Mortality after HIV diagnosis compared to the general population

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Background

The beneficial effect of HAART on survival of HIV-infected patients has been well established. Recently, we showed that mortality amongst successfully treated patients, i.e. low-level HIV-RNA and high CD4 cell counts at 24 weeks after start of HAART, approaches that of the general population (JAIDS 2005). In this analysis, we study progression to death from HIV diagnosis onwards.

Methods

- 4985 adult patients were selected from the ATHENA national observational cohort who were diagnosed between 1998 and 2005 and were therapy naïve if starting HAART.
- A CD4 T-cell count and HIV-RNA value within 12 weeks after diagnosis but before initiation of HAART were required.
- The most serious CDC-B or CDC-C (AIDS) event occurring within four weeks after diagnosis was considered.
- A time-dependent multivariate hazards model was used to model the hazard of progression to death compared to the age and gender matched general Dutch population.
- An “intention-to-treat” approach was used: initiation of HAART is not included in the model as such.
- Standardised mortality ratio were defined as the one-year mortality of HIV-infected patients relative to the general population.

Study population

		N=4985
gender, male		3745 (75.1%)
transmission risk		
homosexual contact		2478 (49.7%)
heterosexual contact		2022 (40.6%)
intravenous drug use (IDU)		74 (1.5%)
region of origin		
the Netherlands		2659 (53.3%)
sub-Saharan Africa		1141 (22.9%)
CDC stage at diagnosis:	CDC-B	390 (7.8%)
	CDC-C (AIDS)	822 (16.5%)
CD4 at diagnosis (10^6 cells/l)		300 (IQR 114-500)
$\log_{10}$ RNA at diagnosis ($\log_{10}$ copies/ml)		4.8 (4.2-5.2)
age at diagnosis (years)		36.4 (30.2-43.4)
initiated HAART		3502 (70.3%)
time from diagnosis to start of HAART (years)		0.2 (0.1-0.4)
progression to death		153 (3.1%)
before initiation of HAART		28 (0.6%)
follow-up (years)		2.7 (1.2-4.6)
total person-years follow-up		15087

Mortality

The table shows the overall mortality for each CDC stage at diagnosis and the mortality before and after initiation of HAART.

	mortality per 100 person-years		
stage	overall	never HAART	HAART
none	0.53 (0.40-0.68)	0.33 (0.18-0.56)	0.65 (0.47-0.87)
CDC-B	1.81 (1.15-2.72)	1.36 (0.17-4.93)	1.87 (1.16-2.86)
AIDS	2.64 (2.06-3.34)	6.79 (3.51-11.9)	2.35 (1.79-3.03)
overall	1.04 (0.86-1.19)	0.62 (0.41-0.89)	1.18 (0.99-1.41)

Note the high mortality amongst AIDS patients before HAART.

Results – Hazards model

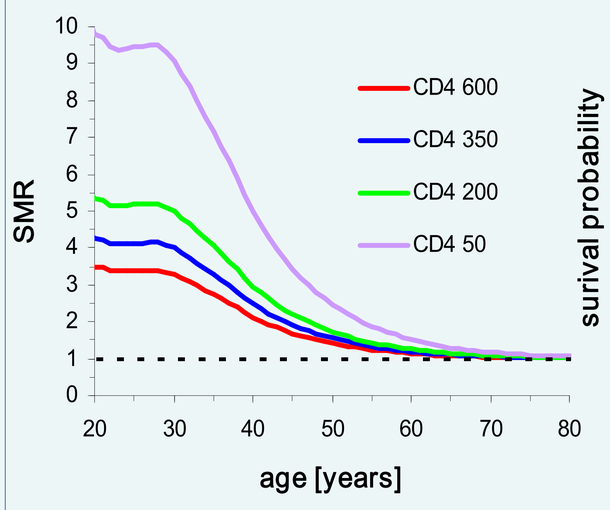
- The high pre-HAART mortality amongst patients diagnosed with AIDS complicated the model fit. In order to obtain a stable fit, patients with an AIDS event at diagnosis were excluded. IDUs were also excluded, restricting the population to 4096 patients of whom 77 died.
- The only two covariates significantly associated with survival were (HR: hazard ratio)

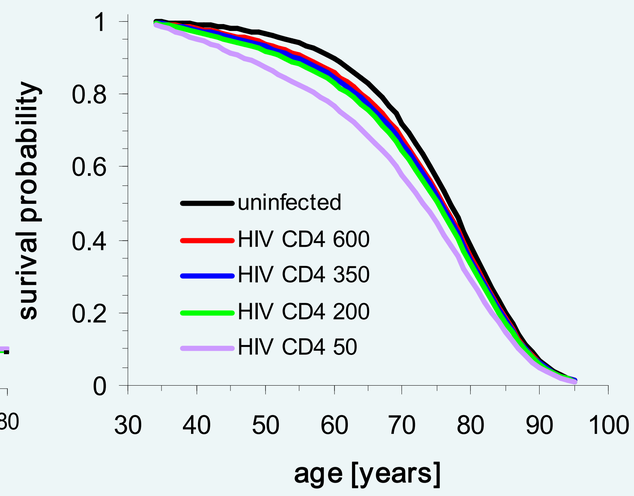
CDC-B event at diagnosis	HR 3.35 (95% CI 1.59-7.05)
log CD4 at diagnosis	HR 0.58 (95% CI 0.30-0.78)

- The effect of age and gender were taken into account in the baseline hazard.

Results – Model predictions

- Standardised mortality ratio (SMR) decreases with age.
- The plot on the left shows SMRs for men without a CDC-B diagnosis for various CD4 counts at diagnosis.
- For 34-year old men with a CDC-B event SMRs are 2.5-3 times higher than without a CDC-B event.
- SMRs for women <30 years of age are twice as large as general population mortality is smaller than amongst men.
- SMRs around 4 are comparable with those observed in diabetes patients.





- The plot on the right shows the predicted probability of survival up to the age on the horizontal axis for 34-year old uninfected individuals and for HIV-infected patients who were diagnosed at the age of 34 with various CD4 counts at diagnosis.
- Expected survival probabilities hardly deteriorates with decreasing CD4 counts at diagnosis, provided they exceed 200×10^6 cells/l.

Conclusions & discussion

- SMRs for non-IDU patients without AIDS at HIV-diagnosis <30 years of age are high, even when CD4 counts approach normal levels.
- However, survival probabilities in the years following diagnosis are not much lower than for HIV-negative individuals if CD4 counts exceed 200×10^6 cells/l.
- The number of deaths used during fitting of the model is small. This might have a negative impact on the power to discriminate between patients with CD4 cell counts exceeding 200×10^6 cells/l.

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