Substantial decline in virological failure after cART initiation in treatment-naïve HIV-positive adults in the Netherlands from 1996 to 2016

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Background

We evaluated the incidence of, and factors associated with, virological failure (VF) after combination antiretroviral therapy (cART) initiation in adults in the Netherlands, since the introduction of cART in 1996.

Methods

We assessed the incidence of VF (i.e. the first of two consecutive viral load measurements ≥200 copies/ml after >6 months of cART) among HIV-1 positive, ART-naïve, non-pregnant adults in the ATHENA-cohort between 1996-2016.

Time was censored at the date of last contact with HIV-care, or at the last date of cART when cART was interrupted for >2 weeks.
We assessed the incidence of VF since cART initiation, and assessed socio-demographic and clinical factors associated with time-to-VF specifically for cART initiation between 2011-2016 using Cox regression.

ATHENA is a nationwide observational HIV cohort study, which monitors all HIV-positive adults and children who do not opt-out of data collection from the moment of entry into HIV care in the Netherlands.

Extensive clinical and laboratory information relevant to HIV infection and treatment, co-infections, and comorbidities recorded during clinical follow-up is extracted from the medical record, at time of enrolment into the cohort and regularly thereafter. Specific data collection protocols exist for pregnant women and children, and hepatitis B and C virus co-infection.

As of May 2017, 26,409 HIV-positive people had ever been registered in the ATHENA national HIV cohort.

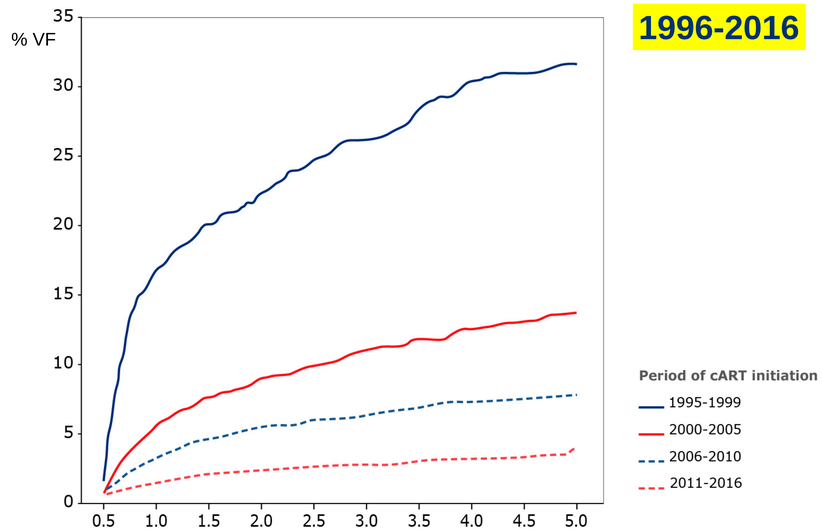

Figure 1. Kaplan-Meier estimates of virological failure according to calendar period of starting cART, from 1996-2016. *Log-rank p<0.001.*

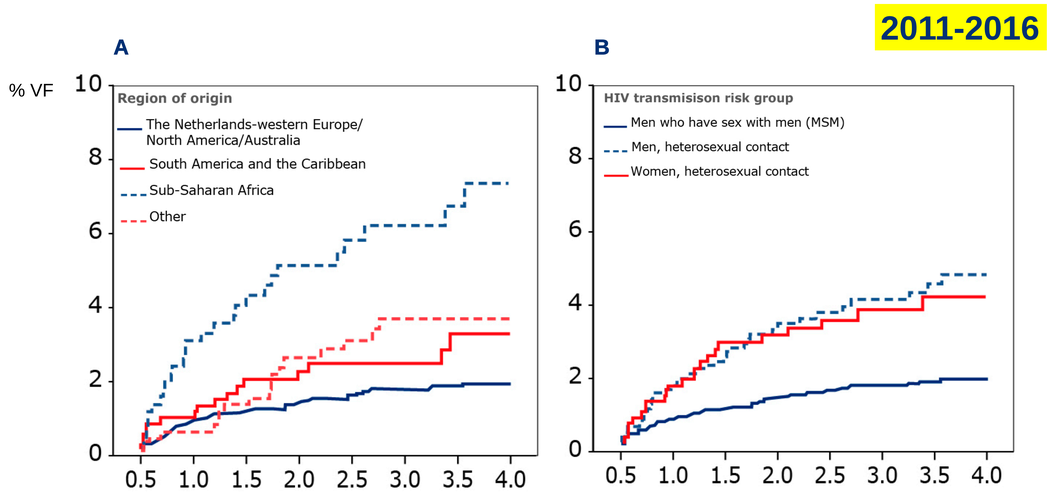

Figure 2. Kaplan-Meier estimates of viral rebound according to region of origin (A) HIV-transmission risk group (B), among previously ART-naive individuals receiving cART, since 2011. *Both log-rank p<0.001.*

Results

During 1996-2016, 1,807 (10.6%) out of 17,044 adults experienced VF after a median of 1.4 [IQR 0.7-3.4] years since cART initiation.
The likelihood of VF decreased substantially by year of cART initiation: unadjusted hazard ratio (uHR) 12.6 (95%CI 10.4-15.2) in 1996-1999, 5.2 (4.3-6.3) in 2000-2005, and 2.6 (2.1-3.2) in 2006-2010, respectively compared to 2011-2016 (***Figure 1***).

During 2011-2016, 133 (2.1%) out of 6,228 people who initiated cART experienced VF after a median of 1.6 (IQR 0.7-2.0) years. Before VF, 106 out of 133 people had ≥1 VL measurement available, of whom 66 had an undetectable VL. HIV-transmission risk group and region of origin were independently associated with VF: adjusted hazard ratio (aHR) 1.7 (95%CI 1.0-2.7) for men with heterosexual acquired HIV-1 compared to men who have sex with men (MSM), and aHR 2.3 (1.3-4.1) for people originating from sub-Saharan Africa compared to Western Europe/North America/Australia (***Figure 2***). Additionally, a higher VL (aHR 1.5 [95%CI 1.2-2.0] per $\log_{10}$ cps/ml) and lower CD4-cell count (aHR 2.3 [1.0-5.1] for <50 cells/mm^3, and aHR 2.1 [1.0-4.5] for 50-199 cells/mm^3, compared to >500 cells/mm^3) at cART initiation were independently associated with VF.

Conclusions

VF after cART initiation has decreased substantially over the last two decades in the Netherlands.

While the risk of VF continues to decline, additional support for non-MSM, late-presenters, and those originating from sub-Saharan Africa is warranted to further optimize cART outcomes.

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