Sexual networks across risk groups persistently contribute to local spread of HIV

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Introduction

Despite the sharp drop in influx of immigrants from HIV endemic countries since 2003, HIV incidence is not decreasing in the Netherlands. We aimed to get insight in local transmission dynamics.

Methods

- Clinical and virological data collected of nearly all newly diagnosed HIV-patients of the UMC Utrecht and Rijnstate Arnhem from 2004 until 2013 (n=1220), with *pol* sequences available for 973 patients.
- Maximum likelihood phylogenetic tree was constructed and clusters were identified using 95% support and genetic distance <0.015 or <0.045.
- Duration of circulation of large clusters was established based on prior negative HIV-1 test results of patients in the clusters
- Subtyping was performed with COMET v0.5
- Transmitted drug resistance mutations (TDRM) were defined using the 2009 epidemiological list of the WHO (Bennett *et al)*

Results

Table 1. Baseline characteristics

	Utrecht (n=709)	Arnhem (n=511)
Male	84.9%	84.8%
Mean age at diagnosis	39 ± 11	39 ± 11
Route of transmission MSM HSX IDU	 65.6% 27.2% 0.8%	 64.4% 25.3% 0.2%
Region of origin NL Europe (other than NL) Sub Saharan Africa	 73.9% 3.8% 11.6%	 73.6% 4.8% 13.1%
Median viral load, log	5.0 (4.5-5.5)	4.9 (4.4-5.4)
Median CD4 count	352 (170-535)	340 (175-505)

Table 2. Transmission clusters

Cluster definition		
Genetic distance	<0.015	<0.045
Unique viral variants in cohort	502 (51.6%)	324 (33.3%)
Small clusters (2-5 patients)	108 (n=258, 26.5%)	93 (n=221, 22.7%)
Large clusters (>6 patients)	19 (n=213, 21.9%)	34 (n=428, 44.0%)

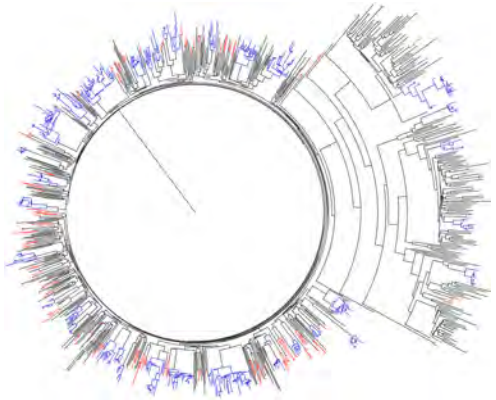


Figure 1. Phylogenetic tree.
Maximum likelihood phylogenetic tree of our cohort, showing small clusters in red and large clusters in blue (defined with genetic distance <0.045).

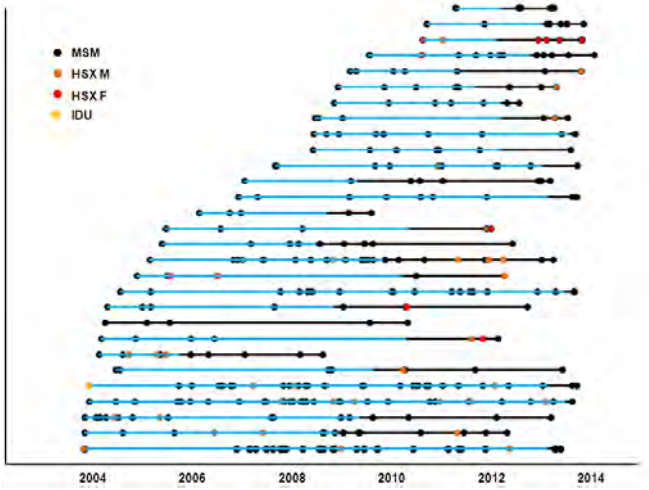


Figure 2. Large subtype B clusters
We identified 29 large clusters of patients infected with subtype B. Patients that are part of the same cluster are plotted on a horizontal line. Every dot represents a patient in the cluster, depicted at date of diagnosis. The colouring of the dots shows their transmission risk group. 18 clusters included patients from different risk groups. For 28 clusters, we could determine the minimal duration of circulation based on last negative HIV test results of patients in the cluster (indicated by the blue line). These 28 cluster variants circulated on average at least 53 months, with a range from 10-111 months.

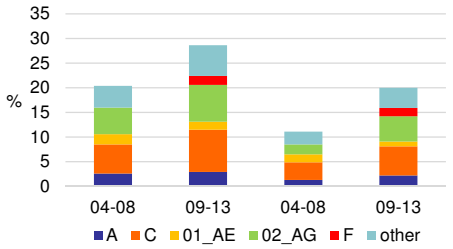


Figure 3.
In more recent years, we observed a significant increase in HIV non-B subtypes in all HIV-patients in our cohort (2 left bars, p 0.008). This significant difference was also observed in patients from Dutch origin (2 right bars, p 0.005).

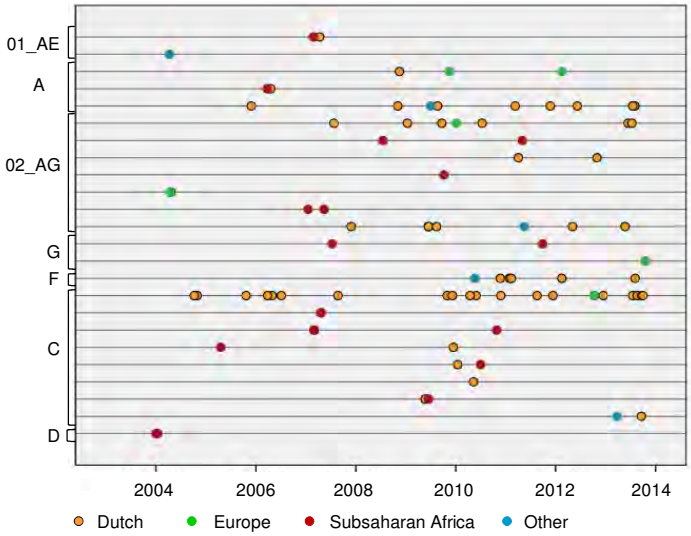


Figure 4. Clusters of HIV non-B subtypes
We identified 24 clusters of patients infected with non-B subtypes. Patients that are part of the same cluster are plotted on a horizontal line. Every dot represents a patient in the cluster, depicted at date of diagnosis. The colouring of the dots shows their continent of origin. Patients from sub Saharan Africa are only represented in small clusters, often with other patients from this region. The four large clusters of non-B subtypes consisted of patients of Dutch origin from different risk groups (HSX and MSM).

Conclusion

- Half of the newly diagnosed patients could be attributed to a cluster in the cohort.
- Viral strains from large subtype B clusters were shown to be circulating for a prolonged period, up to more than 9 years.
- Longstanding clusters of non-B subtypes were seen in patients of Dutch origin transcending different risk groups, suggesting the increase in non-B HIV is due to local spread in the Dutch population.

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