European HIV-1 A6 International Transmission Networks Are Enriched by Migrating Populations

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BACKGROUND

→**The A6 sub-subtype** drives the expanding HIV epidemic in Eastern Europe and is increasingly detected across multiple European countries.

→Long-standing migration and recent war-related displacement from Ukraine have contributed to **cross-border spread of the A6 lineage across Europe**

→Our goal was to characterize **international transmission patterns of HIV-1 A6** across Czechia, Poland, Israel, and Germany, and to assess cluster enrichment associated with migration

METHODS

→We assembled all publicly available HIV-1 A6 partial *pol* sequences (n=15,666) and defined an analytic subset with migration-related metadata from **Poland** (n=2,067), **Czechia** (n=304), **Israel** (n=293), and **Germany** (n=88); Total study-country sequences (n=2,752)

→Maximum-likelihood phylogenies were reconstructed (IQ-TREE; SH-aLRT >70%), and broad transmission clusters were delineated when study-country sequences grouped with global reference sequences

→We inferred transmission links using distance-based network analysis (HIV-TRACE), selecting an epidemiologically plausible mean pairwise TN93 threshold.

RESULTS

→ML analysis identified 4,093 sequences (26.1%) forming broad transmission clusters, including 2,434 (59.4%) from the four-country subset and 1,659 (40.6%) from background regions

→Using a TN93 genetic distance threshold of 0.010 substitutions/site, selected based on epidemiological plausibility, a clustering rate of 44.5% was observed. The inferred network comprised 5,093 links, with a mean node degree of 5.5 (range: 2–718)

RESULTS continued

→Over time, the probability of migrant inclusion in transmission links increased significantly (OR/year 1.080; 95% CI 1.047–1.114; p<0.0001), rising from 6.3% (2011) to 14.6% (2023); (Figure 1)

→We also observed a significant increase in transmission links involving female individuals (OR/year 1.088; 95% CI 1.010–1.172; p<0.05), from 2.2% to 5.8% over the study period; (Figure 2)

→After link-level normalization, within-country transmission predominated; however, notable cross-border links were identified between Germany and Poland (n=107; 1.1%), and between Czechia and Poland (n=67; 0.7%); (Figure 3)

→ Cross-border transmission is an expanding component of the European HIV-1 A6 epidemic

→Rising migrant and female representation within A6 transmission networks signals shifting epidemic dynamics that require coordinated international action.

CONCLUSIONS

→Cross-border clustering of HIV-1 A6 reflects sustained international transmission across Europe

→Transmission networks of HIV-1 A6 are becoming increasingly heterogeneous, with a rising contribution of migrants and female individuals over time

→Coordinated, cross-jurisdictional prevention strategies targeting mobile populations are essential to address evolving transmission patterns and limit further HIV spread

PLAIN LANGUAGE SUMMARY

A specific form of HIV called A6 is spreading within and between European countries. Our genetic analysis shows that international transmission links are becoming more common, with increasing involvement of migrants and women over time. HIV prevention programs need to work across national borders and better address the needs of mobile populations.

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Figure 1.

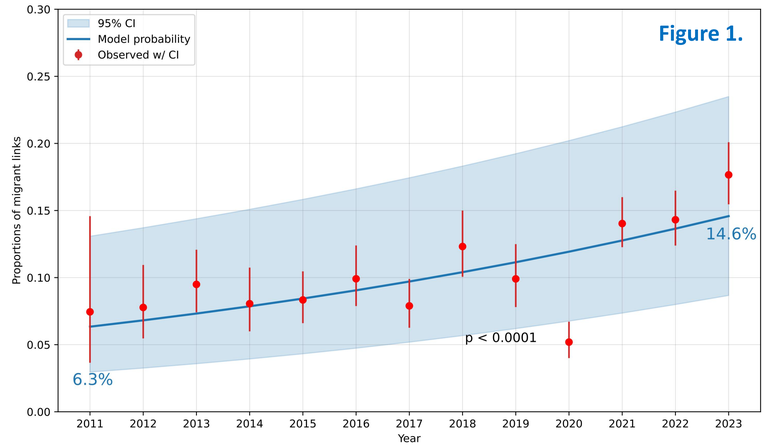


Figure 2.

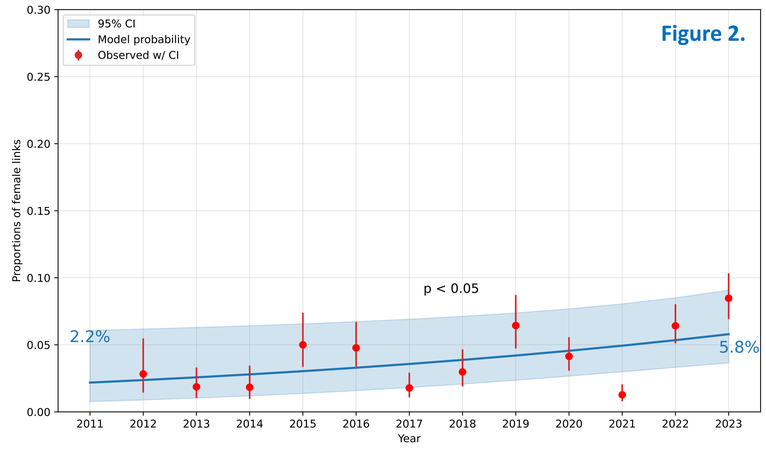


Figure 3.

