

Retention of People Living with HIV and Factors Associated with Attrition at 36 Months: Case of Patients Followed at the Outpatient Treatment Center in Dakar Fann

Ngom Ndeye Fatou^{1*}, Ndiaye Kine², Lawson AT Dela-dem³, Faye Mame Awa⁴, Faye Fulgence Abdou¹, Doutchi Mahamadou⁵, Mboup Ahmadou², Gueye Mamadou², Ba Awa¹, Ka Ousseynou⁶, Seydi Moussa⁴, Amandine counil⁷ and Eric Delaporte⁷

¹Department of Health and Sustainable Development Alioune Diop University (UAD), Bambey, Senegal

²Outpatient Treatment Center, Fann University Hospital, Dakar, Senegal

³Clinic of infectious Diseases, Tivaoune Hospital, UFR of health Thies, SenegalThiès, Senegal

⁴Clinic of Infectious Diseases, Fann University Hospital, Dakar, Senegal

⁵Department of Health Science, Zinder University, Niger Zinder, Niger

⁶Unit of Community Health, Department of Health and Sustainable Development, Alioune Diop University (UAD), Bambey, Senegal, Bambey, Senegal

⁷TransVIHMI, UMI233- Institute of Research and Development, U1175-Inserm, University of Montpellier, Montpellier, France

Abstract

Introduction: Retention has become a challenge for AIDS programs, especially in countries with limited resources. However, for better care, it is essential that infected people stay in treatment programs for a long time. It is in this context that we conducted this study which focused on the retention of PLHIV on ARVs at the Dakar CTA.

Methodology: This was a retrospective descriptive and analytical study on patients over 15 years of age living with HIV naïve to antiretroviral treatment and whose file was opened between 2011 and 2016 at the Fann outpatient treatment center with at least 36 months of follow-up under treatment.

Results: The study population was 432 patients with a predominance of women (57.2%), married (47.9%), informal sector workers (67.8%), and patients from the Dakar region (94%). The median age was 36 years with a predominance of patients aged 30 to 39 years. The majority of patients were classified as stage III and IV by WHO (52.3%). BMI between 18 and 25 affected 54.3% of patients. The majority of patients (94.2%) were infected with HIV-1 and the median LTCD4 baseline was 235 cells/mm³. The 36-month retention rate (86%) of patients at CTA. The factors significantly associated with attrition at 36 months were age, sex, BMI, clinical stage and CD4 count, but these factors differ depending on whether one is looking at the lost to follow-up or death. The factors significantly associated with attrition at 36 months were age, sex, BMI, clinical stage and CD4 count, but these factors differ depending on whether one is looking at the lost to follow-up or death, while sex and region of residence were associated with the risk of being lost to follow-up. Only BMI was associated with both the risk of death and loss of vision, with a stronger association with mortality.

Conclusion: The outcome of patients on treatment in patients followed by CTA was good. However, additional efforts must be made to achieve 90% retention on treatment and contribute to the eradication of the virus by 2030.

Keywords: HIV/AIDS; Retention; Fann; CTA

Introduction

By the end of July 2017, 20.9 million people living with HIV initiated antiretroviral therapy worldwide, representing 53% coverage. This access to therapy has increased in sub-Saharan Africa, where two-thirds of PLHIV live [1]. UNAIDS has set the goal of ending the HIV epidemic by 2030, with an intermediate target of 90% of HIV-positive people knowing their status by 2020, 90% of people tested initiating antiretroviral treatment and 90% of people put on treatment remaining in care with a controlled viral load [2]. Several studies conducted in developed countries have observed a progressive decline in retention according to the duration of treatment at 12 (77%-81%), 24 (69%-77%) and 36 (63%-72%) months and consistently regardless of the study period [3-7]. Overall, in Africa, retention is 80% at 12 months and 65% at 36 months.

Regarding attrition, many studies have revealed that death occurs early in the first six months after initiation of treatment [8,9]. In contrast, attrition is often observed late in treatment and it is difficult to identify true attrition, deceased attrition, self-transfers and those not found for false or changed addresses [10].

Few studies have been conducted to assess long-term treatment retention in Senegal. The GARP 2016 report shows ARV coverage of 50% in 2016 with 12-month VDPs at 9.1% and 3% of deaths. Retention

rates at 12, 24 and 36 months were 75.7%; 65.4% and 58.8% for the period 2013-2015 [11]. The Outpatient Treatment Centre (CTA) in Dakar is one of the first three HIV treatment sites in Senegal and has experienced the different historical periods in the evolution of the Senegalese HIV Control programme. The proportion of naive people who initiated antiretroviral treatment at the centre increased sharply between 1998 and 2015 in parallel with the expansion of the eligibility criteria for starting ART from 200 to 350 and then 500 CD4/mm³. This proportion increased from 25%; 47%; 75% to 82% in 1998-2003, 2004-2010, 2011-2013 and 2014-2015 respectively [12]. The objective of this study was to assess the evolution of retention based on the follow-up time, considering the different changes in eligibility

***Corresponding author:** Ngom Ndeye Fatou, Département de Médecine de l'UFR Santé et Développement Durable, Université Alioune Diop (UAD), Bambey, Sénégal, E-mail: ndeyefatou.ngom@uadb.edu.sn

Received date: January 05, 2022; **Accepted date:** January 19, 2022; **Published date:** January 26, 2022

Citation: Ngom NF, Ndiaye K, Lawson DAT, Faye MA, Faye FD, et al. (2022) Retention of People Living with HIV and Factors Associated with Attrition at 36 Months: Case of Patients Followed at the Outpatient Treatment Centre in Dakar Fann. J Infect Dis Ther S1:004.

Copyright: © 2022 Ngom NF, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

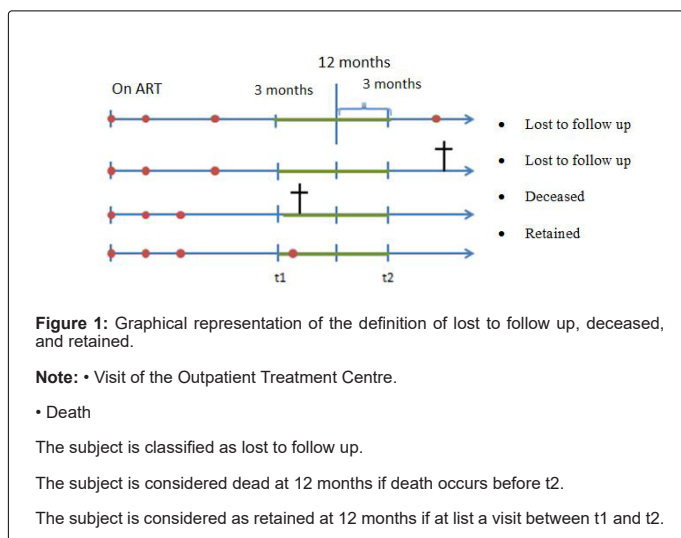
criteria. Finally, we plan to determine whether the progress in access to therapy observed at the Outpatient Treatment Centre is followed by an improvement in retention among treatment-naive patients in care at 12, 24 and 36 months, depending on the period, and to identify the sociodemographic, bio clinical and therapeutic factors associated with attrition on treatment at 36 months.

Methodology

Population and type of study

We conducted a retrospective cohort study of Antiretroviral Therapy (ART)-naive patients aged 15 years or older who initiated ART at the Outpatient Treatment Centre between August 1, 1998, and March 31, 2016, and followed them up until June 30, 2018, to reach at least 27 (24+3) months of follow-up by June 30, 2018, for all patients. For the 36-month analysis, patients who started treatment after 31 March 2015 were excluded from the analysis. Transferred patients who have not had 12, 24 or 36 months of follow-up at the time of analysis will not be considered for retention assessment at the 12, 24 and 36 months.

The definitions for the classification of patient as retained, LDP or dead at 12 months are shown in Figure 1. The same definitions apply for 24 and 36 months of follow-up.



Retention on ART at 12, 24 or 36 months is the proportion of patients who started treatment and not transferred before 12, 24 or 36 months and who are retained at 12, 24 or 36 months.

ART attrition at 12, 24 or 36 months is the proportion of patients who started on ART and not transferred before 12, 24 or 36 months and who died or are lost to follow-up at 12, 24 or 36 months.

Four periods were defined according to the recommendations on HIV management in Senegal: 1998-2003 (P1), 2004-2010 (P2), 2011-2013 (P3), and 2014-2016 (P4).

The time to ART is the time between eligibility and initiation of ART.

Data collection

The Outpatient Treatment Centre has a computerized database of a cohort of 3,651 naive patients. A retrospective catch-up of routine data was carried out until March 2012 for patients recorded at the centre since the start of activities on 1 August 1998, until March 2012, when

the files were entered prospectively, and new visits were entered in real time.

An active search by phone calls or home visits of those lost to follow-up was organised in 2016. The results of the search were updated before the database was frozen. Regarding follow-up, patients who were late for their appointments received reminder by phone calls. Those who were lost to follow-up were traced by telephone and home visits by the team of social workers. Following these visits, information was recorded in the database. Information on dates and causes of death, for those known, is entered into the database. If a patient is transferred or self-transferred, the doctor closes the file, and the data entry team enters the date, reason, and place of transfer. Patients not found for false addresses or change of address is considered as Lost to follow up.

Statistical analysis

Findings Continuous variables will be described as median and interquartile range, categorical variables as percentage to describe socio-demographic, clinical and biological characteristics of the treatment-naive population. The characteristics of the analysis population were compared according to the period of initiation of ART using the Chi-2 test (categorical variables) or the Kruskal-Wallis's test (continuous variables).

Factors associated with attrition at 36 months were identified using a Cox model. We then used a competitive hazard model to separately identify factors associated with the risk of death or being lost to follow-up using the Fine and Gray method [13]. All available variables likely to be associated with attrition were tested.

All variables associated in bivariate with a p-value of less than 0.20 with the risk of attrition, death or loss to follow up was retained in the 3 multivariate models. The variable "period of initiation of treatment" was retained in the models as a specific variable of interest, irrespective of its association with the risk of attrition. Adjusted Hazard Ratios (HRa) and their 95% confidence intervals were estimated for the variables retained in the model. The models were also used to estimate cumulative incidences (deaths or attrition) by period, which were presented in graphical form.

Statistical analyses were carried out using Stata version 14 software. The original date was the date of initiation of ARV treatment. The duration of follow-up since the date of initiation of ARV treatment was expressed in months. It corresponds to the difference between the date of initiation of ARV treatment and the date of censoring or death. The date of censoring may be the date of transfer to another care centre, the date of last consultation for patients lost to follow-up, or the date at the end of the 12-month follow-up (point date) for those who were still in active follow-up.

A patient was declared lost to follow-up when there was no news of the patient for at least six months after the date of the last consultation. Before declaring a patient lost to follow-up and when possible, we initiate telephone contact to make sure that the patient is not died.

Survival curves were estimated using the Kaplan-Meier method. The comparison of the survival curve of patients put on ARV treatment within ≤ 4 weeks to that of patients treated after 4 weeks was done using the Log-rank test.

Results

Characteristics at inclusion

In total, our analysis covered 1853 naive patients aged over 15 years

who initiated treatment between 1st August 1998 and 30th March 2016 at the Dakar Outpatient Treatment Centre. The median age of treated patients was 38 years [IIQ: 31-46] over the entire period; it decreased over time from 40 years in the first period (1998-2003) to 36 years in the last two periods (2011 to 2016). There was a female predominance (58.8%) in all periods. More than half of the patients (63%) worked in the informal sector and about 10% lived outside Dakar (Table 1).

At inclusion, the body mass index was less than 18.5 kg/m² for one third of the treated patients and half of the cases were in WHO

stage III or IV. At ART initiation, 1316 (71%) patients had an LTCD4 test. The median CD4 count was 148 [IIQ: 56-249] cells/mm³ over the entire period. There was an increase in the proportion of people with CD4 ≥ 350 cells/mm³ from 2011 onwards in line with the broadening of the eligibility criteria for treatment. This proportion increased from 4.5% in 2004-2010 to 19% in 2011-2013 and then to 38% in 2014-2016. However, it is important to note that, the proportion of people with a CD4 count < 100 cells/mm³ was still high after 2011, representing 30% and 21% of people put on ART in 2011-2013 and 2014-2016 respectively (Table 2).

| | Periods (at initiation) | | | | |
|--|-------------------------|--------------|--------------|---------------|--------------|
| | 1998-2003 | 2004-2010 | 2011-2013 | 2014-2016 | |
| | n=335 | n=1095 | n=230 | n=193 | n=1853 |
| Age, median [IIQ], years | 40 [32-47] | 39 [32-46] | 36 [28-44] | 36 [28-45] | 38 [31-46] |
| Age range (years) %, *** | | | | | |
| 15-29 | 17.3 | 17.5 | 27.4 | 29.0 | 20.0 |
| 30-39 | 32.5 | 35.3 | 32.2 | 28.0 | 33.7 |
| 40-49 | 30.7 | 30.3 | 27.0 | 32.1 | 30.2 |
| >50 | 19.4 | 16.8 | 13.5 | 10.9 | 16.2 |
| Sex (% female) ** | 56.1 | 60.2 | 58.7 | 55.4 | 58.8 |
| Marital status %*** | | | | | |
| Single | 14.9 | 16.7 | 26.5 | 30.6 | 19.0 |
| Married | 53.4 | 54.0 | 50.9 | 44.0 | 52.5 |
| Widows/widowers | 20.0 | 15.3 | 10.9 | 9.3 | 15.0 |
| Divorced | 11.6 | 14.0 | 11.7 | 16.1 | 13.5 |
| Occupation %*** | | | | | |
| Unemployed | 35.5 | 26.5 | 28.7 | 18.6 | 27.6 |
| Informal sector | 54.3 | 63.8 | 63.9 | 73.1 | 63.1 |
| Employee | 10.1 | 9.7 | 7.4 | 8.3 | 9.3 |
| Region of residence %*** | | | | | |
| Dakar | 83.3 | 90.2 | 93.9 | 93.8 | 89.8 |
| Centre | 14.9 | 8.3 | 6.1 | 5.7 | 9.0 |
| North | 1.2 | 0.8 | 0.0 | 0.5 | 0.8 |
| Southeast | 0.6 | 0.6 | 0.0 | 0.0 | 0.5 |
| WHO clinical stage %*** | | | | | |
| 1 | 7.5 | 11.3 | 20.9 | 38.9 | 14.7 |
| 2 | 50.7 | 36.9 | 16.5 | 19.7 | 35.1 |
| 3 | 39.7 | 37.8 | 37.4 | 25.9 | 36.9 |
| 4 | 2.1 | 14.0 | 25.2 | 15.5 | 13.4 |
| Body mass index (BMI) n | 324 | 1081 | 209 | 183 | 1797 |
| Groups %, kg/m ² *** | | | | | |
| <18.5 | 28.1 | 39.9 | 30.1 | 28.4 | 35.4 |
| 18.5-25 | 58.3 | 47.8 | 51.7 | 48.6 | 50.2 |
| >25 | 13.6 | 12.3 | 18.2 | 22.9 | 14.3 |
| Tuberculosis %*** | 20.0 | 17.7 | 7.8 | 5.7 | 15.6 |
| Type of HIV | | | | | |
| HIV-1 | 91.3 | 92.4 | 94.8 | 93.8 | 92.7 |
| HIV-2 | 5.4 | 5.7 | 3.9 | 5.2 | 5.3 |
| HIV-1 & HIV-2 | 3.3 | 1.9 | 1.3 | 1.0 | 2.0 |
| Missing CD4 count, %, n | 35.8 (n=215) | 28.8 n=780) | 27.4 n=167 | 20.2 n=154 | 29.0 n=1316 |
| Median CD4 count [IIQ], cells/mm ³ ** | 128 [54-221] | 131 [47-220] | 199 [62-322] | 272 [136-391] | 148 [56-249] |
| Groups %, CD4 cells/mm ³ *** | | | | | |
| <100 | 41.9 | 40.5 | 30.5 | 20.8 | 37.2 |
| 100-199 | 29.3 | 28.5 | 20.4 | 16.2 | 26.1 |
| 200-349 | 24.2 | 26.5 | 30.5 | 24.7 | 26.4 |
| ≥ 350 | 4.6 | 4.5 | 18.6 | 38.3 | 10.3 |

Table 1: Characteristics at inclusion of patients started on ART at the Outpatient Treatment Centre in Dakar, Senegal (n=1853).

| | RDR period | | | | Total |
|------------------|------------|------------|-----------|-----------|-----------|
| | 1998-2003 | 2004-2010 | 2011-2013 | 2014-2016 | |
| Initial protocol | 335 | 1095 | 230 | 193 | 1853 |
| 2NRTI+IDV | 98(29.2) | 56(5.1) | 0(0.0) | 0(0.0) | 154(8.3) |
| 2NRTI+EFV | 138(41.2) | 516 (47.1) | 144(62.6) | 178(92.2) | 976(52.7) |
| 2NRTI+NVP | 80(23.9) | 447(40.8) | 64(27.8) | 3(1.5) | 594(32.1) |
| 2NRTI+LPVr | 0(0.0) | 25(2.3) | 12(5.2) | 12(6.2) | 49(2.6) |
| Other | 16(4.8) | 12(1.1) | 5(2.2) | 0(0.0) | 33(1.8) |
| Missing | 3(0.9) | 39(3.6) | 5(2.2) | 0(0.0) | 47(2.5) |

Table 2: Distribution of patients according to treatment at initiation, outpatient treatment centre in Dakar, Senegal (n=1853).

Time to start ART

The median time to initiation of treatment was 1 month in the latest period, compared to 4.5 months in the first period. While overall, more than half of the patients had initiated ART within three months of eligibility, they represented only 32% of those on ART from 1998-2003 compared to 69% from 2014-2016 and even 73% from 2011-2013. However, the proportion of people not put on ART 12 months after eligibility is relatively high (18%). This proportion does not decrease over time; it was 17% in 1998-2003 and 18% in 2014-2016 respectively (Table 3).

Retention, mortality, and attrition in patients on ART

As of 30 June 2018, out of a total of 1,853 naive patients who initiated antiretroviral treatment, 36% were retained in care with 32% lost to follow-up and 15% dead. With the decentralization policy and the bringing of patients closer to their place of residence or work, 16% were transferred (Table 4).

Over the whole study period, retention rates were 84%, 77% and 73% at 12, 24 and 36 months, respectively. There was an increase in retention at 12 and 24 months of more than 7 points between 2011-13 and 2014-16. At 36 months, this improvement in the latter period was no longer observed. Retention rates for the 1,626 patients analysed at

36 months were stable across the study period. The improvement in the latter period for retention at 12 and 24 months was mainly related to a decrease in the proportion of patients lost to follow-up, which was no longer observed at 36 months (Table 5 and Figure 2). This is highlighted in Figure 3 showing that the onset of loss to follow up was later in the last period compared to the other periods.

Deaths represent 6%, 9% and 10% at 12, 24 and 36 months. The evolution of the proportion of deaths according to the period was marked by a higher proportion for the period 2011-2013. At 12 months, the proportion of deaths was 10% for this period. It was between 5 and 6% for the other periods, and most deaths occurred within 3 to 6 months after initiation of ART.

Factors associated with attrition at 36 months

Among patients on ART, factors significantly associated with attrition at 36 months were age, sex, BMI, clinical stage and CD4 count, but these factors differed between those lost to follow-up and those who died. Age, WHO clinical stage, and CD4 count were associated with the risk of death, while gender and region of residence were associated with the risk of being lost to follow-up. Only BMI was associated with both risk of death and loss to follow up, with a stronger association with mortality (Table 6).

| | RDR period | | | | Total |
|--------------------------------------|---------------|---------------|---------------|---------------|---------------|
| | 1998-2003 | 2004-2010 | 2011-2013 | 2014-2016 | |
| Number of individuals initiating TAR | 335 | 1095 | 230 | 193 | 1853 |
| Median time [IIQ], months | 4.6 [2.5-9.2] | 2.3 [1.1-7.0] | 0.7 [0.3-3.2] | 1.0 [0.4-5.3] | 2.3 [0.9-7.3] |
| Time %, months | | | | | |
| <3 | 109 (32.5) | 633 (57.8) | 169 (73.5) | 133 (68.9) | 1044 (56.3) |
| 3-5 | 93 (27.8) | 163 (14.9) | 8 (3.5) | 13 (6.7) | 277 (14.9) |
| 6-11 | 77 (23.0) | 121 (11.0) | 12 (5.2) | 13 (6.7) | 223 (12.0) |
| ≥ 12 | 56 (16.7) | 56 (16.7) | 41 (17.8) | 34 (17.6) | 309 (16.7) |

Table 3: Time to treatment.

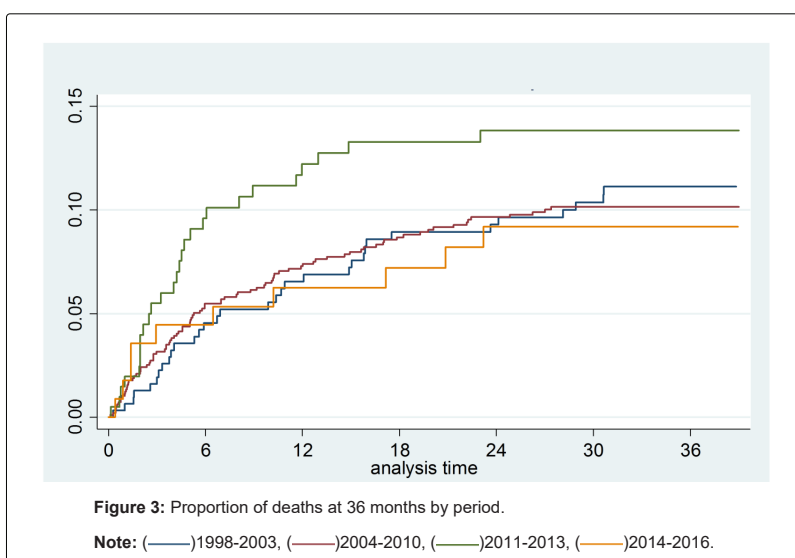
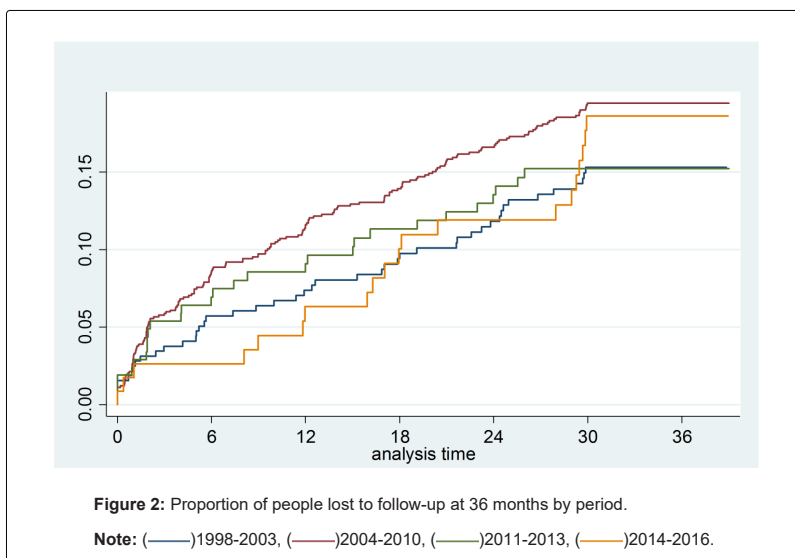
| | RDR periods | | | | Total N=1853 |
|-------------------|--------------------|---------------------|--------------------|--------------------|-----------------|
| | 1998-2003 N=335 | 2004-2010 N=1095 | 2011-2013 N=230 | 2014-2016 N=193 | |
| Withheld | 100(29.8) | 352(32.1) | 102(44.3) | 105(54.4) | 659(35.6) |
| Lost to follow up | 118(35.2) | 367(33.5) | 66(28.7) | 48(24.9) | 599(32.3) |
| Dead | 69 (20.6) | 166(15.2) | 36(15.6) | 17(8.8) | 288(15.5) |
| Transferred | 48(14.3) | 210(19.2) | 26(11.3) | 23(11.9) | 307(16.6) |

Table 4: Outcome of ART-naive patients as of 30 June 2018, Dakar outpatient treatment centre, Senegal (n=1853).

| | Periods (at initiation) | | | | Total |
|-----------------------------|-------------------------|-----------|-----------|-----------|--------|
| | 1998-2003 | 2004-2010 | 2011-2013 | 2014-2016 | |
| 12 months, n | n=332 | n=1053 | n=218 | n=189 | n=1792 |
| Retention under ART %*** | 81.0 | 84.9 | 82.6 | 90.5 | 84.5 |
| Lost to follow-up (LF) %*** | 13.2 | 9.6 | 7.8 | 4.2 | 9.5 |
| Deceased (DCD) %*** | 5.7 | 5.5 | 9.6 | 5.3 | 6.0 |
| 24 months, n | n=328 | n=1005 | n=213 | n=182 | n=1728 |
| Retention under ART %*** | 79.6 | 76.1 | 74.6 | 81.9 | 77.2 |
| Lost to follow-up (LF) %*** | 11.3 | 15.5 | 13.1 | 9.3 | 13.8 |
| Deceased (DCD) %*** | 9.1 | 8.4 | 12.2 | 8.8 | 9.0 |
| 36 months, n | n=321 | n=982 | n=208 | n=115 | n=1626 |
| Retention under ART %*** | 75.1 | 72.4 | 73.0 | 73.9 | 73.1 |
| Lost to follow-up (LF) %*** | 14.3 | 18.3 | 13.9 | 17.4 | 16.9 |
| Deceased (DCD) %*** | 10.6 | 9.3 | 13.0 | 8.67 | 10.0 |

Note: P-values for comparison between time-periods: ***<0.0001, **<0.001, *<0.01.

Table 5: Treatment outcome: retention, mortality, and attrition.



| | Attrition | | Lost to follow up | | Mortality | |
|--|-----------|-----------|-------------------|-----------|-----------|-----------|
| | aHR | 95% CI | aHR | 95% CI | aHR | 95% CI |
| Age, years | | | | | | |
| 30-40 vs. 15-29 | 1.35* | [1.0-1.8] | 1.15 | [0.8-1.6] | 1.72* | [0.9-3.0] |
| 40-49 vs. 15-29 | 1.19 | [0.8-1.6] | 0.99 | [0.6-1.4] | 1.60 | [0.9-2.8] |
| ≥ 50 vs. 15-29 | 1.28 | [0.9-1.8] | 0.96 | [0.6-1.4] | 2.07* | [1.1-3.7] |
| Gender | | | | | | |
| Female vs. male | 0.70** | [0.5-0.8] | 0.65** | [0.5-0.8] | 0.87 | [0.6-1.2] |
| Region of residence | | | | | | |
| Other regions vs. Dakar | 1.32* | [0.9-1.8] | 1.47* | [1.0-2.1] | 1.04 | [0.5-1.8] |
| TAR initiation period | | | | | | |
| 1998-2003 vs. 2014-2016 | 0.83 | [0.5-1.3] | 0.77 | [0.4-1.3] | 0.94 | [0.4-2.0] |
| 2004-2010 vs. 2014-2016 | 1.06 | [0.7-1.5] | 1.14 | [0.7-1.8] | 0.84 | [0.4-1.7] |
| 2011-2013 vs. 2014-2016 | 0.97 | [0.6-1.5] | 0.79 | [0.4-1.4] | 1.20 | [0.5-2.7] |
| WHO clinical stage | | | | | | |
| 1 vs. 2 | 1.27 | [0.8-1.8] | 1.16 | [0.7-1.7] | 1.70 | [0.7-3.8] |
| 1 vs. 3 | 1.51* | [1.0-2.1] | 1.15 | [0.7-1.7] | 2.71* | [1.2-6.0] |
| 1 vs. 4 | 1.2 | [0.8-2.0] | 0.95 | [0.5-1.6] | 2.48* | [1.0-6.0] |
| Body mass index, Kg/m² | | | | | | |
| 18.5-25 vs. <18.5 | 0.59*** | [0.4-0.7] | 0.73* | [0.5-0.9] | 0.48*** | [0.3-0.6] |
| >25 vs. <18.5 | 0.77 | [0.5-1.0] | 1.00 | [0.6-1.4] | 0.52* | [0.2-0.9] |
| CD4 at ART initiation | | | | | | |
| <100 vs. >200 | 1.91*** | [1.3-2.7] | 1.41 | [0.9-2.1] | 3.21** | [1.5-6.6] |
| 100-200 vs. >200 | 1.37 | [0.9-2.0] | 1.45* | [0.9-2.2] | 1.31 | [0.5-3.0] |
| CD4 Missing | 2.22*** | [1.5-3.1] | 1.76** | [1.1-2.6] | 3.33** | [1.6-6.7] |

Table 6: Factors associated with attrition, mortality and loss of sight at 36 months.

Thus, patients older than 50 years versus 15-29 years, those with WHO clinical stage III and IV versus WHO stage I and those with CD4 counts <100 or missing versus CD4 >200 cells/mm³ at ART initiation were at higher risk of death. BMI between 18.5-25 versus BMI <18.5 as for attrition reduced mortality risk. Furthermore, women and people living in Dakar had a lower risk of being lost to follow-up at 36 months compared to men and people living outside Dakar respectively.

Finally, we did not find any effect of the ART period on the risk of attrition at 36 months.

Discussion

Retention, mortality, and attrition in patients on ART

The challenge is not only to get new patients on ART early, but to keep all patients on treatment alive and with a controlled viral load for as long as possible. As observed in many other studies, our results confirm the difficulty of keeping patients on treatment for a long time. At the same time, the attrition rates (death and loss to follow up) that we observed corroborate those found in other African studies at 12 months (16%) such as in Uganda ([14] and more generally in resource-limited countries (15%) [9]. Other studies have found lower attrition rates, notably in China and Uganda [15]. In developed countries, attrition rates are even lower at less than 5% [9].

Of 1,853 treatment-naïve patients who initiated treatment at the Outpatient Treatment Centre in Dakar between August 1998 and March 2016, retention rates were 84%, 77% and 73% at 12, 24 and 36 months respectively. These rates are similar to those found in most African reviews and studies [3-5,7]. A recent publication by Haas et al. in 2018 on the IeDEA cohort of adults and children who initiated treatment between 2009-2014 found similar results with 83.1%; 77.3% and 72.2% respectively at 12, 24 and 36 months [6]. However, our results are better compared to those observed in the Senegalese HIV Control programme over the period 2014-2016 [16].

Our results show a significant improvement in retention for the most recent period (2014-2016) with rates reaching 90% and 82% at 12 and 24 months. This progress is largely the result of a significant decrease in the number of patients lost to follow-up. The decrease in the proportion lost to follow-up could be explained by the improvement in the median initial LTCD4 level from 138 to 272 cells/mm³ with a proportion of 38% of patients initiating ART with LTCD4 ≥ 350 cells/mm³ in the latter period. This improvement in retention could also be related to the fact that most patients residing in the regions were transferred. It is also important to note that the improvement in retention observed at 12 and 24 months is not maintained over time. Indeed, at 36 months, retention on treatment was stable over the entire study period, with an overall rate of 73%. Loss to follow up occurred later in the most recent period but at 36 months the proportion was no different from that of the earlier periods. The evolution of mortality rates according to periods shows a higher mortality rate in the period 2011-2013 compared to earlier or later periods. This higher mortality may be due to immune restoration phenomena or to the fact that the most fragile patients who died before being put on ART in periods 1 and 2, die after being put on ART after 2011 and are counted in the mortality rate on ART.

To this, we can add the inadequacy of the technical platform and the lack of means to diagnose certain infections and opportunistic conditions associated with HIV to manage them adequately.

Factors associated with attrition

In this analysis, we found different predictors of mortality and lost

to follow up at 36 months over the entire study period. The association between attrition or mortality and low LTCD4 levels at initiation was found in many studies conducted in resource-limited countries [3,8,15,17-22].

Our results also show that people submitted to treatment at advanced stages of the disease (stage 3 and 4) have a higher risk of death than those at stage 1 and thus confirm the relationship between advanced disease stage and mortality observed in several studies as previously cited.

Like in other studies in sub-Saharan Africa, we found that people over 50 years of age who initiate ART are at higher risk of death at 36 months compared to younger people, regardless of CD4 count and clinical stage [23-25].

Age is known to be a major factor in mortality. The increased frequency of age-related co-morbidities in PLHIV probably contributes to the increased risk of mortality in older people [26,27]. On the other hand, unlike what is observed in some studies, we did not find evidence of a higher risk of being lost to follow-up among people with a high LTCD4 [15,22,28,29]. This result can be explained by the fact that over the whole period, the proportion of asymptomatic patients with high CD4 counts was quite low, and there may not be sufficient evidence to establish this association.

All these results are in line with the Test and Treat strategy as recommended by the WHO and adopted by Senegalese HIV control programme, as this strategy should allow patients to be put on treatment more quickly and therefore at a less advanced stage of immunodepression, with expected benefits in terms of mortality reduction. The challenge today is screening and linkage to care [17]. In fact, at the Outpatient Treatment Centre as elsewhere, we note that a significant proportion of patients arrive at health facilities late and are put on ART at an advanced stage of immunodepression, despite the extension of the criteria for putting patients on ART [12,30-32]. We identified two main factors associated with the risk of being lost to follow-up at 36 months: Region of residence and gender.

At the beginning of the programme, only the Dakar region had treatment facilities. Some patients travelled many Kilometers (km) to obtain treatment and keep their appointments (more than 800 km). They had to pay for transport, which could cost up to CFA 80,000 for a return trip (Matam), without taking into account accommodation and food costs [33]. The results observed by Van der Kop in his study, which found that the distance from the place of residence to the place of care could be a cause of lost to follow up, confirm our results [34]. Much has been done in terms of decentralisation and geographical accessibility of health care facilities. Nevertheless, with the stigma attached to HIV infection, some patients continue to receive care in sites where they feel safe. Interventions are needed despite efforts to facilitate access to treatment follow-up, at a lower cost, for an acceptable duration and at a sustainable pace. Bringing care sites closer to where patients live, supporting transport, reducing waiting time, reducing appointments (3-6 months for people stable on ART), community-based treatment delivery, could contribute to a low risk of lost to follow up [35-37].

The higher risk of lost to follow up in men should be of concern to caregivers [4,19,21]. Support strategies that specifically target men such as enhanced counseling, targeted therapeutic education sessions, reorganisation of working hours and days, should be implemented to minimise the risk of lost to follow up in men [15]. Innovative strategies to help with appointment reminders such as texting, beeping, etc. are essential [38,39].

The absence of a period effect indicates that the evolution of adherence enhancement measures and the extension of eligibility criteria for ART did not have a significant impact on attrition (deaths or attrition) in the medium term (36 months), but there are encouraging signs of a decrease in attrition in the last period, in the shorter term (12 and 24 months). It is important to conduct further qualitative studies to better assess the factors associated with attrition, death and loss to follow up and to put in place appropriate prevention measures.

The limitations of the study are: The lack of qualitative data to better explain the determinants of mortality and loss to follow up, the fact that several of the factors tested for their association with attrition, such as clinical stage, BMI, marital status or professional activity are only available in this analysis for the initial visit. Controlling for these variables during follow-up would have allowed a more refined analysis of the associated factors.

Conclusion

Despite its experience and the mechanisms put in place to support the treatment of PLHIV, the retention rate at the outpatient treatment centre is comparable to those of many African countries. These results are acceptable, but the practices must be reviewed (evaluated) and additional efforts must be made for the achievement of the retention rate of 90% on treatment to contribute to the eradication of the virus by 2030. This goal remains a challenge in 2021 for many African countries, especially in West Africa.

References

- UNAIDS (2017) Gap Report.
- Joint United Nations Programme on HIV/AIDS (UNAIDS). An ambitious treatment target to help end the AIDS epidemic. Geneva UNAIDS (2014).
- Dalhatu I, Onotu D, Odafe S, Abiri O, Debem H, et al. (2006) Outcomes of Nigeria's HIV/AIDS treatment program for patients initiated on antiretroviral treatment between 2004-2012. *PLoS ONE* 12: e0170912.
- Fox MP, Rosen S (2010) Patient retention in antiretroviral therapy programs up to three years on treatment in sub-Saharan Africa, 2007-2009: Systematic review. *Tropical Med and Int Health* 15:1-15.
- Fox MP, Rosen S (2015) Retention of adult patients on antiretroviral therapy in low- and middle-income countries: systematic review and meta-analysis 2008-2013 HHS public access. *J Acquir Immune Defic Syndr* 69:98-108.
- Haas AD, Zaniewski E, Anderegg N, Ford N, Fox MP, et al. (2018) The African regions of the international epidemiologic databases to evaluate AIDS (IeDEA). Retention and mortality on antiretroviral therapy in sub-Saharan Africa: Collaborative analyses of HIV treatment programmes. *J Int AIDS Society* 21:e25084.
- Mutasa-Apollo T, Shiraishi RW, Takarinda KC, Dzangare J, Mugurungi O, et al. (2014) Patient retention, clinical outcomes and attrition-associated factors of HIV-infected patients enrolled in zimbabwe's national antiretroviral therapy programme 2007-2010. *PLoS ONE* 9: e86305.
- Lawn SD, Myer L, Harling G, Orell C, Bekker LG, et al. (2006) Determinants of mortality and nondeath losses from an antiretroviral treatment service in south africa: implications for program evaluation. *Clin Infect Dis* 43:770-776.
- Braitstein (2006) Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: Comparison between low-income and high-income countries. *The Lancet* 367:817-824.
- Wilkinson LS, Skordis-Worrall J, Ajose O, Ford N (2015) Self-transfer and mortality amongst adults lost to follow-up in ART programmes in low- and middle-income countries: Systematic review and meta-analysis. *Trop Med Int Health* 20: 365-379.
- GARP Senegal Report 2016-2017.
- Ngom NF, Faye MA, Ndiaye K, Thiam A, Ndour CT, et al. (2018) ART initiation in an outpatient treatment center in Dakar, Senegal: A retrospective cohort analysis (1998-2015). *PLoS One* 13: e0202984.
- Fine JP, Gray RJ (1999) A proportional hazards model for the subdistribution of a competing risk a proportional hazards model for the subdistribution of a competing risk. *J American Stat Ass* 94:496-509.
- Geng EH, Glidden DV, Emenyonu N, Musinguzi N, Bwana MB, et al. (2010) Tracking a sample of patients lost to follow-up has a major impact on understanding determinants of survival in HIV-infected patients on antiretroviral therapy in africa. *Trop Medicine & Int Health* 15:63-69.
- Zhu H, Napravnik S, Eron J, Cole S, Ma Y, et al. (2012) Attrition among human immunodeficiency virus (HIV)-infected patients initiating antiretroviral therapy in China, 2003-2010. *PLoS ONE* 7: e39414.
- Annual activity report of the National AIDS Council (2016).
- Alvarez-Uria G, Agbor AA, Bigna JJR, Billong SC, Tejiokem MC, et al. (2013) Factors associated with attrition, mortality, and loss to follow up after antiretroviral therapy initiation: Data from an HIV cohort study in India. *Global Health Action*.
- Clouse K, Pettifor A, Maskew M, Bassett J, Van Rie A, et al. (2013) Initiating ART when presenting with higher CD4 counts results in reduced loss to follow-up in a resource-limited setting. *AIDS (London, England)* 27: 645-650.
- Cornell M, Myer L, Kaplan R, Bekker LG, Wood R (2009) The impact of gender and income on survival and retention in a south african antiretroviral therapy programme. *Trop Med & Int Health* 14:722-731.
- Egger M, May M, Chene G, Phillips AN, Ledergerber B, et al. (2002) ART cohort collaboration prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: A collaborative analysis of prospective studies. *Lancet* 360:119-129.
- Ekouevi DK, Balestre E, Ba-Gomis FO, Eholie SP, Maiga M (2010) IeDEA west africa collaboration low retention of HIV-infected patients on antiretroviral therapy in 11 clinical centers. *Trop Med & Int Health*, 15:34-42.
- Tang Z, Pan SW, Ruan Y, Liu X, Su J, et al. (2017) Effects of high CD4 cell counts on death and attrition among HIV patients receiving antiretroviral treatment: An observational cohort study. *Scientific Rep* 7:3129.
- Auld AF, Mbofana F, Shiraishi RW, Sanchez M, Alfredo C, et al. (2011) Four-year treatment outcomes of adult patients enrolled in mozambique's rapidly expanding antiretroviral therapy program. *PLoS One* 6:e18453.
- Drain PK, Losina E, Parke RG, Giddy J, Ross D, et al. (2013) Risk factors for late-stage hiv disease presentation at initial HIV diagnosis in durban, south africa. *PLoS One* 8:e55305.
- Kiplagat J, Mwangi A, Keter A, Braitstein P, Sang E, et al. (2018) Retention in care among older adults living with HIV in western Kenya: A retrospective observational cohort study. *PLoS One* 13: e0194047.
- Agaba PA, Meloni ST, Sule HM, Agbadji OO, Sagay AS (2017) Treatment outcomes among older human immunodeficiency virus-infected adults in Nigeria. *Open Forum Infect Dis* 4:1-9.
- Negin J, Nemser B, Cumming R, Lelera E, Ben Amor Y, Pronyk P (2012) HIV attitudes, awareness and testing among older adults in Africa. *AIDS and Behavior* 16:63-68.
- Ahmed I, Gugsu ST, Lemma S, Demissie M (2013) Predictors of loss to follow-up before HIV treatment initiation in Northwest Ethiopia: A case control study. *BMC Public Health* 13:1.
- Schöni-Affolter F, Keiser O, Mwango A, Stringer J, Ledergerber B, et al. (2011) Estimating loss to follow-up in HIV-Infected patients on antiretroviral therapy: the effect of the competing risk of death in zambia and switzerland. *PLoS ONE* 6: e27919.
- Hall HI, Halverson J, Wilson DP, Suligoi B, Diez M, et al. (2013) Late diagnosis and entry to care after diagnosis of human immunodeficiency virus infection: A country comparison. *PLoS ONE* 8: e77763.
- Lahuerta M, Wu Y, Hoffman S, Elul B, Kulkarni SG (2014) For the multi-level determinants of late art initiation in sub-saharan Africa team and the identifying optimal models of HIV care in sub-saharan Africa collaboration. *An Official Publication of the Infectious Diseases Society of America* 58:432-441.
- The IeDEA and COHERE Cohort Collaborations (2018) Global trends in cd4 cell count at the start of antiretroviral therapy: collaborative study of treatment programs. *Clin Infect Dis* 6:893-903.
- Van der Kop ML, Ekström AM, Awiti-Ujiji O, Chung MH, Mahal D, et al. (2014) Factors associated with attrition from HIV care during the first year after antiretroviral therapy initiation in kenya. *J AIDS Clin Res* 5:354.

-
34. Hardon AP, Akurut D, Comoro C, Ekezie C, Irunde HF (2007) Hunger, waiting time and transport costs: Time to confront challenges to ART adherence in Africa. *AIDS Care* 19:658-665.
 35. Avong YK, Alivu GG, Jatau B, Gurumnaan R, Danat N (2018) Integrating community pharmacy into community based anti-retroviral therapy program: A pilot implementation in Abuja, Nigeria. *PLoS ONE* 13: e0190286.
 36. Bemelmans M, Baert S, Goemaere E, Wilkinson L, Vandendyck M (2014) Community-supported models of care for people on HIV treatment in sub-Saharan Africa. *Trop Med Int Health* 19:968-977.
 37. Keane J, Pharr JR, Buttner MP, Ezeanolue E (2017) Interventions to reduce loss to follow-up during all stages of the hiv care continuum in sub-saharan africa: A systematic review. *AIDS and Behavior* 21:1745-1754.
 38. Mbuagbaw L, Mursleen S, Lytvyn L, Smieja M, Dolovich L (2015) Mobile phone text messaging interventions for HIV and other chronic diseases: An overview of systematic reviews and framework for evidence transfer. *BMC Health Services Res.*
 39. Brinkhof MWG, Boule A, Weigel R, Messou E, Mathers C, et al. (2009) Mortality of HIV-Infected patients starting antiretroviral therapy in sub-saharan africa: comparison with HIV- unrelated mortality. *PLoS Med* 6: e1000066.