

REVEALING THE MOLECULAR EPIDEMIOLOGY OF THE COLOGNE, GERMANY, HIV EPIDEMIC

Melanie Stecher¹, **Martin Hoenig**^{2,3}, Joerg Janne Vehreschild¹, Clara Lehmann¹, Gerd Fätkenheuer¹, Rolf Kaiser¹, Sanjay R. Mehta², Antoine Chaillon²

¹University of Cologne, Cologne, Germany, ²University of California San Diego, La Jolla, CA, ³Medical University of Graz, Graz, Austria, Veterans Affairs

Martin Hoenig, MD
 UCSD
 200 Arbor Drive,
 San Diego, CA 92103, USA
 E-mail: mhoenigl@ucsd.edu

Antoine Chaillon, MD, PhD
 UCSD
 E-mail: achaillon@ucsd.edu



Background

- ▶ By inferring potential transmission links between risk groups, demographic subpopulations, and geography, one may better understand the drivers of spread locally, and the links between epidemics outside the region.
- ▶ Cologne is one of the cities with the highest rate of new HIV infections in Germany with a HIV incidence of 15.5 per 100.000 in 2014 (https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2015/Ausgaben/27_15.pdf?__blob=publicationFile).

Objective

To use molecular epidemiology to characterize the transmission dynamics of the Cologne HIV epidemic.

Methods

- **Participants:** 1,507 unique HIV positive antiretroviral therapy (ART) naïve individuals, receiving care at the University Hospital of Cologne, Germany. HIV partial *pol* sequences were obtained between 1999 – 2016.
- **Measures**
 - Phylogenetic and network analyses were performed to infer putative relationships between all HIV partial *pol* sequences.
 - After quality filtering, putative transmission linkages were inferred when two sequences were ≤1.5% genetically different (TN93 distance measure).
 - Multiple inferred linkages were resolved into transmission clusters
 - All sequences were screened for drug resistance mutations using the Calibrated population resistance tool (*Stanford Algorithm*).
 - We further applied a computationally efficient network based approach to analyze relationships between all publicly available HIV sequences found in the Los Alamos National Laboratory HIV Sequence database (<https://www.hiv.lanl.gov/content/index>)

Acknowledgements
 This research was supported by funds from the following: Interdisciplinary Research Fellowship in NeuroAIDS (R25-MH081482), and grants from the National Institutes of Health: AI043638, AI074621, AI106039, MH100974, AI036214, DA034978, AI100665 and AI108351.

Results

- ▶ The sampled population was predominantly male (80%). The most common HIV risk group in the sampled population were men reporting sex with men (MSM, 54.8%), while only 3.6% reported injection drug use as their main risk factor.
- ▶ A German map of the sampled population using the first 3 numbers of the zip code of residency is displayed in **FIGURE 1**.
- ▶ 248/1,507 (16.5%) sequences linked with at least one other sequence, forming 83 transmission clusters, ranging in size from 2 to 10 sequences, **FIGURE 2**.
- ▶ Clustering individuals were significantly more likely to be younger and reporting MSM contact as main risk factor, **TABLE 1**.
- ▶ Drug resistance screening showed that 24.4% and 26.6% of sequences harbored at least one Nucleoside or Non-Nucleoside Reverse Transcriptase Inhibitor (NRTI/NNRTI) mutation, respectively. The presence of a mutation was significantly less common among clustering sequences (NRTI 9.2% vs 27.4%, $p < 0.001$; NNRTI 18.5% vs 27.7%, $p = 0.02$).
- ▶ Among clustering sequences, we found 10 sequences with K103N mutations (90% from MSM), of which 6 were linked, **FIGURE 2**.
- ▶ By combining local data with 119,222 publicly available HIV *pol* sequences, we found a total of 78 clusters (91% subtype B) that included both sequences from Cologne and other regions in Germany (64 clusters, 82%) or predominantly European Countries.

Figure 1: German Map of sampled population

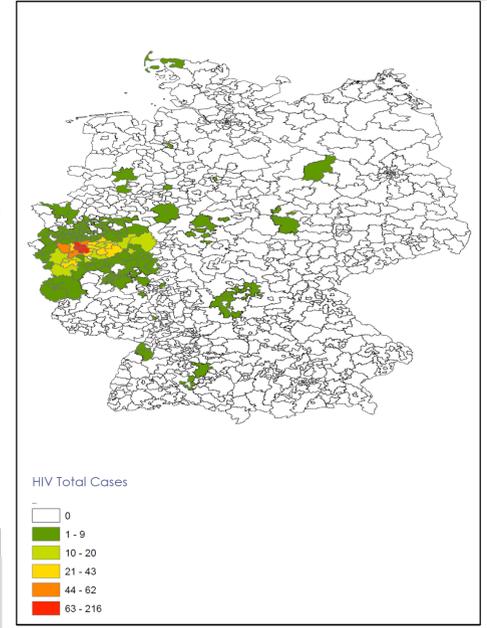
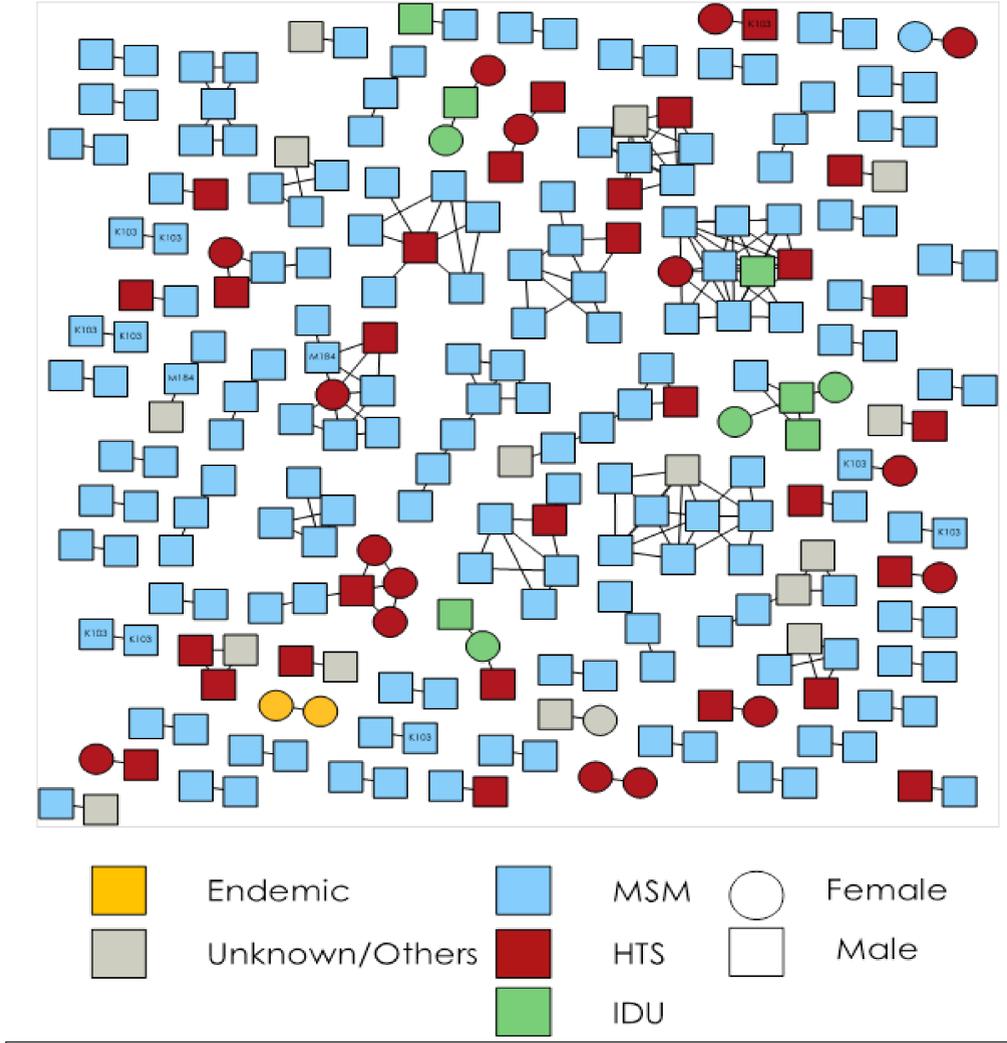


Table 1. Population characteristics

	Not clustering, N (%)	Clustering, N (%)	p-value
N	1259 (83.5)	248 (16.5) ^a	-
Age [median (IQR)]	40 (34-48)	36 (30-44)	<0.001
Gender			<0.001
- Male	987 (78.4)	224 (90.2)	
- Female	268 (21.3)	23 (9.3)	
Subtype			<0.001
- B	928 (73.7)	222 (89.5)	0.001
- A	28 (2.2)	16 (6.5)	<0.001
- CRF	115 (9.1)	5 (2.0)	<0.001
- El Salvador	109 (8.7)	5 (2.0)	<0.001
Risk			<0.001
- MSM	651 (51.7)	175 (70.6)	0.030
- HTS	307 (24.4)	45 (18.1)	n.s.
- PWID	44 (3.5)	10 (4.0)	<0.001
- ENDEMIC ^b	136 (10.8)	2 (0.8)	n.s.
- Others/Unknown	121 (9.6)	16 (6.5)	n.s.
Year of Diagnosis	2009 (2006-2012)	2010 (2008-2012)	-

Legend: ^a83 clusters in total were observed. ^bMRRecent immigration from a country with a HIV prevalence >1%. DRF, circulating recombinant forms MSM, men who have sex with men; PWID, people who inject drugs; HTS, heterosexual.

Figure 2: Cologne HIV Transmission Network



LEGEND: HIV-1 transmission clusters (networks) identified in Cologne, Germany. Sex of the individuals (nodes) is indicated by shape, nodes are colored by their reported risk factor. All edges represent a genetic distance 1.5% separating nodes. K103 and M184 drug resistance mutations are indicated in the nodes.

Conclusions

- ▶ In the sampled Cologne HIV epidemic, we found that transmission clusters were predominantly comprised of younger MSM.
- ▶ We also found multiple putative transmission links between this epidemic and those across Germany and around the world.
- ▶ These results highlight the pitfalls of focusing prevention efforts and monitoring on specific risk groups or specific locales, and not taking into consideration the overall HIV epidemic.