

HIV Transmission Networks Among the USA, Mexico and Central America

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Background

- The role of migration in shaping genetic diversity of viral populations has been well established.
- We show results of a large collaborative effort to assess epidemiological networks and dispersion routes between the HIV epidemics in the United States, Mexico and Central America, including Guatemala, Belize, Honduras, El Salvador, Nicaragua and Panama.

Methods

- We analyzed 12,595 HIV-1 pol sequences collected from Mexican and Central American national HIV sequence databases, and local databases located at the University of North Carolina and the University of California, San Diego.
- Sequences were aligned to the reference sequence HXB2. We then estimated Tamura-Nei (TN) 93 pairwise genetic distances among all sequences.
- A putative transmission linkage was inferred when two sequences were found to be $\leq 1.5\%$ divergent calculated using the TN93 distance.
- We then constructed transmission clusters by linking sequences through shared potential transmission partners.
- Clustering information and demographic information were plotted geographically using ArcGIS (ESRI, Redlands, CA).
- Maximum clade credibility phylogeny of selected clusters was inferred using the BEAST software package (V1.8.1).
- Differences between groups were analyzed using the Pearson's χ^2 test for categorical variables, and the Kruskal-Wallis Test for continuous variables. We used logistic regression models to evaluate characteristics associated with cluster membership.

Results

- In total, 2,866 (23%) sequences had an inferred potential transmission partner in the network, comprising 1,031 distinct transmission clusters.
- Clusters were predominately observed within a single country (986 clusters, 95.6%).
- The majority of clusters were located within highly represented countries (USA 39.2%, Mexico 33.8%).
- Most clusters were pairs (71.2%) while only four clusters included more than 20 members.
- Only 45 (4.5%) clusters included sequences isolated from at least two individuals in different countries.
- Of sequences in clusters, 878 (31%) were linked to a sequence sampled from another city/state, with highest rates of these “trans-regional” links in Guatemala(47%) and Mexico (43%), compared to the US (17%) [$P<0.001$]
- Fourteen clusters included linkages between sequences isolated in San Diego and in Mexico (mainly Tijuana).
- Factors associated with cluster membership, both in bivariate and multivariate models, included residence in Mexico or Guatemala, MSM risk factor, younger age, higher CD4 T cell counts, higher HIV VL and more recent sampling date.
- Using a multivariate model, factors associated with membership in a transnational cluster included residence in Mexico, younger age, more recent sampling year and higher HIV VL.
- Similar findings were seen for trans-regional clusters.
- Risk factors for HIV acquisition were mostly heterosexual risks in Guatemala, Honduras, Nicaragua and Panama.
- MSM transmission predominated in most Mexican states (mainly Veracruz, Tabasco, Campeche, Yucatán, Michoacán, Mexico City and Puebla) and at USA sites.

Table 1. Description of Study Population

Variable

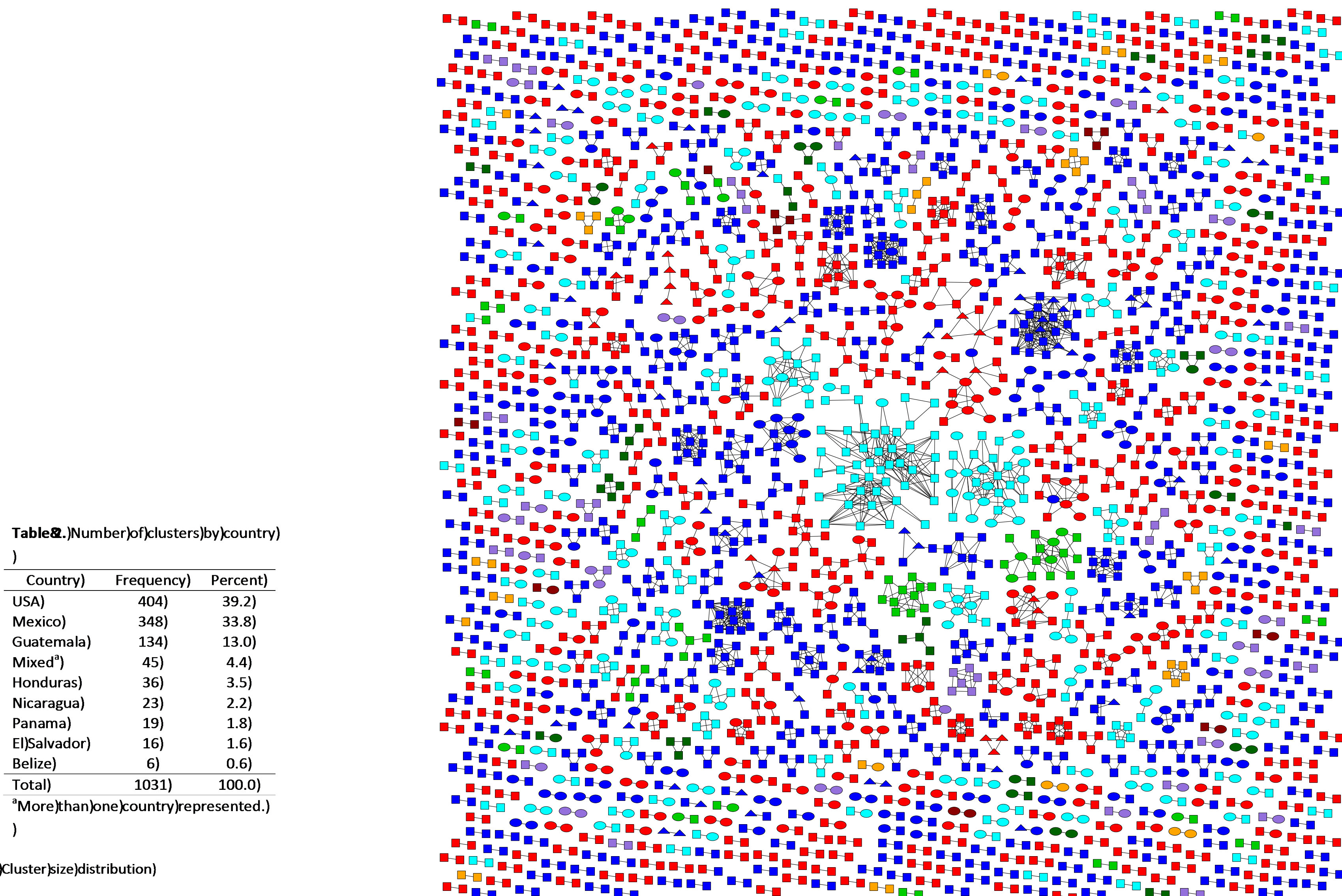


Figure 1. Cluster analysis for 12,595 *pol* sequences from the USA, Mexico and Central America. Tamura-Nei (TN) 93 pairwise genetic distances were calculated between all sequences and linkages were inferred between those $\leq 1.5\%$ apart. Multiple linkages were resolved into clusters. 1,031 clusters were identified. Nodes are shaded by country of origin. Squares, males; ovals, females.

Table 2. (Number of clusters by country)

Country	Frequency	Percent
USA	404	39.2
Mexico	348	33.8
Guatemala	134	13.0
Mixed*	45	4.4
Honduras	36	3.5
Nicaragua	23	2.2
Panama	19	1.8
El Salvador	16	1.6
Belize	6	0.6
Total	1031	100.0

*More than one country represented.)

Table 3. (Cluster size distribution)

Cluster Size	Frequency	Percent	Cumulative Percent
2)	734	71.2	71.2
3)	147	14.3	85.5
4)	66	6.4	91.9
5)	28	2.7	94.6
6)	16	1.6	96.1
7)	9	0.9	97.0
8)	5	0.5	97.5
9)	9	0.9	98.4
10)	4	0.4	98.7
11)	4	0.4	99.1
12)	2	0.2	99.3
13)	2	0.2	99.5
16)	1	0.1	99.6
24)	1	0.1	99.7
25)	1	0.1	99.8
29)	1	0.1	99.9
45)	1	0.1	100.0
Total	1031	100	

Table 4. Bivariable associations with clustering

Variable

year, and higher HIV RNA remain significant.

e recent sampling

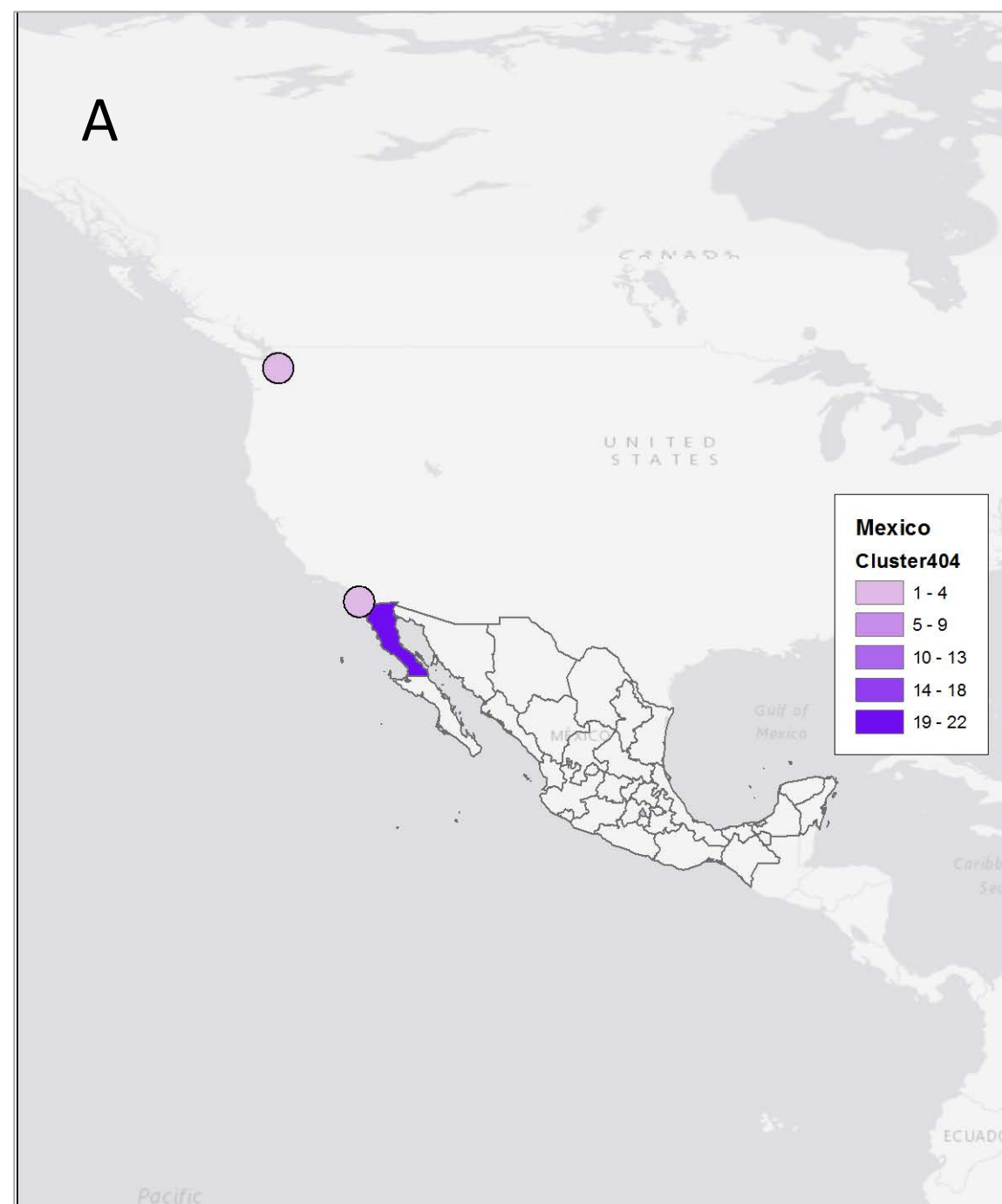
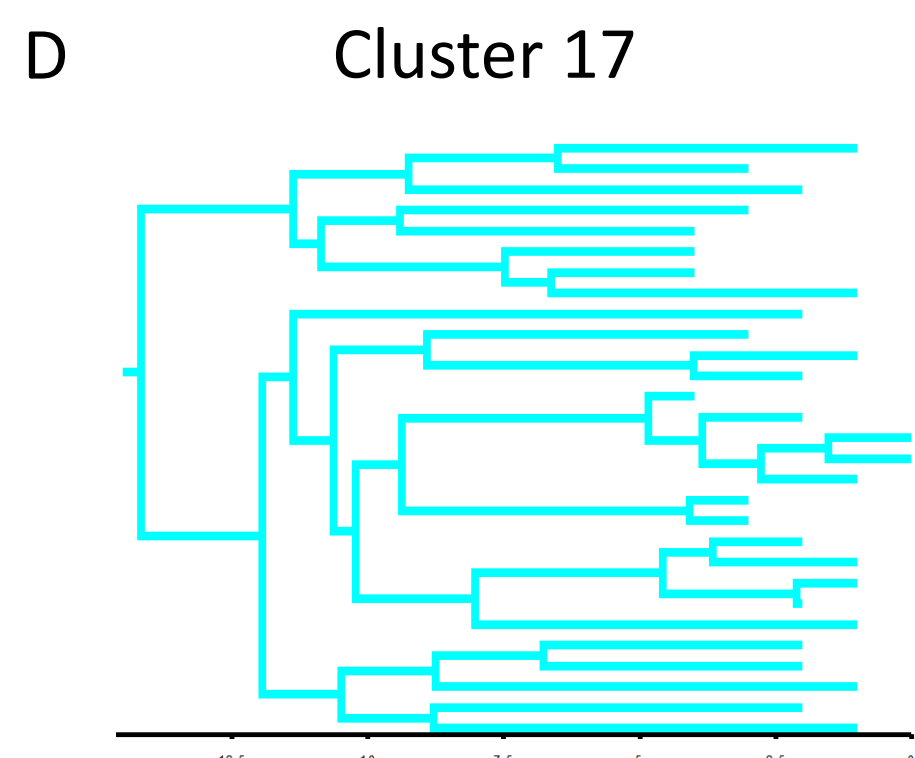
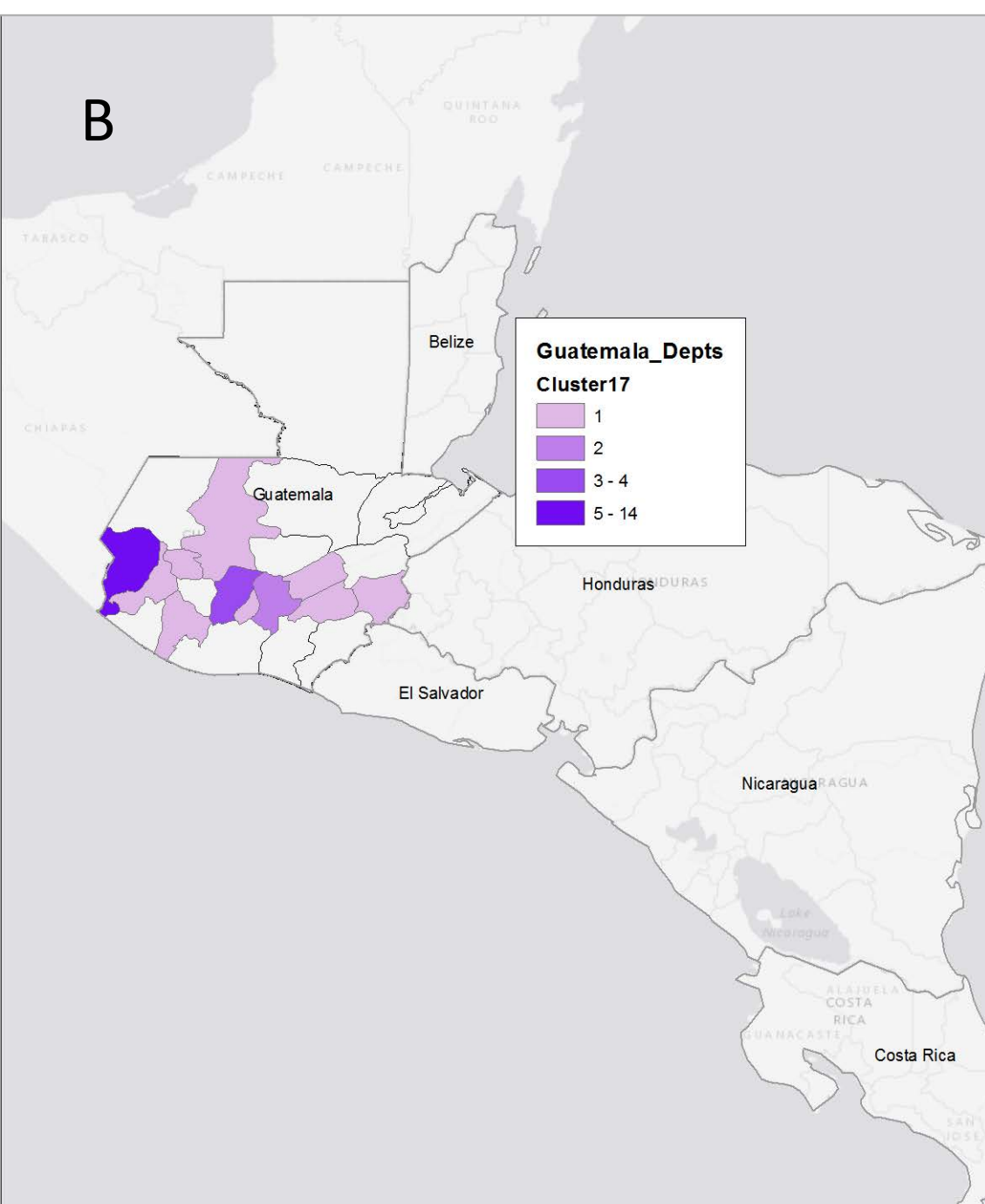


Figure 3. Geographic distribution and MCC trees of the largest inferred transmission clusters. A. Cluster 404 (n=25); B. Cluster 17 (n=29); C. Cluster 31 (n=45). Cluster 404 represents a USA-Mexico transnational cluster and Clusters 17 and 31 represent Guatemalan national clusters. Below maps are MCC trees of clusters with diversification timeline. D. Cluster 17 (n=29); E. Cluster 31 (n=45); F. Cluster 339 (n=24), USA is shown separately. Timeline in years.

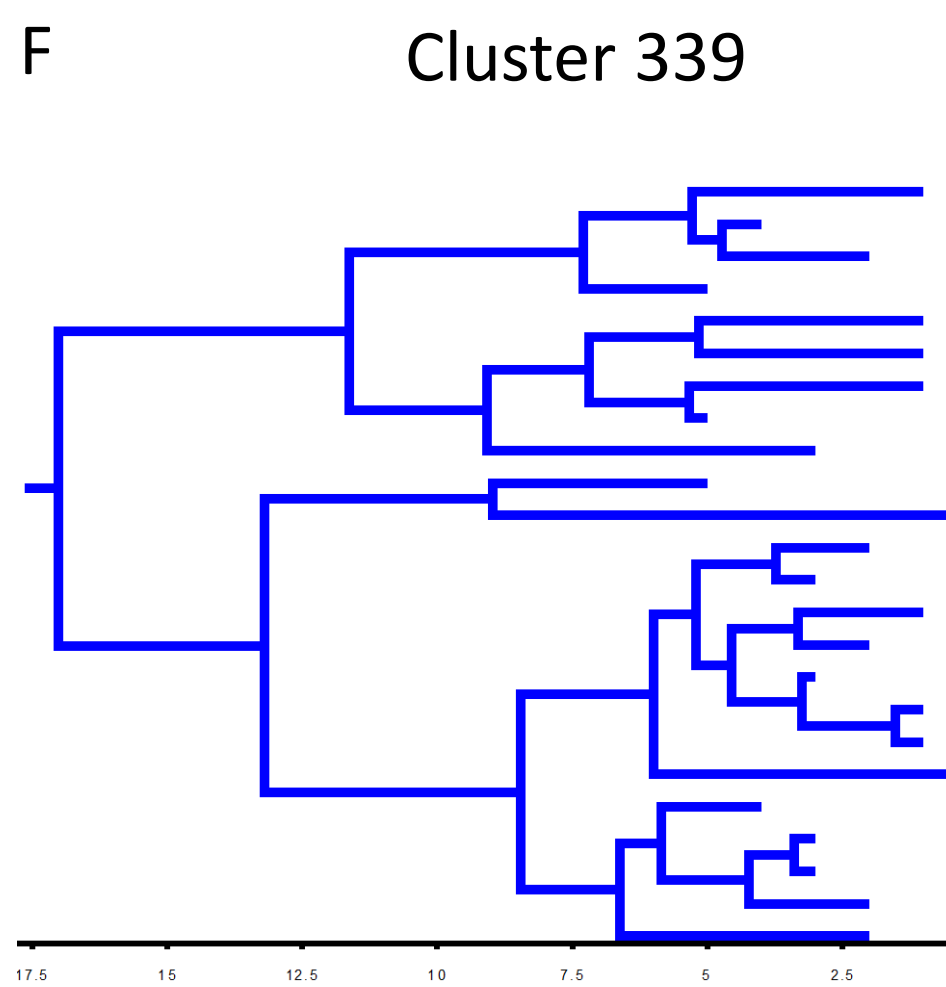
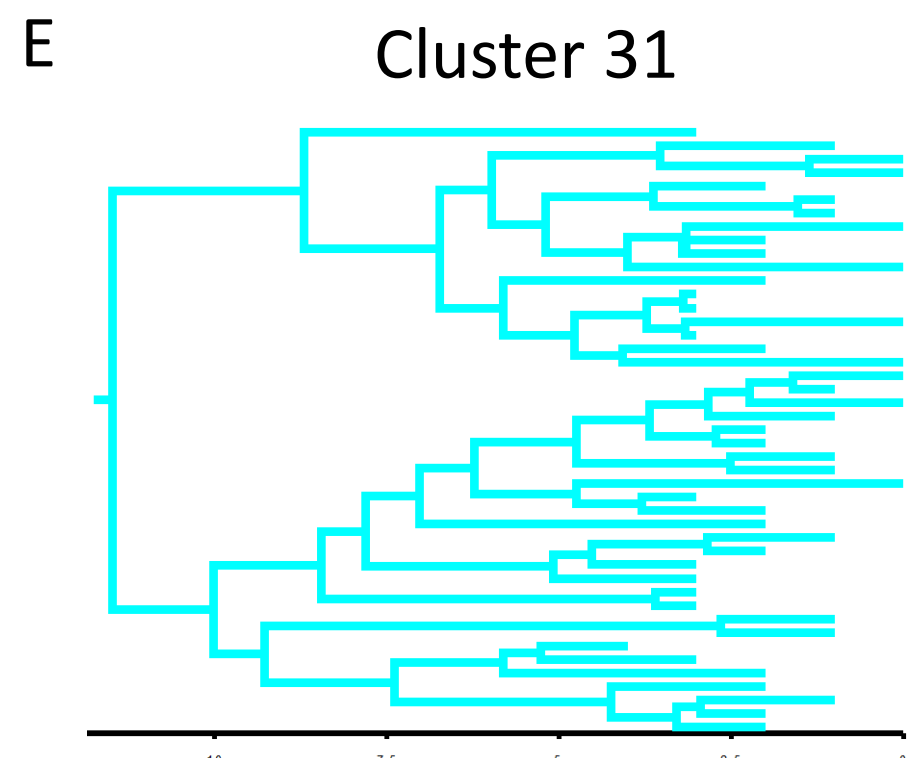
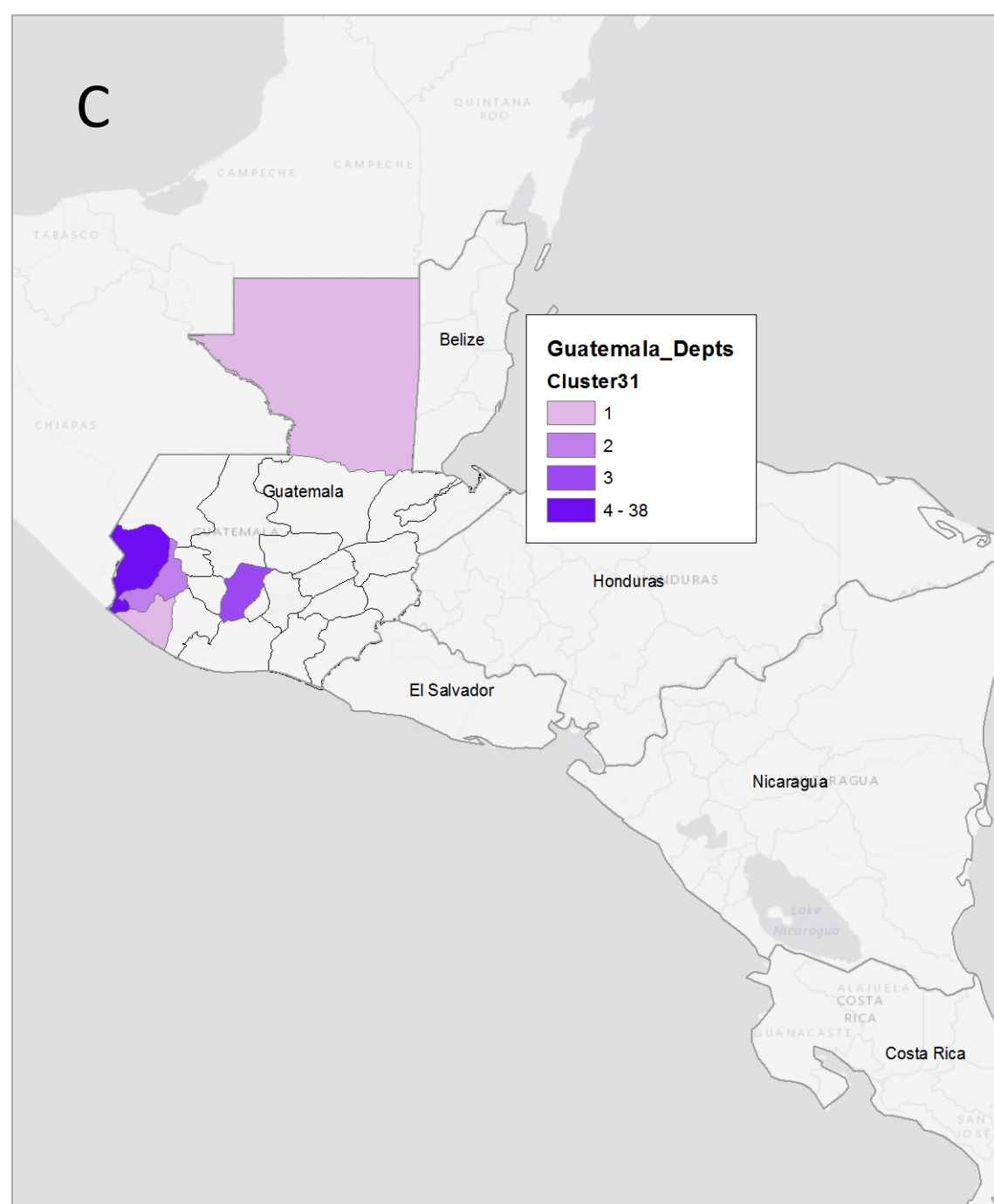
Table 5. Description of Large Clusters

Variable

ed in Baja California (mainly Tijuana), 1 in Distrito Federal.



*Cluster 339 is not represented geographically as all sequences are from San Diego
** A MCC tree is not presented for cluster 404 as convergence was not achieved.



Conclusions

- Our work underlines the importance of political and cultural barriers in HIV transmission among the USA, Mexico and Central America, with most transmission events occurring within countries.
- Nevertheless, the presence of international connections was observed at rates similar to other published work. These viral migrations may be important in influencing the spread and diversity of HIV in the region.

Funding

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