

Mortality of HIV-infected patients starting HAART in sub-Saharan Africa: Comparison with the general population in four countries

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Background: Mortality in HIV-infected patients receiving HAART in resource-limited settings has declined, but it is unclear how it compares to the mortality of the general population. We compared all-cause mortality in HIV-infected patients starting HAART with non HIV-related mortality in the general population.

Methods: We used data collected by the ART-LINC Collaboration, a multinational network of HIV treatment programs in Africa, Brazil, and Asia. Eligible patients came from 5 cohorts, in 4 sub-Saharan African countries (Côte d'Ivoire, Malawi, South Africa, Zimbabwe), that actively followed-up patients on treatment for at least two years. Patients were aged over 16 years, previously treatment naïve and starting with at least 3 antiretroviral drugs, and had at least 1 day of follow up. We used multiple imputation procedure to account for missing information on baseline CD4 cell count, clinical stage and the outcome. Population data on estimated non-HIV background mortality by country, age (5-year age bands) and sex were obtained from WHO's Global Burden of Disease Project. Poisson regression was used to estimate excess mortality (additive model) and standardized mortality ratios (SMRs, multiplicative model). Multivariable models included month on ART, age, sex, baseline CD4 cell count, initial treatment regimen (NNRTI-based vs. PI-based vs. other), and stage of disease at start of treatment.

Results: 13,249 patients (67% female), 17,480 person-years of follow up and 1340 deaths were analysed. The median baseline CD4 cell count was 109 cells (IQR: 48-179) and 84% started treatment with advanced disease. Combined cumulative expected and observed survival over the first two years were 0.987 and 0.857, respectively. Excess mortality was 6.94 per 100 person-years and the SMR was 18.7 (95% CI 17.7-19.8). SMRs varied widely (Table) according to patient characteristics at baseline and time period after starting HAART: from 323.1 (276.0-378.3) during months 1-3 for patients starting HAART with <25 CD4 cells and advanced stage to 0.7 (0.4-1.2) during months 13-24 among patients who started with ≥ 200 cells and no advanced stage (and survived to the second year of HAART), indicating that there was no excess mortality in this patient group and period. However, the SMR was 3.4 (1.9-6.2) for the same group for the whole period, and in all groups substantial excess mortality was observed during the first months of treatment.

Conclusions: The massive excess mortality early after starting therapy reflects advanced immunodeficiency and clinical stage. Even patients starting with higher CD4 counts and less advanced disease have substantially increased mortality, possibly due to selection mechanisms, which mean that in all groups sick patients gain access to HAART.

Table: Standardized mortality ratios by baseline CD4 count, clinical stage and time period after starting HAART.

CD4 count	Clinical stage	Time period (months)				Overall (1-24)
		1-3	4-6	7-12	13-24	
< 25	Advanced	323.1 (276.0-378.3)	124.5 (106.3-145.9)	33.7 (26.3-43.0)	10.1 (8.4-12.1)	47.1 (39.1-56.6)
	Less advanced	111.8 (69.3-180.3)	43.1 (25.9-71.8)	11.6 (6.4-21.1)	3.5 (2.2-5.6)	15.8 (9.0-27.9)
25-49	Advanced	215.3 (188.6-245.6)	83.0 (70.8-97.2)	22.4 (17.8-28.2)	6.7 (5.6-8.0)	31.4 (26.1-37.7)
	Less advanced	74.5 (46.5-119.2)	28.7 (17.2-47.8)	7.8 (4.3-14.0)	2.3 (1.5-3.7)	10.6 (6.1-18.4)
50-99	Advanced	138.6 (117.3-163.7)	53.4 (42.8-66.7)	14.4 (10.9-19.2)	4.3 (3.6-5.3)	19.6 (15.1-25.5)
	Less advanced	48.0 (28.3-81.2)	18.5 (10.4-32.9)	5.0 (2.6-9.5)	1.5 (0.9-2.5)	6.6 (3.6-12.1)
100-199	Advanced	95.3 (85.8-105.8)	36.7 (31.4-42.9)	9.9 (8.0-12.4)	3.0 (2.5-3.5)	13.6 (11.5-16.1)
	Less advanced	33.0 (20.7-52.5)	12.7 (7.6-21.2)	3.4 (1.9-6.2)	1.0 (0.6-1.6)	4.6 (2.7-7.8)
≥ 200	Advanced	66.7 (50.3-88.4)	25.7 (19.8-33.3)	6.9 (5.0-9.6)	2.1 (1.5-2.8)	10.2 (7.6-13.7)
	Less advanced	23.1 (14.1-37.8)	8.9 (5.3-14.8)	2.4 (1.3-4.4)	0.7 (0.4-1.2)	3.4 (1.9-6.2)
Overall	Overall	130.0 (110.9-152.4)	49.6 (42.2-58.3)	13.4 (10.4-17.3)	4.0 (3.3-5.0)	18.7 (17.7-19.8)

