

10 years HAART

Did it change mortality and survival?

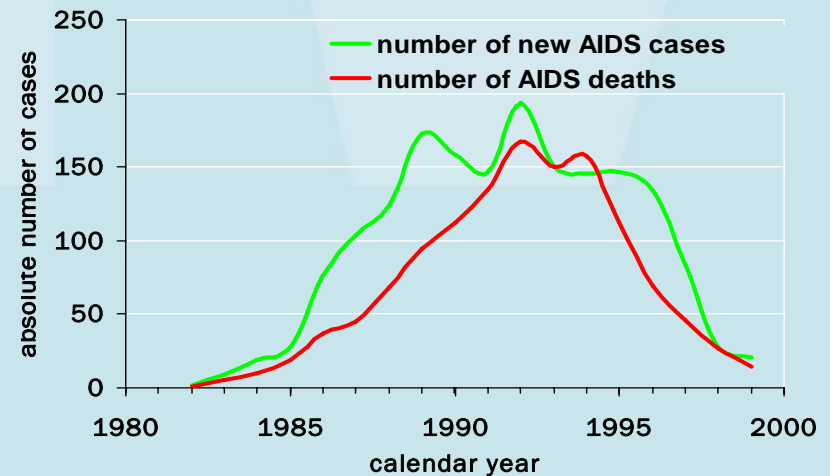
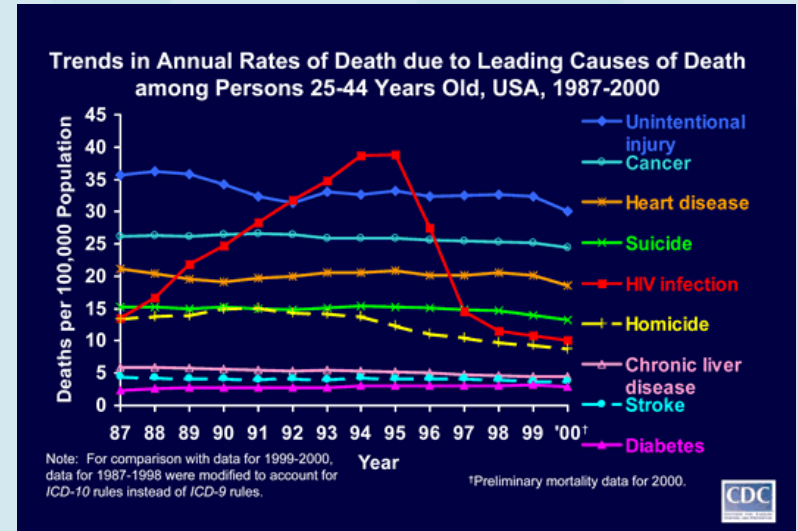
Ard van Sighem

HIV Monitoring Foundation

Amsterdam, 1 December 2006

Introduction

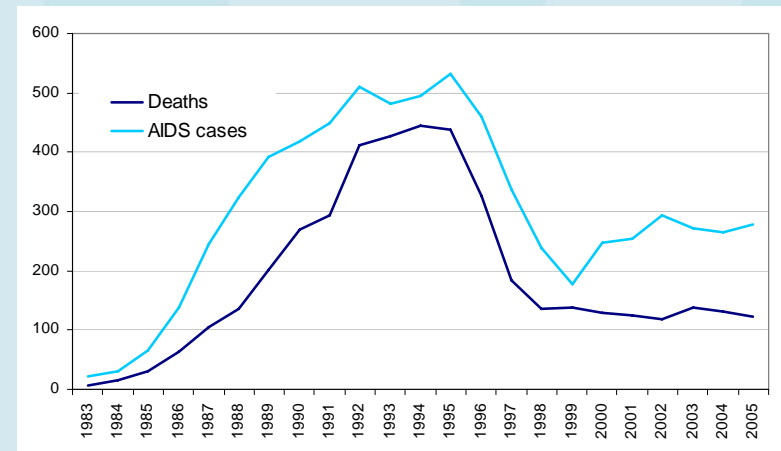
- In the early 90s, HIV/AIDS was the leading cause of death among young adults.
- The widespread use of HAART since 1995 reduced mortality.
- In Amsterdam, the reduction in mortality was earlier
 - early reduction in new infections
 - dual therapy
 - participation in trials



Source: Smit et al., *Epidemiology* 2004

Death and AIDS in the Netherlands

- By the end of 2005, 6931 AIDS cases and 4398 cases of death had been registered.
- Proportion of MSM among reported AIDS cases declined from 77% in 1988 to 43% in 2005, whereas the proportion of heterosexuals increased from 6% to 40%.

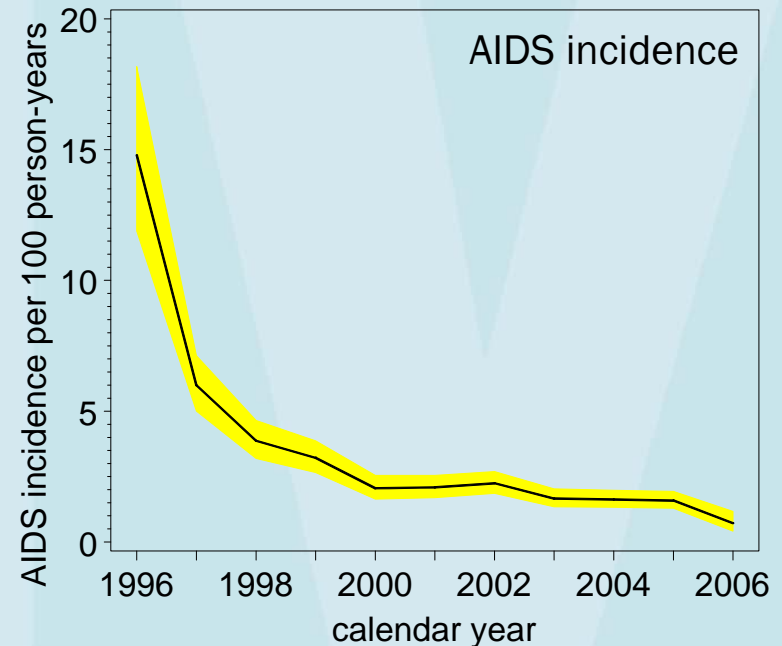
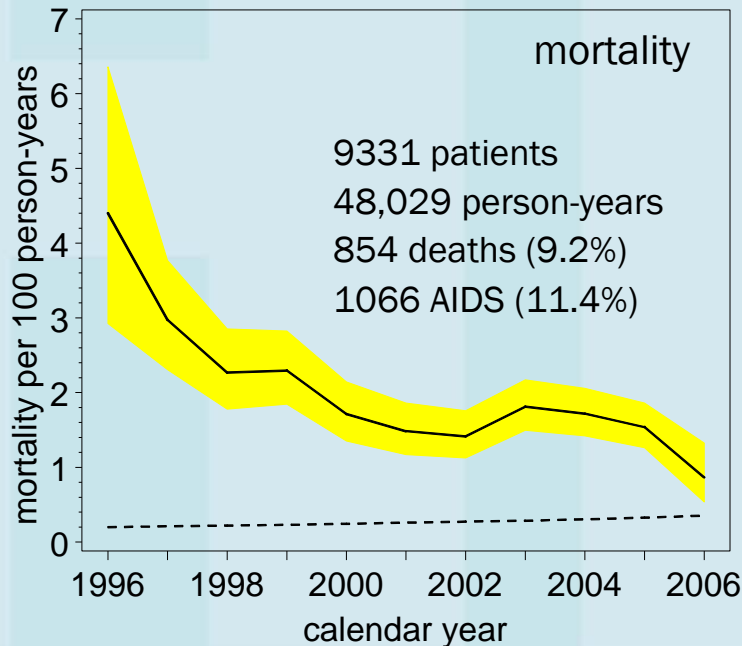


Source: De Boer et al., RIVM 2006

Sources AIDS: AIDS registration Health Inspectorate <2000, HMF ≥2000.

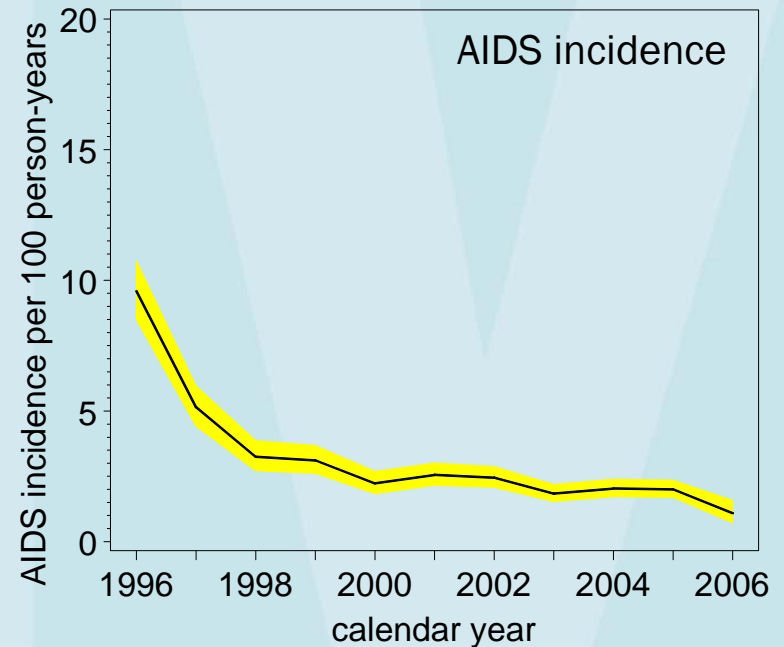
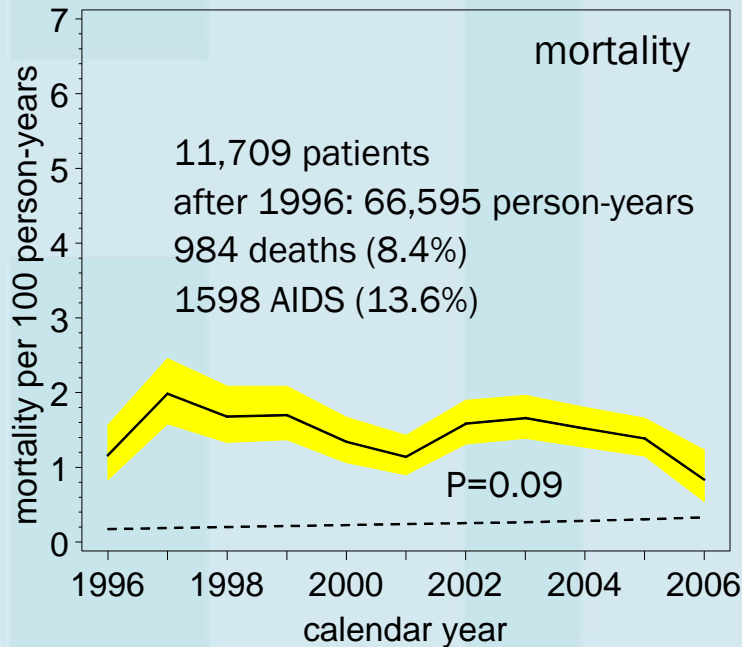
Sources deaths: CBS <2002, HMF ≥2002.

Death and AIDS after start of HAART



- No change in mortality when pre-treated patients were excluded.
- Mortality in the pre-treated population 2 times higher than in the therapy naïve population, but incidence of AIDS is similar.

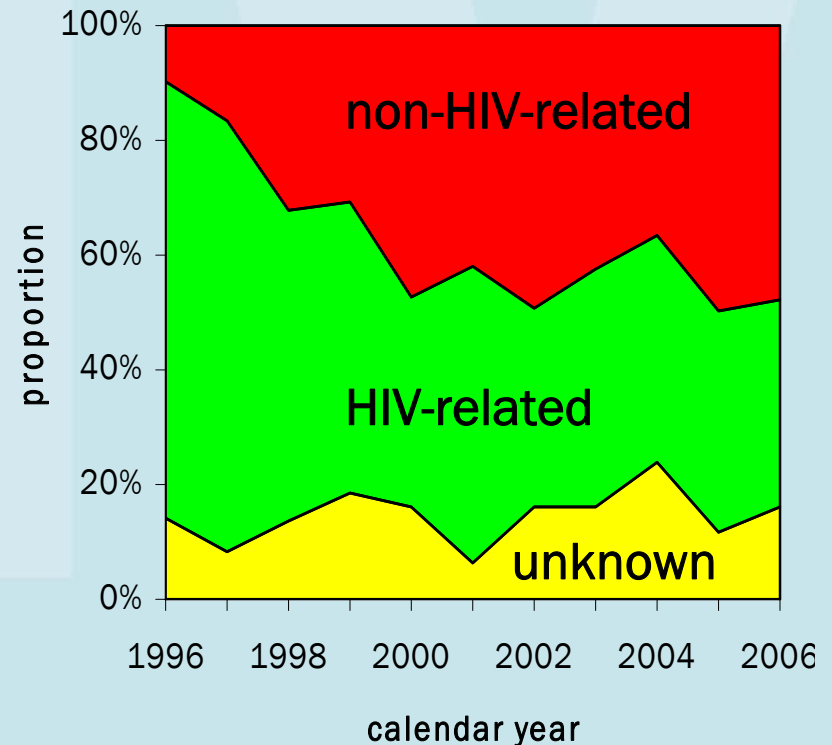
Death and AIDS after HIV diagnosis



- No decline in mortality was observed in the total HIV-infected population as pre-treated patients account for only 20% of the total population.

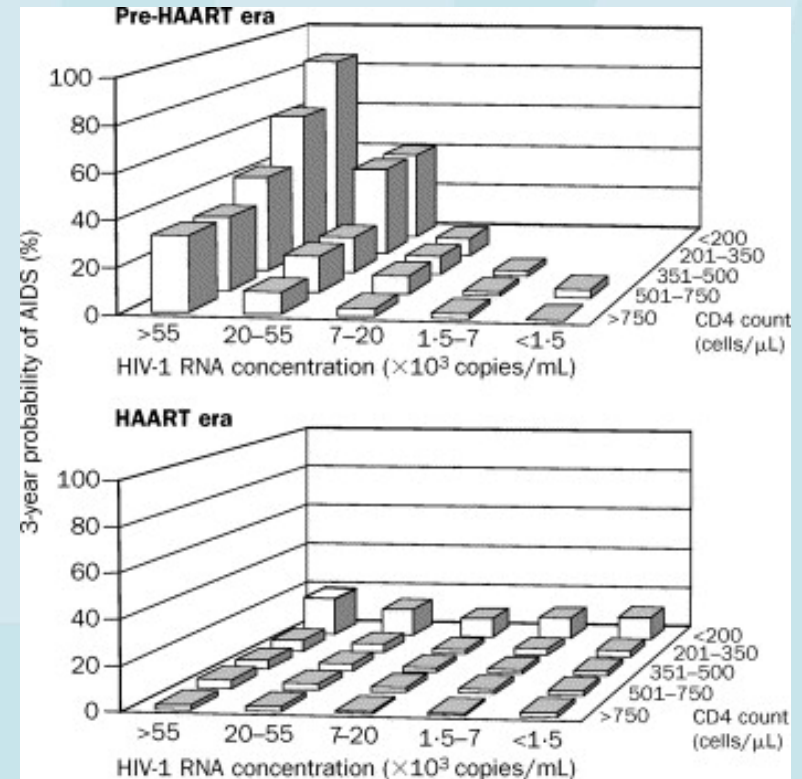
(non-)HIV-related mortality

- HIV-related mortality decreased since 1996:
 - 391 (39.7%) HIV-related cases of death
 - 226 (58%) in patients with AIDS diagnosis in the year before the start of HAART
- Causes of death in 2005:
 - 39% HIV-related
 - 50% non-HIV-related
 - 11% unknown



Prognosis pre-HAART and HAART era

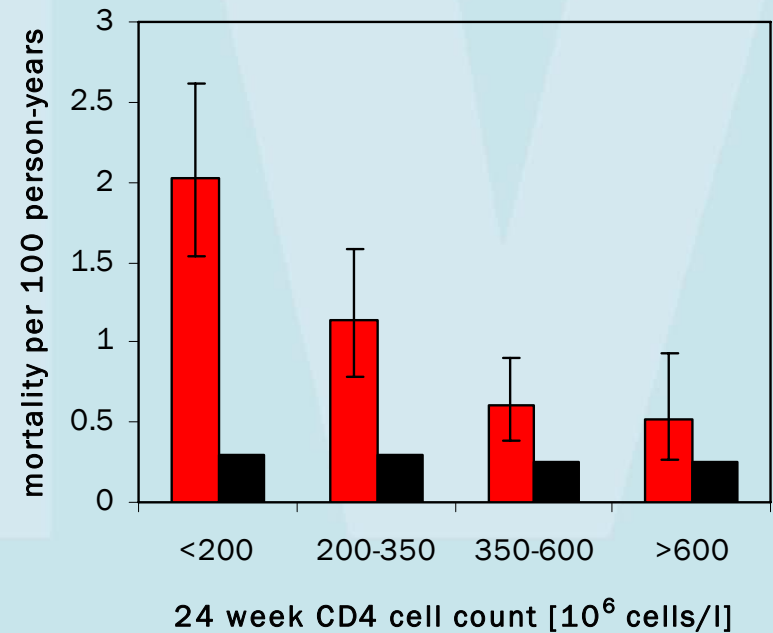
- Prognosis of HIV-infected patients has improved.
- Models for progression to death and/or AIDS:
 - MACS
 - 209 patients
 - ART Cohort Collaboration
 - 12,574 patients
 - 24,310 person-years
 - 1094 AIDS/death



Source: Egger et al., Lancet 2002

ATHENA/HMF prognostic model

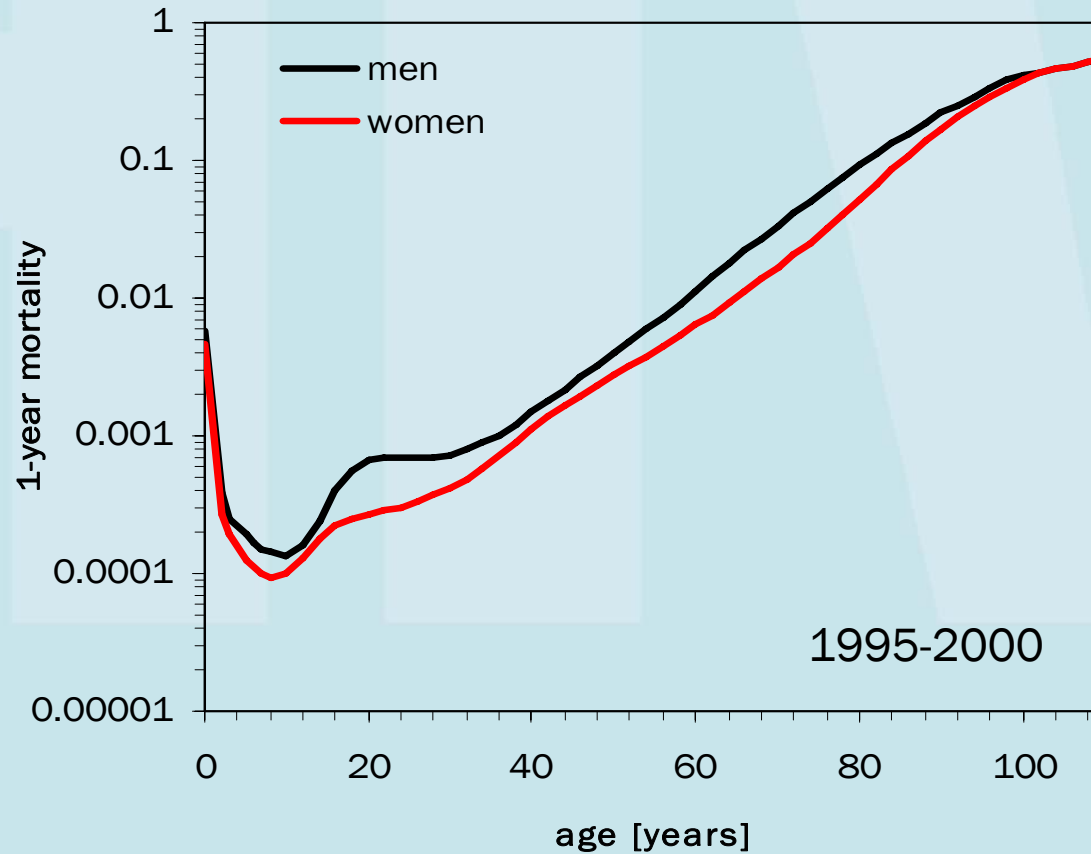
- HMF developed prognostic models for AIDS and death
 - using information at start of HAART (AIDS 2003)
 - using response to HAART after 24 weeks (JAIDS 2005)
- Important predictors are
 - CD4 count
 - intravenous drug use
 - prior AIDS
 - RNA suppressed or not



Statistical model

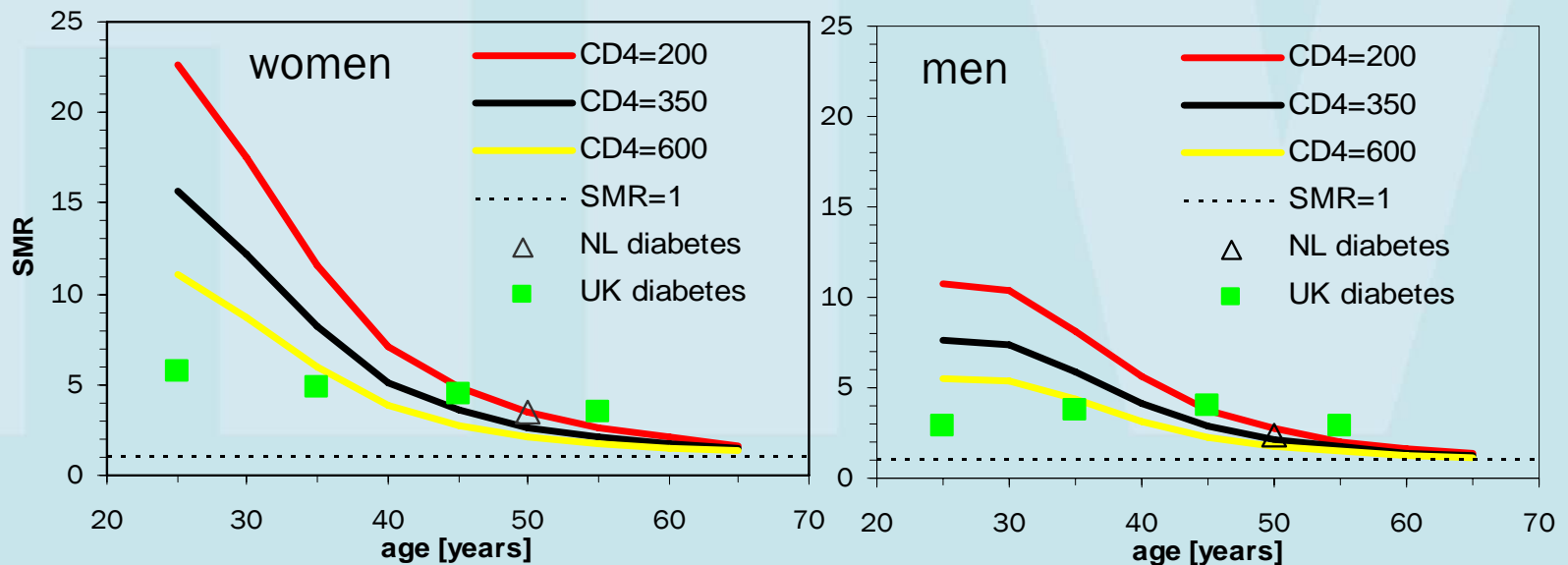
- time-dependent hazards model for the prediction of n -year survival probabilities (Cox model)
- risk (hazard) of death is modelled as the sum of two terms:
 - **expected risk** given the patient's age and gender and the probability of death in the general Dutch population
 - **patient-specific risk** based on covariates, e.g. CD4 counts
- effect of covariates on progression to death is expressed by hazard ratios (HR)
- Standardised Mortality Ratio (SMR): ratio of probability of death within one year for HIV-infected patients and non-infected individuals

General population mortality



Standardised Mortality Ratio

- SMR r : patient has r times higher probability of death than a non-infected individual



Source diabetes data: Baan et al., *Epidemiology* 2004;
Laing et al., *Diabet Med.* 1999

New model...

- around 20% of HMF patients are not yet treated
- develop a model that uses information at diagnosis
- model based on 4142 patients
 - diagnosed between 1998 and 2005
 - untreated or starting HAART without prior antiretroviral treatment
 - no concurrent AIDS event at diagnosis
 - 81 (2.0%) deaths, 13,219 person-years of follow-up
- use same mathematical structure as previous model
- “intention-to-treat” approach: initiation of HAART is not included as such

Patient characteristics

CDC status	asymptomatic		CDC-B		CDC-C		total	
at diagnosis	3864	75.3%	404	7.9%	862	16.8%	5130	
male gender	2840	73.5%	325	80.4%	693	80.5%	3858	75.2%
transmission								
homo	1995	51.6%	222	55.0%	364	42.2%	2581	50.3%
hetero	1576	40.8%	141	34.9%	369	42.8%	2086	40.7%
IDU	56	1.4%	7	1.7%	9	1.0%	72	1.4%
other	237	6.1%	34	8.4%	120	13.9%	391	7.6%
origin								
NL	2055	53.2%	254	62.9%	423	49.1%	2732	53.3%
SSA	894	23.1%	65	16.1%	205	23.8%	1164	22.7%
HAART	2452	63.5%	365	90.3%	823	95.5%	3640	71.0%
death	66	1.7%	25	6.2%	80	9.3%	171	3.3%
bef. HAART	16	24%	4	16%	11	14%	31	18%

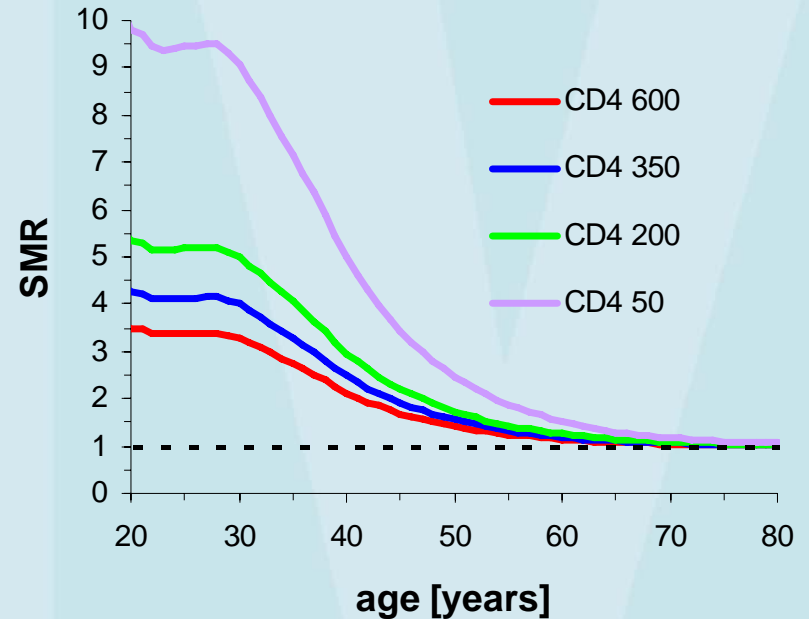
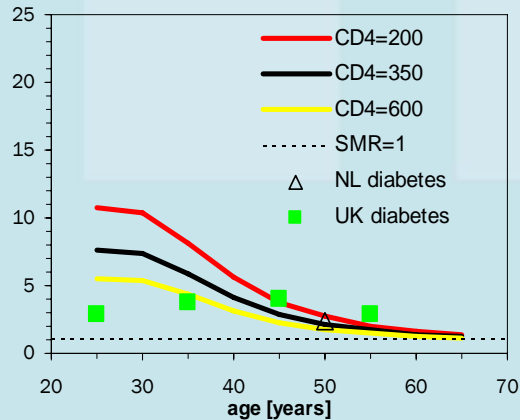
Mortality and predictors

mortality per 100 person-years			
stage	overall	never HAART	HAART
CDC-A	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)

- Only predictors for progression to death are
 - CD4 count at diagnosis HR 0.66 (95% CI 0.51-0.85)
 - CDC stage B vs. A HR 3.50 (95% CI 1.67-7.32)

Mortality ratios

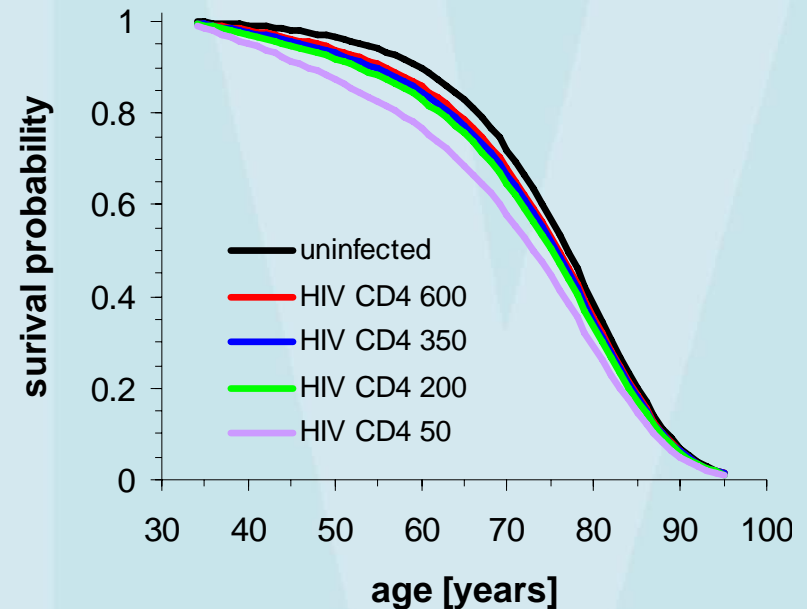
- The variation of SMR with CD4 count is small.
- This most likely indicates that HAART is started in time for those diagnosed above 200 cells/mm³.



SMR for asymptomatic male patients

Predicted survival probability

- predicted probability to reach a specific age for an asymptomatic male patient diagnosed at the age of 34.
- probability to reach age of 70
 - 72% non-infected
 - 68% CD4 600 cells/mm³
 - 67% CD4 350 cells/mm³
 - 65% CD4 200 cells/mm³
 - 58% CD4 50 cells/mm³



Conclusions

- Overall mortality in the HIV-infected population in the Netherlands remained stable at a level between 1 and 2 deaths per 100 person-years.
- In contrast, mortality rates in the HAART-treated population declined, but only in the pre-treated population, accounting for 20% of the HIV-infected population.
- Causes of death changed from mostly HIV-related in 1996 to half now resulting from conditions not directly attributable to the HIV infection.

Conclusions

- Extra mortality relative to non-infected individuals is high, but decreases with age.
- Mortality among HIV-infected patients is comparable with that observed for chronic diseases like diabetes.
- HIV is gradually acquiring the characteristics of a chronic, rather than a lethal disease.
- HMF models encouraged insurance companies to offer life insurance policies to HIV-infected patients.

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