

Stable HIV-1 Epidemic among Heterosexual Men and Women in the Netherlands

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Background

Increasing risk behaviour and resurgent HIV epidemics have been widely reported amongst men who have sex with men (MSM) in the era of combination antiretroviral therapy (cART). We analysed the impact of cART on the transmission dynamics of HIV-1 among patients in the Netherlands infected via heterosexual contact.

Methods

Mathematical model

- A mathematical model based on Bezemer *et al.* (AIDS 2008) was used to estimate the changes in transmission and diagnosis rates, and the changes in immigration patterns needed to explain the observed data on HIV and AIDS diagnoses and the transmission of non-B subtypes.
- The model incorporated
 - infection with HIV in the Netherlands
 - import of HIV infections from abroad
 - natural disease progression and HIV diagnosis
 - subsequent use of cART and therapy failure
- The transmission rate was related to
 - the stage of infection (primary, chronic, AIDS)
 - awareness of HIV-positive status
 - treatment (viral load suppression, therapy failure)
- Sensitivity analyses (Latin Hypercube sampling) were performed to assess the dependence of the model results on input parameter values.

Reproduction number

- The reproduction number $R(t)$ was calculated as the average number of individuals infected by each HIV-infected patient during his infectious lifespan.
- $R(t)$ was calculated in three distinct historical intervals:
 - 1984-1995: pre-cART (serological testing, HIV awareness)
 - 1996-1999: early cART
 - 2000-2006: late cART

Study population

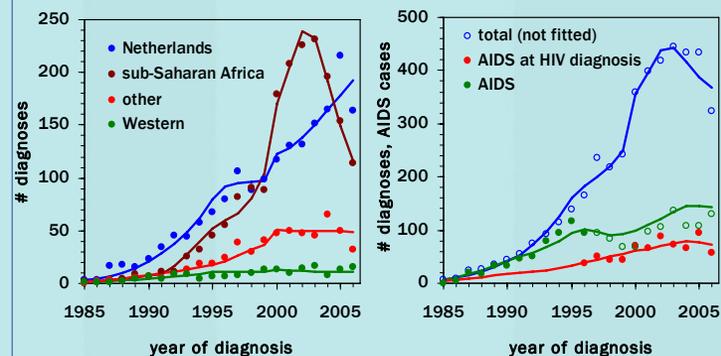
- 4295 patients infected via heterosexual contact and diagnosed up to 2006 were selected from the ATHENA national observational cohort in the Netherlands.
- Patients were classified according to their region of infection:

region of infection	N	%
Netherlands	1778	41.4
sub-Saharan Africa	1778	41.4
other Western countries	180	4.2
other countries	559	13.0

- For 1215 (28.3%) patients, the HIV-1 subtype was known; 724 (59.6%) were infected with a non-B subtype.
- Of the 3672 patients diagnosed with HIV from 1996 onwards, 692 (18.8%) were already having AIDS.

Results – model fit to diagnoses and AIDS cases

- The figures show the annual number of diagnoses (total and per region of infection) and AIDS cases. Lines represent the model fit. Data used in the fit are represented by dots, whilst open circles are data that were not used in the fit.



- The proportion of patients infected with a non-B subtype in the Netherlands restricted the extent to which imported infections contribute to new infections.

Results – estimated parameters

- The table shows estimated values and 95% marginal confidence intervals for the time to diagnosis and the transmission rate in each time period.

	period		
	1984–1995	1996–1999	≥2000
time to diagnosis [years]	3.74 3.47-4.02	3.68 3.45-3.93	3.02 2.87-3.17
transmission rate	0.87 0.84-0.90	0.74 0.66-0.81	0.95 0.91-0.98
$R(t)$	1.37 1.32-1.41	0.88 0.79-0.95	1.06 1.02-1.09

- According to the model, the transmission rate increased 28% in 2000-2006 compared to 1996-1999, resulting in an increase of $R(t)$ to 1.06, despite a shorter time between infection and diagnosis.
- Patients who were not yet aware of their HIV infection accounted for 91% of new infections after 2000.

Sensitivity analyses

- The sensitivity analyses showed that the increase in transmission rate was robust to changes in input parameters.
- In all model variants, $R(t)$ in the period 2000-2006 was estimated to be above or near 1.
- Estimates were similar when 876 patients with unknown transmission route were considered as heterosexuals.

Conclusion

- Our model indicates that transmission rates in the heterosexual population in the Netherlands have increased in recent years.
- Though these increases are less marked than in the MSM population, the current reproduction number is near or above the epidemic threshold, and the local HIV epidemic amongst heterosexuals appears to be self-sustaining.