

# 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  
E-mail: [mhoenigl@ucsd.edu](mailto:mhoenigl@ucsd.edu)

### Funding

NIH: MH081482, AI043638, AI074621, AI106039, MH100974, AI036214, DA034978, AI100665 and AI108351.

## 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.
- High rates of new HIV diagnoses are observed in Cologne/Bonn, Hannover, and Munich; regions which host some of the largest annual festivals in Europe (i.e. Oktoberfest, Carnival, Schuetzenfest, Christopher Street Day with 1 to 6 million visitors each).

## 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>)

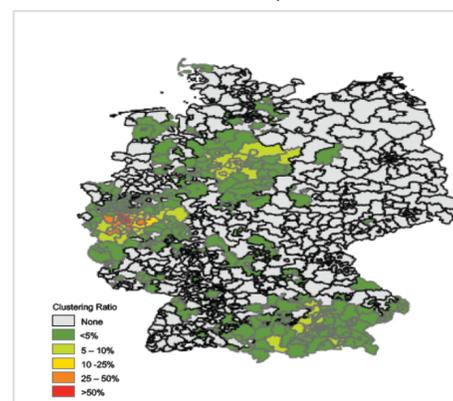
## Results

- Characteristics of the sampled population are displayed in the **TABLE**.
- A German map of the sampled population using the first 3 numbers of the zip code of residency is displayed in **FIGURE 1**.
- 595/2,774 (21.4%) sequences linked with at least one other sequence, forming 184 transmission clusters, ranging in size from 2 to 18 sequences; **FIGURE 2**.
- Clustering individuals were significantly more likely to be younger, reporting MSM contact as main risk factor and infected with subtype-B **TABLE**.
- Among those reporting heterosexual sex as main risk factor, men were more likely to cluster than women ( $p < 0.01$ ). Of the 78 clustering men reporting heterosexual sex as main risk factor, 34 (43.6%) had links only with men reporting MSM contact.
- 32/184 transmission clusters contained sequences from more than one region.
- Clustering men were significantly more likely to be found in a position bridging regional HIV epidemics than clustering women ( $p = 0.03$ ).
- By combining our sample with publicly available HIV sequences, we found a total of 236 clusters that linked sequences from our sample (total n=547) and LANL database (n=1,407, of which 31% were from other German centres).

**Table. Population characteristics**

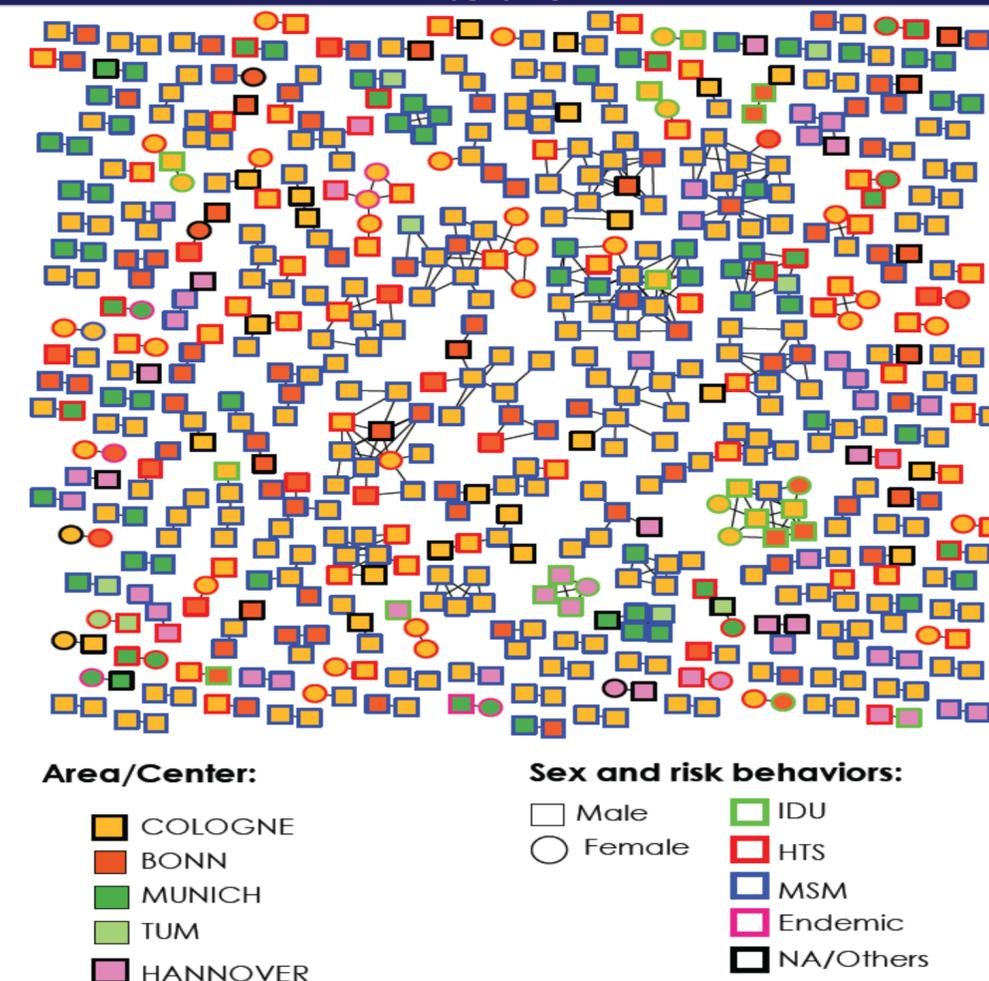
	Not clustering, N=2,179 (78.6%)	Clustering, N=595 (21.4%)	p-value
Age [median (IQR)]	40 (34-49)	36 (30-45)	<0.01
Male Sex	1,681 (77.1)	540 (90.7)	
Subtype B	1,510 (69.2)	532 (89.4)	<0.01
Risk			<0.01
- MSM	1,053 (48.3)	395 (66.3)	
- HTS	509 (23.3)	113 (18.9)	
- IDU	111 (5)	26 (4.3)	
- ENDEMIC*	285 (13)	7 (1.1)	
Cohort			<0.01
- 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)	

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



**Figure 1: Map of sampled population**

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



## Conclusions

- Transmission clusters were mostly comprised of younger MSM.
- Links between HIV risk groups were frequent and mostly observed between men reporting heterosexual sex as main risk and MSM.
- Regional epidemics were interlinked (primarily men to men links) and also linked to other epidemics across Germany and the world.
- Men were more likely to be found in a position bridging regional HIV epidemics than women.
- Results highlight the pitfalls of focusing prevention efforts on specific risk groups or specific locales.