

Spatiotemporal Dynamics of HIV-1 Transmission in France, 1999-2014

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Background

Identifying and monitoring HIV transmission networks can be important in understanding the evolutionary patterns and geospatial spread of the epidemic.

Objective

To reconstruct the broad molecular epidemiology of HIV in France from individuals enrolled at the time of primary HIV-1 infection in the national ANRS PRIMO Cohort over 15 years.

Table 1. Population Characteristics at baseline

	Total	Not in cluster	In clusters (≥2)	p
N	1356	71.5% (969)	28.5% (387)	
Age median (min-max)	35 (17-79)	36 (17-79)	32.5 (18-68)	<i>p</i> <0.01
Sex				<i>p</i> <0.01
-Male	86.7%(1175)	83.0%(804)	95.9% (371)	
-Female	13.0% (176)	16.6%(161)	3.9%(15)	
-NA	0.3%(5)	0.4%(4)	0.2%(1)	
Ethnicity				<i>p</i> <0.01
- White	85.9%(1165)	83.7%(811)	91.5%(354)	
- Black	10.8%(146)	12.8%(124)	5.7%(22)	
- Asian	1.5%(20)	1.5%(15)	1.3%(5)	
- Others	1.3%(17)	1.3%(13)	1%(4)	
- NA	0.6%(8)	0.6%(6)	0.5%(2)	
Origin				<i>p</i> =0.66
-Pairs area*	38%(515)	38.4%(372)	37%(143)	
-Outside Paris area	55.7% (755)	55.3%(536)	56.8% (220)	
- Overseas	6.3%(86)	6.3%(61)	6.2%(24)	
Risk				<i>p</i> <0.01
-MSM	71.4% (968)	65.6% (636)	85.8% (332)	
-HTS	21.8% (296)	27.6% (267)	7.5% (29)	
-Blood	0.1% (1)	0.1% (1)	0	
-IDU	0.2% (3)	0.3% (3)	0	
-Others/NA	6.5% (88)	6.4% (62)	6.7% (28)	
Year of Diagnosis				<i>p</i> <0.01†
-before 2006	34.5% (468)	38.4% (372)	24.8% (96)	
-2006 to 2010	36.1% (489)	34.2% (332)	40.6% (157)	
-2011 to 2014	29.4% (399)	27.4% (265)	34.6%(134)	
CD4 count (range)	547 (22-2872)	543 (22-2872)	559 (54-1930)	<i>p</i> =0.25
HIV RNA Level (range)	5.13 (1.0-8.11)	5.1 (1.0-8.1)	5.2 (1.8-8.1)	<i>p</i> =0.15
HIV Subtype:				<i>p</i> =0.01
-B	71.5% (969)	70.5%(683)	73.9%(286)	
-CRF02_AG	15.3% (208)	13.4%(130)	20.2%(78)	
-A	2.1% (28)	2.9% (28)	0	
-C	1.6% (22)	2.3% (22)	0	
-Others	9.6% (129)	11.0%(106)	5.9%(23)	

*zipcodes 75, 91, 92,93, 94 and 95; †: chi-square test for Trend.

Methods

Sociodemographic, clinical, and *pol* sequence data from 1356 cohort participants were collected between 1999 and 2014 (Chaix, 2013, Frange, 2015).

Network analysis was performed to infer genetic relationships between HIV sequences (Little, 2014, Wertheim 2014).

Bayesian coalescent-based methods were used to examine the temporal and spatial dynamics of identified clusters and the spread of HIV-1 subtype B and CRF02_AG epidemics (Fig. 1).

Figure 1. Bayesian time-scaled tree of the HIV transmission network

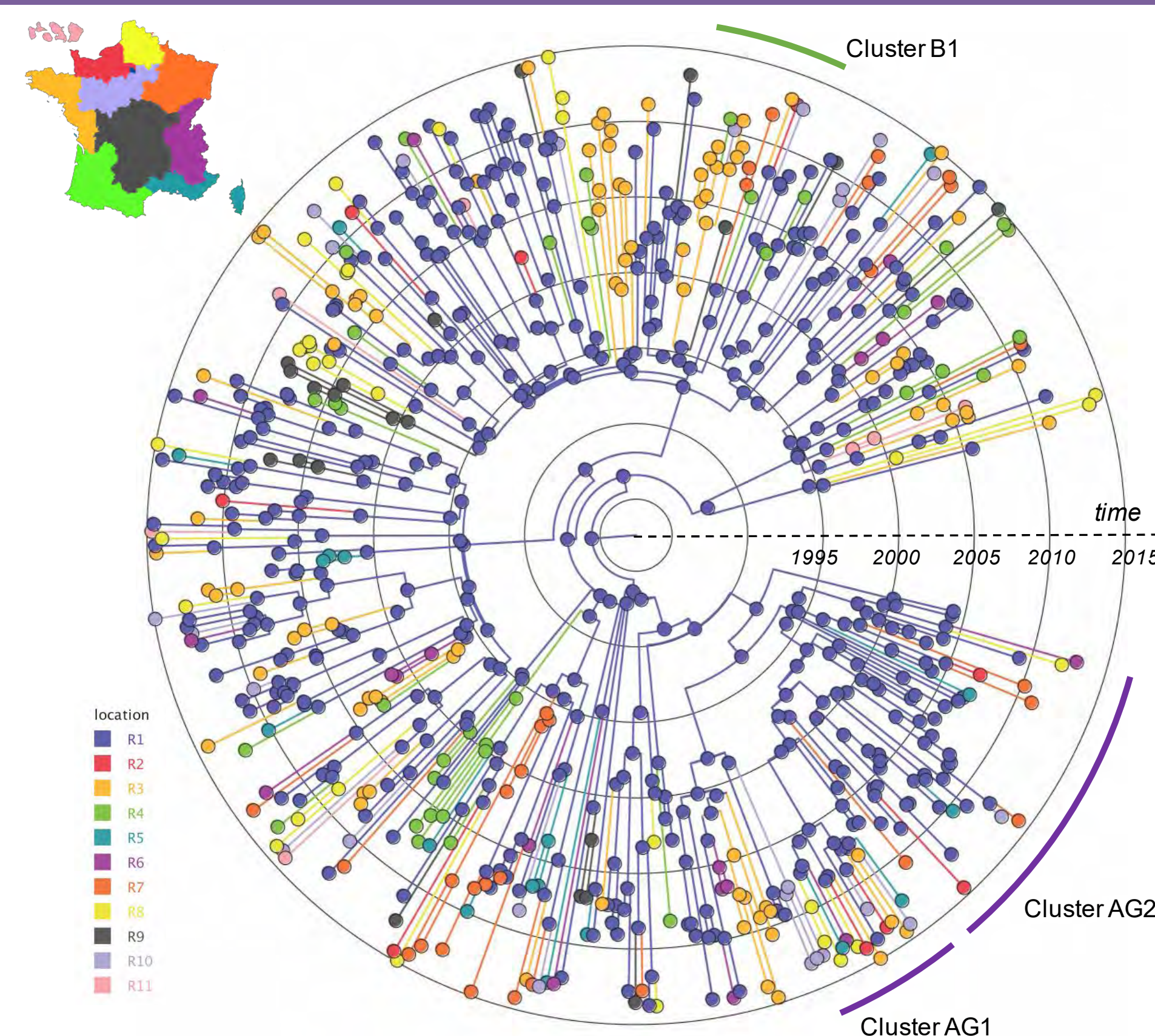


Figure 1. Time scaled in year. Branches are colored according to the most probable location state of their descendent nodes with the color codes corresponding to the 11 equally populated regions. Subtypes B and CRF02AG are highlighted in light green and blue respectively.

References

Chaix et al. CID, 2013, Frange et al. JAC, 2015, Wertheim et al. JID, 2014; Little et al. PONE ,2014

Results

Compared to those who did not cluster (n=969), those in clusters (n=387) were more frequently men (95.9% vs 83%, *p*<0.01), MSM (85.8% vs 65.6%, *p*<0.01) and infected with CRF02_AG (20.2% vs 13.4%, *p*<0.01) (Table 1 and Fig. 2).

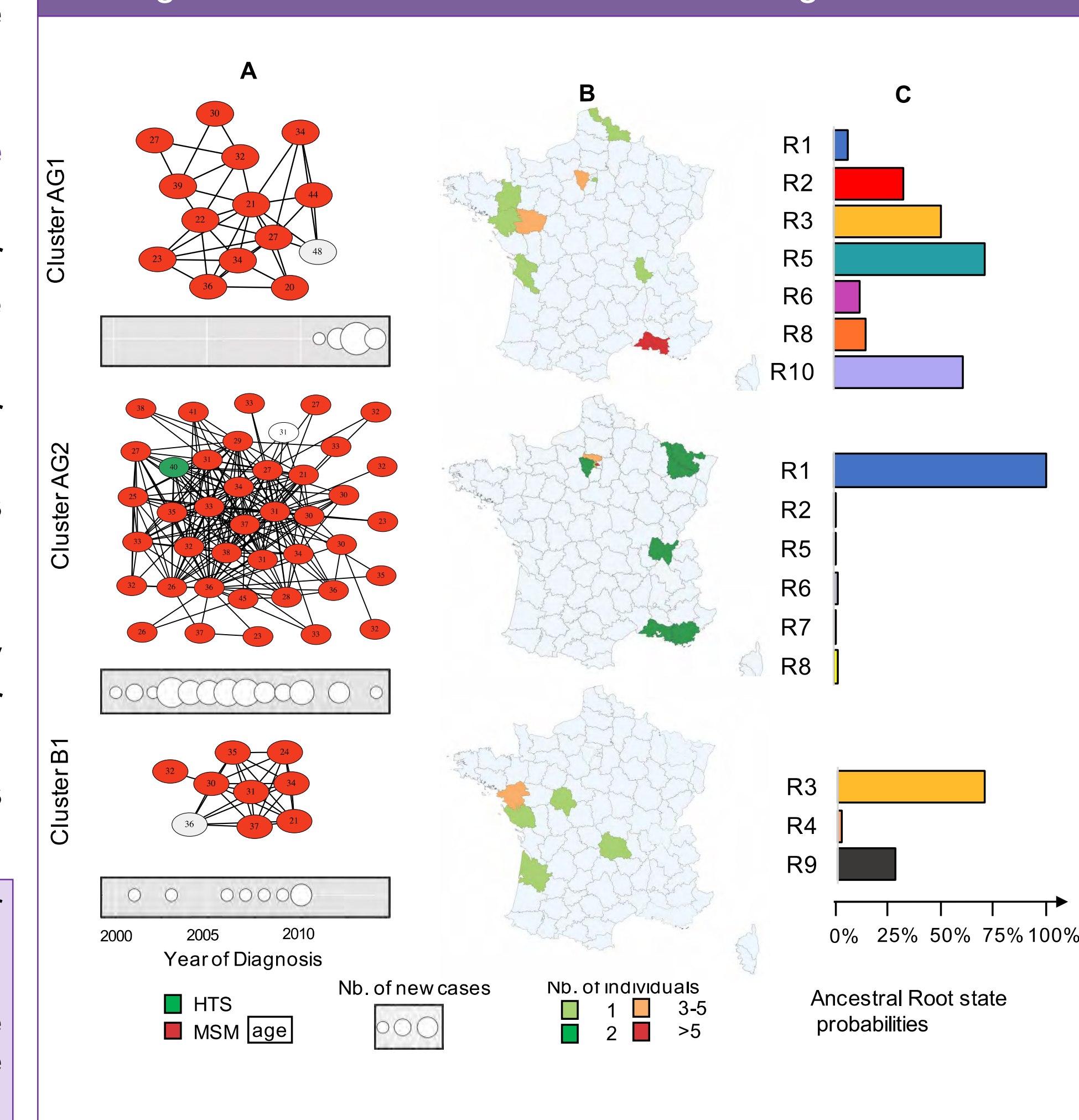
The likelihood to be involved in a cluster significantly increases overtime (chi-square test for trend, *p*<0.01).

Phylogeographic analyses found a higher density of CRF02_AG clustering among participants residing in Paris area versus those living outside Paris area (*p*<0.01)(Fig.1).

Evolutionary analyses revealed that HIV-1 CRF02_AG epidemic arose more recently (time from the most common ancestor [TMRCA]=17.3 years, among individuals with PHI in France than subtype B lineages (TMRCA=26.4 years) (Fig. 1).

Figure 2. A. Transmission network of the three larger cluster AG1 (n=14), AG2 (N=41) and B1 (n=9) and evolution of the main clusters over the study period. B. Map representing the location of residence of the clustering individuals C. Ancestral root state probabilities.

Figure 2. Characteristics of the three larger clusters



Conclusions

The rapid diffusion of CRF02_AG in highly connected networks of MSM could lead to a substantial and rapid reshaping of the HIV epidemic in Western Countries. Targeting prevention efforts based on network connectivity may be an efficient way to deliver prevention interventions.

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