

CHANGES OVER TIME IN THE RISK OF AIDS BY SEX: SLOWER PROGRESSION IN WOMEN IN RECENT PERIODS

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OBJECTIVE

To evaluate the effect of sex on survival and on the risk of AIDS (overall) and on each specific AIDS-defining disease or death without AIDS, and investigate changes over calendar period.

METHODS

CASCADE data restricted to seroconverters infected through injecting drug use (IDU) and heterosexual intercourse were analysed. The effect of sex on overall progression to AIDS and death was investigated using Cox proportional hazard models. Sex differences in the risk of specific AIDS-defining diseases (ADD) were assessed by modelling the hazard that is derived from the cause-specific cumulative incidence function through Cox proportional hazard models. We evaluated whether the effect of sex had changed over calendar period (pre-1997 and 1997-onwards) by including the interaction between sex and calendar period in multivariable models. All models allowed for late-entry and were adjusted by age at seroconversion (continuous) and exposure category.

RESULTS

Of 6923 seroconverters, 50.7% were men, 44.7% injecting drug users and 1238 (17.9%) died. A higher proportion of men had been infected through injecting drug use compared to women (59.0% vs. 30.1%, $p < 0.001$). Of 6702 people included in the analyses of progression to AIDS, 1417 (21.1%) progressed to the disease and 402 (7.6%) died without an AIDS diagnosis.

The introduction of HAART altered the differences in AIDS and mortality risk between men and women. While before 1997, no sex differences were found, from 1997-onwards women experienced a much lower hazard of AIDS (aHR: 0.74; 95%CI: 0.62 to 0.88) and death (aHR: 0.68; 95%CI: 0.56 to 0.82) (Table 1), despite apparently similar person-time spent on HAART as men (51.4% and 46.8% in men and women, respectively) (Figure 1).

TABLE 1. Effect of sex on progression to AIDS and death from HIV seroconversion, in the eras pre-1997 and 1997-onwards

	Progression to AIDS		Progression to death	
	< 1997	1997-onwards	< 1997	1997-onwards
Sex				
Men	1.00	1.00	1.00	1.00
Women	0.99 (0.85 – 1.14)	0.74 (0.62 – 0.88)	0.89 (0.76 – 1.05)	0.68 (0.56 – 0.82)
	$p = 0.85^*$	$p = 0.001^†$	$p = 0.17^*$	$p < 0.001^†$
p		0.011		0.024

Results from a multivariable Cox regression model that includes the interaction between sex and calendar period, age at seroconversion (continuous) and exposure category. Data are HR (95% CI). ^{*} For variation of sex within calendar period. [†] For variation of effect of sex over calendar period.

Table 2 shows the frequency and rate per 1000 persons-year of each specific AIDS-defining disease as the first AIDS event (or death without AIDS) by sex, in the eras pre-1997 and 1997-onwards. Women showed lower incidence rates than men for each specific AIDS-defining disease and death without an AIDS diagnosis in period 1997-onwards.

In the pre-HAART era (Figure 2, left) no significant differences between men and women were seen for the cumulative risk of most specific AIDS-defining diseases, except for Kaposi's sarcoma with women showing a lower cumulative risk than men (aCR: 0.06; 95%CI: 0.01 to 0.42). In contrast, in the HAART era (Figure 2, right) we observed a similar pattern to that observed for AIDS overall; namely, women experiencing lower cumulative risks than men. Specifically, women showed significantly lower cumulative risks (aCR, 95% CI) than men for AIDS dementia complex (0.22, 0.07 to 0.69), tuberculosis (0.59, 0.38 to 0.91), Kaposi's sarcoma (0.26, 0.07 to 0.97), lymphomas (0.45, 0.22 to 0.91) and death without AIDS (0.72, 0.54 to 0.95).

FIGURE 1. Proportion of person-time spent on different treatment regimens in the eras pre-1997 and 1997-onwards, according to sex and transmission category

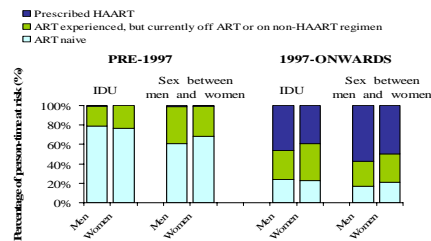
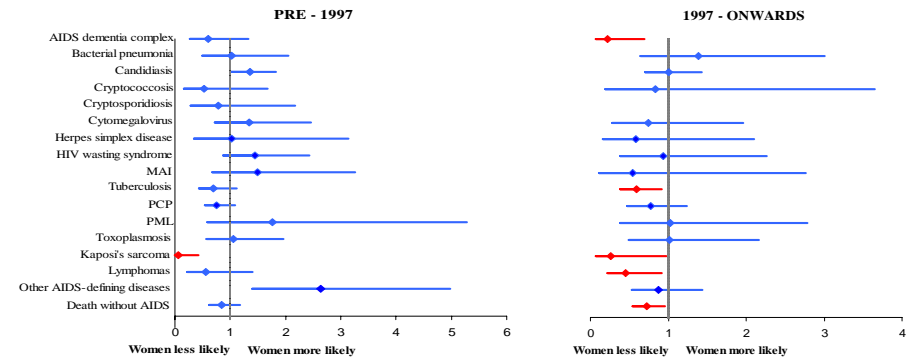


TABLE 2. Frequency and rate (per 1000 persons-year) of each ADD and death without AIDS by sex, in the eras pre-1997 and 1997-onwards

First AIDS defining disease or death without AIDS	PRE - 1997		1997 - ONWARDS					
	Men 8647	Women 7209	Men 11353	Women 12856				
Person year at risk (p-y)	No.	Rate	No.	Rate	No.	Rate	No.	Rate
AIDS dementia complex	27	3.1	8	1.1	23	2.0	4	0.3
Bacterial pneumonia	21	2.4	12	1.7	15	1.3	16	1.2
Candidiasis	105	12.1	85	11.8	69	6.1	62	4.8
Cryptococcosis	9	1.0	4	0.6	4	0.4	4	0.3
Cryptosporidiosis	12	1.4	9	1.2	3	0.3	0	-
Cytomegalovirus	24	2.8	28	3.9	9	0.8	9	0.7
Herpes simplex disease	9	1.0	7	1.0	6	0.5	4	0.3
HIV wasting syndrome	37	4.3	32	4.4	13	1.1	9	0.7
MAI ^a	15	1.7	17	2.4	5	0.4	3	0.2
Tuberculosis	54	6.2	27	3.7	63	5.5	32	2.5
PCP ^b	97	11.2	53	7.4	41	3.6	33	2.6
PML ^c	7	0.8	6	0.8	9	0.8	6	0.5
Toxoplasmosis	26	3.0	19	2.6	14	1.2	15	1.2
Kaposi's sarcoma (KS)	17	2.0	1	0.14	9	0.8	3	0.2
Lymphomas	17	2.0	7	1.0	25	2.2	11	0.9
Other ADD ^d	16	1.9	23	3.2	41	3.6	26	2.0
Death without AIDS	129	14.9	58	8.0	143	12.6	72	5.6

^a Mycobacterial diseases not including tuberculosis
^b Pneumocystis carinii pneumonia
^c Progressive multifocal leucoencephalopathy
^d Includes: cervical cancer, focal brain lesion, isosporiasis, leishmaniasis, salmonella bacteremia and diagnosis unknown

FIGURE 2. Effect of sex (men as reference category) in time to specific first AIDS-defining disease or death without AIDS in the eras pre-1997 and 1997-onwards (adjusted cumulative risk; 95% CI)



* Results from multivariable Cox regression models that include the interaction between sex and calendar period, age at seroconversion (continuous) and exposure category. Data are cumulative risks (95% CI).

CONCLUSIONS

- Women showed slower progression to AIDS compared to men only for period 1997-onwards, with remarkable reductions for some AIDS-defining conditions such as AIDS dementia complex, tuberculosis, Kaposi's sarcoma and lymphomas.
- Women also have lower mortality compared to men in period 1997-onwards for both all cause-mortality and death without AIDS, despite apparently similar person-time on HAART
- These differences maybe attributable to reported differences in exposure to other agents (such as mycobaterium tuberculosis and HHV8) as well as to behavioural differences in health seeking patterns, which are difficult to measure in our cohort.
- Given that, from the general (uninfected) population in western countries, women have better survival than men, longer follow-up is needed in order to establish whether the sex mortality ratio for HIV infected individuals will come to resemble more closely that of the HIV negative population.