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BACKGROUND

- According to the European Centre for Disease Prevention and Control (ECDC), almost half of the new HIV diagnoses were among people originating from outside the reporting country (migrants) in Europe the last few years [1]. Unfortunately, there is a gap in our knowledge related to the geographic origin of HIV-1 acquisition that could impact public health policies.
- In France, it is assessed that in 2018, 180,000 [150,000 – 210,000] people lived with the HIV (PLWHIV). According to the PARCOURS study, the migrants are infected for nearly 49% after their arrival in France [2].
- Considering that CRF02_AG is the most prevalent non-B clade in Paris, France, we aimed to trace the geographic origin of HIV-1 acquisition for CRF02_AG-infected migrants diagnosed in Paris, using a novel approach based on current state-of-the-art molecular epidemiology methods.

METHODS

- We studied the first available *pol* gene sequence for all PLWHIV infected with CRF02_AG (N=2,146), diagnosed in two large Parisian University hospitals (Bichat-Claude Bernard and Pitié-Salpêtrière) (Figure 1).
- HIV-1 subtyping was carried out by automated subtyping tools (COMET, REGA).
- We analysed phylogenetically the CRF02_AG sequences from migrants (N=567) along with all the available CRF02_AG sequences from non-migrant PLWHIV (N=1,579) to determine the local transmission networks (LTNs) for sequences from migrants. We also included all publicly available CRF02_AG sequences (N=3,476), and unpublished CRF02_AG sequences from Spain, Italy and Greece (N=1,193), as references. LTNs were phylogenetic clusters including sequences from France at proportions >70%, receiving bootstrap value >70% or SH-support >0.8. Phylogenetic trees were estimated by the maximum likelihood method (RAxML v8.0.20, FastTree v2.1).
- The putative origin of HIV-1 acquisition for those infected with CRF02_AG strains was traced by using a combination of the clustering pattern for each sequence (within or outside a local transmission network) and an estimation of this parameter provided by phylogeographic analysis and

This is one of the few *molecular* studies showing that even for **CRF02_AG**, a large proportion of *transmissions* among *migrants* occur in *Paris (post-migration)*.

METHODS (Cont.)

- ancestral character reconstruction using the criterion of parsimony (Mesquite v3.5).
- We performed statistical analysis which was based on chi-square tests for simple comparisons and multivariable logistic regression models for the investigation of parameters associated with clustering as implemented in STATA 12-StataCorp LP.

Figure 2 Unrooted phylogenetic tree estimated by RAxML v8.0.20 of HIV-1 CRF02_AG sequences sampled in France, and a global reference dataset. Local transmission networks are indicated as triangles.

RESULTS

- In our study population, most of the migrants infected with CRF02_AG strains were heterosexuals (78.8%), originating from Western Sub-Saharan Africa (83.4%) and especially from Ivory Coast (36.3%) and Cameroon (18.3%). The distribution of transmission risk group in migrants was: Heterosexuals (N=447; 78.8%), MSM (N=37; 6.5%), and Others/Unknowns (N=83; 14.7%).
- Phylogenetic analysis revealed that 198 (34.9%) sequences from migrants clustered within LTNs (Figures 1 and 2).
- Phylogeographic analysis showed that 29.3% of the CRF02_AG HIV-transmissions within migrants occurred in Paris, France.
- The proportion of migrant MSM within the LTNs was significantly higher (83.8%) than the corresponding proportion of heterosexuals (31.5%) ($p < 0.001$).
- Multivariable logistic regression analysis showed that parameters associated with clustering:
 1. Within the large LTNs (≥ 10 sequences) were MSM risk group (MSM vs heterosexuals OR: 10.3, 95% CI: 6.5-16.5) and French origin (non-migrants vs migrants OR: 2.4, 95% CI: 1.5-3.9).
 2. In migrants were MSM risk group (MSM vs heterosexuals OR: 8.6, 95% CI: 3.0-24.8) and origin from Central and Eastern Sub-Saharan Africa, and Western Europe (Central and Eastern Sub-Saharan Africa vs Western Sub-Saharan Africa OR: 2.7, 95% CI: 1.2-5.9; Western Europe vs Western Sub-Saharan Africa OR: 9.5, 95% CI: 2.0-45.3).

Africa Asia Europe
America Oceania France

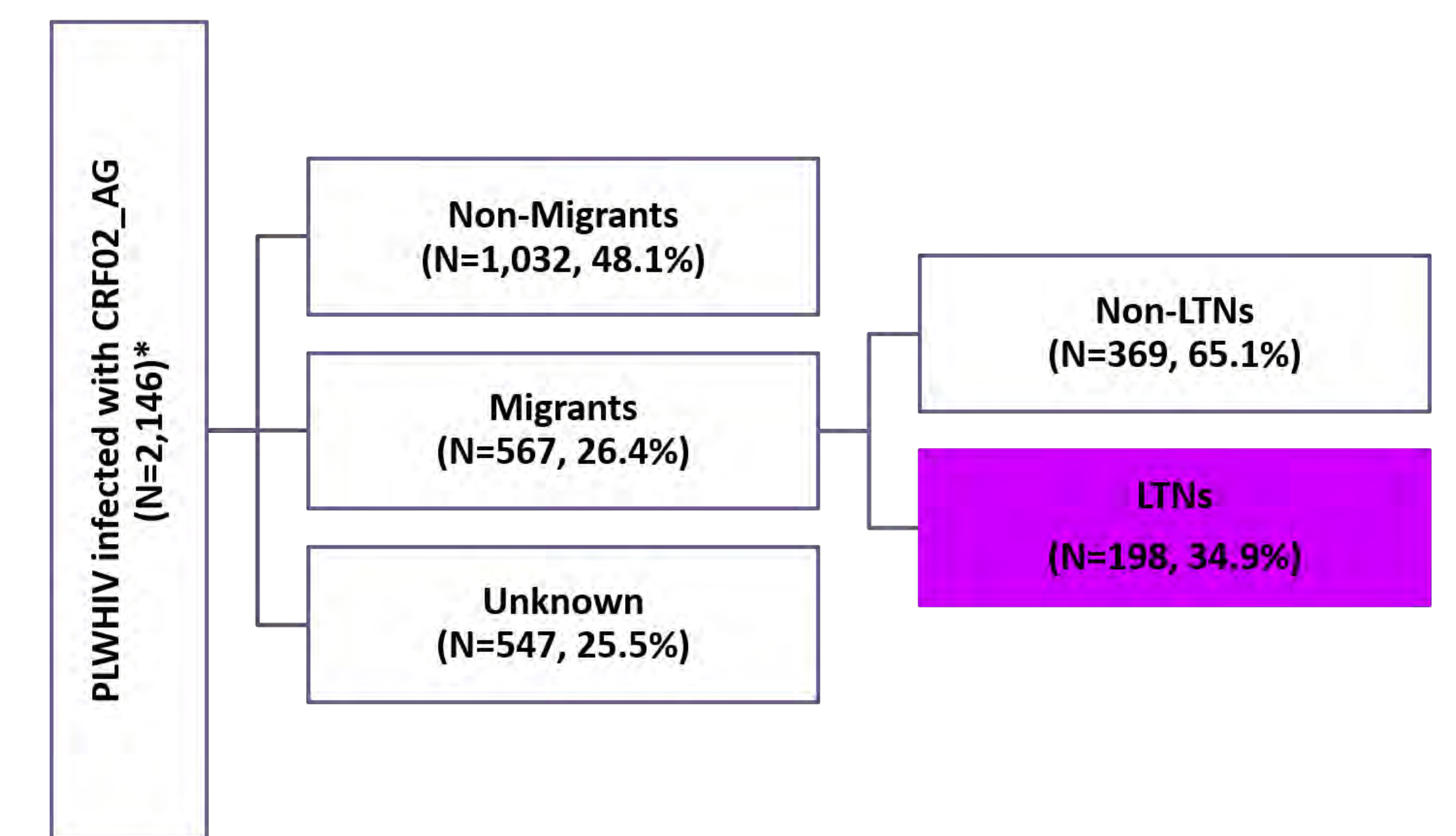
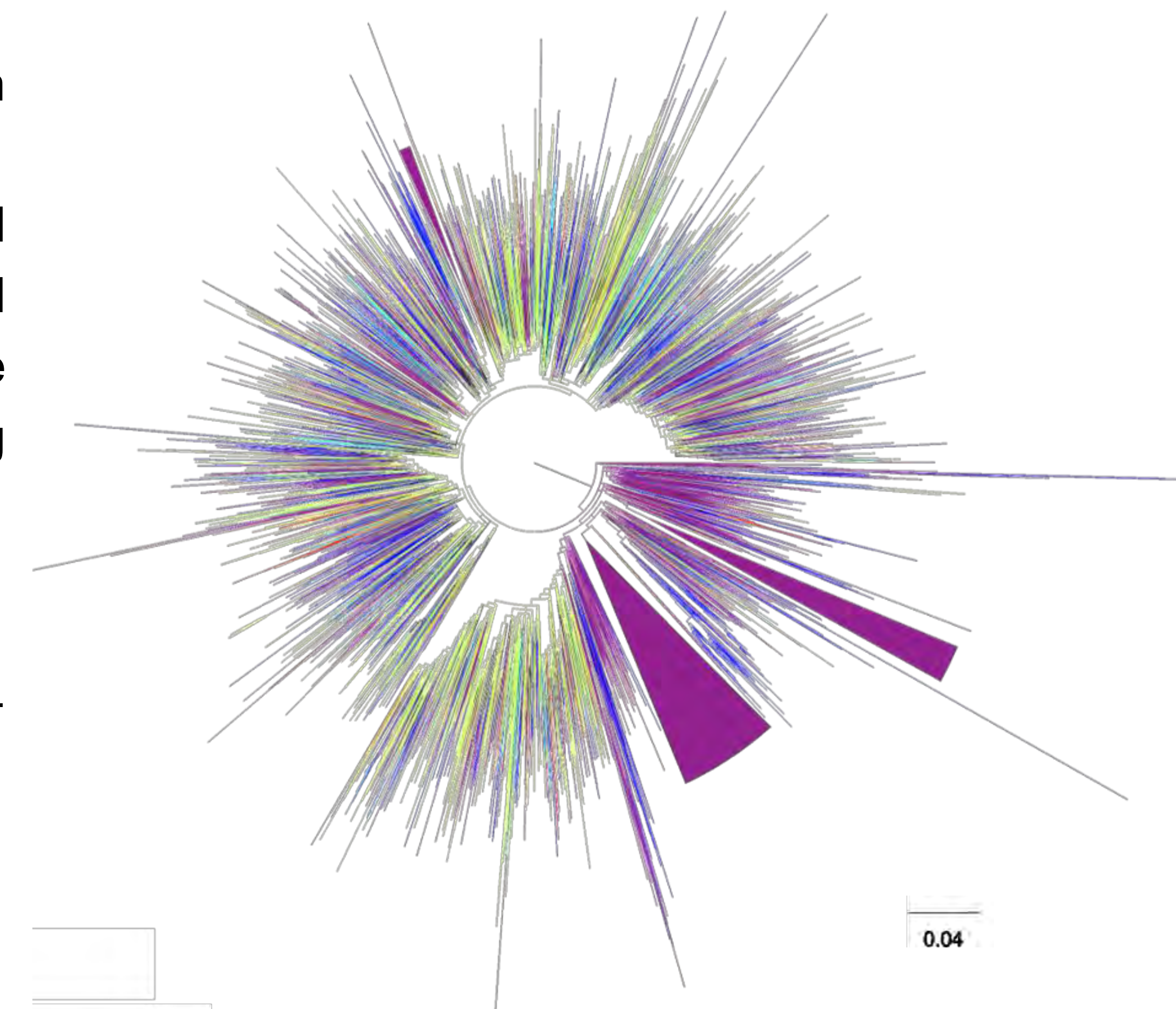


Figure 1 Study population. The highlighted box corresponds to migrants diagnosed in Paris, infected with HIV-1 CRF02_AG within local transmission networks (LTNs). Abbreviations: PLWHIV, People Living With HIV

CONCLUSIONS

- ✓ The 29.3% of CRF02_AG HIV-transmissions within migrants originated in Paris.
- ✓ Transmissions among migrants within LTNs were associated with MSM risk group.
- ✓ Transmissions within large LTNs were more frequent among MSM and non-migrants.
- ✓ This is one of the few molecular studies showing that even for CRF02_AG, which is prevalent in Sub-Saharan Africa, a large proportion of transmissions among migrants occur in Paris.
- ✓ It is important to test and implement new molecular tools, such as proposed in this to study, to better monitor the changing trends of the HIV epidemic. Knowing whether HIV acquisition occurs pre-migration or post-migration, is critical in designing adequate public health interventions in HIV prevention and testing strategies.

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