

# Carnival meets Oktoberfest: Molecular Epidemiology of the HIV Epidemic in Three German Metropolitan Regions

Martin Hoenigl<sup>1,2</sup>, Melanie Stecher<sup>3,4</sup>, Johannes Bogner<sup>5</sup>, Clara Lehmann<sup>3,4</sup>, Josef Eberle<sup>6</sup>, Christoph Spinner<sup>7,8</sup>, Rolf Kaiser<sup>9</sup>, Georg Behrens<sup>10,11</sup>, Gerd Fätkenheuer<sup>3,4</sup>, Sanjay R. Mehta<sup>1</sup>, Joerg Janne Vehreschild<sup>3,4</sup>, Antoine Chaillon<sup>1</sup>

<sup>1</sup> Division of Infectious Diseases, University of California San Diego, San Diego, United States, <sup>2</sup> Medical University of Graz, Graz, Austria, <sup>3</sup> University of Cologne, Cologne, Germany, <sup>4</sup> German Center for Infection Research (DZIF), Partner Site Bonn-Cologne, Cologne, Germany, <sup>5</sup> Sektion Klinische Infektiologie, Medizinische Klinik und Poliklinik IV, Klinikum der Universität, Ludwig-Maximilians-Universität München, Munich, Germany, <sup>6</sup> LMU München, Munich, Germany, <sup>7</sup> Department of Medicine II, Technische Universität München, Munich, Germany, <sup>8</sup> German Center for Infection Research (DZIF), Partner Site Munich, Munich, Germany <sup>9</sup> Institute of Virology, University Hospital of Cologne, Cologne, Germany, <sup>10</sup> Medizinische Hochschule Hannover, Hannover, Germany, <sup>11</sup> German Center for Infection Research (DZIF), Partner Site Hannover, Hannover, Germany



Martin Hoenigl, MD  
UCSD  
200 Arbor Drive,  
San Diego, CA 92103, USA  
E-mail: [mhoenigl@ucsd.edu](mailto:mhoenigl@ucsd.edu)

Antoine Chaillon, MD, PhD  
UCSD  
E-mail: [achaillon@ucsd.edu](mailto:achaillon@ucsd.edu)

## Background

- By inferring potential transmission links between risk groups, demographic subpopulations, and geography, one may better understand the drivers of HIV spread locally, and the links between epidemics outside the region.
- The incidence of HIV remains highest in large cities, with Munich and Cologne among the cities with highest incidence rates in Germany ([https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2015/Ausgaben/27\\_15.pdf?blob=publicationFile](https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2015/Ausgaben/27_15.pdf?blob=publicationFile)).
- Similar to the epidemic across the European Union, men who have sex with men (MSM) bear the major burden of new infections

## Objective

To use molecular epidemiology to characterize the transmission dynamics of the HIV epidemic in three German metropolitan regions.

## Methods

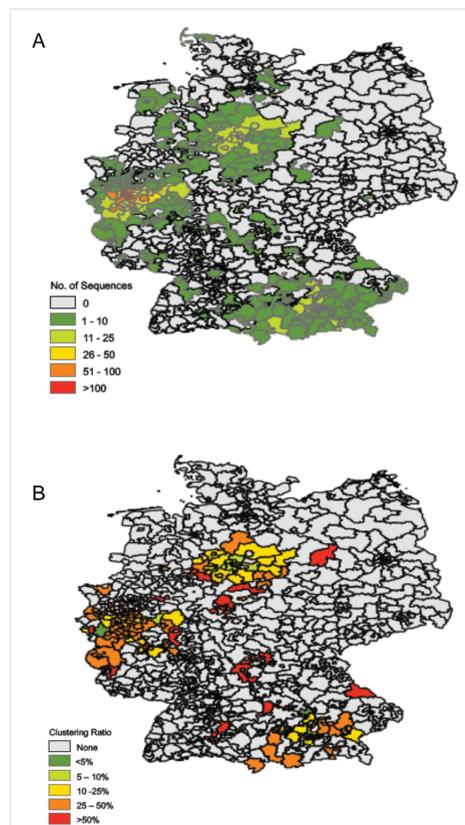
- Participants:** 2,774 unique HIV positive individuals, receiving care at the University Hospital of Cologne/Bonn (n= 1,766), Munich (n=641) and Hannover (n=334) in Germany.
  - HIV partial *pol* sequences, clinical and socio-demographic data were obtained between 1999 – 2016.
- Measures**
  - Phylogenetic 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  $\leq 1.5\%$  genetically different (TN93 distance measure).
  - Multiple inferred linkages were resolved into transmission clusters
  - We further applied a computationally efficient network based approach to analyze relationships between all publicly available HIV sequences (n=150,396) found in the Los Alamos National Laboratory HIV Sequence database (<https://www.hiv.lanl.gov/content/index>)

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## Results

- The sampled population was predominantly male (80%). The most common HIV risk group was MSM, 52%, while only 4.9% reported injection drug use (IDU) as their main risk factor.
- A German map of the sampled population (A) using the first 3 numbers of the zip code of residency and the ratios of sequences clustering (B) in each area are displayed in **FIGURE 1**.
- 595/2,774 (21.4%) sequences linked with at least one other sequence, forming 184 transmission clusters, ranged in size from 2 to 18 sequences, **FIGURE 2**.
- Clustering rate ranged from 12.5% in Munich, over 15% in Hannover to 26.1% in Cologne/Bonn.
- Clustering individuals were significantly more likely to be younger and reporting MSM contact as main risk factor and infected with subtype-B **TABLE**.
- By combining local data with 150,396 publicly available HIV *pol* sequences, we found a total of 236 clusters that linked sequences from our sample (total n=547) and publicly available sequences (total n=1,407) predominantly from European countries.



**Figure 1: Map of sampled population**

**Table. Population characteristics**

	Not clustering, N (%)	Clustering, N (%)	p-value
<b>N</b>	2,179 (78.6)	595 (21.4)	-
Age [median (IQR)]	40 (34-49)	36 (30-45)	<0.001
Sex			<0.001
- Male	1,681 (77.1)	540 (90.7)	
- Female	492 (22.5)	53 (8.9)	
Subtype			<0.001
- B	1,510 (69.2)	532 (89.4)	
- Non-B	669 (30.7)	63 (10.5)	
Risk			<0.001
- MSM	1,053 (48.3)	395 (66.3)	
- HTS	509 (23.3)	113 (18.9)	
- IDU	111 (5)	26 (4.3)	
- ENDEMIC*	285 (13)	7 (1.1)	
- Others/Unknown	221 (10.1)	54 (9.1)	
Cohort			<0.001
- Bonn	155 (7.1)	104 (17.4)	
- Cologne	1,150 (52.7)	357 (60)	
- Hannover	284 (13)	50 (8.4)	
- Munich LMU	566 (25.9)	75 (12.6)	
- Munich TUM	24 (1.1)	9 (1.5)	
Sample year (IQR)	2009 (2006-2012)	2010 (2008-2013)	<0.001

**Legend:** \*Recent immigration from a country with a HIV prevalence >1%. DRF, circulating recombinant forms MSM, men who have sex with men; IDU, people with injected drug use; HTS, heterosexual.

**Figure 2: HIV Transmission Network by region, sex and risk behavior**



**Area/Center:**

COLOGNE  
BONN  
MUNICH  
TUM  
HANNOVER

**Sex and risk behaviors:**

Male  
Female  
IDU  
HTS  
MSM  
Endemic  
NA/Others

**LEGEND:** HIV-1 transmission clusters (networks) identified in Cologne, Bonn, Munich and Hannover, Germany. Sex of the individuals (nodes) is indicated by shape, nodes are colored by area/center and framed by their reported risk factor. All edges represent a genetic distance 1.5% separating nodes.

## Conclusions

- In this molecular analysis of the HIV epidemics of Cologne/Bonn, Munich, and Hannover, 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 on specific risk groups or specific locales, and not taking into consideration viral migration.