

Global Burden of Cervical Cancer in HIV-Positive Women on Antiretroviral Therapy

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**Abstract
617**

Background

HIV-positive women are at increased risk of human papillomavirus (HPV) infection and progression to invasive cervical cancer (ICC). HIV and HPV epidemics as well as access to cervical cancer screening vary between geographical regions.

Objectives

To compare ICC risk in HIV-positive women on combination antiretroviral therapy (ART) between different geographical regions.

Methods

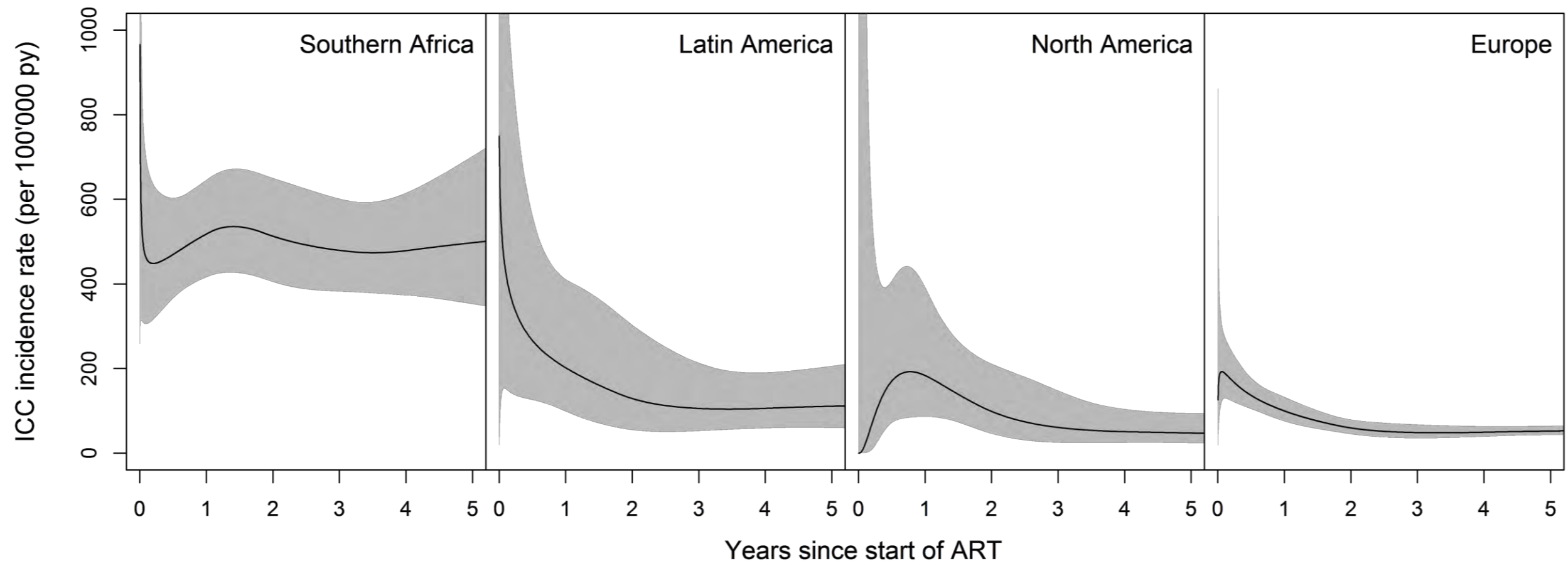
- We analyzed data from the International Epidemiologic Databases to Evaluate AIDS (leDEA) and the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord.
- We included HIV-positive women (≥16 years) who initiated ART after enrollment into cohort from 1996 onwards.
- We used flexible parametric survival models with region-specific baseline hazards adjusted for time-updated CD4 cell counts, age, and year of ART start to compare regional ICC rates. We excluded the Asia-Pacific region from multivariable analyses due to the small sample size.
- We present incidence rates and adjusted hazard ratios (aHR) with 95% confidence intervals (CI).

Table: Characteristics of included women.

	Asia-Pacific	Southern Africa	Latin America	North America	Europe
Women (N)	809	13,845	2,289	4,124	44,659
Median follow-up time [years]	2.8 (1.6-3.9)	2.1 (0.7-4.0)	4.9 (2.1-8.4)	5.4 (2.3-9.9)	4.7 (2.0-8.5)
Median age at ART start [years]	36 (31-42)	35 (30-42)	35 (29-44)	39 (32-45)	35 (29-42)
Median CD4 count at ART start [cells/μl]	146 (52-227)	115 (50-182)	179 (74-281)	241 (107-385)	241 (129-363)

ART, combination antiretroviral therapy; N, number. Medians are presented with interquartile ranges.

Figure: Hazards and 95% CIs for invasive cervical cancer in different regions.



ART, combination antiretroviral therapy; CI, confidence interval; ICC, invasive cervical cancer.

Results

- We included 65,726 HIV-positive women from 55 countries in the Asia-Pacific, Southern Africa, Latin America, North America, and Europe (Table).
- During 323,224 person-years (pys) 390 women developed incident ICC on ART: The incidence rate per 100,000 pys was highest in Southern Africa (497, 95%CI 429-577) followed by Latin America (152, 95%CI 97-238), North America (76, 95%CI 48-119), Europe (71, 95%CI 62-83) and the Asia-Pacific (42, 95%CI 6-297).
- With the exception of Southern Africa regional ICC incidence rates decreased with time since ART start (Figure).
- Adjusted hazard ratios comparing Europe with other regions at 2 and 5 years were 8.9 (95%CI 6.0-13.3) and 12.4 (95%CI 7.8-20.0), respectively, for Southern Africa, and 2.1 (95%CI 0.8-5.0) and 2.2 (95%CI 1.2-4.2), respectively, for Latin America. No difference was observed between North America and Europe.

Limitations

- Only women who started ART were included in the analyses
- Access to cervical cancer screening varies between regions which might have introduced ascertainment bias

Conclusions

HIV-positive women in Southern Africa and Latin America had a markedly higher ICC risk than women from North America and Europe, and rates did not decline with time on ART in Southern Africa. These regional differences were not explained by differences in CD4 cell counts, age, or year of ART initiation, but might be due to higher prevalence and incidence of HPV infection and limited access to effective cervical cancer screening.

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