SPREAD Program

HIV Molecular Surveillance in Europe
SPREAD Program

Aims:

Study the spread of transmitted drug resistant HIV

To get insight in characteristics of new HIV patients in Europe

• Started in 2001
• Established via European Framework Programmes
Sampling Strategy

Two sampling strategies have been developed which enable sampling of data which are representative and can be generalized

- **Strategy I**
  - Access to >80% of newly diagnosed patients:
  - A random sample is taken

- **Strategy II**
  - Access to <80%:
  - Stratified inclusion according to risk group and geographical distribution
Data collection and analysis

- Demographic, clinical and virological data
- QC via ENVA programme
- General data verification, missing data, unlogical data
- Random sample for in depth data verification
- Data analysis team for primary analysis
- Possibility to submit study proposals for scientific studies for all data submitters
Prevalence of Drug-Resistant HIV-1 Variants in Untreated Individuals in Europe: Implications for Clinical Management

Transmission of Drug-Resistant HIV-1 Is Stabilizing in Europe

HIV-1 subtype distribution and its demographic determinants in newly diagnosed patients in Europe suggest highly compartmentalized epidemics

Limited cross-border infections in patients newly diagnosed with HIV in Europe

Persistence of frequently transmitted drug-resistant HIV-1 variants can be explained by high viral replication capacity

Increase in transmitted resistance to non-nucleoside reverse transcriptase inhibitors among newly diagnosed HIV-1 infections in Europe

Patterns of Transmitted HIV Drug Resistance in Europe Vary by Risk Group

Global Dispersal Pattern of HIV Type 1 Subtype CRF01_AE: A Genetic Trace of Human Mobility Related to Heterosexual Sexual Activities Centralized in Southeast Asia

Trends and Predictors of Transmitted HIV Drug Resistance (TDR) and Clusters with TDR in a Local Belgian HIV-1 Epidemic

Evolution

Research

Tracing the HIV-1 subtype B mobility in Europe: a phylogeographic approach

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Overview of results surveillance of transmitted drug resistant HIV
## Baseline characteristics

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<tr>
<td><strong>Male sex</strong></td>
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<tr>
<td></td>
<td>2337 (78.2)</td>
<td>1952 (79.4)</td>
<td>3406 (82.3)</td>
<td>3968 (83.7)</td>
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<td><strong>Age at diagnosis, years, median</strong></td>
<td>38 (29-42)</td>
<td>36 (29-42)</td>
<td>37 (29-43)</td>
<td>36 (29-44)</td>
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<tr>
<td><strong>MSM HSX IDU</strong></td>
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<td></td>
<td>1486 (49.7)</td>
<td>1060 (35.5)</td>
<td>1169 (47.6)</td>
<td>2314 (55.9)</td>
<td>2756 (58.2)</td>
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<tr>
<td></td>
<td>1060 (35.5)</td>
<td>812 (33.0)</td>
<td>812 (33.0)</td>
<td>1323 (32.0)</td>
<td>1326 (28.0)</td>
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<tr>
<td></td>
<td>245 (8.2)</td>
<td>174 (7.1)</td>
<td>174 (7.1)</td>
<td>188 (4.5)</td>
<td>184 (3.9)</td>
</tr>
<tr>
<td><strong>HIV RNA load, log copies/mL, median (IQR)</strong></td>
<td>4.9 (4.3-5.3)</td>
<td>4.8 (4.2-5.3)</td>
<td>4.8 (4.2-5.3)</td>
<td>4.9 (4.3-5.4)</td>
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<tr>
<td><strong>CD4 count, cells/mm³, median (IQR)</strong></td>
<td>355 (180-547)</td>
<td>360 (192-535)</td>
<td>393 (202-544)</td>
<td>368 (198-555)</td>
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<tr>
<td><strong>Subtype</strong></td>
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<td>A</td>
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<tr>
<td></td>
<td>234 (7.8)</td>
<td>174 (7.1)</td>
<td>224 (5.4)</td>
<td>277 (5.9)</td>
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<td>2010 (67.2)</td>
<td>1519 (61.8)</td>
<td>2781 (67.2)</td>
<td>3135 (66.2)</td>
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<tr>
<td></td>
<td>190 (6.4)</td>
<td>141 (5.7)</td>
<td>221 (5.3)</td>
<td>228 (4.8)</td>
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<td>100 (3.3)</td>
<td>87 (3.5)</td>
<td>122 (2.9)</td>
<td>160 (3.4)</td>
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<td>277 (5.9)</td>
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<td>49 (1.6)</td>
<td>23 (0.9)</td>
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<td>29 (1.0)</td>
<td>72 (2.9)</td>
<td>111 (2.7)</td>
<td>107 (2.3)</td>
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<tr>
<td>02_AG</td>
<td>72 (2.9)</td>
<td>111 (2.7)</td>
<td>107 (2.3)</td>
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Results 2002-2007

2002-2005:
Overall prevalence in Europe 8.5%

2006-2007:
Prevalence varies by risk group

TDR defined as the presence of at least one mutation of the “SPREAD list” (AIDS 2008 Mar 12;22(5))
Trends over time

% of newly diagnosed HIV-patients

2002-2005 2006-2007 2008-2010

Overall
NRTI
NNRTI
PI
TDRM by risk group/subtype

A. NRTI
- NRTI TDRM more often in MSM and subtype B

B. NNRTI
- NNRTI no difference among risk groups or subtypes

C. PI

2008-2010

- NRTI TDRM more often in MSM and subtype B
- NNRTI no difference among risk groups or subtypes
Predicted susceptibility ART

% of newly diagnosed HIV-patients

High level resistance
Low level/intermediate resistance
Susceptible
Insight in characteristics of new HIV patients in Europe
Recently infected patients

We determined how many patients with laboratory evidence of recent infection (<1 year) (N=1422) would be classified as late presenter based on different definitions.
Late presentation over time
Duration of infection unknown for 80% of patients

Late presenter

Advanced HIV Disease

CDC stage C

CD4 > 500

Late presentation over time
Duration of infection unknown for 80% of patients
Prevalence resistance mutations

- Overall: $P < 0.04$
- NRTI
- NNRTI
- PI: $P < 0.02$

Legend:
- Recently infected
- Late presenters
- Advanced HIV Disease
- AIDS
Summary

The SPREAD program is a long term collaboration of an expanding network and has resulted in insight in the dynamics of HIV transmission

• 10 year surveillance shows a stable prevalence of transmitted resistance (8-10%)
• 20% of patients have evidence of recent infection
• Late presentation decreases over time but is still observed in 50% of newly diagnosed patients
Acknowledgements


ESAR Coordination Office: A. van Kessel, K. Siebelt.

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http://www.esar-society.eu/
How to join the SPREAD program

• Dataset: no selection bias regarding offering of drug resistance testing

• Inclusion criteria
  – Therapy naive patients
  – Above 18 years of age
  – Viral load (>1000 cps/mL)
  – Sampling within 6 months of diagnosis

• www.esar-society.eu / info@esar-society.eu