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# Transmitted drug resistance in dated transmission networks

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12<sup>th</sup> EU HIV & Hepatitis workshop, Barcelona

## Background & Aim

### HIV transmission networks

- Patients linked by transmission edges
- Constructed by thresholding genetic distance of viruses sampled from patients

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Incorporate sampling time

### Transmitted drug resistance (TDR)

- HIV evolves drug resistance during therapy
- Individuals infected with viral strains carrying drug resistant mutations (DRM)

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Measure TDR on networks



# Outline

Patient data

Methods

Network construction

Results

Network characteristics

Transmitted drug resistance

Conclusions



## Data overview

HIV-1 B *pol* gene (PR+RT-DRM): 705 nt  
Earliest sample from each patient

### EuResist

Country	Patients
Italy	9632
Germany	2144
Portugal	1225
Sweden	980
Unknown	8429

Transmission	Patients
MSM	5035
HET	5511
IDU	3836
Unknown	12235
<b>Total</b>	<b>27124</b>

## DRM in therapy naive patients

- Earliest sample is before start of therapy
- DRM from WHO list [Bennet et. al., 2009]

	Therapy status		
	Naive	Experienced	Unknown
No DRM found	6623	2550	7279
DRM found (%)	610 (8%)	3294 (56%)	6768 (48%)

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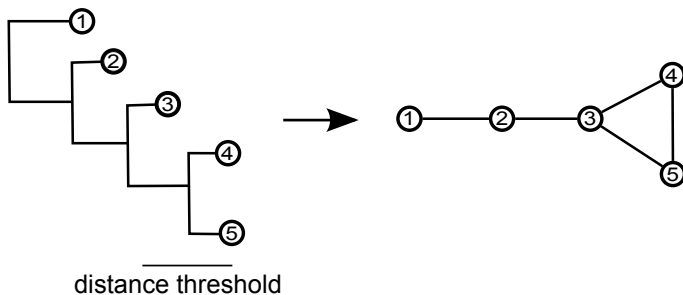
Transmitted drug resistance

Conclusions



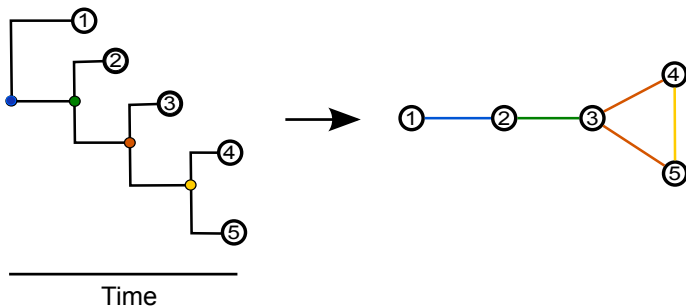
## Transmission network

- An undirected graph representing transmission between patients.
- Graph constructed by thresholding evolutionary distance
- Distance on phylogenetic tree is thresholded



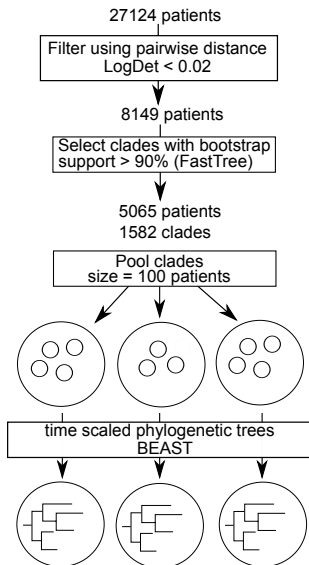
## Dated transmission network

- Molecular clock phylogenetics can be used to estimate divergence time
- Transmission time is approximated with divergence time





# Work flow



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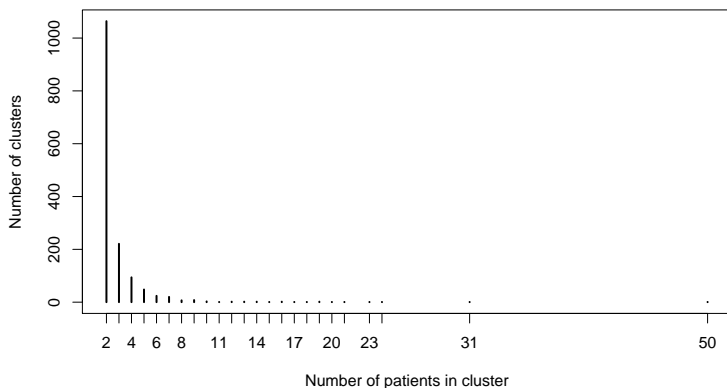
Conclusions



# Transmission network

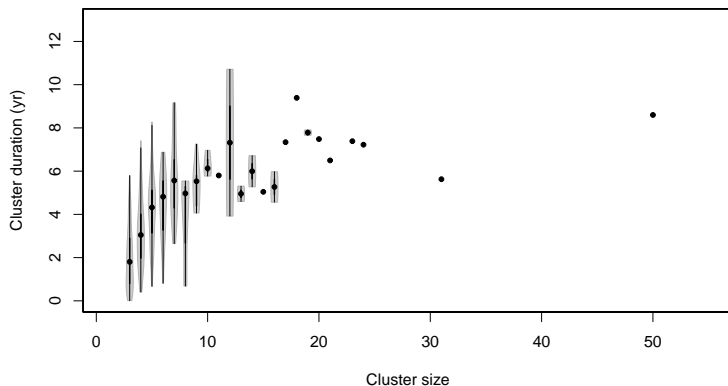
Transmission threshold of 6 years

- 4227 patients (16% of EuResist)
- 1509 clusters (no edges joining supported clades)



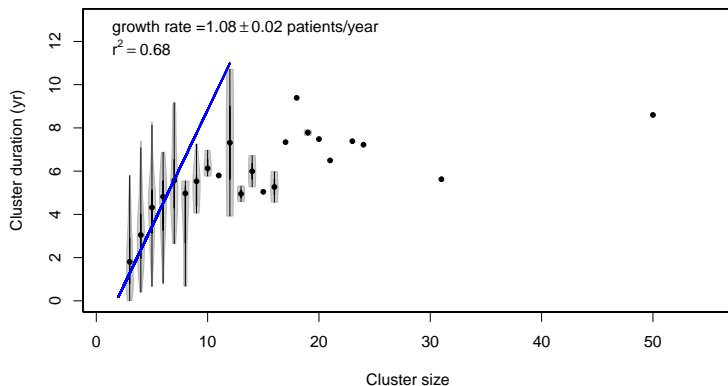
# Cluster duration

Time elapsed between first and last transmission within a cluster



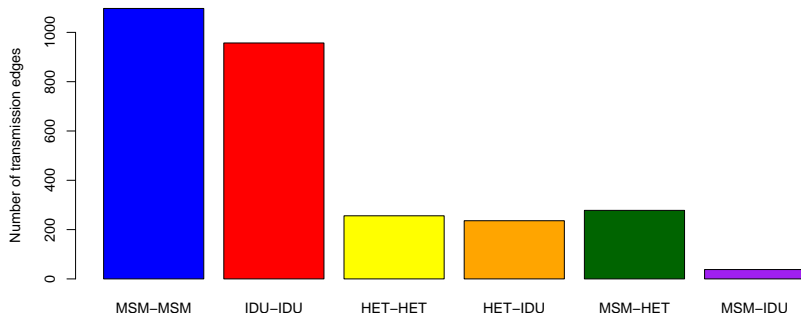
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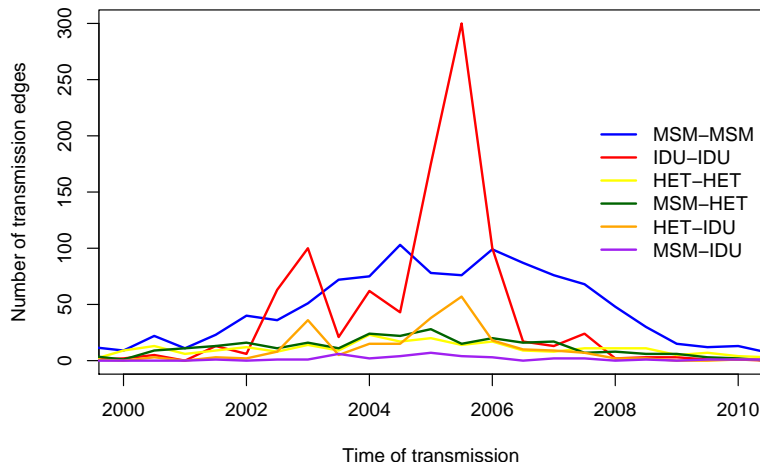


# Compartmentalization by risk group

Number of edges within and between risk group pairs



# Time trend of risk group pair transmission



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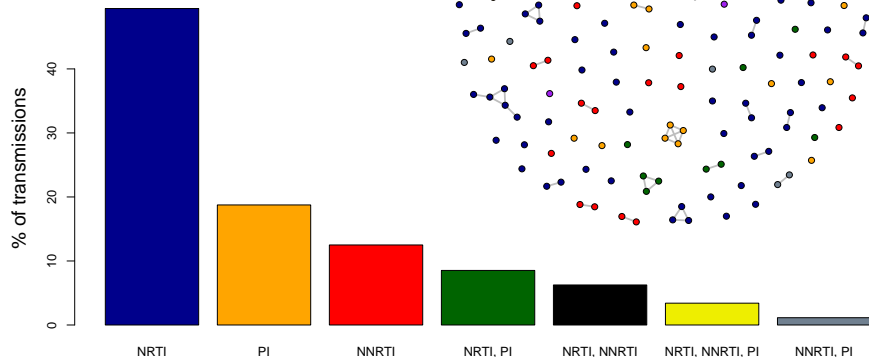
Conclusions



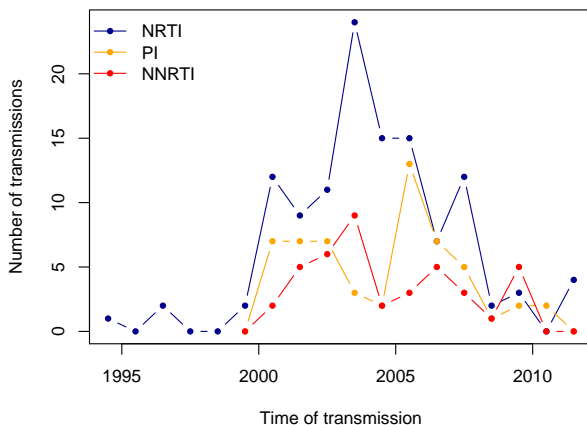


# Distribution of drug class

176/610 patients



# Drug class prevalence over time



## Distribution of risk group

Risk group	EuResist	TDR in EuResist	TDR in network
MSM	5035	286	78
IDU	3836	60	7
HET	5511	169	24
Unk	8360	211	39

TDR is significantly lower in IDU

# Conclusion

- Clusters grow at a rate of 1 patient/year with evidence of large rapid growing clusters
- NRTI class of DRM
  - comprises 50% of TDR network
  - peaks between 2000 and 2008
- Lack of TDR in IDU could be due to separate MSM and IDU epidemics



# Acknowledgments

Department of Computational Biology and Applied Algorithmics

Thomas Lengauer  
Glenn Lawyer  
Mathieu Flinders

Rolf Kaiser  
Maurizio Zazzi  
Eugen Schülter



EuResist Network Study Group