



GEOSPATIAL SPREAD OF HIV IN THE COLOGNE-BONN REGION, GERMANY-FROM 2001-2016

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Background

- The overall rate of new HIV infections is still increasing with a current incidence of 4.5 per 100.000, in Germany [1].
The metropolitan region of Cologne-Bonn has one of the highest rates of new HIV infections in Western Europe (13.7 per 100k) in 2016 [1].
Men having sex with men (MSM) bear the major burden, with 67.4% of all new HIV diagnoses in Germany occurring among MSM in 2017 [1].
The high incidence among MSM in the Cologne-Bonn region may be related to several factors.
There is a well-known MSM party scene in central Cologne [2].
An increased prevalence of high risk behaviors associated with chemsex, which involves the use of methamphetamine, mephedrone, poppers, or cocaine [3].

Objective

Providing insights into the drivers of the HIV-1 transmission of the Cologne-Bonn area

Methods

Population:

- Sociodemographic, geographic data, and pol sequence data were collected from individuals diagnosed at the University Hospital in Cologne and Bonn, between 2001 and 2018.
714 HIV-1 infected Antiretroviral Therapy (ART) naive individuals, followed at the University Hospital Cologne (n=558; 78.2%) and Bonn (n=156; 21.9%) between 2001 and 2016.

Sequence Analysis and Network Inferences:

- Genetic network analyses were performed to infer putative relationships between HIV partial pol sequences.
We used HIV-TRACE software (HIV TRANsmission Cluster Engine: www.hivtrace.org) to infer transmission links between sequences with a genetic distance <=1.5% [4].

- Sociodemographic and geographic data were used to characterize transmission clusters (Table1).

Geospatial analyses:

- Assortativity index (AI, i.e. shared attributes) and characteristics of genetically linked individuals were analyzed.
The geospatial diffusion of the local epidemic (i.e. viral gene flow) was evaluated using a Slatkin-Maddison approach [5] implemented in HyPhy [6].
Geospatial dispersal of the clusters was determined by calculating the average distance between reported residence (centroids of 3-digit zip code, ArcGIS®) of genetically linked individuals using R packages mapproj [7] and mapdata [8].

Results

- The HIV transmission network annotated by risk group and residence location is displayed in Figure 1A&B. 217/714 (30.4%) sequences had a putative linkage with at least one other sequence, forming 77 transmission clusters ranging in size from two to eight individuals.
Figure 2 shows the inferred putative links and numbers of clustering individuals (blue circles) based on the centroid of zip code of residency.
Median distance between genetically linked individuals was 23.4 kilometers (IQR 11.3-34.6), which was significantly lower than the median distance of any random sub-sampled population (median 39.68 kilometers (IQR 23.79-62.59), p<0.001) (Figure 3A).
Slatkin-Maddison analyses revealed increased gene flow from central Cologne towards the surrounding areas (p<0.001) (Figure 3B).
Assortativity analysis showed, that genetically linked individuals were more likely to live in a different zip code (AI= -0.0026, p=0.046) (Figure 3C).

Table 1. Population Characteristics. Baseline demographic, risk- and viral characteristics in clustering and non-clustering individuals.

Table with 8 columns: Study population, N (%), Non-clustering, N (%), Clustering, N (%), Univariate analysis (OR, p-value), Multivariable analysis** (OR, p-value). Rows include Age, Gender, Subtype, Risk, and Residential area.

*MSM, men who have sex with men; HTS, heterosexuals; PWID, persons who inject drugs; Endemic, recent immigration from a country with a HIV prevalence >1%. **Adjusted multivariable logistic regression model for gender, region of origin and risk. *Zip codes: 501, 502, 503, 507, 508, 509, 510, 511, 513, 514, 515, 520, 521, 531, 532, 533, 534, 535, 536, 537, 538 *Zip code: 506

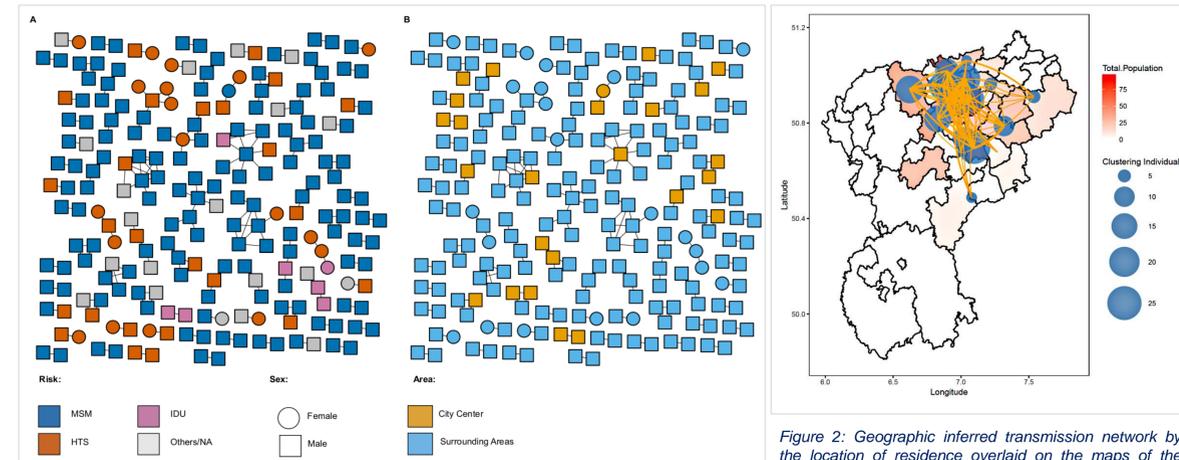


Figure 1: Transmission network of HIV in the Cologne-Bonn region. Sex of individuals (nodes) is indicated by shape. In A) the color indicates the reported risk group. In B) the color indicated the residence location, i.e. living in the city center(yellow) or surrounding areas (orange) of Cologne-Bonn. All edges represent a genetic distance of <=1.5%.

Figure 2: Geographic inferred transmission network by the location of residence overlaid on the maps of the Cologne and Bonn area. The size of the dots defining the number of clustering individuals in each specific area. The golden lines representing the links between different areas. Most of the larger cluster (>20 individuals) are located in the central parts of Cologne and Bonn (n=217).

Conclusion

- We inferred significant gene flow from the city center of Cologne to the surrounding areas, highlighting the role of this area in the transmission dynamics of the regional epidemic.
We found evidence that HIV-1 transmission in Cologne-Bonn is between MSM residing closer together, but not in the same neighborhood, suggesting that geographically focused prevention efforts should encompass clusters of adjacent neighborhoods
Our findings highlight the importance of phylogeographic analysis to get a better understanding of local transmission clusters.
The knowledge of these patterns can improve the efficiency of prevention and intervention efforts and can help health entities to allocate resource.
In addition, resources can be used to ensure that strategies are optimal for priority risk groups and areas of greatest need.

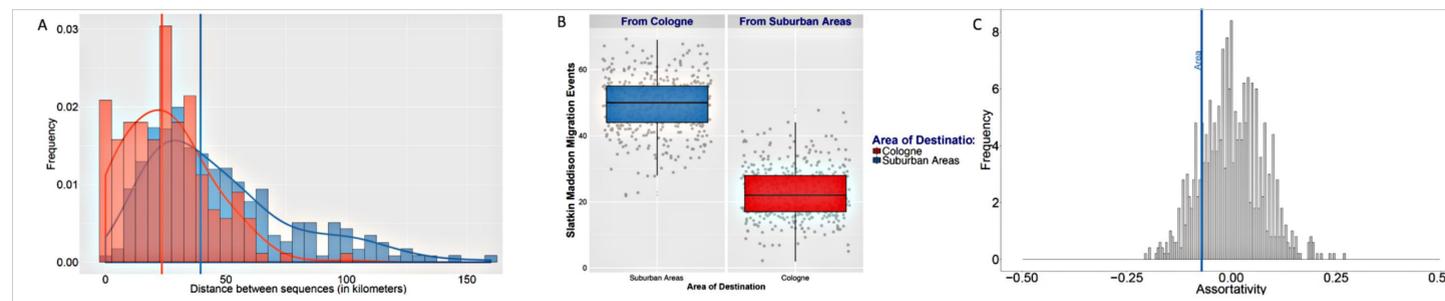


Figure 3: A) Median Euclidean distance between linked sequences vs. median distance between random selection of sequences. Simulation were repeated 1000 iterations. (red=genetically linked; blue= random) B) Viral gene flow within the sampled epidemic between central district of Cologne and the surrounding areas. Viral migration was inferred using the Slatkin-Maddison index on phylogenetic trees constructed from 1,000 random subsets of equal number of sequences per location to identify the diffusion of the epidemic in the region between central Cologne and surrounding areas. C) Geospatial mixing between genetically linked individuals using assortativity coefficients by area of residency (n= 714).