Gender Differences in Loss to Follow-up and Mortality in Older Adults on ART in Sub-Saharan Africa

Mansi Agarwal[1,2]; Matthew R. Lamb[1,2]; Veronicah Mugisha[1]; Davies Kimanga[3]; Bonita Kilama[4]; Andrea A. Howard[1,2]; Elaine J. Abrams[1,2]; Wafaa El-Sadr[1,2]; Batya Elul[1,2]

[1]ICAP-Columbia University, Mailman School of Public Health; [2]Department of Epidemiology, Columbia University Mailman School of Public Health; [3]National AIDS/STI Control Programme, Ministry of Health, Nairobi, Kenya; [4]National AIDS Control Program, Ministry of Health and Social Welfare, Dar es Salaam, Tanzania

Background

People living with HIV (PLWH) ≥50 years of age are a growing but understudied population in Sub-Saharan Africa (1). Older PLWH on antiretroviral therapy (ART) may be at higher risk of loss to follow up (LTF) and mortality compared to younger patients due to their increased likelihood of having concurrent chronic conditions, developing side effects, and poorer immune responses (2-5). However, little is known about whether outcomes differ by gender among older PLWH. Gender differences in outcomes after ART initiation have been well documented for PLWH aged 15-49 years in SSA, with many studies showing higher rates of LTF and mortality among males compared to females (6,7). We explored the effect of gender and age on LTF and recorded mortality after ART initiation among PLWH aged ≥50 years.

Methods

We used routinely collected patient-level data from PLWH ≥50 years initiating ART at 198 HIV clinics supported by ICAP-Columbia University in Kenya (69 clinics), Mozambique (33 clinics), Rwanda (44 clinics), and Tanzania (52 clinics). Age was categorized in 5-year increments based on age at the time of ART initiation.

Kaplan-Meier survival analysis and Cox Proportional Hazards models were used to examine gender and age-related differences in LTF and mortality 12 months after ART initiation. Gender differences were assessed in a model combining all age groups, in age-stratified models, and in gender-stratified models.

All models controlled for disease status (CD4+ <100cells/mL or WHO stage 4 vs. CD4+ ≥100 cells/mL or WHO stage 1-3) at ART initiation, point of entry into HIV care (in-patient ward vs. all other entry points), and country. Patients were considered LTF if they had no record of death or transfer and did not have a recorded clinic visit for 6 months.

References

1.Lamb MR, et al. HIV clinical and program outcomes among older patients with HIV enrolled in HIV care and initiating ART in sub-Saharan Africa. Oral presentation at XIX International AIDS Conference, Washington DC, July 2012. Abstract No. FRLBC02.
2.Blanco JR, Jarrin I, Vallejo M, Berenguer J, Solera C, Rubio R, et al. Definition of advanced age in HIV infection: looking for an age cut-off. AIDS Res Hum Retroviruses 2012;28(9):1000-6.
3.Balestre E, Eholie SP, Lokossue A, Sow PS, Charurat M, Minga A, et al. Effect of age on immunological response in the first year of antiretroviral therapy in HIV-1-infected adults in West Africa. AIDS 2012;26(8):951-7.
4.Mutevedzi PC, Lessells RJ, Rodger AJ, Newell ML. Association of age with mortality and virological and immunological response to antiretroviral therapy in rural South African adults. PLoS One 2011;6(7).
5-Yeung C, et al. Association of aging and survival in a large HIV-infected cohort on antiretroviral therapy. AIDS 2011;25(5):701-5.
6.Cornell, M., et al. (2012). "Gender differences in survival among adult patients starting antiretroviral therapy in South Africa: a multicentre cohort study." PLoS Med 9(9).
7.Centers for Disease, C. and Prevention (2013). "Differences between HIV-Infected men and women in antiretroviral therapy outcomes - six African countries, 2004-2012." MMWR Morb Mortal Wkly Rep 62(47): 945-952.

Table 1. Demographic and clinical characteristics of older adult patients initiating ART at ICAP clinics in Rwanda, Tanzania, Mozambique and Kenya from 2005-2011.

Characteristic	All patients	50-54 years	55-59 years	60-64 years	65-69 years	70+ years
N	21634	10873	5733	2946	1229	853
Age, median (IQR)	55 (52-59)	52 (50-53)	57 (56-58)	61 (60-63)	66 (66-68)	73 (71-76)
Female (n,%)	10992 (50.8)	5747 (52.9)	2824 (49.3)	1549 (52.6)	541 (44.0)	331 (38.8)
Country						
Rwanda	2483 (11.5)	1313 (12.1)	620 (10.8)	319 (10.8)	138 (11.2)	93 (10.9)
Tanzania	3707 (17.1)	1808 (16.6)	982 (17.1)	522 (17.7)	231 (18.8)	164 (19.2)
Mozambique	9820 (45.4)	5092 (46.8)	2559 (44.6)	1302 (44.2)	512 (41.7)	355 (41.6)
Kenya	5624 (26.0)	2660 (24.5)	1572 (27.4)	803 (27.3)	348 (28.3)	241 (28.3)
Point of entry						
Inpatient	1225 (5.7)	601 (5.5)	297 (5.2)	177 (6.0)	82 (6.7)	68 (8.0)
Other	20409 (94.3)	10272 (94.5)	5436 (94.8)	2769 (94.0)	1147 (93.3)	785 (92.0)
CD4 count at ART initiation						
Median (IQR)	168 (91-247)	164 (89-246)	169 (93-250)	169 (91-249)	169 (89-245)	177 (105-255)
<100	4040 (18.7)	2098 (19.3)	1038 (18.11)	549 (18.6)	219 (17.8)	136 (15.9)
100-200	4887 (22.6)	2457 (22.6)	1297 (22.6)	639 (21.7)	287 (23.6)	207 (24.3)
200-350	4533 (20.9)	2252 (20.7)	1197 (20.9)	644 (21.9)	254 (20.7)	186 (21.8)
>350	1029 (4.7)	519 (4.8)	283 (4.9)	126 (4.3)	53 (4.3)	48 (5.6)
Missing	7145 (33.0)	3547 (32.6)	1918 (33.5)	988 (33.5)	416 (33.9)	276 (32.4)
WHO Stage at ART initiation						
1	1451 (6.7)	715 (6.6)	409 (7.1)	202 (6.9)	69 (5.6)	56 (6.8)
2	3222 (14.9)	1638 (15.1)	829 (14.5)	427 (14.5)	192 (15.6)	136 (15.9)
3	6467 (29.9)	3168 (29.1)	1747 (30.5)	933 (31.7)	377 (30.7)	242 (28.4)
4	1844 (8.5)	890 (8.2)	496 (8.7)	258 (8.8)	108 (8.8)	92 (10.8)
Missing	8650 (40.0)	4462 (41.0)	2252 (39.3)	1126 (38.2)	483 (39.3)	327 (38.3)
Advanced HIV at ART initiation (CD4 count <100 or WHO stage 4)						
Yes	5505 (25.5)	2809 (25.8)	1432 (25.0)	748 (25.4)	300 (24.4)	216 (25.3)
No	13105 (60.6)	6539 (60.1)	3501 (61.1)	1777 (60.3)	756 (61.5)	532 (62.4)
Missing	3024 (14.0)	1525 (14.0)	800 (13.9)	421 (14.3)	173 (14.1)	105 (12.3)

Figure 1. Cumulative incidence of loss to follow-up and recorded death 12 months after ART initiation, by gender.

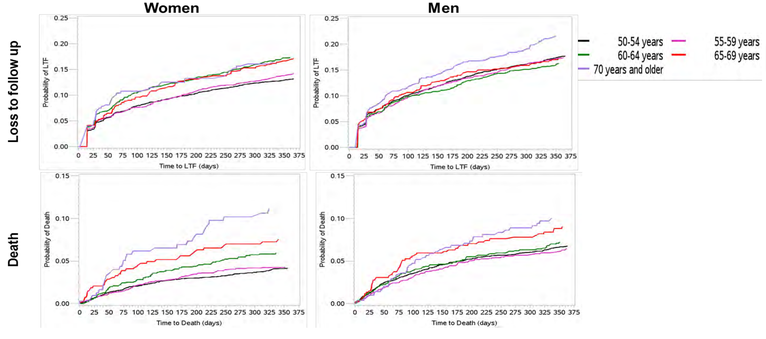

Table 2. Adjusted* hazard ratios and 95% CIs for outcomes 12 months after ART initiation (men compared to women)

	LTF	Death
All age groups	1.23 [1.13-1.34]	1.38 [1.24-1.53]

*Adjusted for advanced HIV disease, point of entry, and country.

Table 3. Adjusted* hazard ratios and 95% CIs for outcomes 12 months after ART initiation by age group

Stratified by age (men compared to women)

Age Group	LTF	Death
50-54 years	1.35 [1.18-1.53]	1.50 [1.29-1.76]
55-59 years	1.23 [1.08-1.39]	1.38 [1.07-1.78]
60-64 years	0.94 [0.78-1.13]	1.20 [0.90-1.59]
65-69 years	1.03 [0.75-1.42]	1.21 [0.80-1.84]
70+ years	1.22 [0.85-1.74]	0.96 [0.62-1.49]

*Adjusted for advanced HIV disease, point of entry, and country.

Table 4. Adjusted* hazard ratios and 95% CIs for outcomes 12 months after ART initiation by gender and age group

Stratified by gender (all age groups compared to ages 50-54)

	LTF	Death
Among women:		
55-59 years	1.08 [0.95-1.22]	1.05 [0.83-1.31]
60-64 years	1.33 [1.14-1.54]	1.40 [1.09-1.81]
65-69 years	1.31 [1.02-1.67]	1.81 [1.26-2.60]
70+ years	1.34 [0.97-1.85]	2.49 [1.70-3.65]
Among men:		
55-59 years	0.97 [0.87-1.08]	0.98 [0.80-1.20]
60-64 years	0.94 [0.83-1.06]	1.11 [0.85-1.46]
65-69 years	1.02 [0.84-1.24]	1.48 [1.07-2.04]
70+ years	1.24 [1.03-1.51]	1.54 [1.10-2.14]

*Adjusted for advanced HIV disease, point of entry, and country.

Results

- From 2005-2011, 21,634 PLWH aged ≥50 years (median (IQR) = 55 (52-59) years) initiated ART. 50% were 50-54 years, 26% 55-59 years, 14% 60-64 years, 6% 65-69 years, and 4% ≥70 years of age (Table 1).
- The proportion of patients who were females decreased across age groups: 53% 50-54 years, 49% 55-59 years, 53% 60-64 years, 44% 65-69 years, and 39% ≥70 years (Table 1).
- Across all age groups, men had significantly higher rates of LTF 12 months after ART initiation (HR: 1.23, 95% CI: 1.13-1.34) and death (HR: 1.38, 95% CI: 1.24-1.53) compared to women (Table 2).
- However, the gender differences in LTF and death were driven largely by men aged 50-59 years. When stratified by age, only men aged 50-54 (HR: 1.35, 95% CI: 1.18-1.53) and 55-59 years (HR: 1.23, 95% CI: 1.08-1.39) had higher rates of LTF and death compared to women (Table 3).
- Stratification by gender showed LTF increased for women aged 60-69 years compared to those aged 50-54 years, and for men ≥70 years compared to those aged 50-54 years (Table 4).
- Mortality rates increased with age for both men and women (Table 4).

Conclusions

In this large cohort of older PLWH on ART, we found inferior outcomes on ART in men compared to women aged 50-59 years , consistent with gender differentials observed in studies among patients aged 15-49 years. Interestingly, the gender difference was not evident among PLWH aged 60 years and older in our study. These results suggest that interventions addressing poor outcomes among men on ART should include older patients.

Acknowledgements

We thank all patients and staff at the HIV care and treatment clinics included in this analysis. We would also like to thank Ministries of Health in Kenya, Mozambique, Rwanda, and Tanzania for their continued collaboration, and all ICAP and clinic staff responsible for collecting the data used in this analysis.

This work has been supported by the President's Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention (CDC) under the terms of Cooperative Agreement Number 5U2GPS001537. The contents are the responsibility of ICAP and do not necessarily reflect the views of the United States Government.

ICAP is a global leader in HIV and public health. Founded in 2004 at Columbia University's Mailman School of Public Health, ICAP has supported work at more than 3,995 health facilities across 21 countries. Nearly 1.8 million people have received HIV services through ICAP-supported programs. **icap.columbia.edu**

CDC Centers for Disease Control and Prevention

ICAP Global. Health. Action. Columbia University Mailman School of Public Health