GEOSPATIAL DISPERSAL OF HIV-1 TRANSMISSION IN SIX MAJOR CITIES IN GERMANY, FROM 2001-2018

Poster no.
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Background

- In Germany, the annual number of HIV infections decreased slightly from 3,100 [2,900-3,300] in 2016 to 2,700 [2,500-2,900] by the end of 2017 [1].
- Rates of new HIV infections remained high among young men between 30-39 and 25-29 years of age (16.1 and 15.9 per 100k) [1].
- Munich, Cologne, and Frankfurt reported the highest rates of new HIV infections (17.3; 13.3 and 12.3 per 100k) in 2017 [2].
- Men having sex with men (MSM) bear the major burden, with 63% of all new HIV diagnoses occurring among MSM in 2017 [1].
- Sexual risk behavior of MSM in commercial (e.g. bathhouse, sex club) or public (e.g. parks) sex venues and/or party venues may contribute to the high rates of new infections in metropolitan cities [3].
- Simultaneous intake of “chemsex” or “party and play drugs” is associated with high risk behavior and HIV transmission [2; 4].

Objective

Providing insights into the drivers of HIV-1 transmission in the German epidemic

Methods

Population:

- Sociodemographic, geographic and HIV-1 *pol* sequence data were collected from newly diagnosed persons living with HIV (PLWH) in six cities (Bonn, Cologne, Frankfurt, Hamburg, Hannover, and Munich) across Germany, between 2001 and 2018.

Sequence Analysis and Network Inferences:

- Genetic-distance based network analyses were performed to infer putative relationships between HIV-1 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% [5].
- Sociodemographic and geographic data were used to characterize transmission clusters (Table 1).

Geospatial Analyses:

- Assortativity index (AI, i.e. shared attributes) and characteristics of genetically linked individuals were analyzed.
- 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 maptools [6] and mapdata [7].

Results

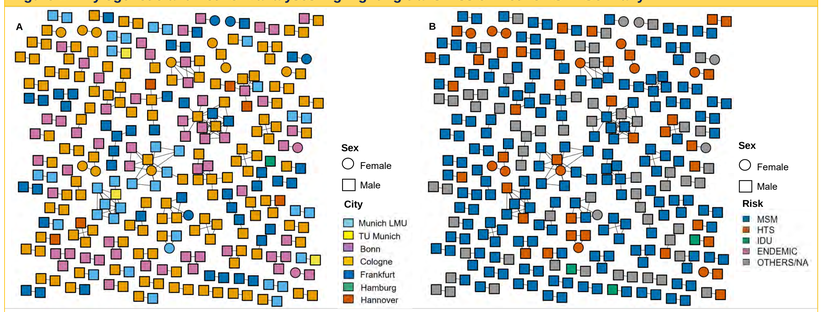
Table 1. Genetically linked individuals were significantly younger and more likely to reside in Bonn and Cologne.

				Univariate analysis		Multivariable analysis**	
	Study population, N (%)	Non-clustering, N (%)	Clustering, N (%)	OR (95% CI)	p-value	OR (95% CI)	p-value
Total	1,397 (100)	1,108 (79.3)	289 (20.7)				
Age							
>45	430 (30.8)	367 (33.1)	63 (21.8)				
25-45	856 (61.3)	671 (60.6)	185 (64.0)	1.60 (1.18-2.20)	0.003	1.75 (1.26-2.43)	**0.001**
<25	111 (7.9)	70 (6.3)	41 (14.2)	3.41 (2.14-5.45)	<0.001	4.22 (2.50-7.14)	**<0.001**
Gender							
Female	239 (17.1)	222 (20.0)	17 (5.9)				
Male	1,158 (82.9)	886 (80.0)	272 (94.1)	4.01 (2.40-6.69)	<0.001	1.98 (1.12-3.53)	**0.020**
Subtype							
non-B	380 (28.2)	360 (32.5)	20 (6.9)				
B	1,017 (72.8)	748 (67.5)	268 (93.1)	6.47 (4.04-10.37)	<0.001	5.61 (3.35-9.42)	**<0.001**
Risk*							
HTS	302 (21.6)	253 (22.8)	49 (17.0)				
MSM	792 (56.7)	580 (52.3)	212 (73.4)	1.89 (1.34-2.66)	<0.001		
ENDEMIC	133 (9.5)	133 (12.0)	-	n.a.			
PWID	24 (1.7)	21 (1.9)	3 (1.0)	0.74 (0.21-2.57)	0.633		
Others/Unknown	146 (10.5)	121 (11.0)	25 (8.7)	1.07 (0.63-1.81)	0.810		
City							
Munich	231 (16.5)	192 (17.3)	39 (13.5)				
Bonn	152 (10.9)	94 (8.5)	58 (20.1)	3.04 (1.89-4.89)	<0.001	2.87 (1.74-4.75)	**<0.001**
Cologne	582 (41.7)	444 (40.1)	138 (47.8)	1.53 (1.03-2.27)	0.034	1.50 (0.99-2.26)	0.051
Frankfurt	215 (15.4)	168 (15.2)	47 (16.3)	1.38 (0.86-2.21)	0.184	1.41 (0.86-2.31)	0.170
Hamburg	48 (3.4)	47 (4.2)	1 (0.3)	0.11 (0.01-0.78)	0.028	0.09 (0.01-0.68)	**0.020**
Hannover	169 (12.1)	163 (14.7)	6 (2.1)	0.18 (0.08-0.44)	<0.001	0.17 (0.07-0.43)	**<0.001**

Legend. Population Characteristics. Baseline demographic, risk- and viral characteristics in clustering and non-clustering individuals. *MSM, men who have sex with men; HTS, heterosexuals; Endemic, recent immigration from a country with a HIV prevalence >1%, PWID, people with injection drug use.**Adjusted binary multivariable logistic regression model for age, gender, subtype, risk, and region of origin; n.a., not applicable because of no cases of clustering individuals. P-values given in bold depict significant result.

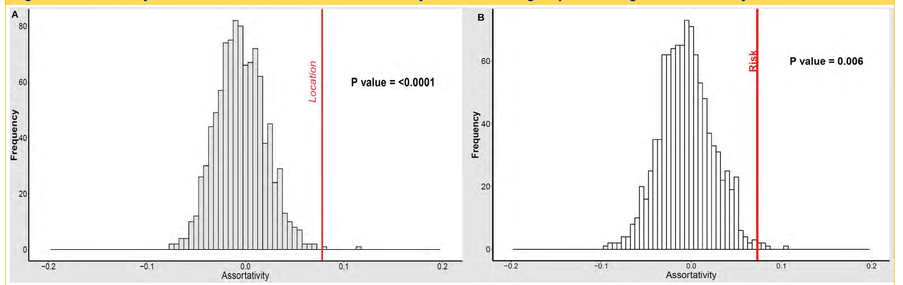
- A total of 1,397 HIV-1 infected Antiretroviral Therapy (ART) naïve PLWH, followed at the University Hospitals of Munich, Bonn, Cologne, Frankfurt, Hamburg, and Hannover were included (Table 1).
- 289/1,397 (20.7%) sequences had a putative linkage with at least one other sequence, forming 102 transmission clusters ranging in size from two to twelve individuals (Figure 1 A&B).

Figure 1. Phylogenetic and network analyses highlighting transmission networks in Germany.



Legend. Transmission network of HIV-1 in six German cities. Shape indicates sex of individuals (male-square, female-circle). In **A)** the color indicates the residence location. In **B)** the color indicates the reported risk group. All edges represent a genetic distance of ≤1.5%.

Figure 2. Genetically linked individuals were more commonly the same risk group and living in the same city



Legend. **A)** Geospatial mixing between HIV-1 genetically linked individuals using assortativity coefficients by cohort and B) risk group. N= 1,397 (Bonn n= 152, Cologne n= 582, Frankfurt n= 215, Hamburg n= 48, Hannover n= 169, Munich n= 231).

- The largest clusters (>10 individuals) consisted mainly of MSM from Bonn, Cologne, and Frankfurt (Figure 1 A&B).
- Genetically linked individuals were significantly younger (<25 years of age vs. >45 years, p=<0.001).
- Sequences from Bonn and Cologne had a higher connectivity than sequences from Munich (p<0.001 for Bonn and p=0.051 for Cologne, respectively) (Table 1)
- Assortativity analysis showed that genetically linked individuals were more likely to cluster with individuals from the same location (AI=0.08, p<0.001) (Figure 2A), the same risk group AI=0.08, p=0.006) (Figure 2B), and the same age group (AI= 0.06, p<0.001).
- Median distance between residences of genetically linked individuals was 78 kilometers (km), which is significantly lower than the expected distance in a randomly sub-sampled population (median 269 km; p<0.001).
- These findings suggests, that genetically linked individuals tended to be linked with partners from nearby communities/areas.

Conclusion

- In Germany, HIV-1 transmission occurs mainly between younger (<25 years of age) MSM who are living in nearby communities.
- Transmission network analysis elucidated that young MSM who are living in the nearby metropolitan cities Cologne, Bonn, and Frankfurt are important drivers of new HIV-1 transmissions in Germany.
- Focusing prevention resources on sex and party venues (commonly frequented by young MSM) in the metropolitan cities may help to prevent new HIV-1 transmissions.
- Our findings highlight the importance for real-time monitoring of HIV-1 transmission using molecular epidemiology, which can be leveraged to target specific geographic areas where new transmissions are being observed.

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