

# SPREAD OF HIV-1 PRE-TREATMENT DRUG RESISTANCE IN THE COLOGNE-BONN REGION, GERMANY

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**524**

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## Background

- In Germany, the prevalence of HIV-1 drug resistance mutations (DRM) remains high, resulting in treatment failure and affecting the choice of antiretroviral therapy (ART) [1].
- Prevalence of transmitted DRM (at least one resistance mutation) remains stable with 10% in Germany [1].
- The overall rate of new HIV infections is still increasing with an incidence of 4.5 per 100.000 [2].
- The metropolitan region of Cologne-Bonn has one of the highest rates of new HIV infections in Germany (11.7 per 100k) in 2015 [2].

## Objective

**Understanding the molecular epidemiology of HIV and DRM transmission in the metropolitan region of Cologne-Bonn, Germany**

## Methods

- **Population:** 714 HIV-1 infected ART naïve individuals, followed at the University Hospital Cologne (n=558; 78.2%) and Bonn (n=156; 21.9%) between 1999 and 2016.
- **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](http://www.hivtrace.org)) to infer transmission links between sequences with a genetic distance ≤1.5%.
  - Sociodemographic and geographic data were used to characterize transmission clusters, **Table 1**.
- **Geospatial analyses:** 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.
- **DRM:** DRM were assessed by <https://hivdb.stanford.edu/>
  - Shared DRM were estimated between genetically linked individuals.

## Results

- Study population median age of 39 years (IQR: 31-47) (**Table 1**).
- Putative transmission links were inferred in 217/714 (30.4%) sequences forming a total of 77 transmission clusters (size ranging from 2-8, **Figure 1A**).
- Individuals younger than 30 years of age and persons who inject drugs (PWID) were more likely to cluster compared to men who have sex with men (**Table 1**).
- People living in the city centers of Cologne and Bonn were more likely to cluster compared to people living in suburbs (62.7% vs. 37.3%, OR 1.39, 95% CI 0.97-1.98).
- DRM frequency was comparable in clustering and not clustering individuals (17.5% vs 17.1%, OR 0.97, 95% CI 0.63-1.51).
- Nucleoside- and non-nucleoside reverse transcriptase inhibitor (NRTI/NNRTI) resistance was detected in clustering individuals 7.8% and 12.9% **Figure 1 A&B**).

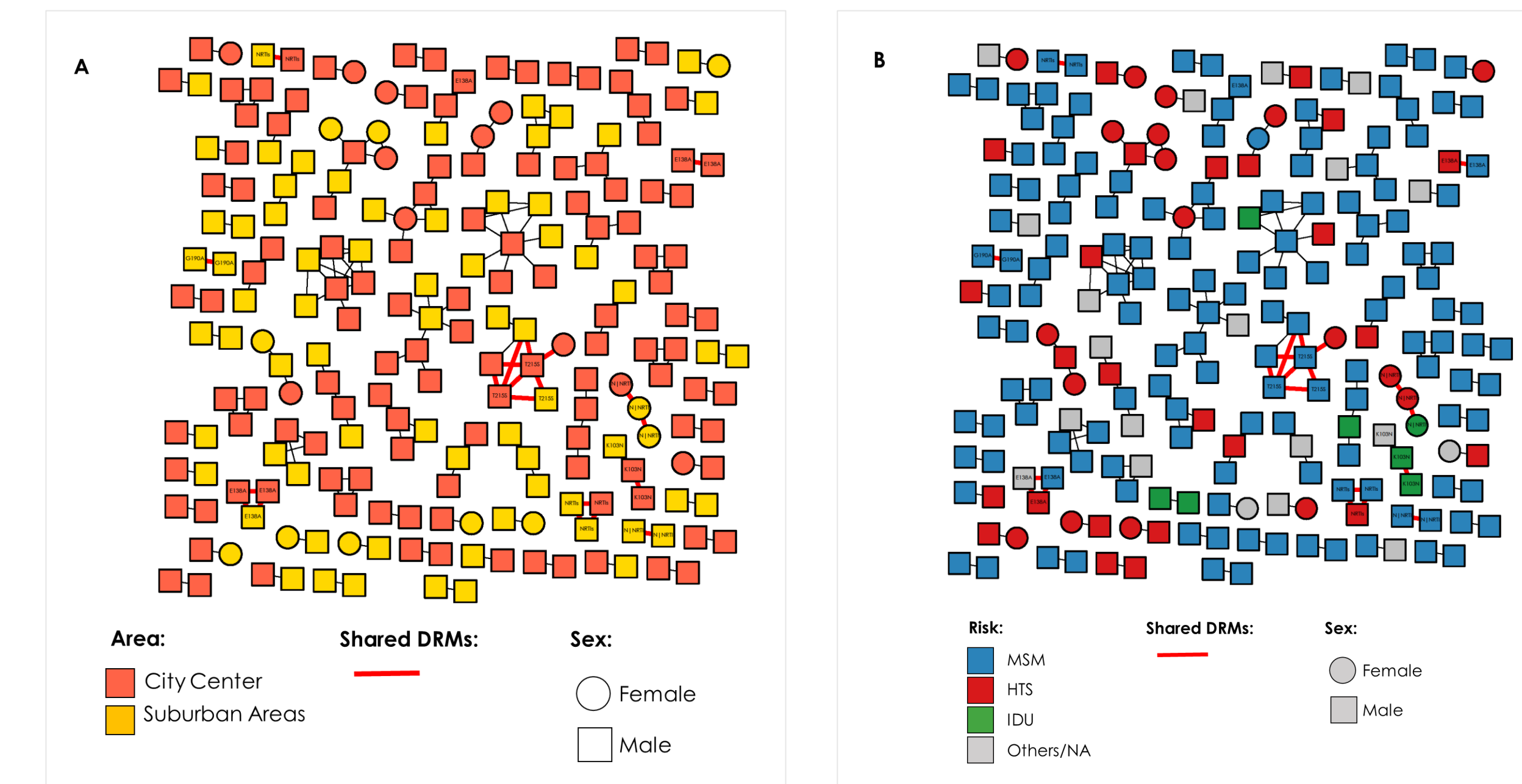
**Table 1:** Patient characteristics, logistic regression analysis of clustering individuals

	Study population	Not clustering, N (%)	Clustering, N (%)	OR (95% CI)**	p-value
<b>Total</b>	714 (100)	497 (69.6)	217 (30.4)		
<b>Age</b>					
<30	137 (19.2)	96 (17.9)	41 (23.2)		
31-40	240 (33.6)	173 (32.2)	67 (37.9)	0.81 (0.51-1.29)	0.379
41-50	211 (29.6)	166 (30.9)	45 (25.4)	0.58 (0.35-0.94)	<b>0.028</b>
>50	126 (17.6)	102 (19.0)	24 (13.6)	0.51 (0.28-0.90)	<b>0.022</b>
<b>Gender</b>					
Male	582 (81.5)	387 (77.9)	195 (89.9)		
Female	129 (18.1)	108 (21.7)	21 (9.7)	0.77 (0.40-1.47)	0.421
<b>DRM</b>					
No	591 (82.8)	412 (82.9)	179 (82.5)		
Yes	123 (17.2)	85 (17.1)	38 (17.5)	0.97 (0.63-1.51)	0.904
<b>Subtype</b>					
B	539 (75.5)	345 (69.4)	194 (89.4)		
non-B	175 (24.5)	152 (30.6)	23 (10.6)	0.41 (0.23-0.72)	<b>&lt;0.001</b>
<b>Risk</b>					
MSM	408 (57.1)	261 (52.5)	147 (67.7)		
HTS	184 (25.8)	141 (28.4)	43 (19.8)	0.89 (0.54-1.47)	0.656
PWID	19 (2.7)	12 (2.4)	7 (3.2)	1.42 (0.52-3.85)	0.489
ENDEMIC*	51 (7.1)	50 (10.1)	1 (0.5)	0.08 (0.01-0.61)	<b>0.015</b>
Others/Unknown	52 (7.3)	32 (6.6)	19 (8.8)	1.27 (0.68-2.38)	0.451
<b>Residential area</b>					
Suburbs	231 (32.4)	150 (30.2)	81 (37.3)		
City	483 (67.6)	347 (69.8)	136 (62.7)	1.39 (0.97-1.98)	0.066

\*Recent immigration from a country with a HIV prevalence &gt;1%. HTS, heterosexual; MSM, men who have sex with men; PWID, persons who inject drugs

\*\* Model adjusted Odds Ratio (OR), 95% Confidence Interval.

- Of the 133 putative links including sequences harboring any DRM, 23 (17.3%) were between genetically-linked partners with shared DRM (**Figure 1 A&B**, red lines), suggesting DRM transmission among ART naïve individuals.
- Number of clustering individuals and clustering individuals harboring DRMs, are mostly located in the city centers of Cologne-Bonn 136 (62.7%) and 22 (57.9%) (**Figure 1 A**) and men reporting MSM contact 25 (65.8%) (**Figure 1 B**).



**Figure 1** Evidence of transmission of pre-treatment drug resistance in the Cologne-Bonn region **A)** Color indicates individuals living in the city center (in orange) or suburban areas (in yellow) of the Cologne-Bonn region. **B)** Color indicates the reported risk group. All edges represent a genetic distance of ≤1.5%. Lines in bold red indicate individuals who shared DRMs. Squares and circles indicating male and female. Only shared DRM are labeled with each nodes. NJNRTIs indicate the presence of ≥1 nucleoside or non-nucleoside reverse transcriptase inhibitor resistance(s).

## Conclusion

- DRMs were mostly observed in men reporting MSM contact.
- We found evidence of transmitted DRM located especially in the city center of Cologne, well known for its districts with strong gay community.
- Phylogenetic and geospatial characterization of HIV revealed close/dense hotspots of HIV transmission that could help identifying targets for treatment and interventions.

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