# Persons living with HIV (PLHIV) with advanced HIV disease: Need for novel care models

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## Background

Differentiated service delivery (DSD) has highlighted the importance of developing diverse, patient-centered models of care for HIV patients on antiretroviral therapy (ART) to enhance their outcomes. However, most of the models utilized thus far have focused on "stable" patients, i.e. those on ART who have achieved virological suppression and or high adherence with immunological response. Similar innovations are not yet available for persons living with HIV (PLHIV) with advanced disease who are at high risk for poor outcomes and who have received little attention beyond recognition of their need for prompt ART initiation.

## Methods

We analyzed data on PLHIV >15 years starting ART with CD4 cell count <200 cells/mm$^3$ at PEPFAR-funded ICAP-supported clinics in Ethiopia, Kenya, Mozambique and Tanzania 2004-2015. Loss to follow-up (LTF), death and a combined endpoint of attrition (LTF and death) following ART start were assessed among those with CD4 101-200, CD4 50-100 and CD4<50 cells/mm$^3$ at ART start using Kaplan-Meier estimators and log-rank tests. LTF after ART initiation was defined as no visit for more than 6 months; deaths were ascertained from medical records. Cox proportional hazards models examined the effect of CD4 at ART start on attrition (LTF and death) adjusted for sex, age, country, year and intrasite clustering.

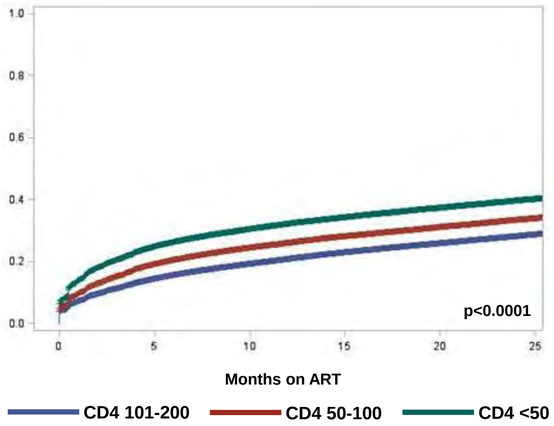
## Results

477,086 PLHIV started ART at 350 clinics, of whom 335,269 (70.3%) had CD4 count at ART initiation; 203,622 (60.7%) had CD4 <200 cells/mm$^3$ and among these, 60.2% were female, median age was 35.0 years [IQR: 28.9-42.1] and 60.7% were WHO stage III/IV (Table 1).

**Table 1. Characteristics of PLHIV starting ART with CD4 count <200 cells/mm$^3$ in Ethiopia, Kenya, Mozambique and Tanzania 2004-2015 (N=203,622)**

| | CD4 count at ART initiation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | All | | 101-200 cells/mm$^3$ | | 50-100 cells/mm$^3$ | | <50 cells/mm$^3$ | | |
| | N | % | N | % | N | % | N | % | p-value |
| | 203,622 | 100.0 | 99,354 | 48.8 | 48,846 | 24.0 | 55,422 | 27.2 | |
| **Country** | | | | | | | | | |
| Tanzania | 31,352 | 15.4 | 14,876 | 15.0 | 7,115 | 14.6 | 9,362 | 16.9 | <0.0001 |
| Mozambique | 57,511 | 28.2 | 29,582 | 29.8 | 13,631 | 27.9 | 14,298 | 25.8 | |
| Kenya | 54,979 | 27.0 | 24,883 | 25.0 | 12,427 | 25.4 | 17,669 | 31.9 | |
| Ethiopia | 59,780 | 29.4 | 30,014 | 30.2 | 15,673 | 32.1 | 14,093 | 25.4 | |
| **Female** | 122,671 | 60.2 | 62,903 | 63.3 | 28,607 | 58.6 | 31,161 | 56.2 | <0.0001 |
| **Age at ART** | | | | | | | | | |
| 15-19 | 3,735 | 1.8 | 1,861 | 1.9 | 783 | 1.6 | 1,091 | 2.0 | <0.0001 |
| 20-29 | 53,781 | 26.4 | 26,977 | 27.2 | 12,378 | 25.3 | 14,426 | 26.0 | |
| 30-39 | 79,702 | 39.1 | 37,649 | 37.9 | 19,514 | 40.0 | 22,539 | 40.7 | |
| 40-49 | 44,727 | 22.0 | 21,560 | 21.7 | 10,910 | 22.3 | 12,257 | 22.1 | |
| 50-59 | 16,232 | 8.0 | 8,346 | 8.4 | 3,912 | 8.0 | 3,974 | 7.2 | |
| 60+ | 5,445 | 2.7 | 2,961 | 3.0 | 1,349 | 2.8 | 1,135 | 2.1 | |
| **WHO stage at ART** | | | | | | | | | |
| I | 22,808 | 13.8 | 14,305 | 17.7 | 4,385 | 11.0 | 4,118 | 9.2 | <0.0001 |
| II | 42,258 | 25.6 | 23,757 | 29.4 | 9,455 | 23.8 | 9,046 | 20.2 | |
| III | 81,453 | 49.3 | 36,309 | 44.9 | 21,141 | 53.1 | 24,003 | 53.7 | |
| IV | 18,842 | 11.4 | 6,476 | 8.0 | 4,812 | 12.1 | 7,554 | 16.9 | |
| Missing | 38,261 | 18.8 | 18,507 | 18.6 | 9,053 | 18.5 | 10,701 | 19.3 | 0.001 |
| **Year initiated ART** | | | | | | | | | |
| 2004-2006 | 27,881 | 13.7 | 12,399 | 12.5 | 7,139 | 14.6 | 8,343 | 15.1 | <0.0001 |
| 2007-2009 | 85,984 | 42.2 | 42,449 | 42.7 | 20,725 | 42.4 | 22,810 | 41.2 | |
| 2010-2012 | 66,978 | 32.9 | 33,211 | 33.4 | 15,594 | 31.9 | 18,173 | 32.8 | |
| 2013-2015 | 22,779 | 11.2 | 11,295 | 11.4 | 5,388 | 11.0 | 6,096 | 11.0 | |

**Figure 1. Probability of combined attrition (LTF and death) among PLHIV starting ART with CD4 count <200 cells/mm$^3$ in Ethiopia, Kenya, Mozambique and Tanzania 2004-2015 (N=203,622)**




## Results *(continued)*

Among all patients with CD4 count <200 cells/mm$^3$, attrition at 3, 6 and 12 months was 14.8% (95%CI 14.6-14.9), 19.7% (95%CI 19.6-19.9) and 25.1% (95%CI 24.9-25.3), respectively (Table 1). Attrition at 12 months was significantly higher among those in lowest CD4 stratum, 32.2% (95%CI 31.8-32.6) of those with CD4<50 cells/mm$^3$ versus 20.8% (95%CI 20.6-21.1) of those with CD4 101-200 cells/mm$^3$ at ART start (p<0.0001).

In multivariable models, compared to PHLIV with CD4 101-200 cells/mm$^3$, those with CD4 <50 cells/mm$^3$ had more than 40% increased risk of attrition (adjusted hazard ratio (AHR) 1.42, 95%CI 1.40-1.44 ) and PLHIV with CD4 50-100 cells/mm$^3$ had 18% increased risk (AHR 1.18, 95%CI 1.16-1.20) (Figure 1).

**Table 2. Cumulative incidence (cum. inc.) of LTF, death and combined attrition among PLHIV starting ART with CD4 count <200 cells/mm$^3$ in Ethiopia, Kenya, Mozambique and Tanzania 2004-2015 (N=203,622)**

| | All CD4 ≤200 cells/mm$^3$ Cum. Inc. (95%CI) | CD4 101-200 cells/mm$^3$ Cum. Inc. (95%CI) | CD4 50-100 cells/mm$^3$ Cum. Inc. (95%CI) | CD4 <50 cells/mm$^3$ Cum. Inc. (95%CI) |
|---|---|---|---|---|
| **LTF at 3 months** | 10.8 (6.9-7.1) | 8.9 (8.8-9.1) | 11.1 (10.8-11.4) | 14.0 (13.7-14.3) |
| **LFT at 6 months** | 15.1 (14.9-15.3) | 12.7 (12.5-12.9) | 15.7 (15.4-16.1) | 19.0 (18.6-19.3) |
| **LTF at 12 months** | 20.0 (19.8-20.1) | 16.8 (16.5-17.0) | 20.6 (20.2-21.0) | 24.2 (23.8-24.6) |
| **Death at 3 months** | 4.4 (4.3-4.5) | 2.6 (2.5-2.7) | 4.6 (4.4-4.8) | 7.5 (7.3-7.7) |
| **Death at 6 months** | 5.4 (5.3-5.5) | 3.4 (3.3-3.5) | 5.7 (5.5-5.9) | 9.0 (8.7-9.2) |
| **Death at 12 months** | 6.4 (6.3-6.5) | 4.1 (4.0-4.3) | 6.8 (6.6-7.1) | 10.4 (10.1-10.7) |
| **Attrition at 3 months** | 14.8 (14.6-14.9) | 11.4 (11.2-11.6) | 15.1 (14.8-15.4) | 20.5 (20.2-20.8) |
| **Attrition at 6 months** | 19.7 (19.6-19.9) | 15.7 (15.5-15.9) | 20.6 (20.2-20.9) | 26.3 (26.0-26.7) |
| **Attrition at 12 months** | 25.1 (24.9-25.3) | 20.8 (20.6-21.1) | 26.1 (25.7-26.5) | 32.2 (31.8-32.6) |

## Conclusion

Even after ART initiation, PLHIV with advanced disease had notably inferior outcomes within lower CD4 strata. With the transition of stable patients to less intensive DSD models, including community ART models, the opportunity exists to focus on optimizing care systems for PLHIV with advanced HIV disease in order to enhance their outcomes. Effective DSD models that include biomedical, psychosocial and structural interventions are urgently needed for this population.

*ICAP is a global leader in HIV and health systems strengthening. Founded in 2003 at Columbia University's Mailman School of Public Health, ICAP has supported more than 5,300 health facilities across more than 21 countries. Over 2.3 million people have received HIV care through ICAP-supported programs. Online at icap.columbia.edu*

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