Ongoing HIV-1 subtype B transmission networks amongst MSM in the Netherlands

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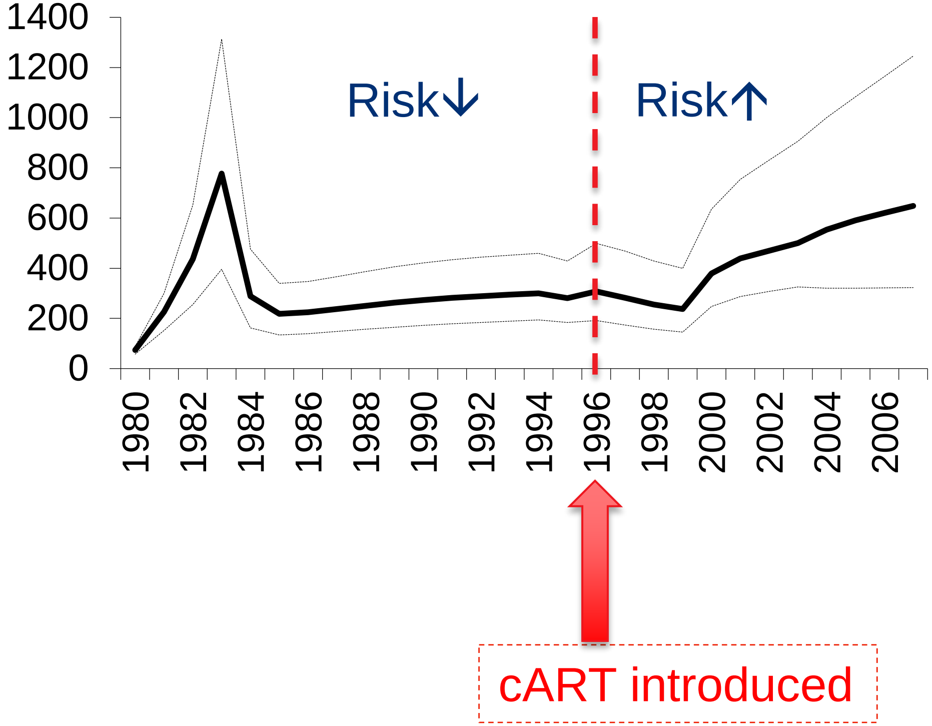
MSM = men who have sex with men

NCHIV 2013

Background

Resurgent HIV-1 epidemic amongst MSM

Estimated annual new HIV-1 infections



Risk↓

Risk↑

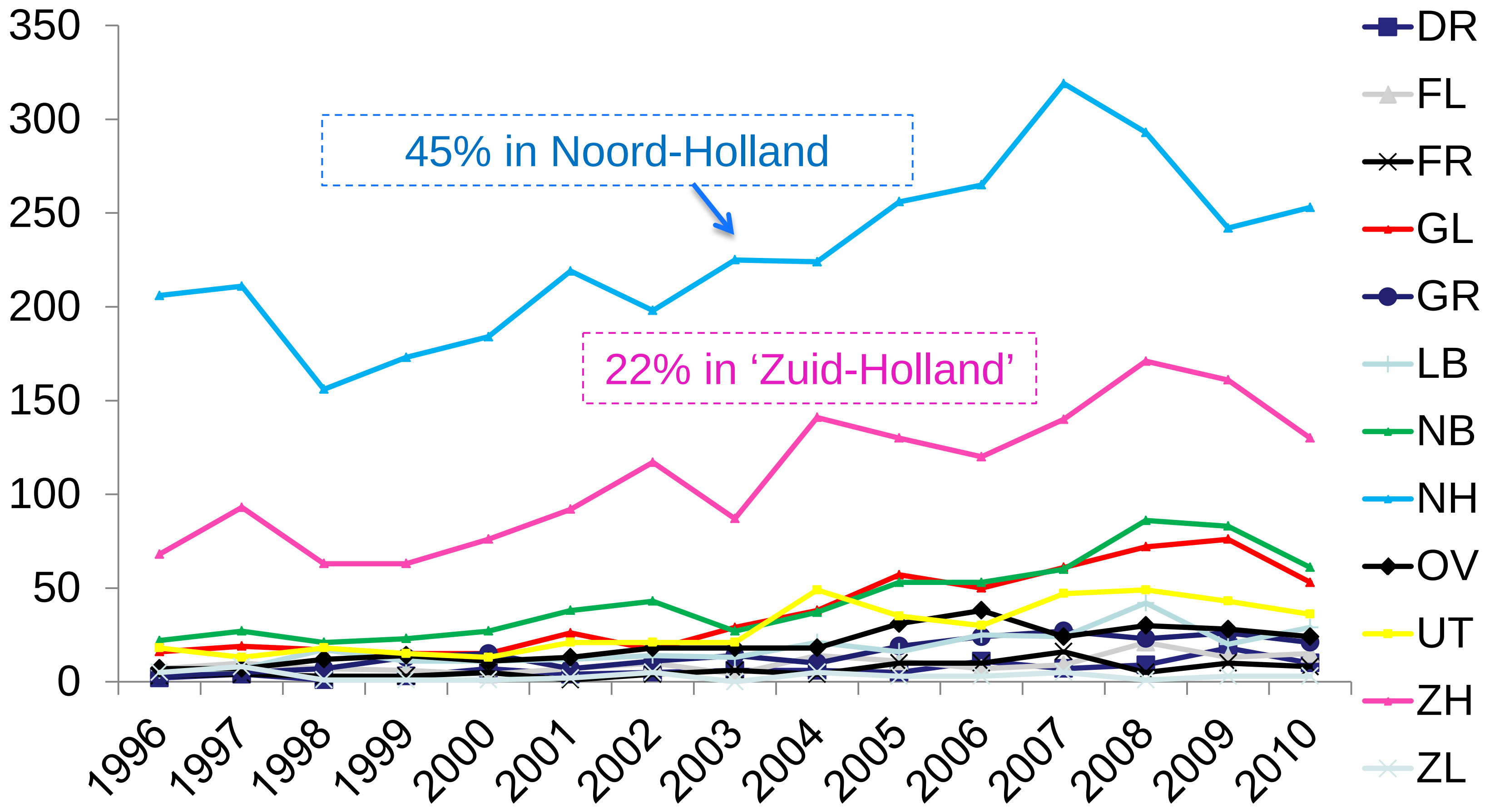
cART introduced

- cART halts onward transmission
- Time to diagnosis ↓
- Risk behaviour ↑
- 90% of new HIV infections from undiagnosed group!
- ~50 MSM/year infected abroad

Bezemer et al, AIDS, 2008; Epidemics, 2010
van Sighem et al., AIDS 2012

Background

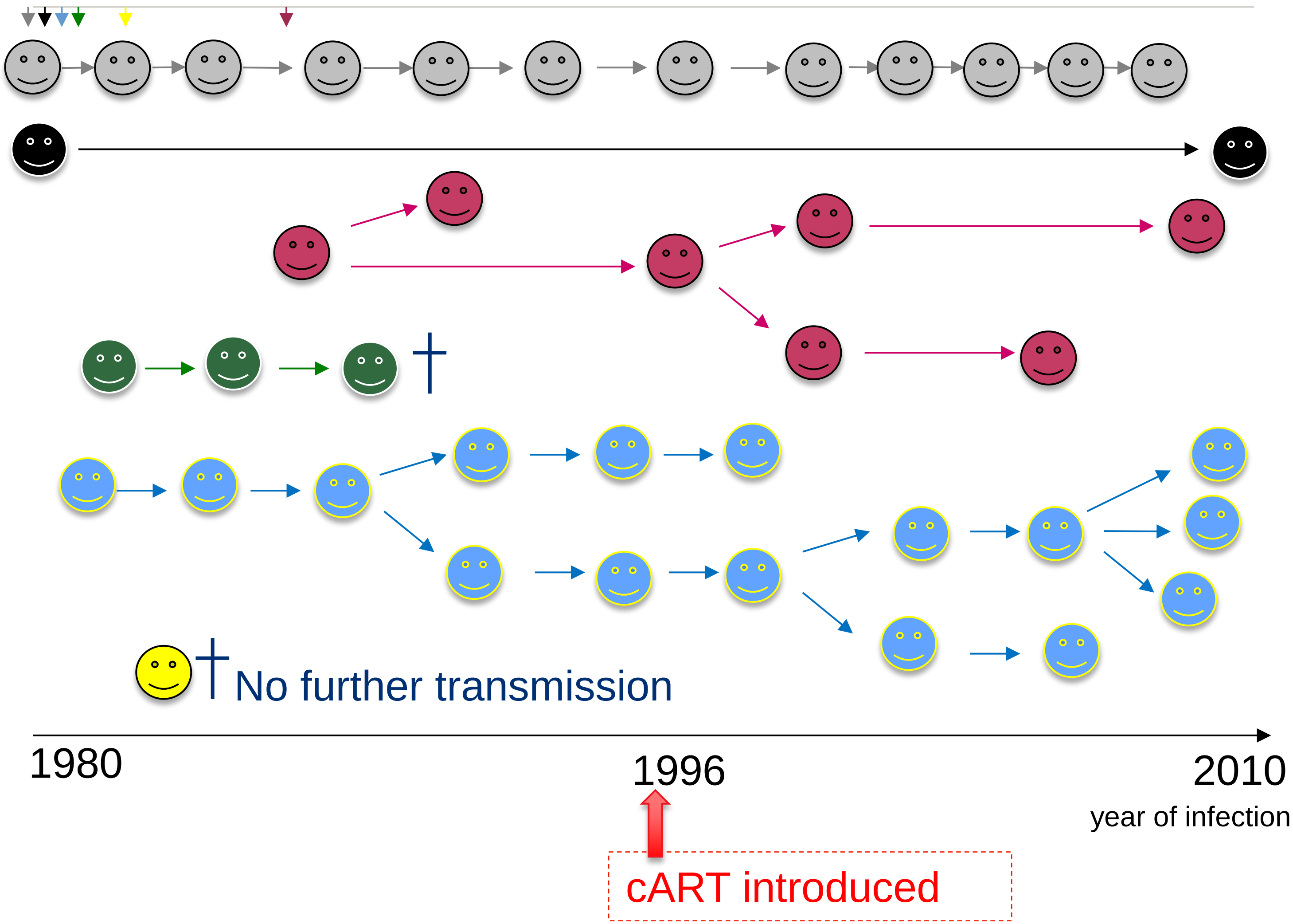
Annual new HIV-1 diagnosis amongst MSM by province



Bezemer et al., NCHIV 2011

OBJECTIVE

Insight into HIV-1 transmission network dynamics



No further transmission

1980

1996

2010

year of infection

cART introduced

METHODS

HIV-1 Polymerase sequences

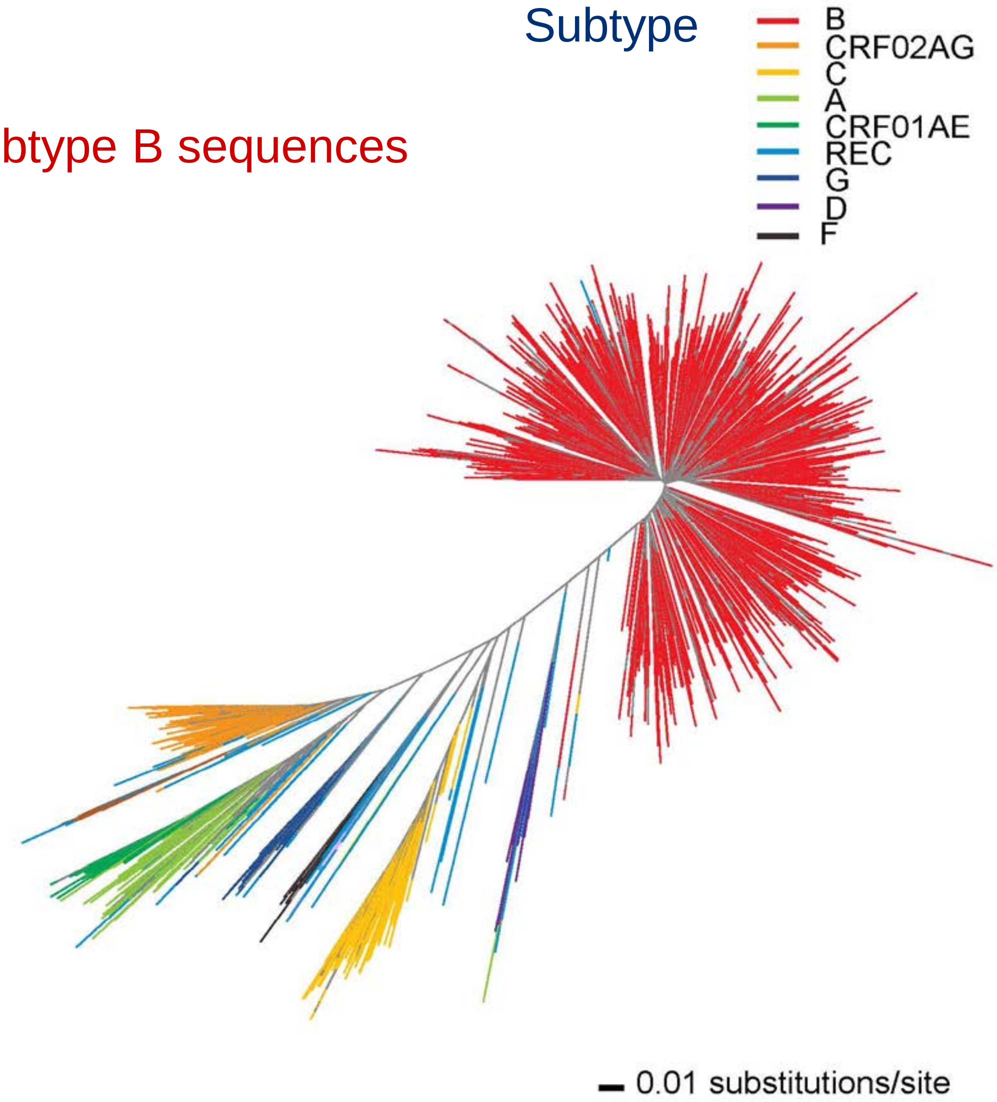
- Available for many patients to check for resistant mutations in order to start (or change) on appropriate therapy

As of November 2011 in ATHENA:

- 19,095 HIV-1-infected patients registered
- 7,589 (40%) have pol sequence available

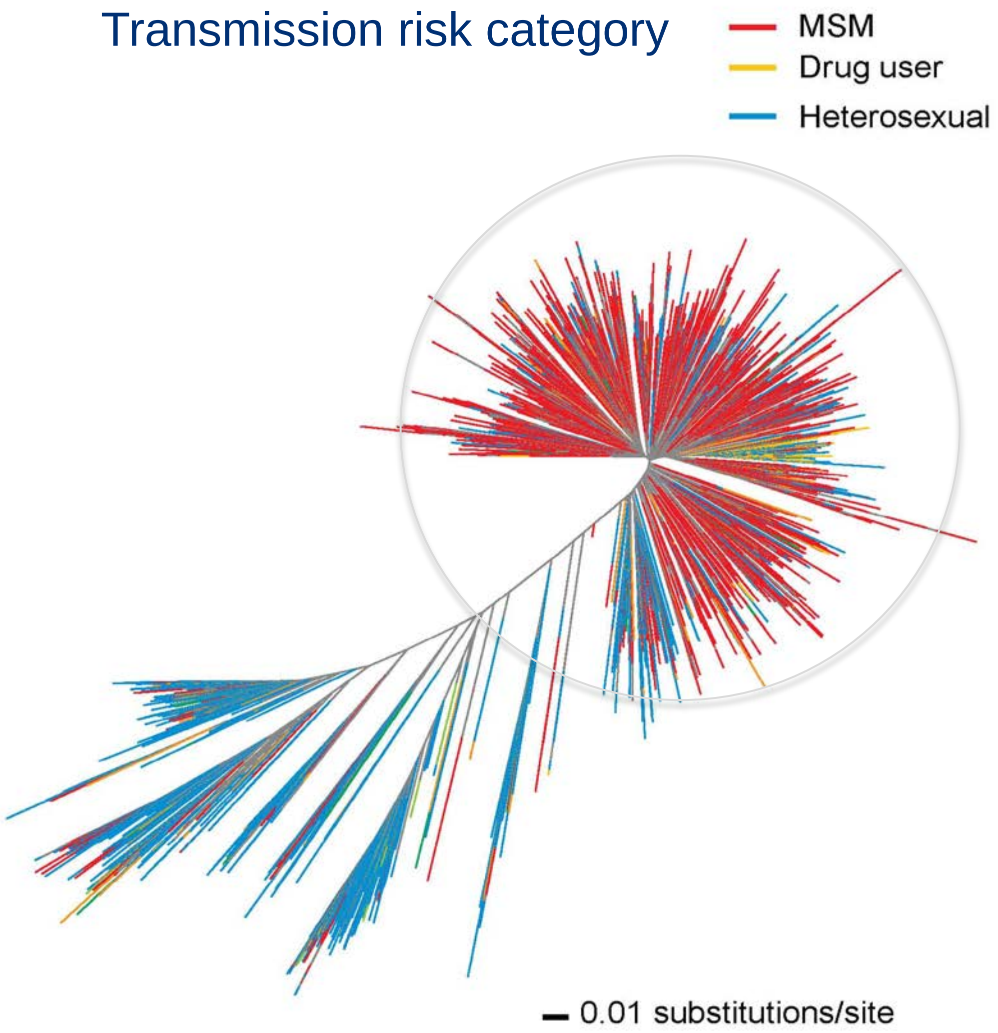
Phylogenetic tree of all sequences in ATHENA

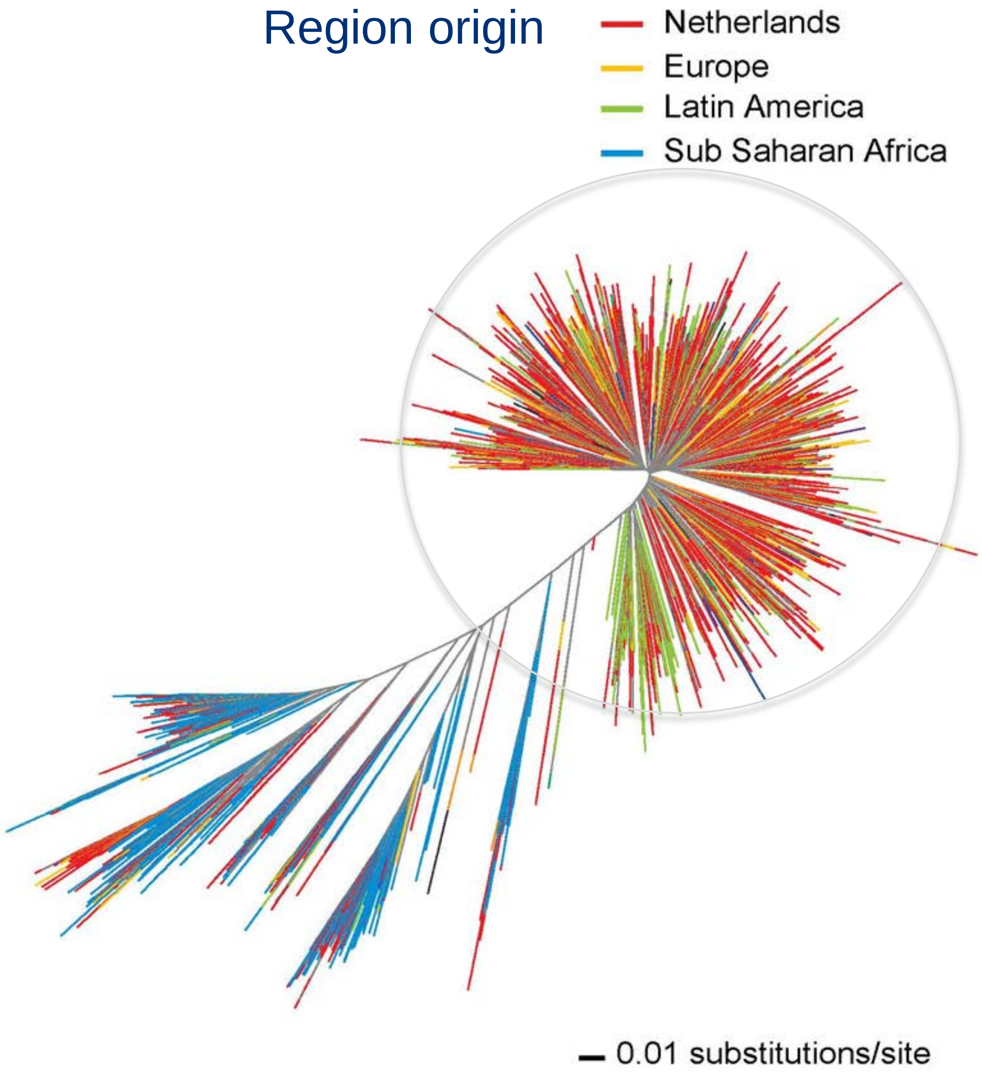
- 5852 (77%) subtype B sequences



Phylogenetic tree of all sequences in ATHENA

Transmission risk category





Phylogenetic tree of all sequences in ATHENA

METHODS

Subtype B sequences selection

5852 Subtype B polymerase sequences in the ATHENA database

- 73% (4288) MSM
- 15% (849) heterosexual
- 4% (207) injection drug use
- 4% (219) registered in Curacao

To get insight into international spread of transmission networks:

- 10 most similar sequences available in Los Alamos database from other countries

→ 2468 sequences added to the phylogenetic tree

METHODS

Transmission network selection

Phylogenetic tree:

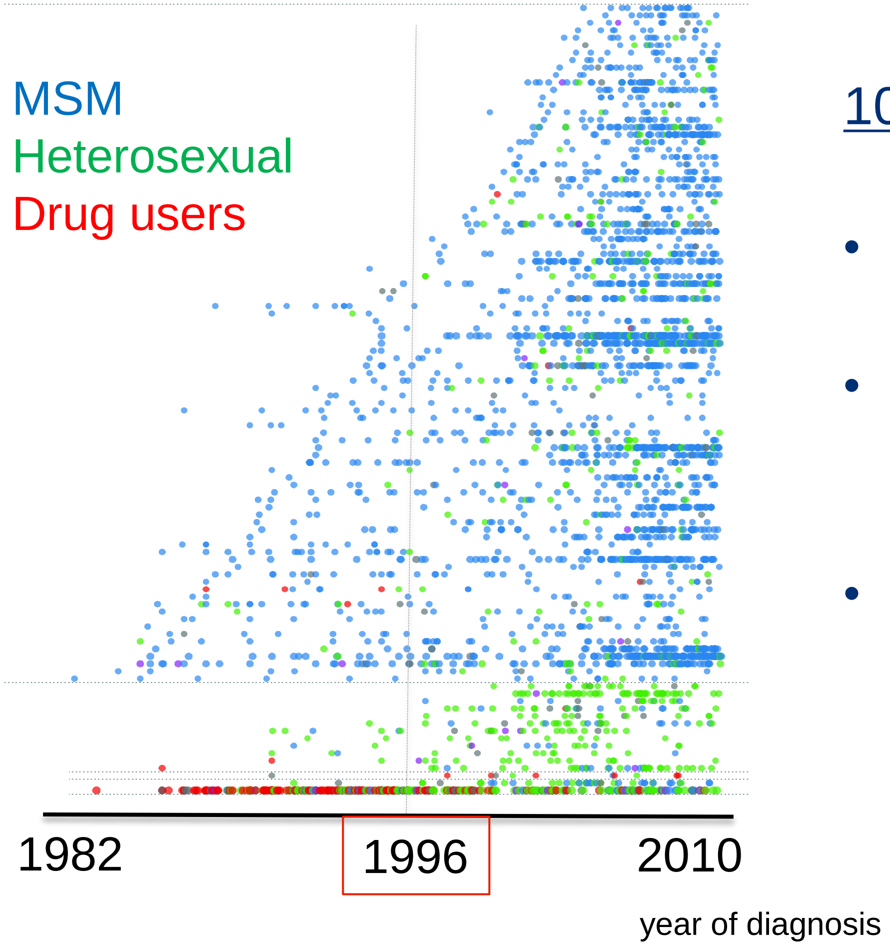
- In total 8,320 subtype B sequences

Definition of established national transmission networks:

- ≥10 ATHENA similar sequences in a phylogenetic cluster
- Bootstrap ≥90%
- Median pairwise patristic distance of the sub-tree is below 5 -10 percentile threshold of the whole-tree patristic distance distribution

Ongoing HIV-1 subtype B transmission networks in the Netherlands !

- MSM
- Heterosexual
- Drug users



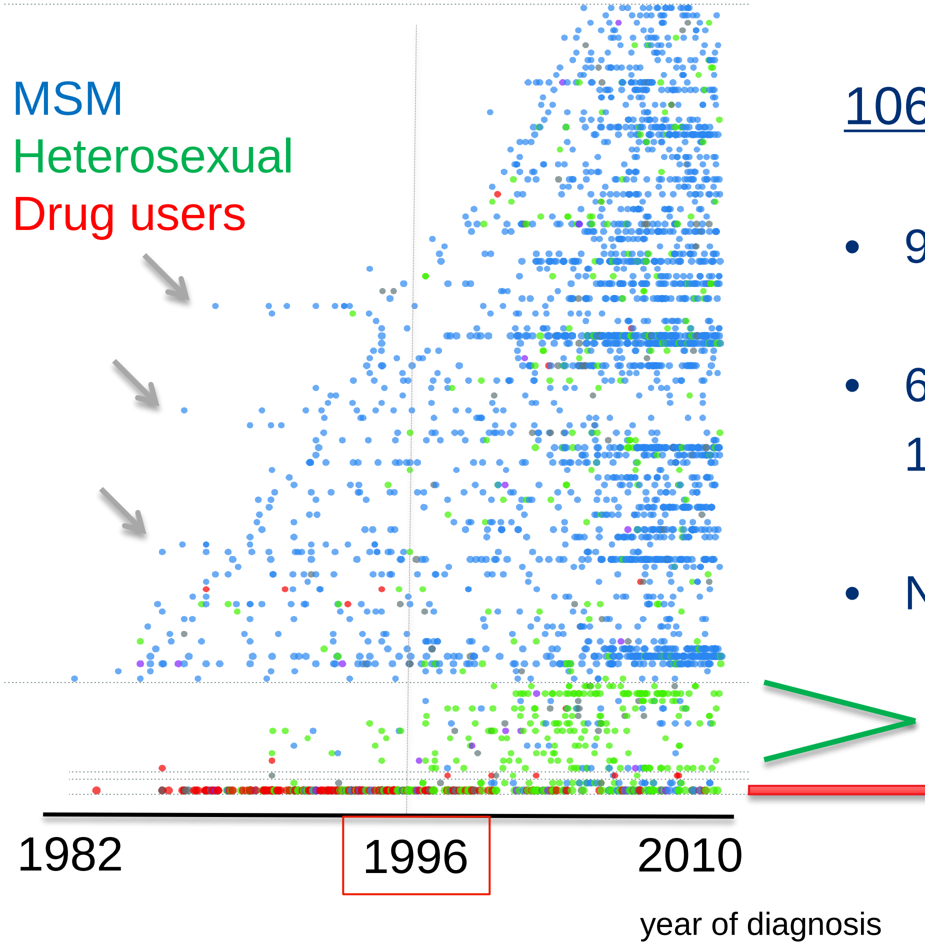
<u>106 networks</u>

- 91 majority MSM networks
- 60% of MSM networks present before 1996 !
- Networks don’t stop !

first date of HIV-1 diagnosis

Ongoing HIV-1 subtype B transmission networks in the Netherlands !

- MSM
- Heterosexual
- Drug users



<u>106 networks</u>

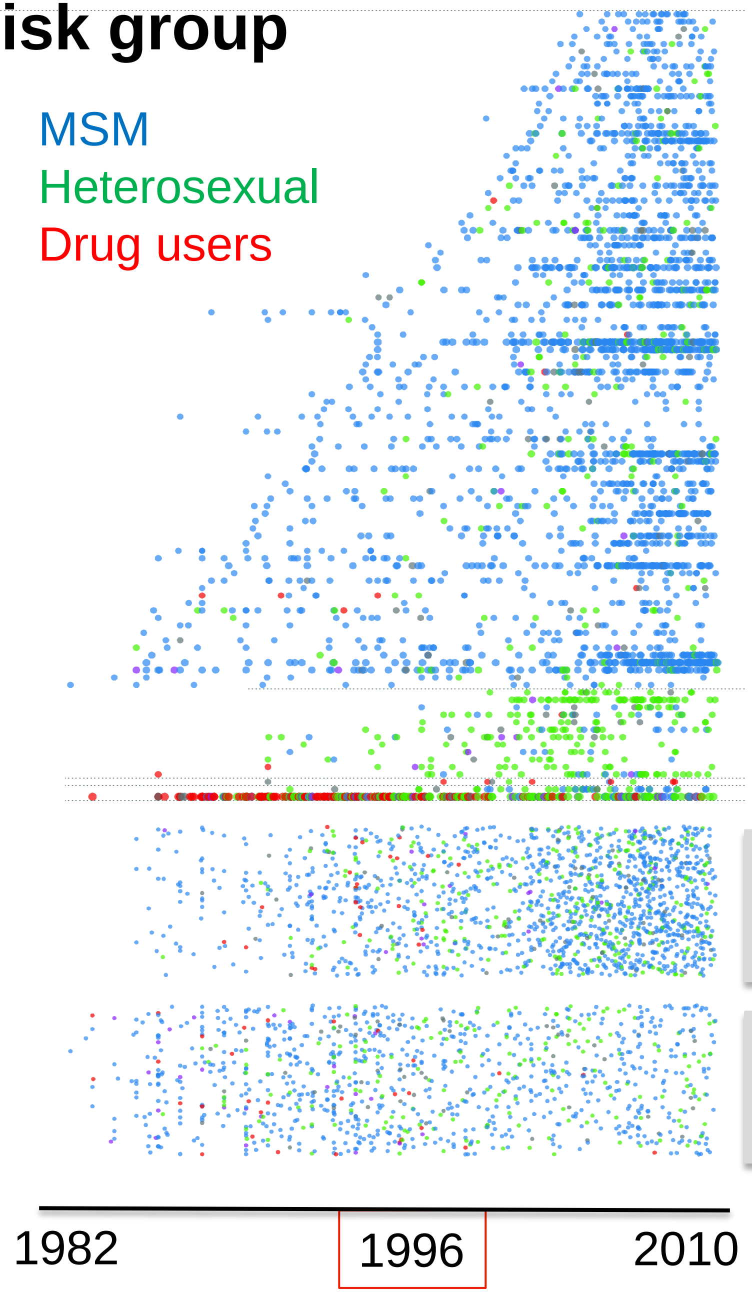
- 91 majority MSM networks
- 60% of MSM networks present before 1996 !
- Networks don’t stop !

Heterosexual networks

66% of all drug users in this study!

Risk group

- MSM
- Heterosexual
- Drug users

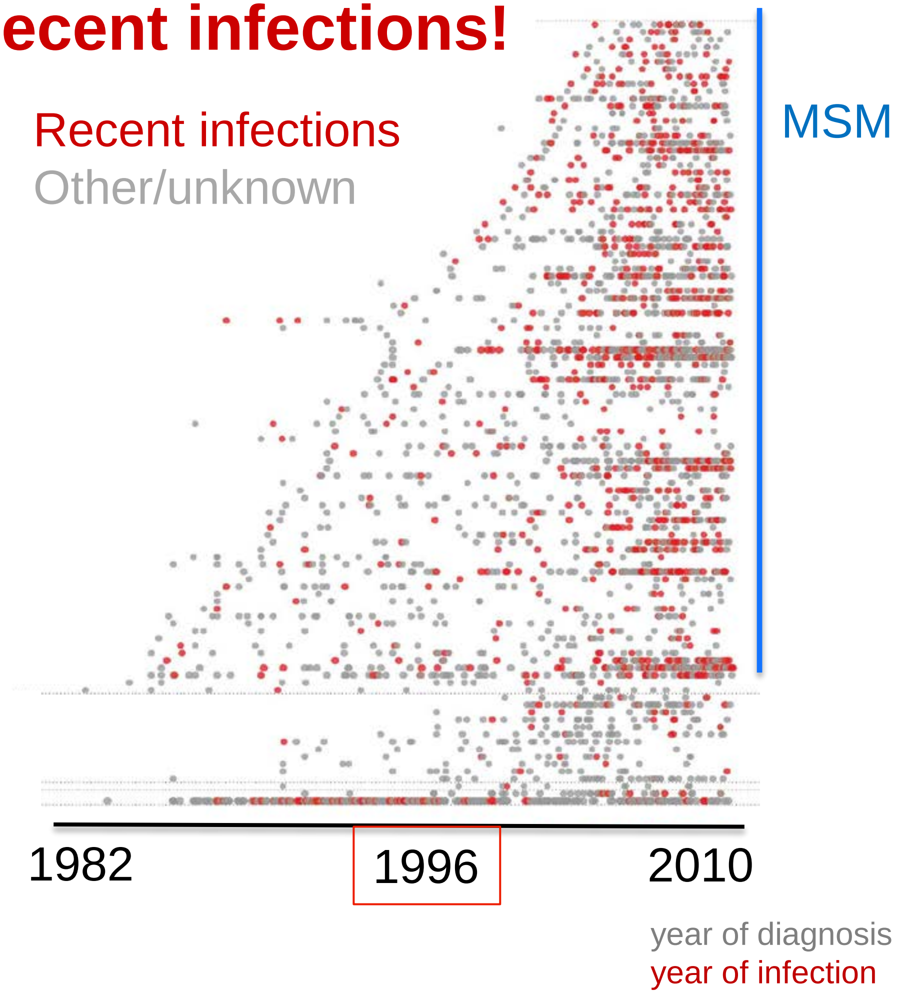


≤10 similar sequences in a cluster

No network identified

Recent infections!

- Recent infections
- Other/unknown



Networks are ongoing !

- Include recent infections and not only diagnosis of older infections

Comparison with Los Alamos database

Countries involved with ≥5 sequences in 91 MSM networks

Country	In MSM networks
SPAIN	58
UNITED KINGDOM	58
BELGIUM	42
ITALY	36
UNITED STATES	31
CANADA	30
BRAZIL	25
CZECH REPUBLIC	22
GERMANY	11
ARGENTINA	10
SWITZERLAND	9
CYPRUS	6
DENMARK	5
PORTUGAL	5

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Conclusion

The resurgent subtype B epidemic amongst MSM is being sustained by transmission networks already established in the pre-cART era, which are still ongoing and have not been brought to an end by earlier diagnosis and the widespread use of cART.

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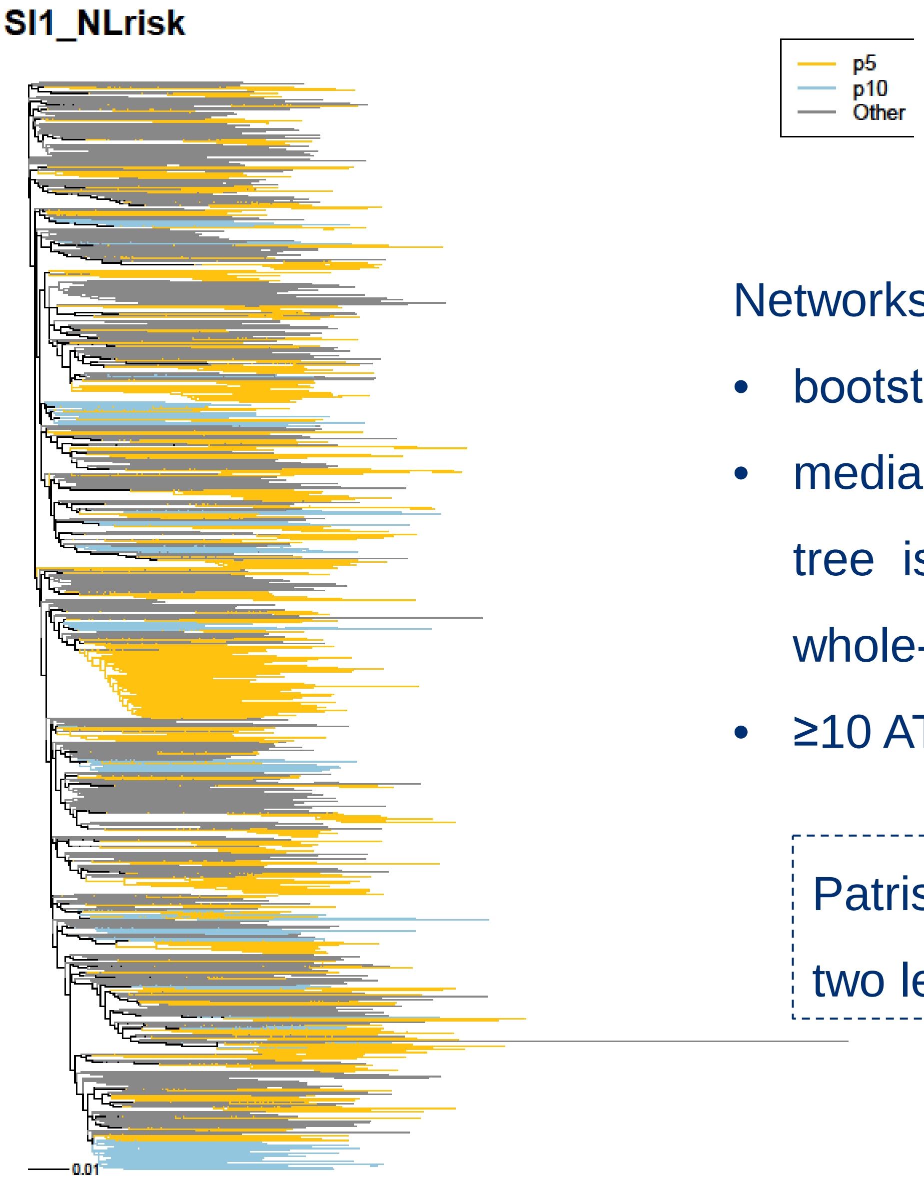
Thank You !

Selected networks using phylopart



Networks:

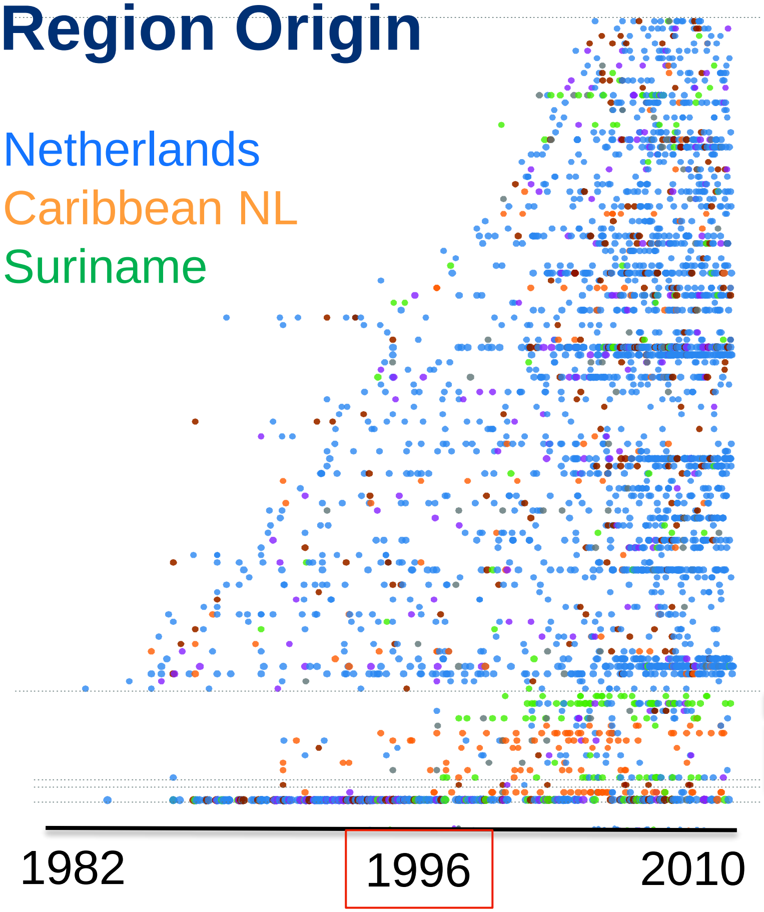
- bootstrap ≥90%
- median pairwise patristic distance of the sub-tree is below 5 -10 percentile threshold of the whole-tree patristic distance distribution
- ≥10 ATHENA sequences.

Patristic distance = the distance between two leaves on the tree

Prosperi et al 2011

Region Origin

- Netherlands
- Caribbean NL
- Suriname



Heterosexual networks:

Suriname related

Networks on Curaçao (NCHIV2012)

Ongoing / Future Research

- Age at diagnosis over time in transmission networks
- Set-point viral load over time in and between transmission networks (Gras et al 2011)
- R0 networks
- MRCA of networks
- Smaller clusters and singletons ?
- Phylogeography
- Sub-networks NL-HT

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