Mortality differences after ART initiation in HIV-positive women from Europe, the Americas and Sub-Saharan Africa; 2000-2014

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Introduction

- Women account for over half of the 36,7 million persons estimated to be living with HIV worldwide in 2016.
- Access to health care and life-saving antiretroviral therapy (ART) varies greatly across regions and depends on both structural and individual factors.
- HIV-positive women, globally, differ in their age distribution, HIV transmission routes, socio-economic status, gender roles and viral and tuberculosis co-infection rates.

Objective

To estimate all-cause mortality after ART initiation, and by duration of ART use, among women living with HIV in Europe, the Americas and Sub-Saharan Africa up to 48 months after ART initiation.

Methods

Setting and data sources

- Five **IeDEA** (International Epidemiologic Databases to Evaluate AIDS) regions: East Africa, West Africa, Southern Africa, North America and Latin America/Caribbean.
- Fourty observational cohorts and cohort collaborations from **COHERE** (Collaboration of Observational HIV Epidemiological Research in Europe) in EuroCoord.

Study population

- Antiretroviral-naïve women, infected through injecting drug use or sex between men and women, aged 18-80 years old at ART initiation who started their first ART regimen between 1st January 2000 and 31st December 2014.
- Only in North America were participants required to have a second visit within 12 months of enrolment.
- We excluded women from the Asia-Pacific region (N=849), Mexico (N=100) and Argentina (N=545).

Ascertainment of mortality

Cohort linkages with mortality registries were reported in South Africa, North America, South America and some sites in Europe, and systematic sample tracing of losses to follow-up was conducted in East Africa. Mortality ascertainment data from East Africa were used to correct under ascertainment in West Africa.

Statistical methods

- Data-contributing regions were categorized as Europe, East Africa, West Africa, Southern Africa, South America, North America, and Central America and the Caribbean.

List of countries represented in each region

Europe	Southern Europe: Croatia, Greece, Italy, Portugal, Serbia, Bosnia and Herzergovina, Slovenia, Spain Western Europe: Belgium, France, Germany, Luxembourg, Netherlands, Switzerland Northern Europe: Denmark, Estonia, Finland, Iceland, Ireland, Latvia, Lithuania, Norway, Sweden, United Kingdom Eastern Europe: Bulgaria, Belarus, Czech Republic, Hungary, Poland, Romania, Russian Federation, Slovakia, Ukraine
East Africa	Kenya, Rwanda, Tanzania, Uganda, Zambia, Zimbabwe
West Africa	Benin, Burkina Faso, Cote d'Ivoire, Ghana, Guinea-Bissau, Mali, Nigeria, Senegal, Togo
South Africa	South Africa
South America	Brazil, Chile, Peru
North America	Canada, United States
Central America and the Caribbean	Honduras, Haiti

- Mortality rates were calculated by region at 0-3, 3-6, 6-12, 12-24 and 24-48 months after ART initiation, and mortality rate ratios were estimated at each interval compared to the rate in Europe using a piecewise exponential parametric survival model fit through Poisson regression.

Results

Women's characteristics

190,175 women:

47% East Africa, 19% South Africa, 16% Europe, 13% West Africa, 3% North America, 2% Central America/Caribbean, 1% South America

Age at ART initiation ranged from 33 years in South Africa to 40 years in North America.

Proportion of **injecting drug users** highest in North America (18%) and Europe (7%).

Proportion of women from **black race/ethnicity** higher in North America (63%) than in Europe (26%), largely migrants from Sub-Saharan Africa.

CD4+ T-cell counts at ART initiation close to 250 cells/mm3 in Europe and North America, 141 cells/mm3 in South Africa and 170-190 cells/mm3 in other regions

Figure1. Crude Mortality Rates per 100 persons-years

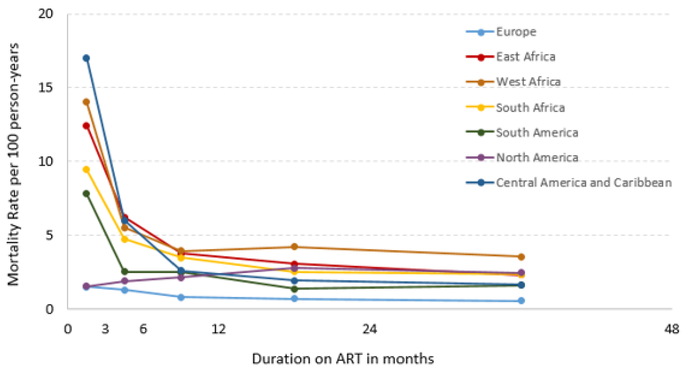

Table1. Mortality rate ratios (95% CI) compared to Europe by duration on ART

Mortality Rate Ratio	Duration on ART				
	0 – 3	3 - 6	6 - 12	12 - 24	24 - 48
East Africa					
Corrected and adjusted for baseline patient characteristics*	7.25 (5.87 – 8.97)	4.24 (3.30 – 5.46)	4.24 (3.35 – 5.37)	3.89 (3.21 – 4.72)	3.63 (3.04 – 4.33)
West Africa					
Corrected by time on ART, age and period of ART initiation	8.95 (7.34 – 10.91)	4.05 (3.21 – 5.11)	4.38 (3.54 – 5.43)	5.37 (4.54 – 6.35)	5.61 (4.84 – 6.51)
Corrected by time on ART, age, period of ART initiation and CD4 in patients with available CD4	3.42 (2.53 – 4.62)	1.44 (0.94 – 2.19)	2.07 (1.46 – 2.94)	2.42 (1.86 – 3.15)	2.49 (1.98 – 3.14)
South Africa					
Adjusted for baseline patient characteristics*	5.42 (4.43 – 6.64)	3.15 (2.50 – 3.97)	3.77 (3.05 – 4.67)	3.05 (2.56 – 3.63)	3.47 (2.97 – 4.06)
South America					
Adjusted for baseline patient characteristics*	4.47 (2.97 – 6.72)	1.67 (0.84 – 3.32)	2.70 (1.62 – 4.52)	1.69 (1.02 – 2.78)	2.42 (1.65 – 3.55)
North America					
Adjusted for baseline patient characteristics*	0.88 (0.53 – 1.44)	1.25 (0.78 – 2.02)	2.30 (1.61 – 3.27)	3.40 (2.64 – 4.37)	3.72 (2.97 – 4.65)
Additional adjustment for transmission category, HIV-RNA and AIDS prior to ART initiation	0.69 (0.42 – 1.14)	0.99 (0.62 – 1.60)	1.80 (1.25 – 2.58)	2.65 (2.03 – 3.44)	2.86 (2.26 – 3.62)
Additional adjustment for transmission category, HIV-RNA, AIDS prior to ART initiation and ethnicity in patients with available info of ethnicity	0.53 (0.31 – 0.89)	0.92 (0.55 – 1.55)	1.48 (0.99 – 2.22)	2.39 (1.77 – 3.24)	2.78 (2.11 – 3.66)
Central America and Caribbean					
Adjusted for baseline patient characteristics*	9.92 (7.79 – 12.63)	4.12 (2.95 – 5.74)	2.93 (2.07 – 4.15)	2.43 (1.82 – 3.26)	2.50 (1.92 – 3.26)

* Baseline patient characteristics are age (<30, 30-44, 45-59, ≥60 years), CD4+ T-cell count (0-24, 25-49, 50-99, 100-199, 200-349, ≥350 cells/mm3, unknown) and period of ART initiation (2000-2003, 2004-2007, 2008-2011, 2012-2014)

Conclusions

- Global variations in all-cause mortality in HIV-positive women initiating ART show distinct geographical patterns for short-, mid- and long-term mortality that may inform context-specific interventions.
- The highest mortality was observed in HIV-positive women living in Central America and the Caribbean and Sub-Saharan Africa, who also had the lowest CD4+ T-cell counts at ART initiation. The lowest mortality was reported in women living in Europe, who had, together with women from North America, the highest CD4+ T cell counts at ART initiation.
- Mortality was highest in the first three months after ART initiation in all regions, except for North America where it was not evaluable due to cohort eligibility criteria, and decreased from then onwards to reach stable rates from the first until the fourth year following ART, where inter-regional differences become less remarkable.

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