Ethnicity has diminished as a risk factor for chronic kidney disease in the current HIV treatment era

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On behalf of the ATHENA national observational cohort study
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Background

Chronic kidney disease (CKD) is an important co-morbidity among people living with HIV. Earlier in the HIV epidemic, CKD in HIV-infected individual was dominated by HIV-associated nephropathy (HIVAN), and predominantly observed in black people. More recently, a shift has occurred towards additional etiologies of CKD.

Purpose of the study

This study within the HIV Monitoring Foundation ATHENA cohort database investigates the role of ethnicity in relation to CKD in recent years, comparing patients originating from Sub-Saharan Africa to patients from other regions, including the Netherlands.

Methods

Definition CKD:

- Estimated glomerular filtration rate (eGFR) below 60 ml/min (calculated by Cockcroft-Gault equation, standardized for body surface area), confirmed after at least 90 days
- Or start of renal dialysis
- Or kidney transplantation

Enrollment of patients aged 16 years and older with available creatinine measurements after 1 January 2007

Analysis CKD incidence between January 2007 and February 2013

- Exclusion of patients with CKD at start of follow-up
- Multivariable Cox proportional hazards analysis

Region of origin

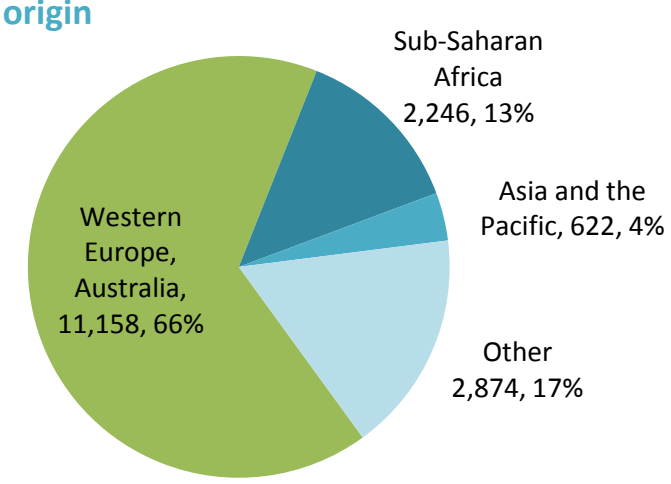

Figure 1. Total cohort, N=16,900

Baseline characteristics

	Total cohort (N=16,900)	Western Europe, Australia (N=11,158)	Sub-Saharan Africa (N=2,246)
Male	14,060 (83.2)	10,162 (91.1)	1,120 (49.9)
Age in years	42.2 [35.1-49.1]	44.0 [37.1-51.1]	36.9 [30.5-43.5]
Mode HIV transmission			
Homosexual	10,409 (61.6)	8,348 (74.8)	134 (6.0)
Heterosexual	4,920 (29.1)	1,872 (16.8)	1,822 (81.1)
Blood(products), i.v. drugs	481 (2.8)	368 (3.3)	283 (12.6)
Other	1,090 (6.4)	570 (5.1)	7 (0.3)
Nadir CD4 count (cells/mm^3)	210 [90-320]	220 [100-328]	168 [70-270]

Table 1. Data are given as number (%) or median [IQR]. IQR: interquartile range, N: number of patients. Mode HIV transmission other: vertical transmission, unknown / other.

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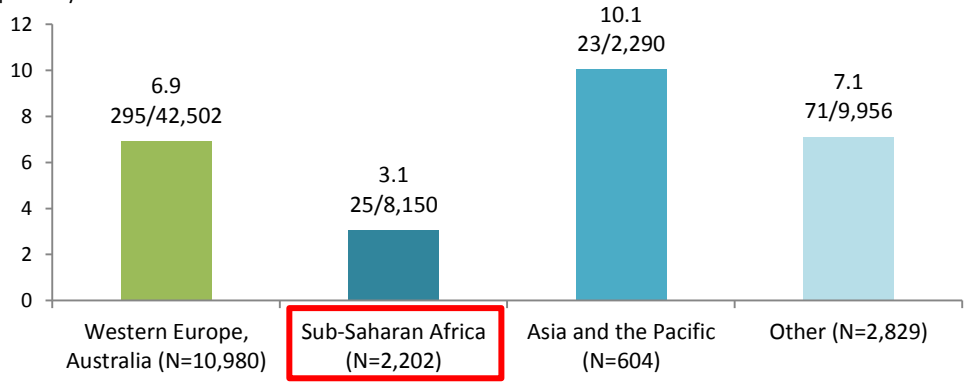
Results - CKD incidence

Included in analysis: N = 16,615 patients
Median duration of follow-up 4.6 years [IQR 2.4-5.2], 62,897 person-years
CKD incidence: 2.5% (414 / 16,615), 6.6 events / 1,000 person-years

Results - CKD incidence per region of origin



Results - multivariable analysis CKD incidence

Variable			Adjusted Hazard Ratio (95% CI)	*P*-value
Age (years)			1.12 (1.11-1.14)	0.00
Sex (female)			2.75 (2.03-3.71)	0.00
Region of origin	Western Europe, Australia		1.00 (Reference)	-
	Sub-Saharan Africa		**0.79 (0.49-1.26)**	**0.32**
	Asia and the Pacific		2.10 (1.33-3.31)	0.00
	Other		1.40 (1.05-1.86)	0.02
Mode of HIV transmission		Homosexual	1.00 (Reference)	-
		Heterosexual	0.95 (0.70-1.30)	0.75
		Blood(products), i.v. drugs	2.57 (1.62-4.10)	0.00
		Other	1.32 (0.92-1.91)	0.13
Nadir CD4 count (cells/mm^3)		**<50**	1.88 (1.21-2.92)	0.01
		50-100	1.76 (1.11-2.78)	0.02
		100-200	1.25 (0.80-1.95)	0.33
		200-350	1.18 (0.76-1.84)	0.46
		>350	1.00 (Reference)	-
On cART			1.24 (0.60-2.56)	0.55
Tenofovir			0.78 (0.63-0.97)	0.03
Atazanavir			1.44 (1.12-1.86)	0.01
Potentially nephrotoxic non-antiretroviral medication			1.49 (1.15-1.95)	0.00
Hepatitis B			1.76 (1.24-2.52)	0.00
Hepatitis C			1.31 (0.93-1.83)	0.12
Hypertension			1.20 (0.92-1.57)	0.18
Dyslipidemia			0.92 (0.71-1.19)	0.51
Diabetes mellitus			1.42 (1.05-1.91)	0.02
Previous cardiovascular event			1.27 (0.90-1.77)	0.17
Smoking			1.26 (1.02-1.55)	0.03

Table 2. Number of subjects: 16,615, number of CKD events: 414
Hepatitis B: Hepatitis B surface antigen-positivity. Hepatitis C: Hepatitis C RNA-positivity

Conclusions

Sub-Saharan African origin was no longer found to be a risk factor for the incidence of CKD in HIV-infected patients in the Netherlands, which suggests a shift in etiology of CKD from HIVAN towards other etiologies. The seemingly protective effect of concurrent tenofovir use most likely reflects selection bias towards patients tolerant of the drug.