An update on the HIV epidemic in the Netherlands

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NCHIV 2013
19 November 2013

HIV Monitoring

Topics

- **Epidemic trends over time**
  - New HIV diagnoses overall and by transmission risk group, gender, and age and stage of infection
  - Time of diagnosis: late vs. early
- **Quality of care**
  - The cascade of care in the Netherlands
- **Combination antiretroviral treatment outcomes**
  - Short- and long-term viro-/immunologic outcomes
  - Trends over time in tolerability of initial treatment
  - Virological failure and antiviral drug resistance
- **HIV in pregnancy, children and adolescents**
- **Mortality and morbidity**
  - AIDS vs. non-AIDS morbidity and mortality
- **Hepatitis B and C co-infection**
- **Conclusions**

HIV Monitoring

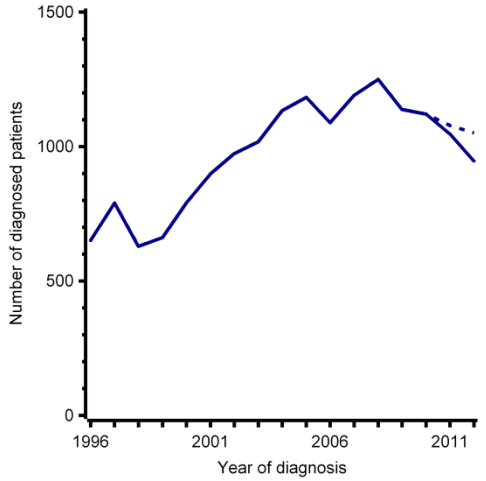
Registered HIV diagnoses

Number per year since 1996:

Stable number **new** registered diagnoses at around 1100 per year

2011: 1047, projected 1078

2012: 947, projected 1051

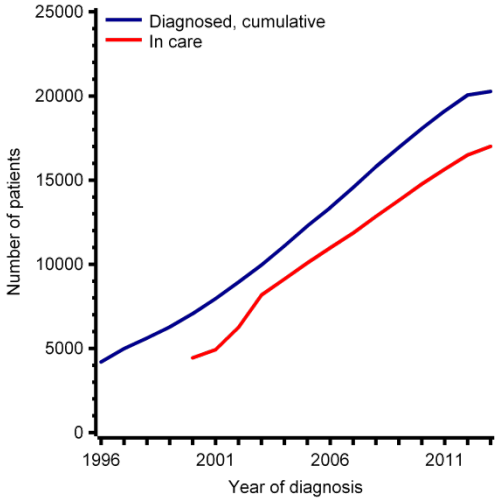


Cumulative number since 1996:

20,761 HIV-1 infected individuals with a registered date of diagnosis

294 children (0-12 yr),
195 adolescents (13-17 yr),
20,272 adults (≥ 18 yr).

17,006 currently in care

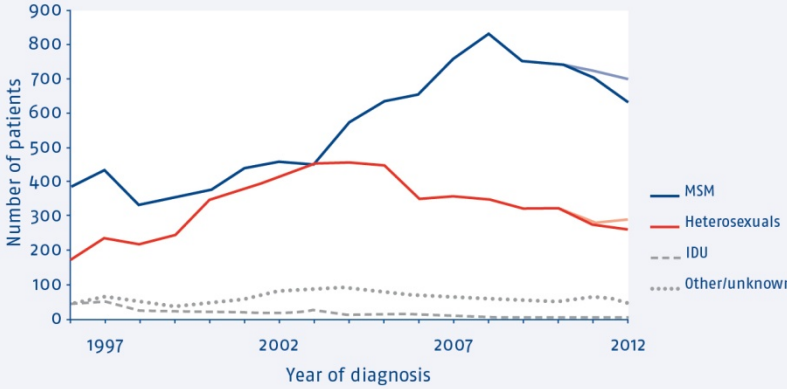


HIV Monitoring

Registered HIV diagnoses

Transmission risk groups:

- **67% MSM**
- **27% heterosexuals**
- 1% IDU



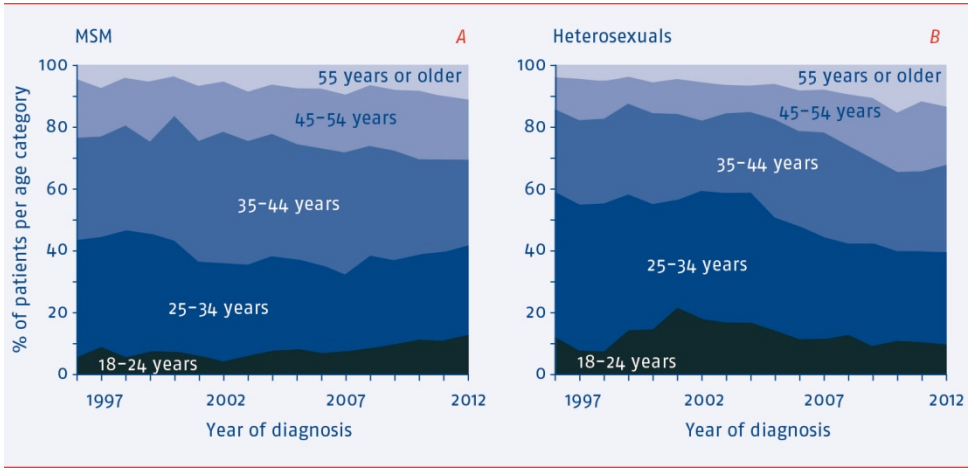
Age at time of diagnosis:

MSM

- **≥45 yrs: ↑ 31%**
- **18-24 yrs: ↑ 12%**
- 25-34 yrs: ↓29%

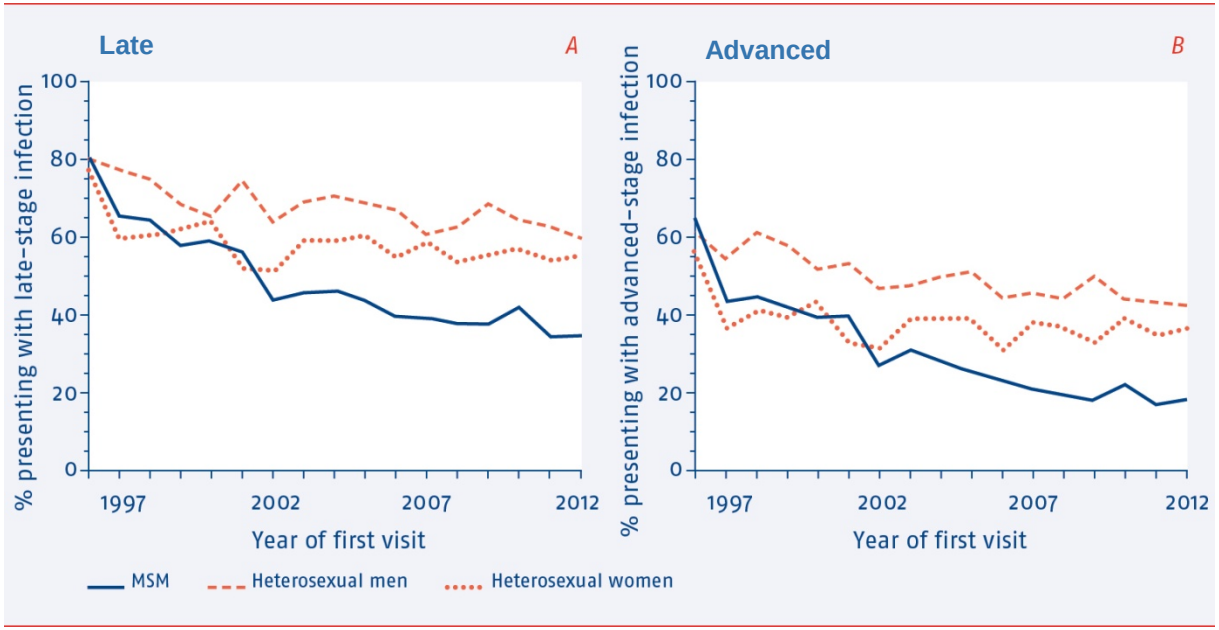
Heterosexuals

- **≥45 yrs: ↑ 32%**
- 25-34 yrs: ↓30%



HIV Monitoring

Late presentation at entry into care remains frequent

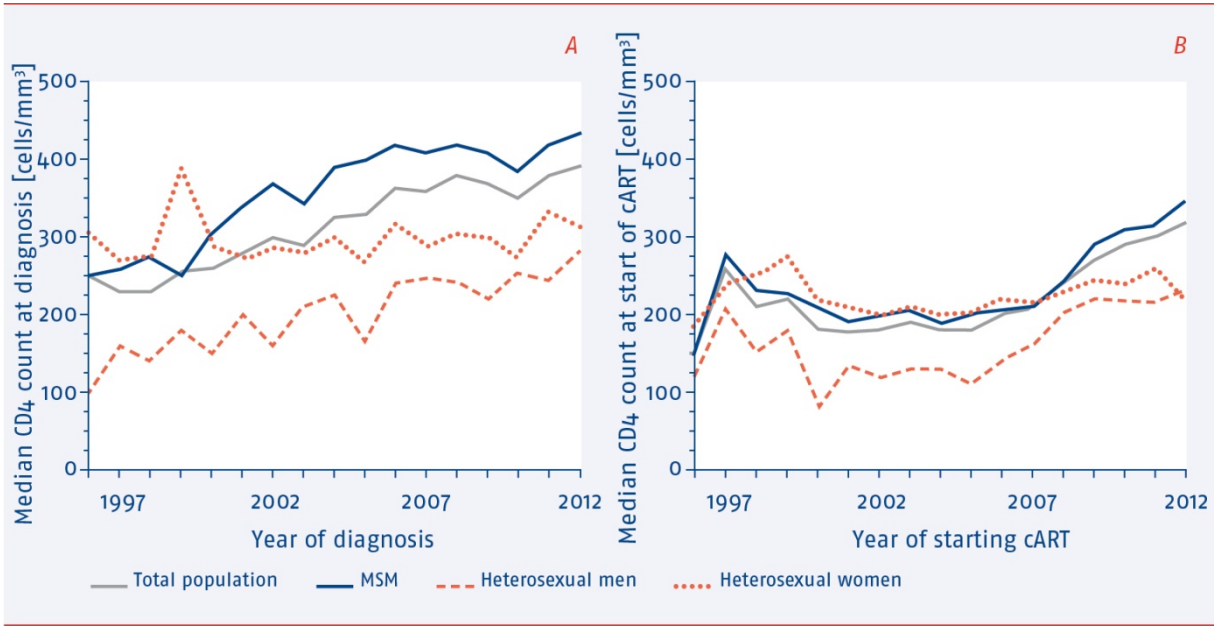


- 2012: 43% late entry into care
- 2012: 26% entry into care with advanced HIV disease

Late = CD4 count <350 cells/mm³ or AIDS
Advanced = CD4 count <200 cells/mm³ or AIDS

HIV Monitoring

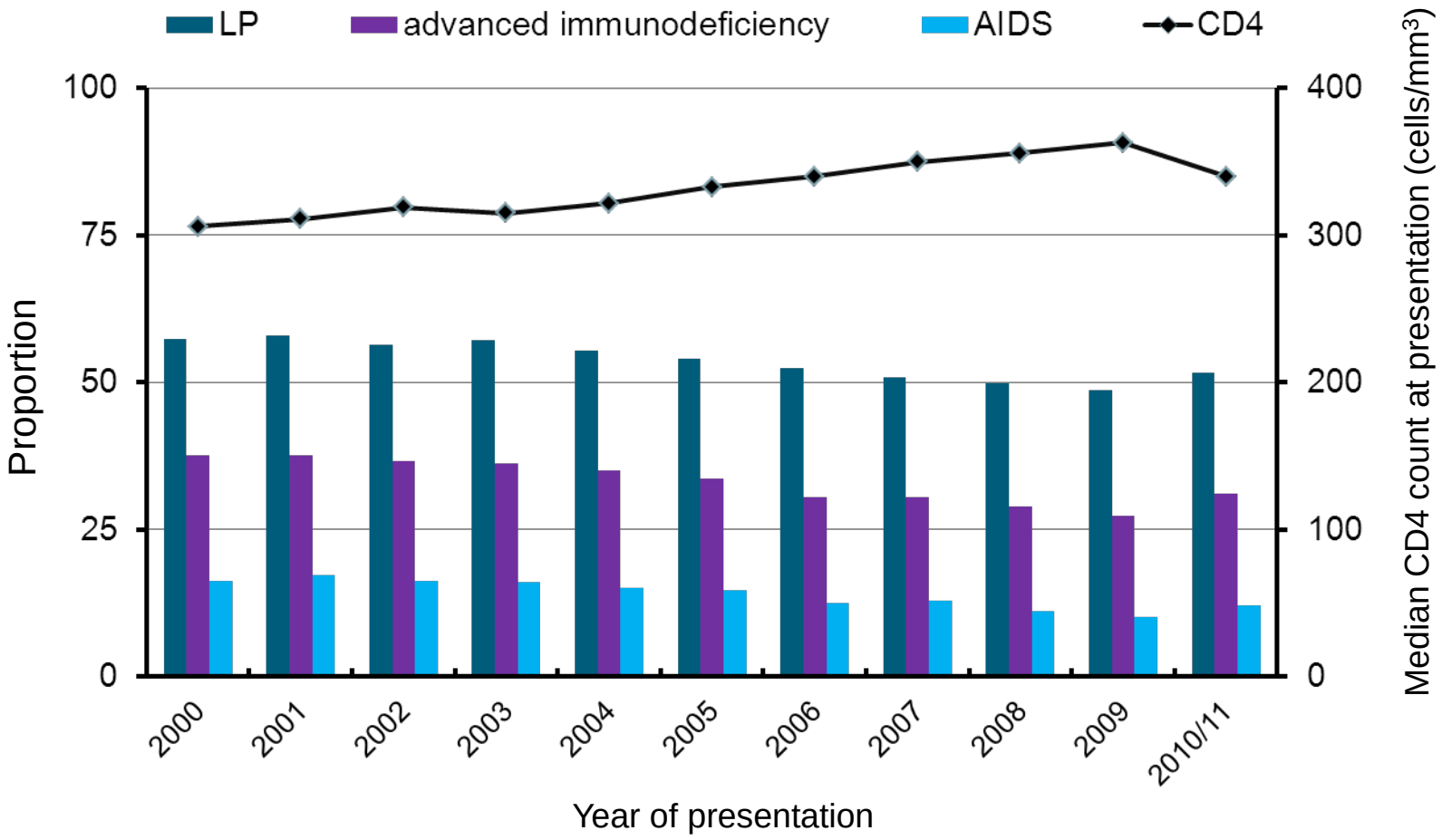
CD4 cell counts at HIV diagnosis & at start of cART



- At entry into care (median) CD4 counts:
  - 1996: 239/mm³
  - 2012: 390/mm³
- At start of cART (median) CD4 counts:
  - 1996→1997: 260 cells/mm³
  - 2012: 320 cells/mm³

HIV Monitoring

Late Presentation– EU trends

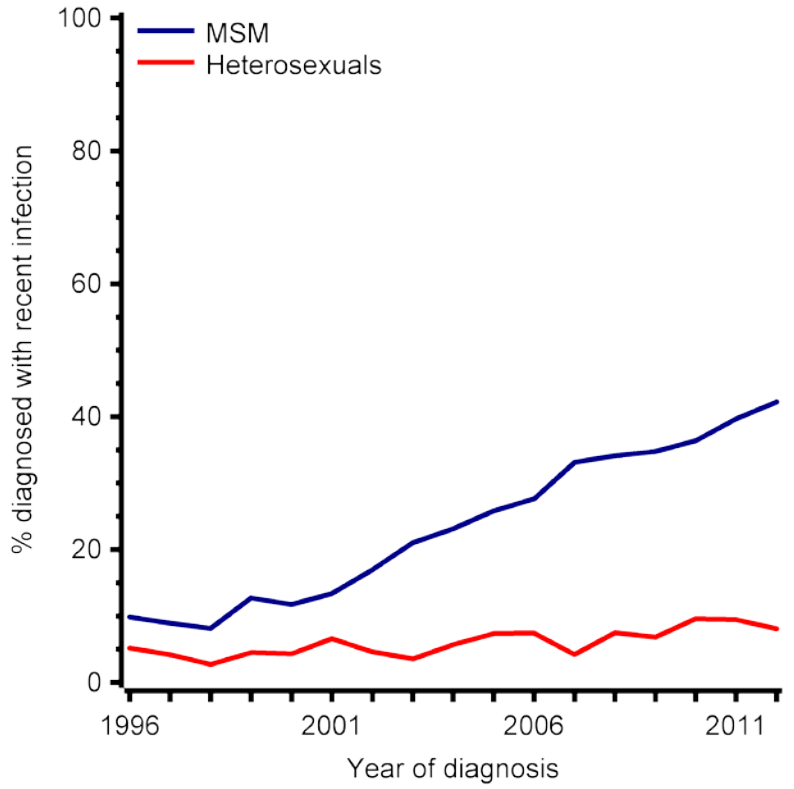


Mocroft A *et al.* PLoS Medicine Epub 2013 Sep 3.

Diagnosis with recent HIV infection

MSM:

- Improvement in diagnosis at earlier stage of infection, also reflected in an increasing proportion diagnosed with recent infection
- Indicates improved testing rates amongst MSM



HIV Monitoring

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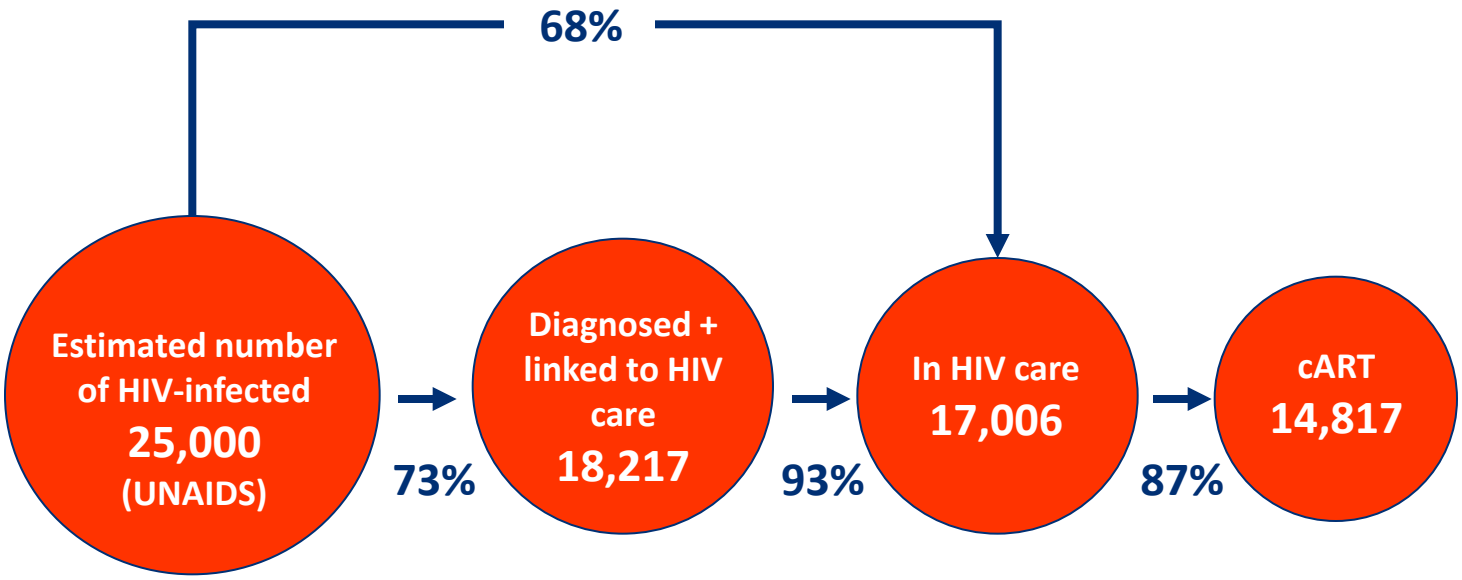
HIV Monitoring

Cascade of care: total population

Estimated number of HIV-infected
25,000
(UNAIDS)

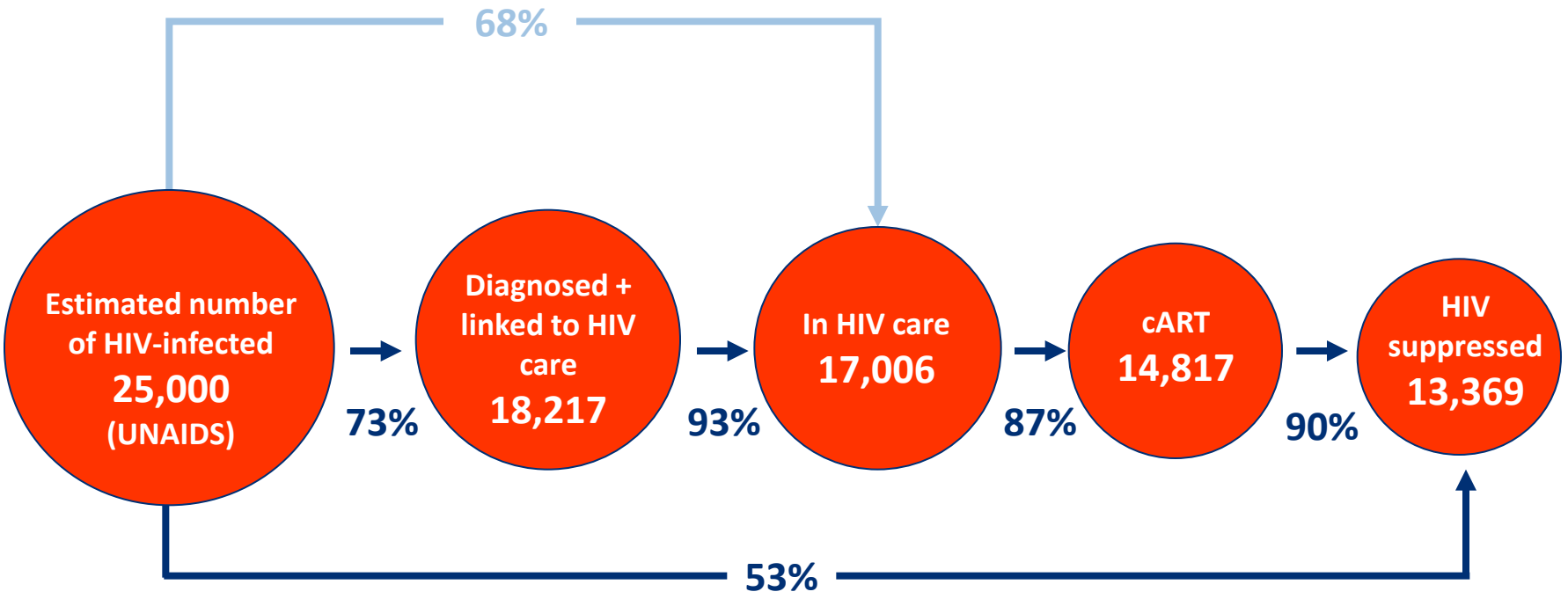
HIV Monitoring

Cascade of care: diagnosed, linked, retained, on cART



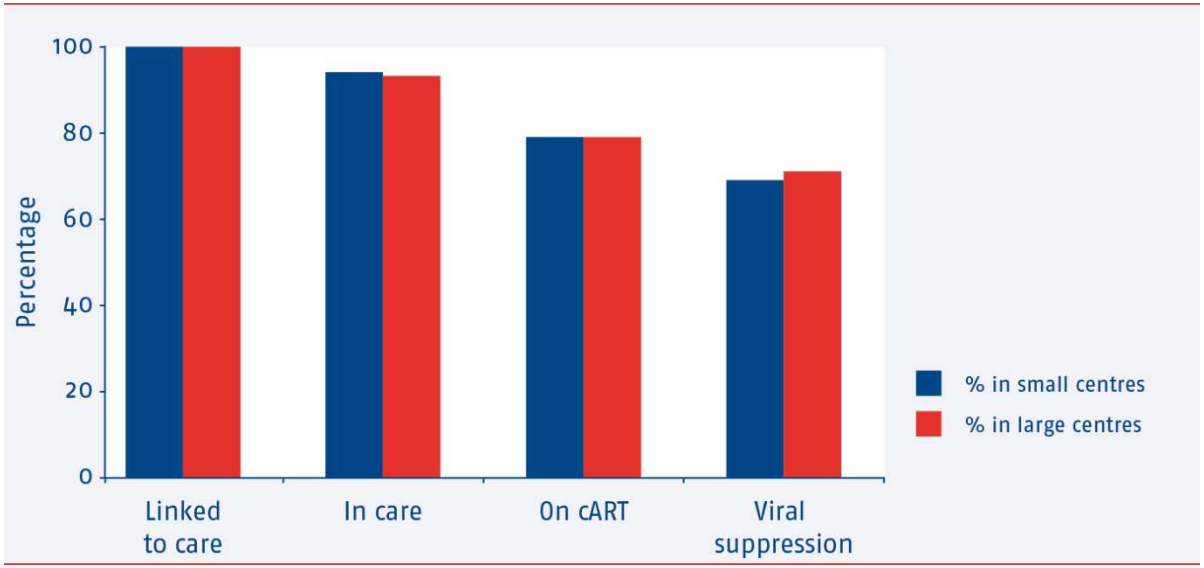
HIV Monitoring

Cascade of care: on cART and suppressed



HIV Monitoring

Cascade of care: small vs large treatment centres



- Q-HIV study initial results

Ref: Esther Engelhard, 14th European AIDS Conference, October 18, 2013

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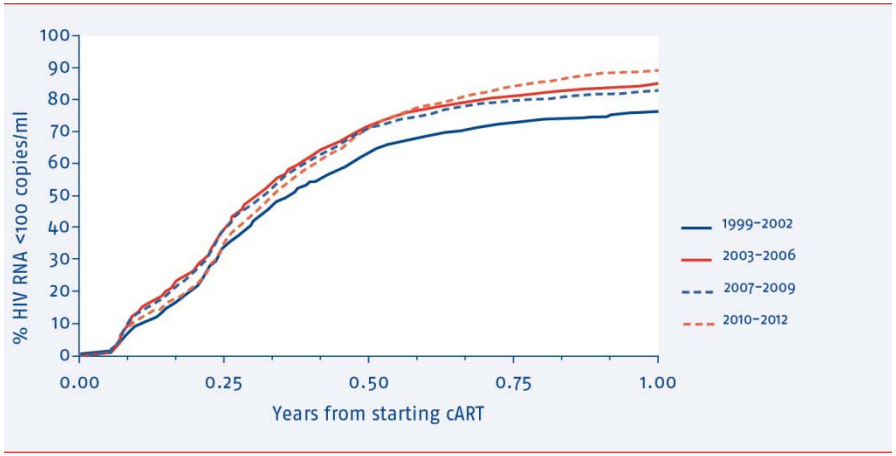
HIV Monitoring

cART: short-term results

- 85% <100 cps RNA/ml plasma at 12 months



- Male gender
- Younger age (<30 years)
- Region of origin (Caribbean/S America, sub-Saharan Africa)

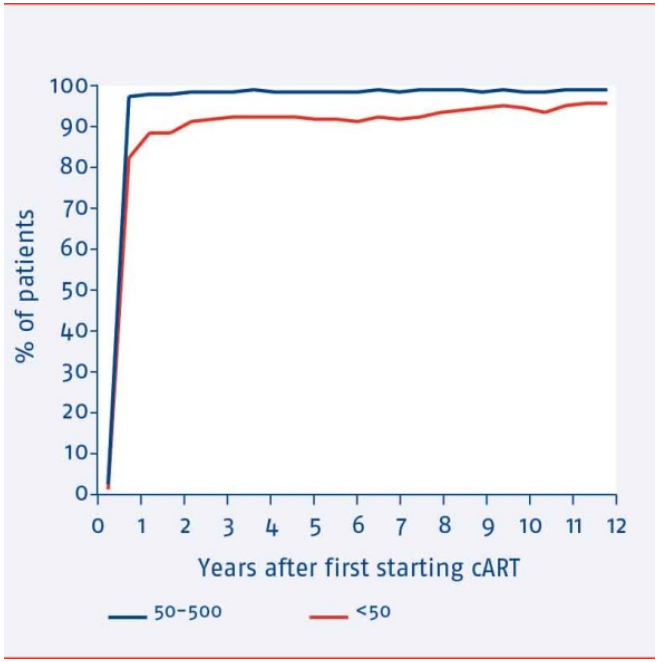
→ Associated with longer time to viral suppression

HIV Monitoring

cART: long-term virological outcome in treatment-naïve patients

Long-term effect of continuous cART:

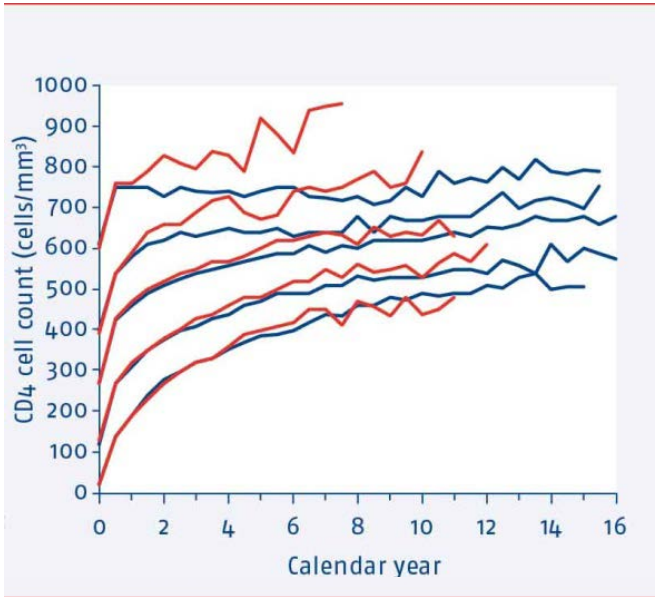
- 94% <50 cps RNA/ml at 12 years



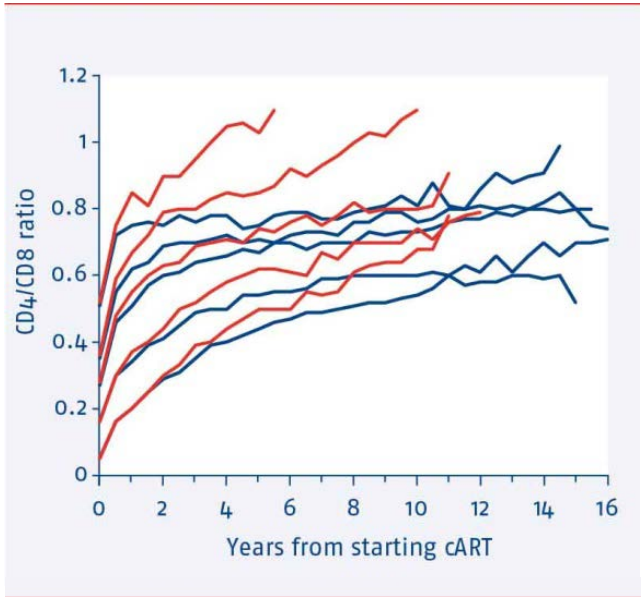
HIV Monitoring

cART: long-term immunological outcome in treatment-naïve patients

CD4 cell count:



CD4/CD8 ratio:



Legend:
- Patients achieving HIV RNA <50 cps RNA/ml ≤9 mths after start of cART and sustained suppression thereafter
- All treatment naïeve patients ever having started cART

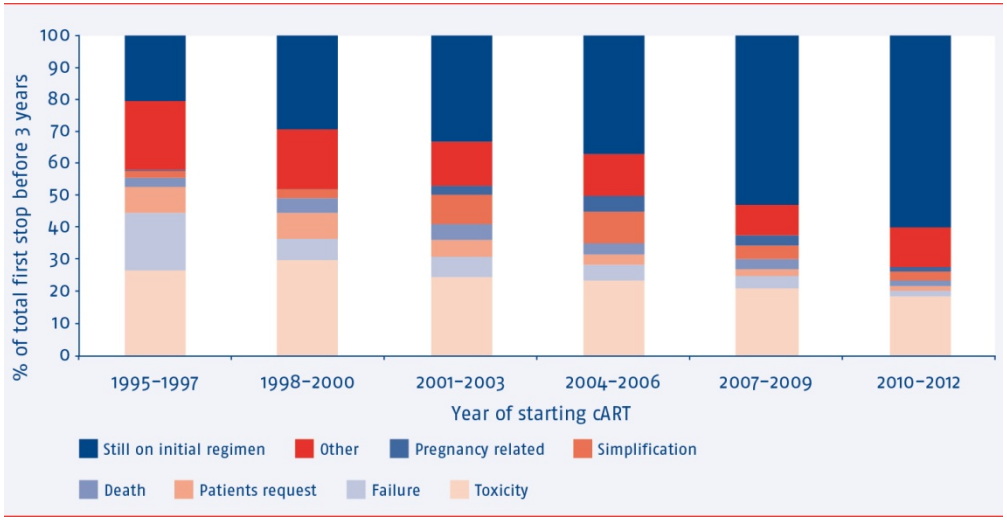
- Optimal immunological recovery associated with starting cART at less advanced infection and maintaining long-term suppression of viraemia

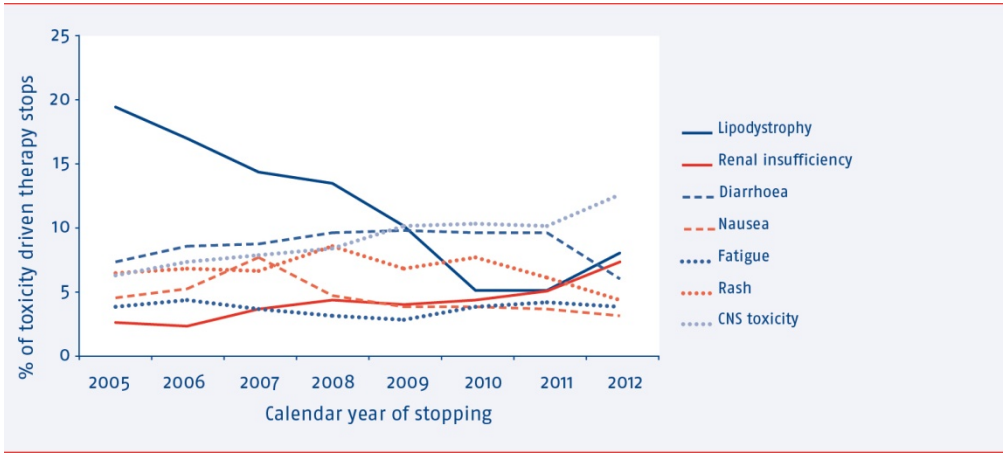
HIV Monitoring

cART: reasons for modifying treatment

- First-line regimens maintained for longer
- Treatment failure has become a rare reason
- Toxicity remains main reason for change

➔ Improved regimens and new drugs still necessary



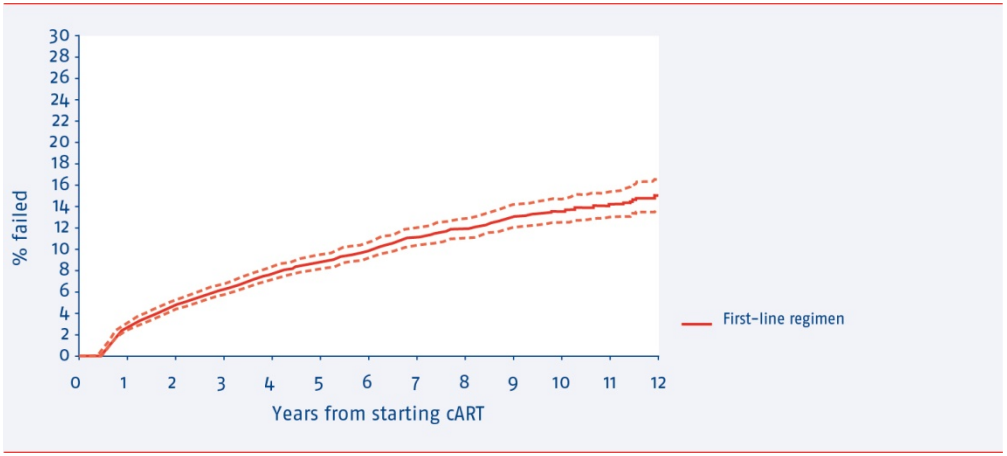


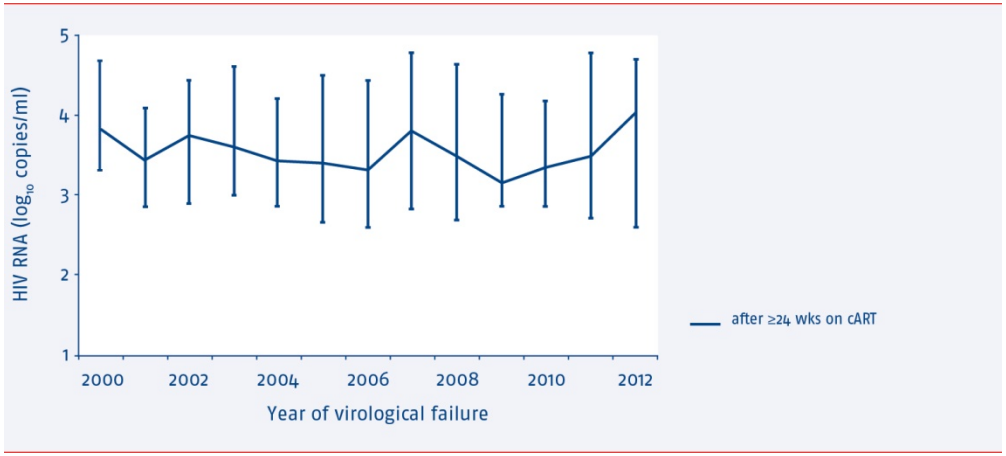
HIV Monitoring

cART: virological failure*

- Virological failure to first-line treatment 15% at 12 years
- Annual proportion of patients with virological failure is low
- HIV levels at time of virological failure relatively low

* HIV RNA (confirmed) >200cps/ml in treatment naïve patients after ≥24 wks on cART





HIV Monitoring

cART: virological failure and drug resistance

- As of June 2013, resistance-associated mutations ever detected in 2,062 of 17,006 (12%) currently in care
- Mutations indicative of high level resistance to at least one drug found in 1,544 of 17,006 (9%) currently in care
  (In 2012: 1,530 (9%) of 16,169)
- Resistance tests available to SHM for only 25% of patients with virological failure
  → True resistance prevalence estimated to be 40% (in line with other EU countries)

HIV Monitoring

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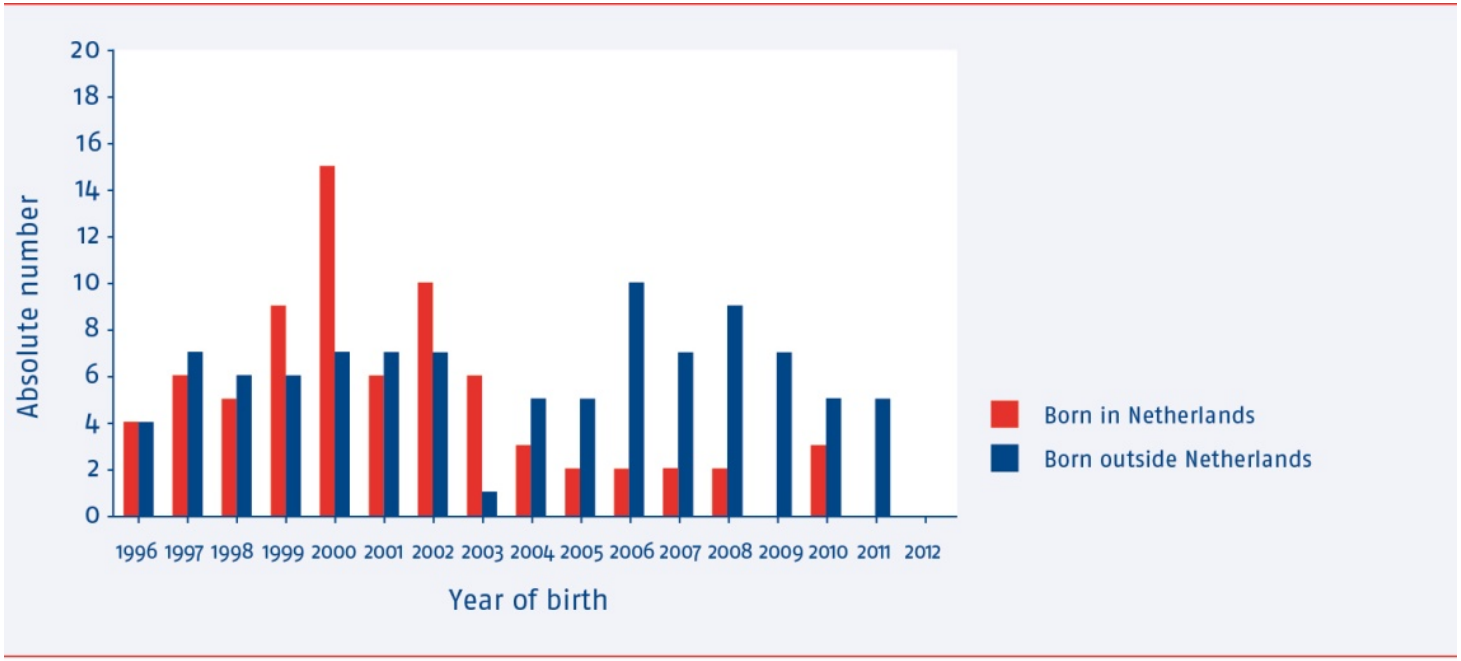
HIV Monitoring

Vertical transmission of HIV

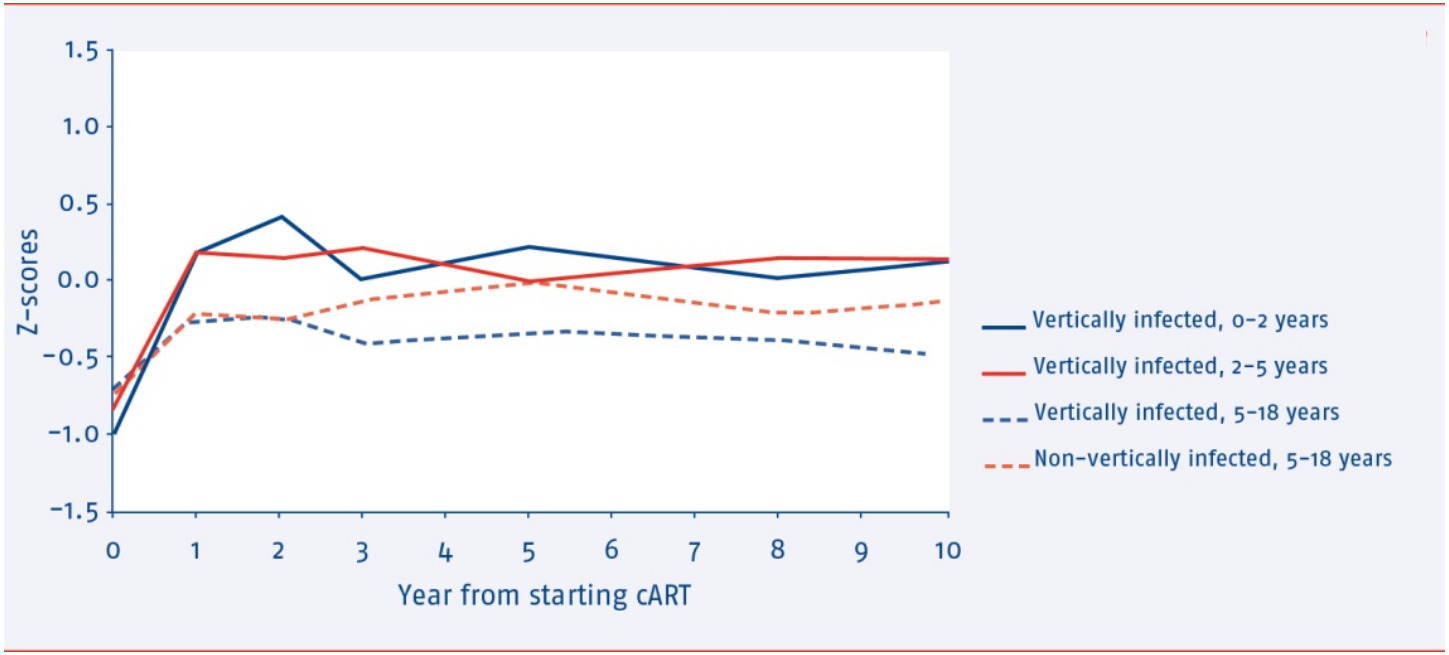


- Vertical transmission of HIV occurring within NL virtually nil
- Overall MTCT risk reduced to <1%

HIV Monitoring

HIV-infected children & adolescents

Long-term immunological recovery on cART



- Immediate treatment leads to better long-term immunological recovery
- 1/3 of children having transitioned to adult care and on cART had detectable HIV RNA at last known measurement (n=21/63)
- Challenge to maintain lifelong adherence to cART

Z-score of 0: Represents the age-appropriate median
Z-score of -1: Child's CD4 count is 1 SD below the age-specific median of an HIV -ve reference population

Cohen S, et al. AIDS. 2013.

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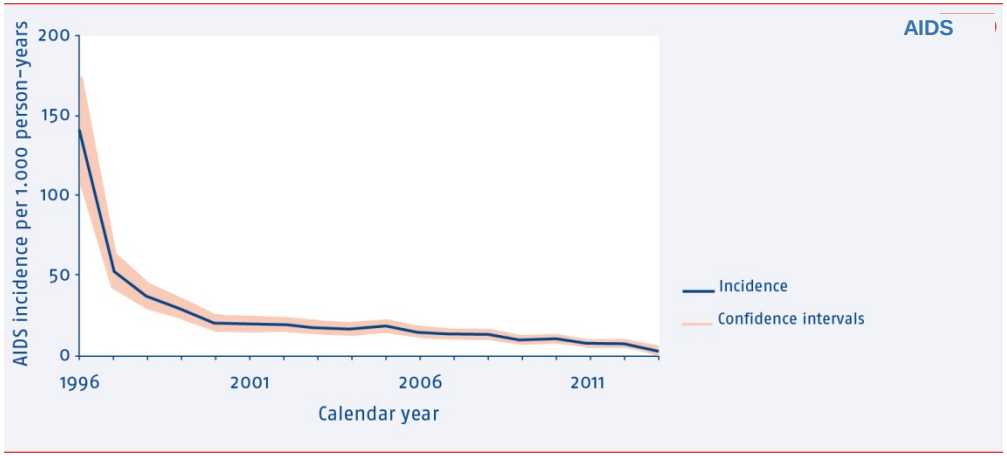
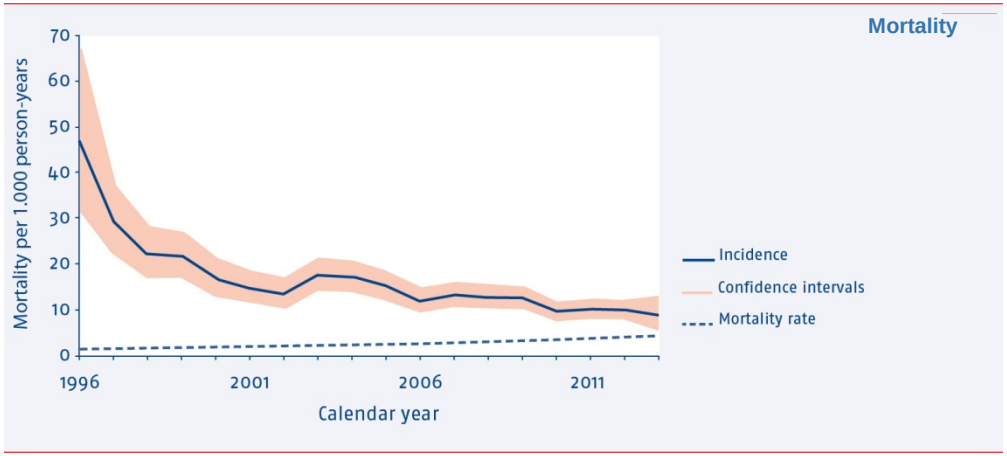
HIV Monitoring

AIDS and death

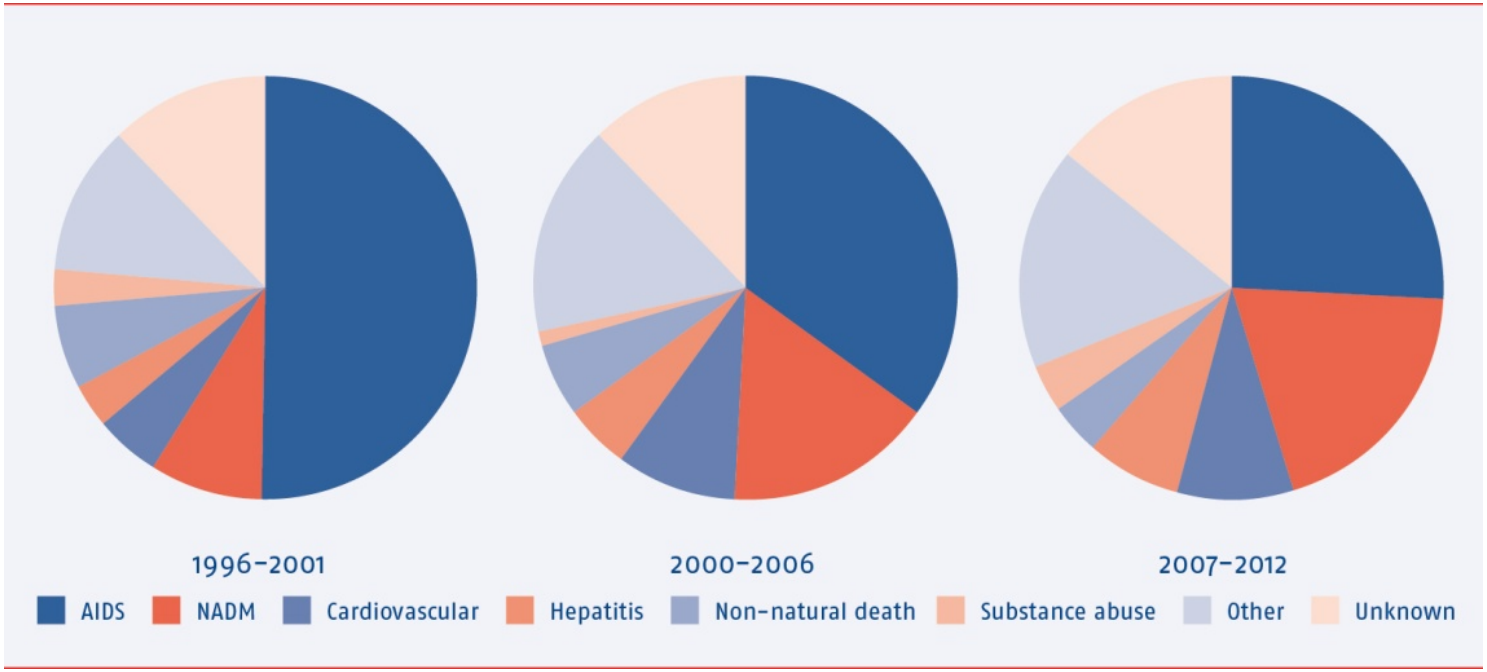
- AIDS down significantly since cART, but still occurs
- Mortality overall still higher than in gender- and age-matched general population
- Mortality of patients successfully treated from an earlier stage of infection approaches that of general population





HIV Monitoring

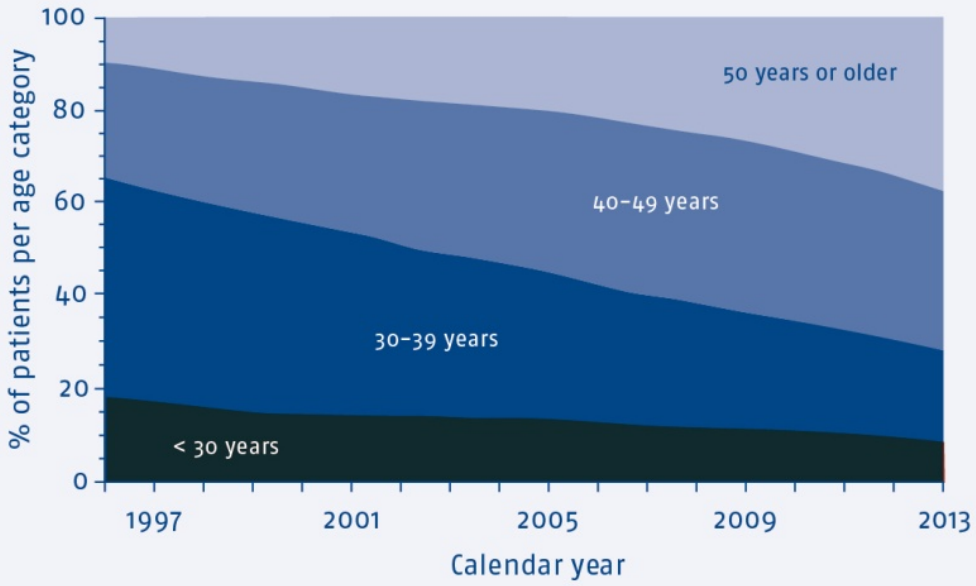
Causes of death



- AIDS remains major cause – 25% (late presentation)
- Shift to non-AIDS causes - NADM (malignancies) and cardiovascular
- Ageing population – more comorbidities

HIV Monitoring

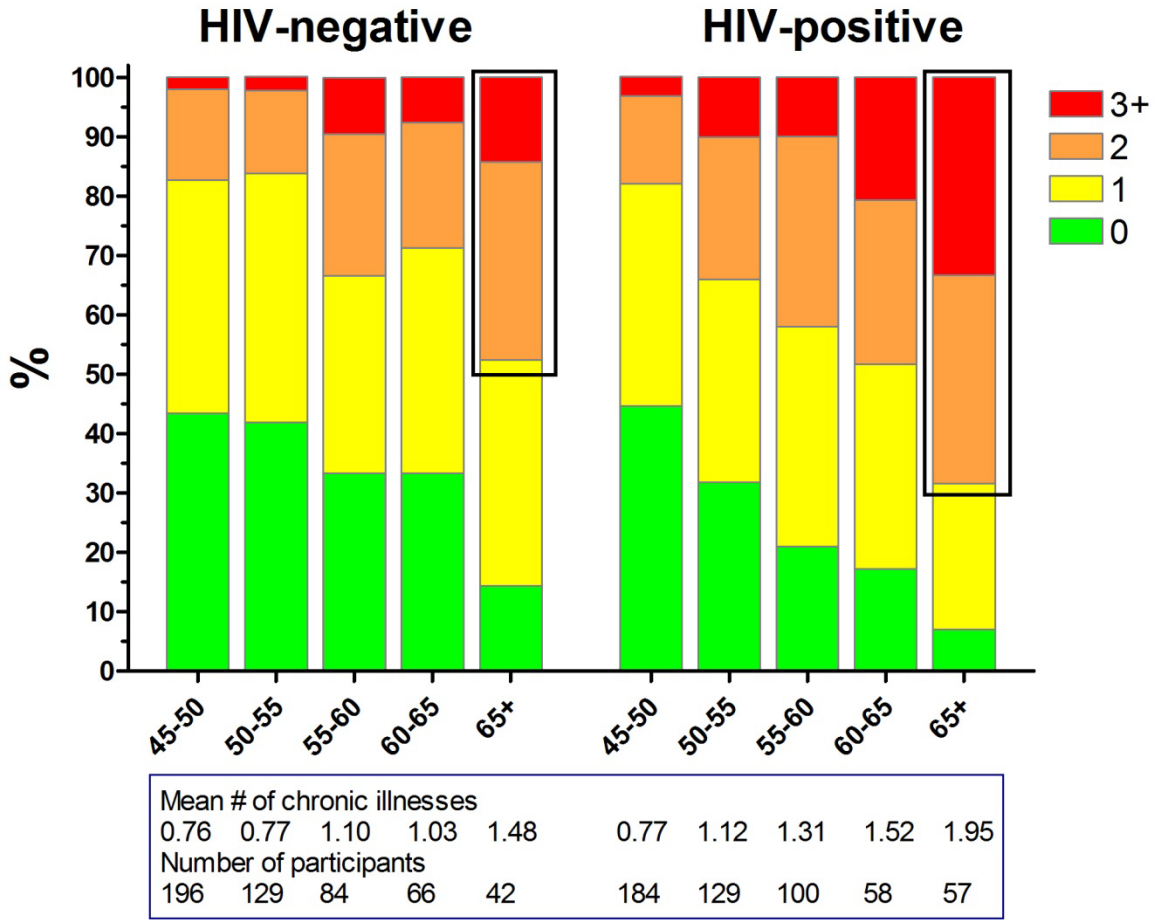
Increasing age of patients in care



- Median age of patients in care = 47 years
- 50 years or older
  - 1996: 9%
  - 2013: 37% (6% ≥65 years)
- Expected increase in age-related comorbidities

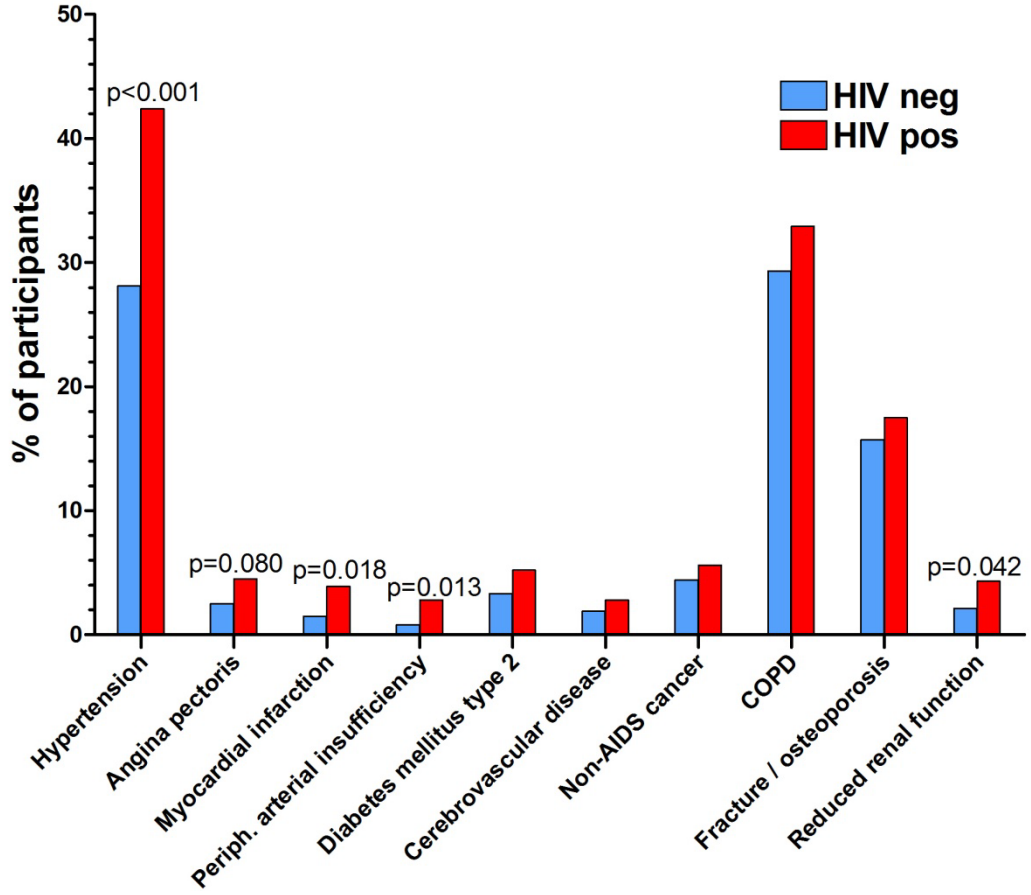
HIV Monitoring

Multiple comorbidity and ageing



- AGE_hIV study – number of comorbidities at time of enrolment
- Multiple comorbidities more prevalent in HIV-infected group, particularly in 65+

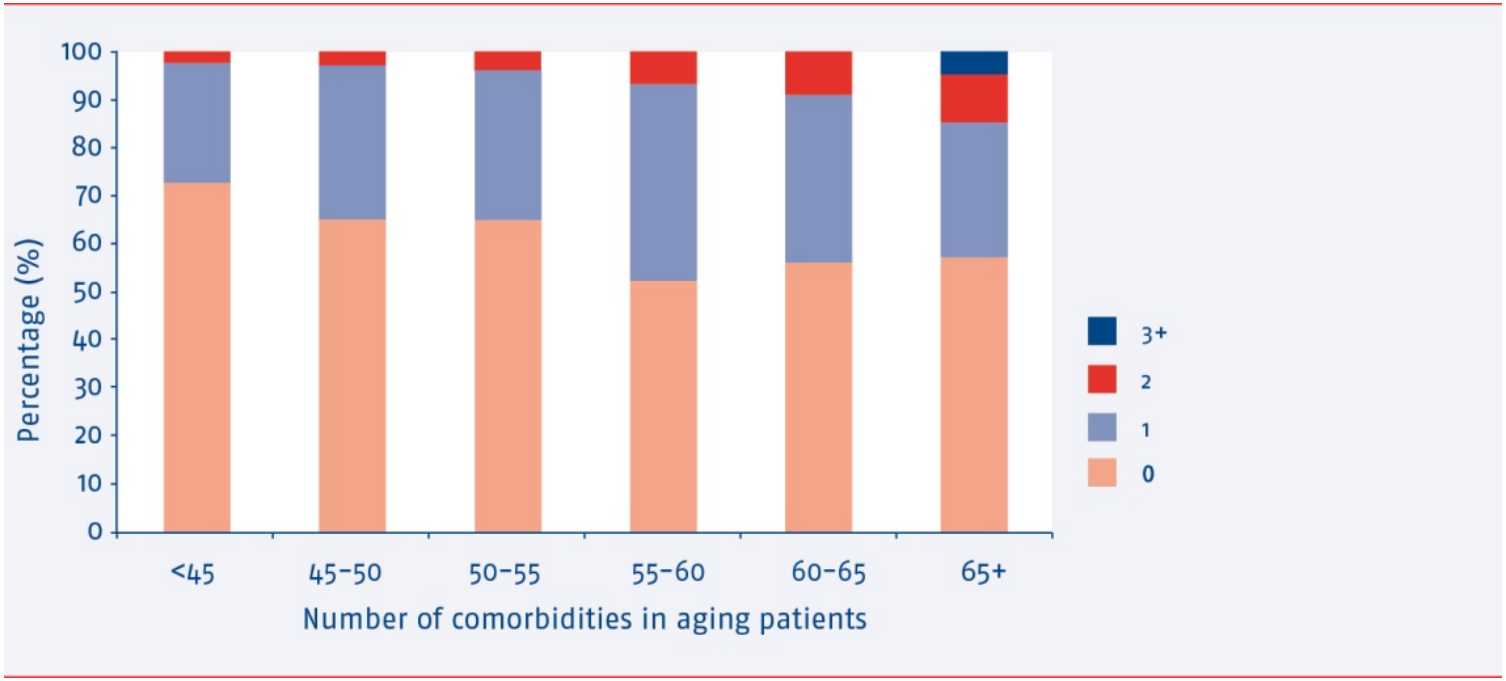
Comorbidities and ageing: HIV vs non-HIV



- AGE_hIV study – prevalence of comorbidities at time of enrolment
- Significantly more cardiovascular disease (CVD) and chronic kidney disease in HIV-infected group

Comorbidities and ageing of patients in care in NL

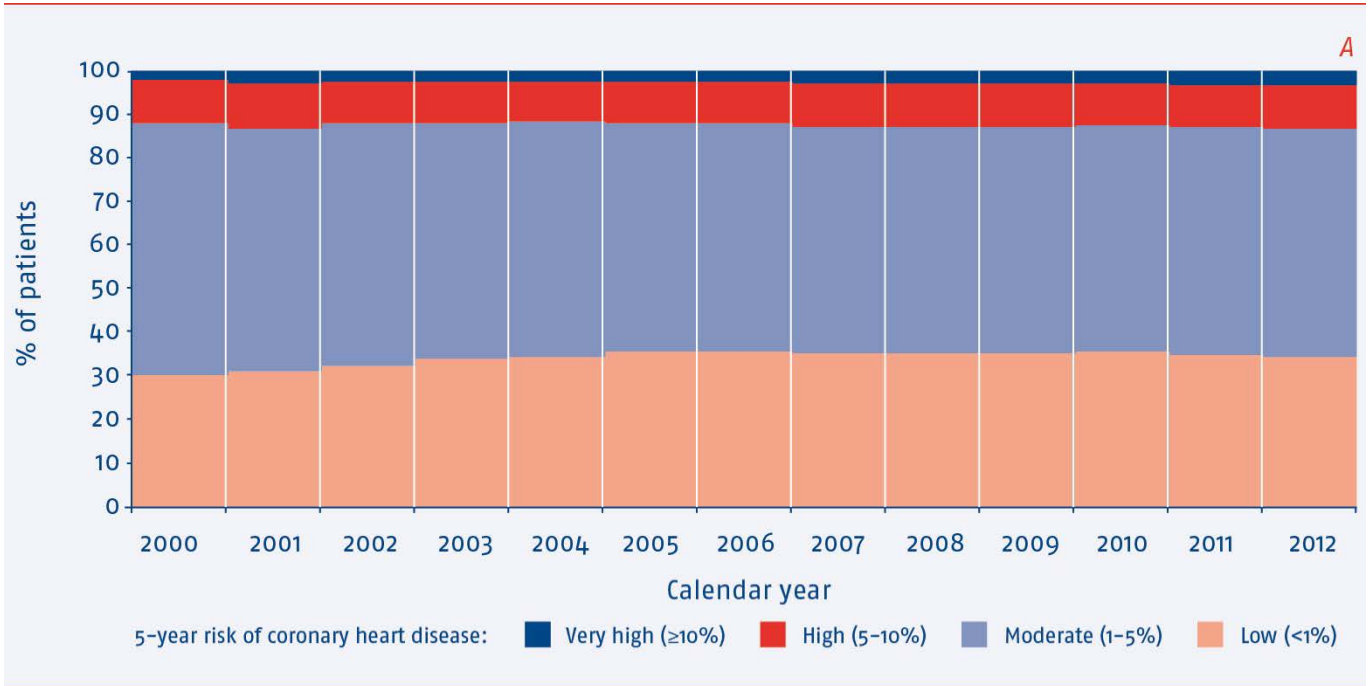
Myocardial infarction, stroke, hypertension, diabetes mellitus, chronic kidney disease and non-AIDS-defining malignancies were assessed.



- Multiple co-morbidities more frequent with age

HIV Monitoring

CVD risk of patients in care in NL



- Calculated using D:A:D study algorithm
- Over time, high risk % and very high risk % remained stable in spite of the population becoming older, suggesting better management of CVD risk

HIV Monitoring

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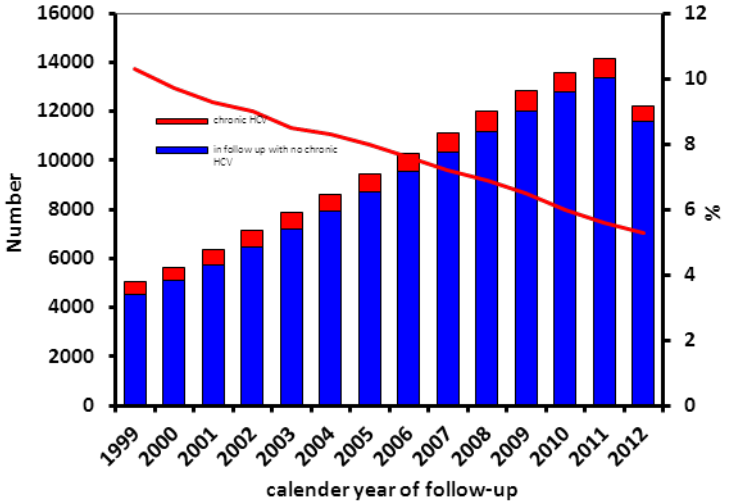
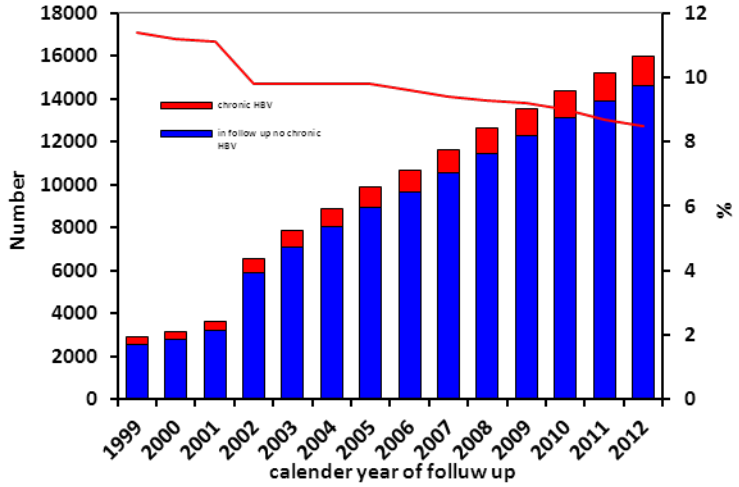
HIV Monitoring

HIV and viral hepatitis

- Annual prevalence of chronic HCV amongst HIV positives tested for HCV slowly decreased from 10% in 1999 to 5% in 2012
- Overall 5.3% of the tested population is diagnosed with chronic HCV

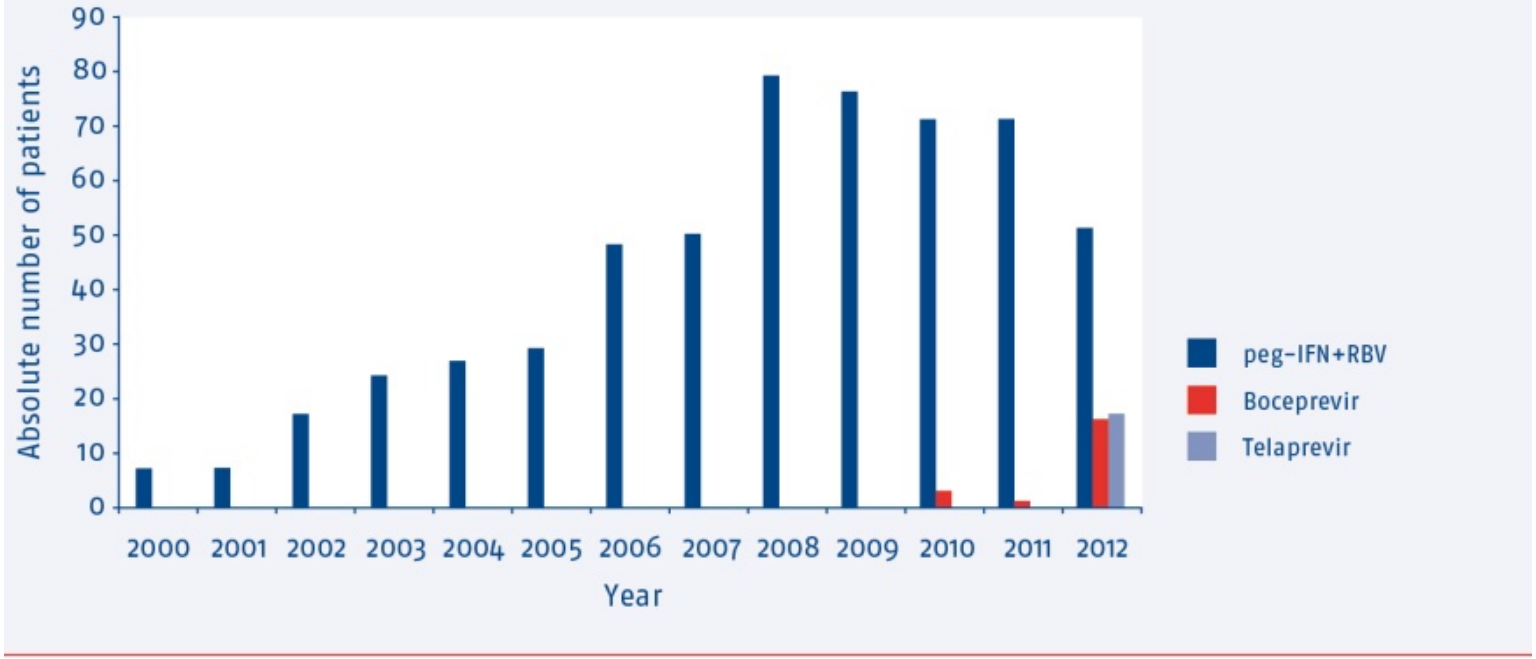


- Prevalence/year of chronic HBV amongst HIV positives decreased from 11% in 2000 to 8% in 2012
- Overall 9% of the tested population is diagnosed with chronic HBV
- Estimated 28% (21% for MSM) not exposed to HBV or vaccinated → increased HBV vaccine efforts necessary



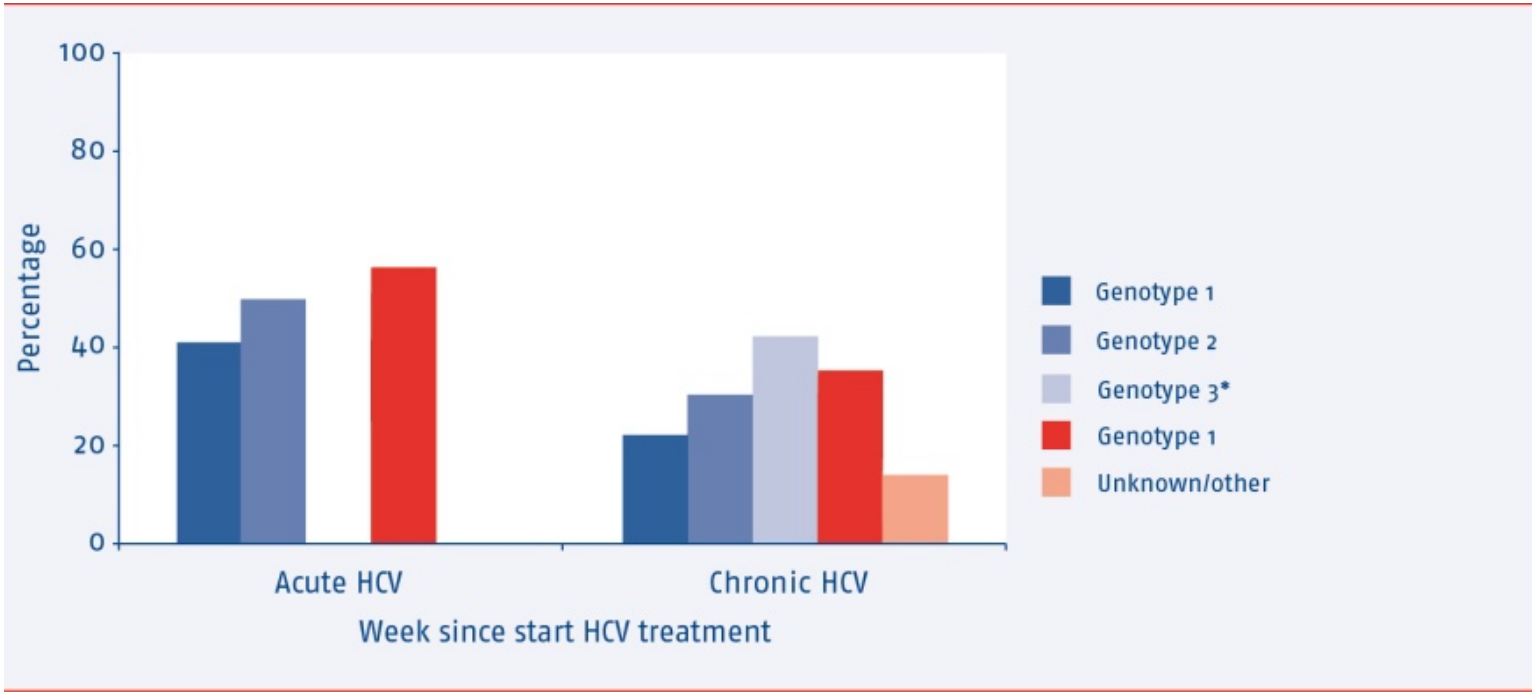
HIV Monitoring

HCV treatment



- HCV treatment uptake has increased with time
- Recent introduction of first-generation direct-acting antivirals

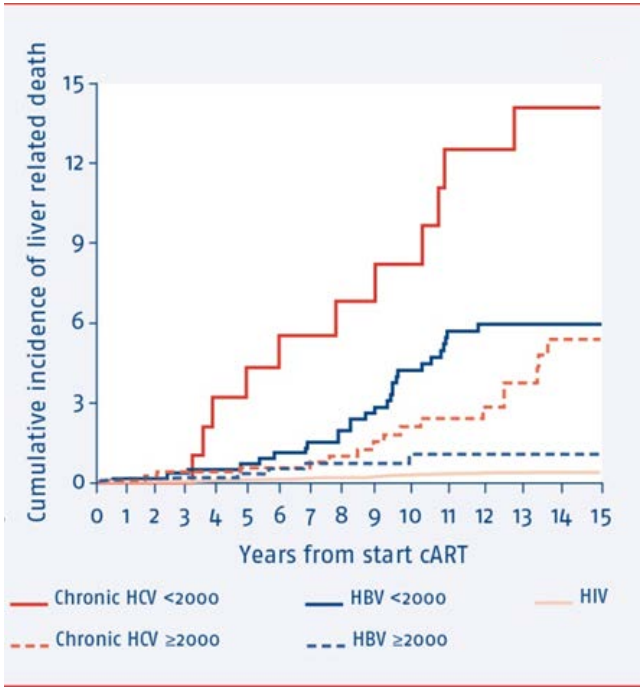
HCV treatment response to (peg)-IFN alfa + ribavirin



- Sustained virological response rates 41-56% for acute HCV and 14-42% for chronic HCV infection

HIV Monitoring

Liver-related death in HIV and HBV / HCV co-infection



	Risk of liver-related death, hazard ratio (95% CI)
HIV	1
HIV/chronic HCV, <2000	7.83 (3.31-18.49)
HIV/chronic HCV, >2000	6.17 (2.85-13.39)
HIV/chronic HBV, <2000	8.01 (4.45-14.39)
HIV/chronic HBV, >2000	3.07 (0.89-10.52)

HBV

- Marked reduction since 2000 (due to tenofovir-containing cART)

HCV

- Some improvement since 2000
- With introduction of new DAA's marked further reduction in liver-related morbidity and mortality expected

HIV Monitoring

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HIV Monitoring

Conclusions

Epidemic trends, quality of care and treatment outcomes

- The annual number of newly diagnosed patients linked to care remains stable, but notably shows no decline
- Two thirds of new diagnoses are in MSM, particularly in both younger and older men
- The rate of late presentation and entry into care remains unacceptably high, especially in heterosexual men and women
- Approximately thirty percent of the total estimated number of PLWHIV in the Netherlands is not in care, most likely unaware of being infected, and importantly contributes to the continuous fuelling of the epidemic
- The large majority of individuals linked to care is retained in care, receives cART and achieves sustained suppression of viraemia
- This has resulted in the prevalence of antiretroviral drug resistance remaining relatively low and stable
- The likelihood of achieving optimal long-term immune recovery is increased with earlier start of cART, both in adults and children

HIV Monitoring

Conclusions

Treatment outcomes, mortality and morbidity

- First-line regimens are increasingly maintained for longer, but toxicities remain the most frequent reason for regimen changes, illustrating the continued need for even better tolerated regimens
- The impact of cART on reducing overall mortality is sustained, but due to late presentation AIDS remains a frequent cause of death, and overall mortality higher than in the general population
- Causes of death in the increasingly aging population of PLWHIV have shifted towards non-AIDS causes, of which CVD and NADM are the most prominent
- Multiple simultaneous co-morbidities are more prevalent in older individuals with HIV on cART than in uninfected individuals
- Preliminary evidence suggests relatively successful management of CVD risk in the aging population of PLWHIV in the Netherlands

HIV Monitoring

Conclusions

HIV and HVB/HCV co-infection

- There remains room for improving vaccination rates in persons at risk of acquiring hepatitis B infection
- Increased use of tenofovir may have contributed to the observed decreased risk of dying from HBV-related liver disease in the last decade
- In spite of increased uptake of treatment, HCV cure rates remain suboptimal
- More effective and especially interferon-free regimens hold great promise for improving cure rates and reducing the future burden of chronic liver disease and liver-related mortality

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Future prospects

- Improved and earlier identification, linkage to care and treatment of persons living with HIV may be expected to:
  - Improve individual prognosis in terms of disease-free survival
  - Contribute to reducing the incidence of new HIV infections

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