diagnosed patients using the preferred first-line regimen consisting of tenofovir (TDF) with lamivudine (3TC) and efavirenz (EFV). This guideline is currently being used all over Cameroon. The patients are monitored regularly in these centers by CD4 determination which is done at first enrolment, at the time of ART initiation and every 6 months as per guideline. However, HIV viral load monitoring is not routinely done in these treatment centers.

Study design and population

The study was a retrospective chart review of records of HIV patients who initiated ART in Buea and LRHs from 1st January, 2013, to 31st December, 2015 to March 2016. We included in the study only adult people living with HIV (PLWH) of age ≥21 years, who were on ART had at least one follow-up clinic visit post-ART initiation and were not on ART for prevention of mother to child transmission (PMTCT) of HIV.

The minimum sample size for this study was determined using single population proportion formula to be 254. A total of 622 files were randomly selected from the 3000 patient who were enrolled on ART from January 1st, 2013, to December 31st, 2015. Out of the 622 files selected, 120 did not fulfill the inclusion criteria and were excluded from the study while the remaining 502 files which met the inclusion criteria were enrolled in the study for further analysis. Of the 120 files, 90 were due to the inadequate follow-up visit, 8 due to early deaths, and the remaining 22 had been on ART for PMTCT of HIV. A predesigned data extraction tool was used to collect the required information from the files.

In this study, modification of ART regimen was defined as either a first-time substitution of one or two drugs in a particular ART regimen or a complete switch of the entire regimen to another. Treatment failure was defined as an immunological failure (fall of CD4 count to pretreatment baseline or below) or clinical failure (new or recurrent WHO stage 4 condition). The reasons for ART regimen modification which were assessed were as follows: drug toxicity, treatment failure, drugs unavailability, nonadherence, concomitant conditions, and prescriber’s error.

Data analysis

Data collected was entered into and analyzed using Epi-info version 7.0 statistical software (CDC, Atlanta, GA, USA). Baseline patient characteristics and the clinical indices at the initiation of treatment were described using percentages for categorical data and median and interquartile ranges for continuous data. The incidence rate for treatment modification was computed per 100 PYs of follow-up. To calculate this incidence rate, the total duration of follow-up for the whole cohort in PY was used. For those who changed their regimen, the follow-up duration was calculated from the date of initiation of ART to either a modification or discontinuation of the original regimen.

Kaplan–Meier curve for a change of initial ART regimen was generated to estimate the median duration for regimen change. Cox proportional hazards model was used in the univariate analysis to determine factors associated with change of initial ART regimen. Statistical significance was set at a $P < 0.05$.

Ethical consideration

Ethical clearance was obtained from the Institutional Ethics Committee for research on human of the University of Douala. Confidentiality was taken into consideration during data collection with no personal identifiable information included in the data collection tool except the ART unique number of each patient.

Results

Characteristics of patients at antiretroviral therapy initiation

A total of 622 HIV patient files were selected following computer-generated simple random numbers, but 502 files which met the inclusion criteria were analyzed. The mean (=standard deviation) age at the initiation of ART was 40 years (±10 years), and 265 (52.8%) of the participants were in the age-group between 21 and 40 years. A majority of the respondents 347 (68.9%) were female. Regarding the level of
education, 17 (3.4%) of the respondents attained below primary (none) education [Table 1].

Out of the 502 patients, 213 (42.4%) had a pre-ART CD4 count below 200 cells/ul. The predominant ART regimen initially prescribed for them was a combination of TDF/3TC/EFV for 389 (77.5%) cases. About 241 (48.0%) were in WHO clinical stage III at the initiation of ART while the WHO clinical stage was not available for 24 (4.8%) patients [Table 2].

### Table 1: Baseline sociodemographic characteristics of study participants

| Characteristics       | Total (n=502), n (%) | Modified (n=92), n (%) | Not modified (n=410), n (%) |
|-----------------------|----------------------|------------------------|----------------------------|
| Gender                |                      |                        |                            |
| Male                  | 156 (31.1)           | 25 (27.2)              | 131 (32.0)                 |
| Female                | 346 (68.9)           | 67 (72.8)              | 279 (68.0)                 |
| Age (years)           |                      |                        |                            |
| 21-40                 | 265 (52.8)           | 52 (55.5)              | 213 (51.9)                 |
| 41-60                 | 220 (43.9)           | 36 (39.1)              | 184 (44.9)                 |
| >60                   | 17 (3.3)             | 4 (4.4)                | 13 (3.2)                   |
| Marital status        |                      |                        |                            |
| Single                | 203 (40.4)           | 39 (42.3)              | 164 (40.0)                 |
| Widowed               | 73 (14.5)            | 10 (11.0)              | 63 (16.4)                  |
| Married               | 202 (40.2)           | 38 (41.3)              | 164 (40.0)                 |
| Separated/divorced    | 24 (4.8)             | 5 (5.4)                | 19 (4.6)                   |
| Level of education    |                      |                        |                            |
| None                  | 17 (3.4)             | 5 (5.4)                | 12 (2.9)                   |
| Primary               | 215 (42.8)           | 40 (43.4)              | 175 (42.7)                 |
| Secondary             | 209 (41.6)           | 41 (44.6)              | 168 (41.0)                 |
| Tertiary              | 61 (12.2)            | 6 (6.6)                | 55 (13.4)                  |

### Table 2: Baseline clinical and immunological status of study participants

| Characteristics       | Total (n=502), n (%) | Modified (n=92), n (%) | Not modified (n=410), n (%) |
|-----------------------|----------------------|------------------------|----------------------------|
| Baseline CD4 count (cells/µl) before starting ART |                      |                        |                            |
| <200                  | 213 (42.4)           | 26 (28.2)              | 187 (45.6)                 |
| 200-350               | 160 (31.9)           | 34 (37.0)              | 126 (30.7)                 |
| >350                  | 88 (17.5)            | 21 (22.8)              | 67 (16.3)                  |
| Missing               | 41 (8.2)             | 11 (12.0)              | 30 (7.3)                   |
| Initial ART regimen   |                      |                        |                            |
| AZT/3TC/EFV           | 11 (2.2)             | 8 (8.7)                | 3 (0.7)                    |
| AZT/3TC/NVP           | 51 (10.2)            | 23 (25.0)              | 28 (6.8)                   |
| d4T/3TC/EFV           | 2 (0.4)              | 1 (1.1)                | 1 (0.2)                    |
| d4T/3TC/NVP           | 7 (1.4)              | 1 (1.1)                | 6 (1.5)                    |
| TDF/3TC/EFV           | 389 (77.5)           | 53 (57.6)              | 336 (82.0)                 |
| TDF/3TC/NVP           | 42 (8.4)             | 6 (6.5)                | 36 (8.8)                   |
| WHO clinical stage at start of ART               |                      |                        |                            |
| Stage I               | 128 (25.5)           | 20 (21.7)              | 108 (26.3)                 |
| Stage II              | 56 (11.1)            | 8 (11.7)               | 48 (11.7)                  |
| Stage III             | 241 (48.0)           | 48 (52.2)              | 193 (47.1)                 |
| Stage IV              | 53 (10.6)            | 12 (12.0)              | 41 (10.0)                  |
| Missing               | 24 (4.8)             | 4 (4.4)                | 20 (4.9)                   |

ART=Antiretroviral therapy, AZT=Zidovudine, d4T=Stavudine, EFV=Efavirenz, NVP=Nevirapine, TDF=Tenofovir, 3TC=Lamivudine

### Incidence rate of initial antiretroviral therapy regimen modification

A total of 502 patients were followed up for a maximum period of 37 months (from ART initiation to time of data collection). The median time of follow-up was 13 months (range: 1–37) and the total PYs contributed was 629.8 years of follow-up. During this period, a total of 92 participants modified their ART regimen resulting with an overall incidence of 14.6/100 PYs (95% confidence interval [CI] 19.6-25.7) for first change. The rate of ART regimen modification varied with the number of years post-ART; 60.3/100 PY at 1st year, 9.7/100 PY at 2nd year, and 0.8/100 PY at >2 years as shown in Table 3 and Figure 1.

A high proportion of patients were on treatment within the 1st year; however, these proportions progressively decreased...
with the number of years spent on treatment as shown in Figure 1.

**Reasons for antiretroviral therapy regimen modification**

The most commonly cited reason for treatment modification was drug shortage 49 (53.3%) followed by drug toxicity 16 (17.4%), while treatment failure, concomitant conditions, and nonadherence accounted for only 10 (10.9%), 7 (7.6%), and 7 (7.6%) respectively. Among the 92 patients who had modifications of their initial ART regimen, 49 (53.3%) were due to drug shortage and 10 (10.9%) were due to treatment failure. Information on drug toxicity was available for 16 of 92 persons who changed regimen. Of these, zidovudine (AZT)-related hematological toxicity (anemia) 9 (9.8%) and hepatotoxicity 5 (5.4%) were the most common documented drug toxicities. Immunological failure accounted for 7 (7.6%) of ART regimen modification while clinical failure was responsible for 3 (3.3%). Tuberculosis was responsible for 4 (4.4%) of regimen modification while defaults amounted for up to 5 (5.4%) [Table 4].

With majority of regimen changes occurring within the 1st year after ART initiation, the most reported reasons for these modifications were still drug shortages 32 (47.1%) followed by drug toxicity 15 (22.0%) as shown in Table 4.

**Factors associated with antiretroviral therapy regimen change**

In the univariate Cox regression analysis, the type of initial ART regimen AZT/3TC/EFV versus TDF/3TC/NVP (aHR 4.78, 95% CI [1.42, 16.12], \( P = 0.012 \)), low baseline CD4 cell count (≤200 cells/ul vs. 201-350 cells/ul, aHR 0.53, 95% CI [0.31, 0.90], \( P = 0.021 \)) and duration on regimen (≤1 year vs. >3 years, aHR 4.11, 95% CI [1.02, 9.22], \( P = 0.0001 \)) were associated with modification of ART regimen as shown in Table 5. AZT-based regimen with the high incidence rates of 65.6/100 PY and 31.4/100 PY were specifically found to be associated with ART regimen modification. The patients who spent <1 year on ART with a high incidence rate of 71.0/100 PY were also specifically associated with modification of ART regimen. In addition, patients who initiated ART at CD4 cell count less than 200 had an incidence rate of 9.3/100 PY were found to be significantly associated (\( P < 0.001 \)) with change of initial ART regimen [Table 5].

**Discussion**

This study was aimed at determining the incidence rate of modification of ART regimen in HIV/AIDS patients in the Southwest regional hospitals of Cameroon. About 92 patients of 502 patients who were included in this study modified their initial ART regimen, representing an incidence rate of 14.6/100 PYs. Drug unavailability (stocks out and cost) was the most common reason for modification of initial highly active antiretroviral therapy regimen. The initial ART regimen, pre-ART CD4 cell counts, and duration on ART regimen were the factors associated with ART regimen modification.

The incidence rate of modification of initial ART regimen of adults enrolled at BRH and LRH HIV/AIDS treatment centers was relatively low compared to similar studies done in developed countries. In the literature, the incidence of change of initial ART regimen varies greatly. It was found higher in a Swiss HIV Cohort study with incidence rate of 41.5/100 PY (95% CI [37.6, 45.8]), Rio de Janeiro 28.3/100 PY (95% CI [26.0, 31.0]). In our setting, the low rate of antiretroviral regimen modification could be explained by the simplified and stable regimen introduced in 2008. A simplified and stable

### Table 3: Incidence rates assessed per increasing number of years postantiretroviral therapy, from January 2013 to December 2015

| Years post-ART Initiation | Person-time (years) | Number of patients on ART | Number of initial ART regimen modifications | Incidence rate (95% CI) |
|--------------------------|---------------------|----------------------------|---------------------------------------------|-------------------------|
| Total                    | 629.8               | 502                        | 92                                          | 14.6 per 100 PY         |
| 0-1 year                 | 112.6               | 211                        | 68                                          | 60.3 per 100 PY         |
| 1-2 years                | 226.8               | 174                        | 22                                          | 9.7 per 100 PY          |
| 2-3 years                | 256.4               | 117                        | 2                                           | 0.8 per 100 PY          |

ART=Antiretroviral therapy, CI=Confidence interval, PY=Person-year

### Table 4: Reasons for antiretroviral therapy regimen modifications

| Reasons                        | Modifications (\( n=92 \), \( n (%) \)) |
|--------------------------------|----------------------------------------|
| Drug toxicity                  | 16 (17.4)                              |
| Anemia                         | 9 (9.8)                                |
| Liver toxicity                 | 5 (5.4)                                |
| Skin rash                      | 1 (1.1)                                |
| Renal                          | 1 (1.1)                                |
| Treatment failure              | 10 (10.9)                              |
| Immunological                  | 7 (7.6)                                |
| Clinical                       | 3 (3.3)                                |
| Concomitant conditions         | 7 (7.6)                                |
| Tuberculosis                   | 4 (4.4)                                |
| Herpes zoster                  | 2 (2.2)                                |
| Kaposi sarcoma                 | 1 (1.1)                                |
| Nonadherence                   | 7 (7.6)                                |
| Defaulter                      | 5 (5.4)                                |
| Missing clinic appointment     | 2 (2.2)                                |
| Drug shortage                  | 49 (53.3)                              |
| Others                         | 3 (3.3)                                |
| Prescriber’s error             | 3 (3.3)                                |

The incidence rate of modification of initial ART regimen of adults enrolled at BRH and LRH HIV/AIDS treatment centers was relatively low compared to similar studies done in developed countries. In the literature, the incidence of change of initial ART regimen varies greatly. It was found higher in a Swiss HIV Cohort study with incidence rate of 41.5/100 PY (95% CI [37.6, 45.8]), Rio de Janeiro 28.3/100 PY (95% CI [26.0, 31.0]). In our setting, the low rate of antiretroviral regimen modification could be explained by the simplified and stable regimen introduced in 2008. A simplified and stable
The Incidence rate of change of initial ART regimen observed in our study (14.6/100 PYs) is comparable to other similar African cohort studies in Mali (16.2/100PY) and also a study by Inzaule et al., in Kenya, who had 18.6/100PY. The slightly higher incidence rates reported in Mali and Kenya were probably due to shorter follow-up periods of 15 and 10.7 months, respectively, compared to 37 months for our study. Even though the rates of initial regimen change has shown to be low in Africa, the goal should always be to strive for a 0% rate of change.

Drug shortage was the most common reason of the initial ART regimen change in this study and was the second reason of modification after drug shortages. Anemia was the most common antiretroviral side effect leading to modification of initial ART regimen. Drug toxicity accounted for 16/92 (17.4%) cases of ART regimen modification in this study and was the second reason of modification after drug shortages. Anemia was the most common antiretroviral side effect leading to modification of initial ART regimen followed by hepatotoxicity. Anemia as the most common drug toxicity has also been reported in a similar study in Latin America. However, this modification rate due to anemia can also be a reflection of baseline anemia and also the fact that anemia is closely monitored in this study setting, and there is always change of ART soon after its occurrence. The side effects reported are as a consequence of the AZT- and NVP- based regimens used in our setting. In our study, 8/92(8.7%) and 23/92(25%) of ART regimen modifications where in AZT/3TC/EFV and AZT/3TC/NVP regimens respectively. These findings may only worsen subsequently, following the new WHO recommendations to treat all HIV-diagnosed patients.

Drug toxicity accounted for 16/92 (17.4%) cases of ART regimen modification in this study and was the second reason of modification after drug shortages. Anemia was the most common antiretroviral side effect leading to modification of initial ART regimen followed by hepatotoxicity. Anemia as the most common drug toxicity has also been reported in a similar study in Latin America. However, this modification rate due to anemia can also be a reflection of baseline anemia and also the fact that anemia is closely monitored in this study setting, and there is always change of ART soon after its occurrence. The side effects reported are as a consequence of the AZT- and NVP- based regimens used in our setting. In our study, 8/92(8.7%) and 23/92(25%) of ART regimen modifications where in AZT/3TC/EFV and AZT/3TC/NVP regimens respectively. In three similar studies, antiretroviral side effects were the most common reasons for change of initial combination therapy, though the different side effects were not specified.

### Table 5: Factors associated with modification of initial antiretroviral therapy regimen

| Variable                        | Incidence of modification (per 100 PYs) | Unadjusted HR (95% CI) | Unadjusted P | Adjusted HR (95% CI) | Adjusted P |
|---------------------------------|----------------------------------------|------------------------|--------------|----------------------|------------|
| **Initial ART regimen**         |                                        |                        |              |                      |            |
| TDF/3TC/NVP                     | 1.024 (0.45-2.43)                      | 0.920                  |              | 0.80 (0.32-2.03)     | 0.640      |
| AZT/3TC/EFV                     | 6.08 (2.12-7.54)                       | 0.001                  | 4.78 (1.42-16.12) | 0.012                |
| AZT/3TC/NVP                     | 3.31 (1.35-8.13)                       | 0.009                  | 5.55 (2.03-15.36) | 0.001                |
| d4T/3TC/EFV                     | 3.83 (0.46-1.83)                       | 0.211                  | 5.43 (0.62-47.93) | 0.130                |
| d4T/3TC/NVP                     | 0.98 (0.12-8.16)                       | 0.992                  | 0.98 (0.21-9.15)  | 0.930                |
| TDF/3TC/EFV                     | 11.2 per 100 PY                        | 1.044                  | 0.820 (0.32-2.03) | 0.640                |
| **Pre-ART WHO stage**           |                                        |                        |              |                      |            |
| Stage IV                        | 1.6.4 per 100 PY                       | 1                      |              | 1                    |            |
| Stage I                         | 12.9 per 100 PY                        | 0.75 (0.37-1.49)       | 0.420        | 0.75 (0.37-1.52)     | 0.420      |
| Stage II                        | 10.3 per 100 PY                        | 0.65 (0.27-1.59)       | 0.341        | 0.69 (0.28-1.71)     | 0.430      |
| Stage III                       | 16.8 per 100 PY                        | 0.97 (0.52-1.86)       | 0.962        | 0.51 (0.52-1.86)     | 0.961      |
| **Pre-ART CD4 (cells/ul)**      |                                        |                        |              |                      |            |
| 201-350                         | 1.75 per 100 PY                        | 1                      |              | 1                    |            |
| <200                            | 9.3 per 100 PY                         | 0.55 (0.33-0.92)       | 0.021        | 0.53 (0.31-0.90)     | 0.021      |
| >350                            | 22.4 per 100 PY                        | 1.27 (0.74-2.19)       | 0.390        | 0.62 (0.62-1.87)     | 1.070      |
| **Duration of ART regimen (years)** |                            |                        |              |                      |            |
| >3                              | 0 per 100 PY                           | 1                      |              | 1                    |            |
| <1                              | 7.10 per 100 PY                        | 5.02 (1.21-4.34)       | 0.0001       | 4.11 (1.02-9.22)     | 0.0001     |
| 1-2                             | 9.5 per 100 PY                         | 0.61 (0.42-1.23)       | 0.024        | 0.59 (0.38-1.01)     | 0.021      |
| 2-3                             | 1.6 per 100 PY                         | 0.83 (0.41-1.75)       | 0.561        | 0.85 (0.47-1.83)     | 0.823      |

ART=Antiretroviral therapy, CI=Confidence interval, HR=Hazard ratio, TDF=Tenofovir, 3TC=Lamivudine, NVP=Nevirapine, AZT=Zidovudine, D4T=Stavudine, EFV=Efavirenz, HAART=Highly active antiretroviral therapy, PY=Person-years
The proportion of ART regimen modification due to treatment failure was 10/92 (10.9%). Studies in India and Ivory Coast reported similar findings of 14% and 12.4% respectively.[11,22] However, these values are relatively high compared to a study in Ethiopia where only 2% of regimen change was due to treatment failure.[13] Low proportion of treatment failure observed in that study can be explained by the short duration of patient follow-up post-ART regimen initiation.

Nonadherence to initial ART accounted for 7 (7.6%) of initial ART regimen modification and was the leading reason for discontinuation of initial ART regimen in our study. Nonadherence was characterized by irregularity in taking the prescribed regimen, default, or nonrespect of clinic appointments. Cicconi et al.[10] found poor adherence as second cause of discontinuation of initial ART regimen after intolerance/toxicity.

Concomitant conditions or comorbidities in the patients with advanced disease and concurrent treatments for opportunistic diseases could affect antiretroviral tolerance and thereby increase the risk of toxicity.[21] Concomitant conditions were the other reasons for ART regimen modifications. Tuberculosis, cerebral toxoplasmosis, Kaposi sarcoma, and herpes zoster were the concomitant conditions reported in this study. The dominant number of tuberculosis cases reported in our study was consistent with studies in the UK and Cote d’Ivoire.[22,23] Due to tuberculosis, a switch was made from d4T/3TC/NVP to d4T/3TC/EFV. The probable suggestion for this change was the overlapping drug toxicity of NVP with antituberculosis drugs, which was hepatotoxicity, and the potential for drug interaction as NVP was a CYP 3A4 enzyme inducer.

The duration on ART regimen <1 year was also found to be associated with change of ART regimen. This was mainly because 68/92 (73.9%) of the treatment modifications occurred within this period and were responsible for the high incidence rate of 71.0/100 PY within the 1st year on ART regimen. It is also worth noting that apart from drug shortages 32 (47.1%) being responsible for most of these early modifications, majority of the ART regimen modifications due drug toxicity (15/16), and treatment failure (8/10) also occurred within the 1st year of treatment. In our setting, more follow-up clinic visits are done within the early months after initiation on ART, and thus, the early detection of drug toxicity and treatment failure. This was further illustrated by anemia which was the most reported drug toxicity leading to treatment modification in our study.

Contrary to other studies, the WHO clinical Stage IV was not associated with initial regimen modification. This can most likely be because, HIV patients at WHO clinical stage IV generally have a low survival rate and may die earlier before a possible ART regimen modification.[14,24]

One of the main limitations of our study was its retrospective design which was an increased risk for misclassification bias since information that was not previously recorded appropriately during the patient follow-up may be misinterpreted or coded wrongly. This could be seen by the absence of data on the other types of drug toxicities (e.g., gastrointestinal and central nervous system toxicities) which could have led to treatment change or modification as reported in other studies. While this may be the case, we believe this was minimized by the use of prestructured questionnaires, which make it easier to collect relevant information and further minimize errors. Selection bias is also likely to have occurred in the case of participants who were lost to follow-up who had only one follow-up visit after treatment initiation. This may lead to underestimation of the magnitude of ART regimen change as well as bias the conclusion about factors associated with ART regimen change.

**Conclusion**

It is important to evaluate reason-specific trends in the incidence of change of initial ART regimen to better understand the determinants of changes. Our study found that the incidence rate of modification of initial ART regimen was 14.6/100 PYs. Drug unavailability (stocks out) was the most common reason for modification of initial ART regimen while factors associated with ART regimen modification were low CD4 count, type of regimen initiated on, and the duration on the specified regimen.

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**Conflicts of interest**

There are no conflicts of interest.

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