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

Daniela Bezemer
HIV Monitoring Foundation
Amsterdam
The Netherlands

MSM = men who have sex with men
Background

Resurgent HIV-1 epidemic amongst MSM

Estimated annual new HIV-1 infections

- 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

45% in Noord-Holland

22% in ‘Zuid-Holland’
OBJECTIVE

Insight into HIV-1 transmission network dynamics

1980 2010 1996

No further transmission

cART introduced

year of infection

No further transmission
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
• 5852 (77%) subtype B sequences
Transmission risk category

Phylogenetic tree of all sequences in ATHENA
Phylogenetic tree of all sequences in ATHENA

Region origin
- Netherlands
- Europe
- Latin America
- Sub Saharan Africa

0.01 substitutions/site
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

106 networks

- 91 majority MSM networks
- 60% of MSM networks present before 1996!
- Networks don’t stop!
Ongoing HIV-1 subtype B transmission networks in the Netherlands!

- MSM
- Heterosexual
- Drug users

106 networks

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

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

<table>
<thead>
<tr>
<th>Country</th>
<th>In MSM networks</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPAIN</td>
<td>58</td>
</tr>
<tr>
<td>UNITED KINGDOM</td>
<td>58</td>
</tr>
<tr>
<td>BELGIUM</td>
<td>42</td>
</tr>
<tr>
<td>ITALY</td>
<td>36</td>
</tr>
<tr>
<td>UNITED STATES</td>
<td>31</td>
</tr>
<tr>
<td>CANADA</td>
<td>30</td>
</tr>
<tr>
<td>BRAZIL</td>
<td>25</td>
</tr>
<tr>
<td>CZECH REPUBLIC</td>
<td>22</td>
</tr>
<tr>
<td>GERMANY</td>
<td>11</td>
</tr>
<tr>
<td>ARGENTINA</td>
<td>10</td>
</tr>
<tr>
<td>SWITZERLAND</td>
<td>9</td>
</tr>
<tr>
<td>CYPRUS</td>
<td>6</td>
</tr>
<tr>
<td>DENMARK</td>
<td>5</td>
</tr>
<tr>
<td>PORTUGAL</td>
<td>5</td>
</tr>
</tbody>
</table>
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.
Acknowledgements

Imperial College
Oliver Ratmann
Frank de Wolf
Christophe Fraser

SHM
Ard van Sighem
Rob van den Hengel
Luuk Gras
Peter Reiss

Curaçao
Gonneke Hermanides
Ashley Duits

NCBI
Bas E. Dutilh

Oxford
Nuno Faria

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