

Background

- Although the overall HIV prevalence in Haiti has been stable around 2% for the past 15 years, the prevalence in high risk groups, such as men having sex with men (MSM) and female sex workers (FSW), is much higher, 12.9% and 8.7% respectively.
- Understanding the dynamic of HIV transmission in high-risk groups and targeting the drivers of the epidemic are key to streamline prevention and treatment efforts.

Objective

To characterize the dynamics of HIV transmission among persons living with HIV from high risk groups in Haiti and viral dispersal across the Caribbean.

Methods

- Sampling and cohort.** A total of 119 HIV-1 pol sequences were sampled and analyzed from MSM, FSW and their sexual partners (FSWP) enrolled in 7 healthcare centers in Port-au-Prince, Haiti.
- HIV Transmission network analyses.** Genetic-distance based network analyses were performed to infer putative relationships between HIV-1 partial pol sequences. We used HIV-TRACE software (HIV TRANsmission Cluster Engine: www.hivtrace.org) to infer transmission links between sequences with a genetic distance $\leq 1.5\%$ [1].
- Drug Resistance Mutations.** Screening for HIV drug resistance mutation (DRM) was estimated using the Stanford algorithm (<http://hivdb.stanford.edu>). Shared DRM were defined as DRM present in genetically linked individuals.
- Phylogenetic analysis and subsampling (Fig. 1).** We first performed a phylogenetic analysis combining the Haitian sequences with 3,908 publicly available HIV-1 pol sequences from the Caribbean's and 33,100 sequences from the rest of the world. The purpose of this preliminary analysis was to identify supported monophyletic clades sampled from the Caribbean region. We then subsampled these supported monophyletic clades (≥ 3 sequences) by randomly keeping 1 sequence from each identified cluster.
- Discrete phylogeographic inferences.** Phylogeographic inferences were performed using the discrete diffusion model [2] implemented in BEAST 1.10 [3].
- Generalized Linear Model (GLM) analysis.** GLM analyses were performed to investigate the potential contribution of a series of predictive variables to the dispersal rates among locations.
- Only Bayes Factors (BFs) [4] that remain significant after accounting for the sampling heterogeneity (i.e. BF adjusted) were taken into account to further reduce the false positive rate (see [5] for details).

Fig. 1. Subsampling workflow.

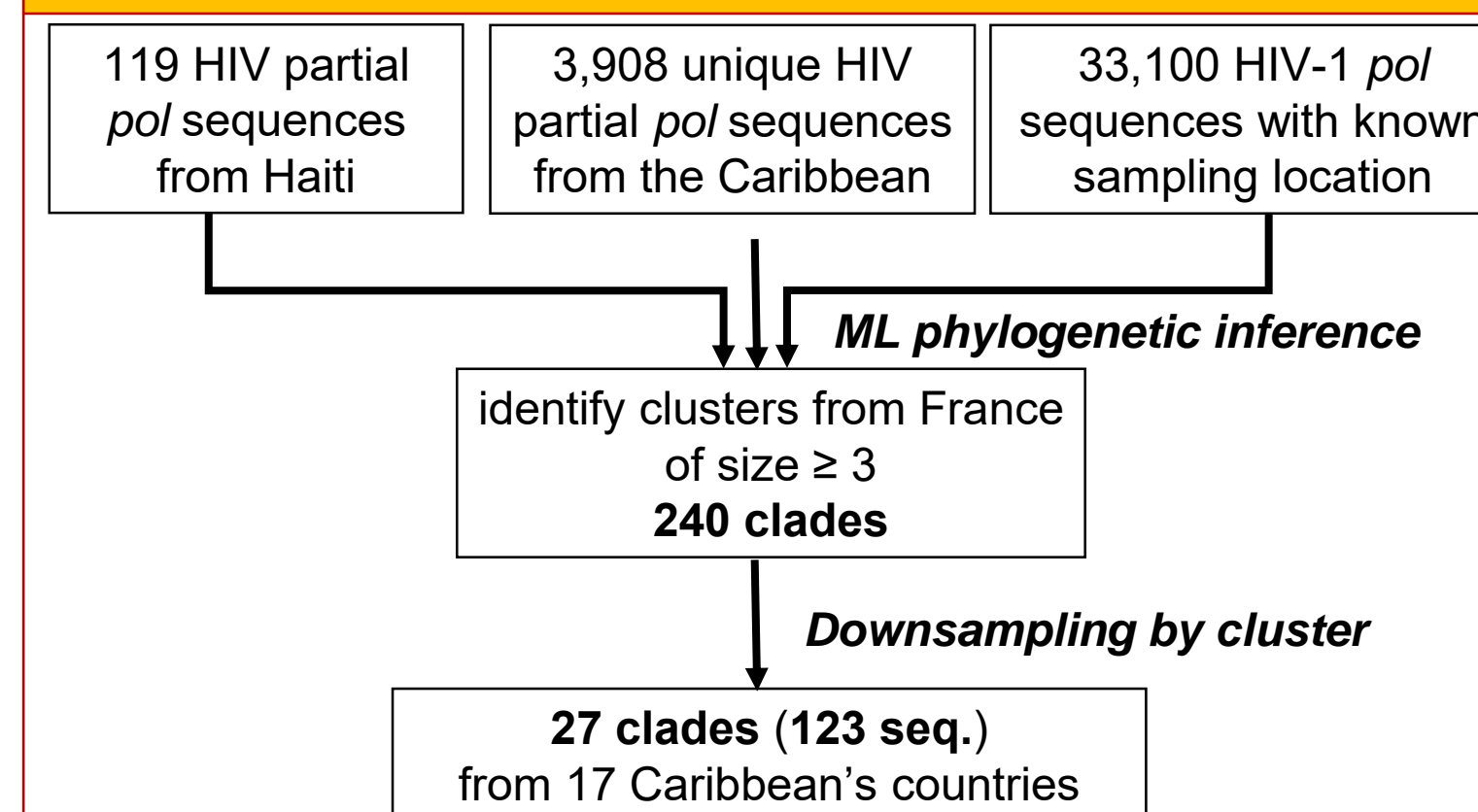
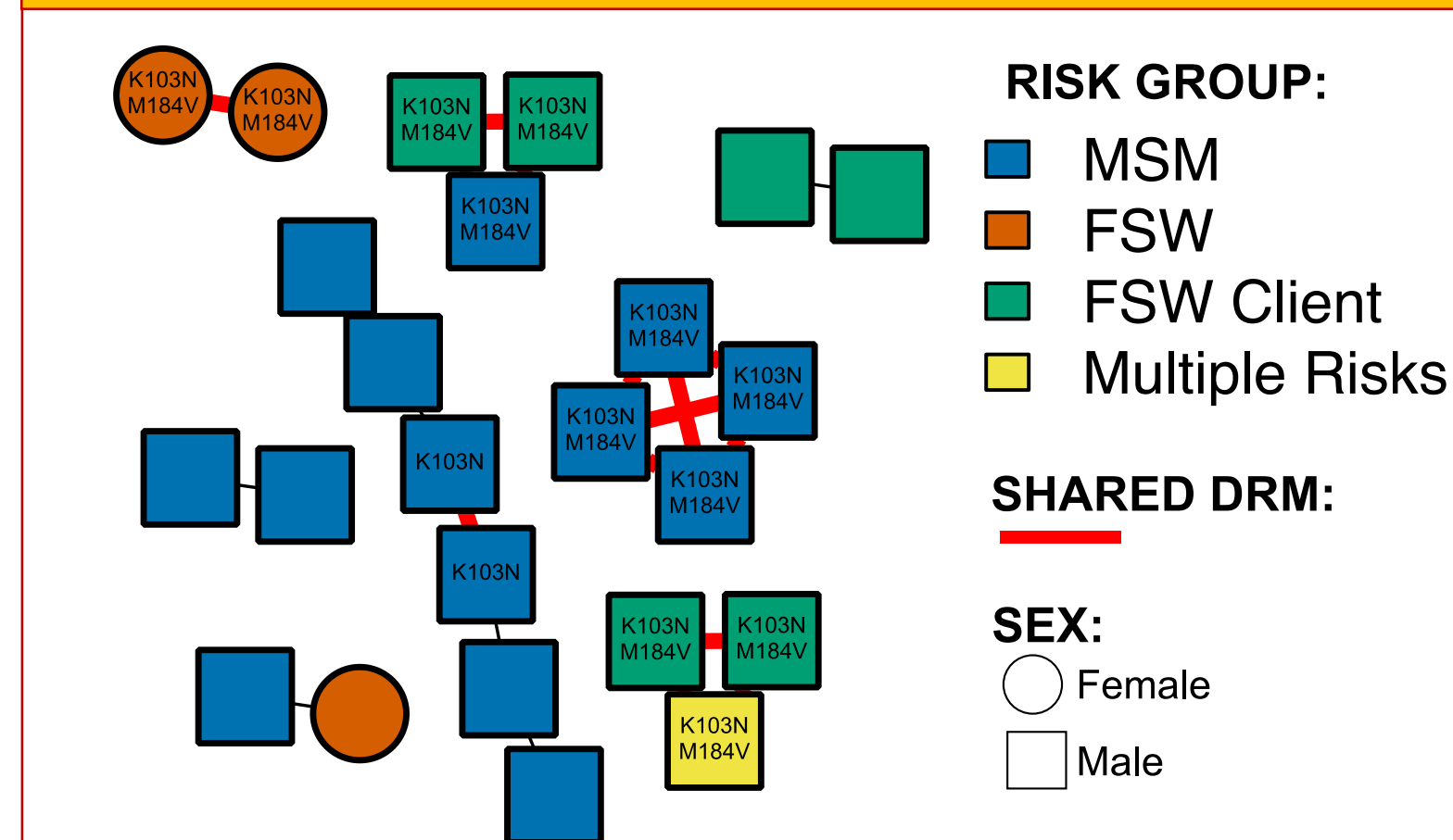


Fig. 2. HIV drug resistance transmission among genetically linked individuals.



- Transmission network analysis identified 24/119 (20.2%) genetically linked individuals forming 8 clusters (size 2-6 individuals). Five clusters had shared resistance mutations. K103N (14/24) or M184V (12/24) were the main shared DRM. The frequency of DRM did not differ between clustering and non-clustering individuals (62.5% (15/24) versus 56.8% (54/95); $p = 0.65$).
- The nodes are colored by risk group, squares and circles indicating male and female. All edges represent a genetic distance of $\leq 1.5\%$. Lines in bold red indicate individuals who shared DRMs. MSM: Men who have sex with men; FSW: Female Sex Worker.

Results

Fig. 3. Evidence of viral trafficking from the Dominican Republic toward Haiti.

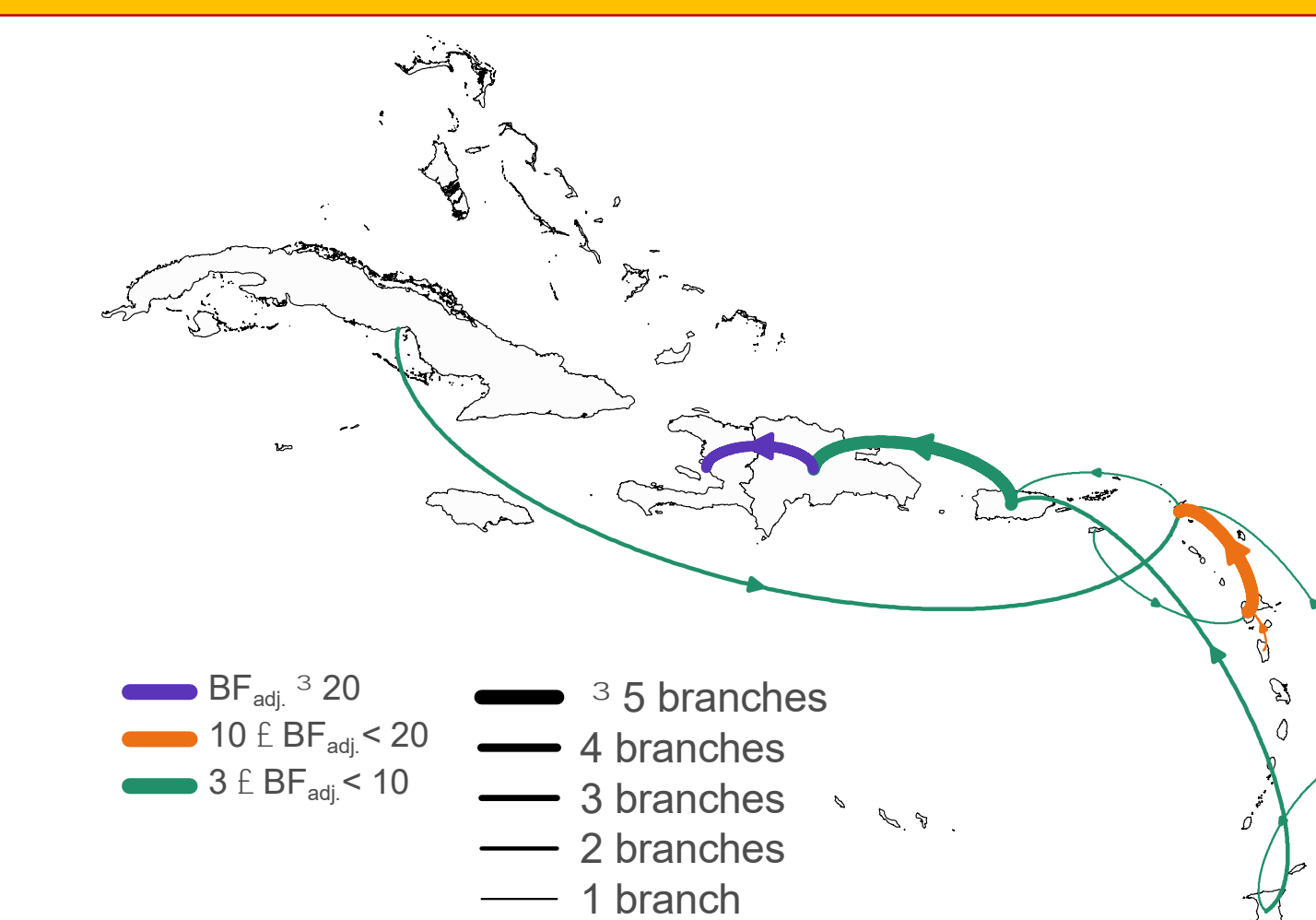


Fig 3. Number of lineage dispersal events between countries. Only transition curves that represent ≥ 2 transition events are shown.

- Population characteristics.** A total of 119 HIV-1 pol sequences were sampled and analyzed from MSM, FSW and FSWP, from September 2018 to July 2019. The majority of participants were male (74/119; 62.2%), and 75.7% of them (56/74) reported MSM as main risk factor. The overall prevalence of DRM was 57.9% (69/119). DRM was observed in 37.5% of MSM (21/56), 80% of FSWs (36/45) and 66.7% (12/18) among FSWP. Of the DRM, K103N (59/119; 49.6%) and M184V (33/119; 27.7%) were the most frequently observed.
- Discrete phylogeographic inferences** Discrete phylogeographic analysis revealed viral trafficking from the Dominican Republic (DR) toward Haiti ($BF_{adj} > 20$) but also from Puerto Rico (PR) and Trinidad and Tobago toward DR and PR respectively (Fig. 3).
- GLM analysis.** After investigating the potential contribution of predictive variables to the dispersal rates among countries in the Caribbean, we showed that countries with limited Circuitscape resistance accessibility were the most likely to show viral exchange ($BF_{adj} = 3.4$, Fig. 4).

Conclusions

- High prevalence of HIV drug resistance was observed among key populations in Port-au-Prince, Haiti.
- Network analysis revealed frequent DRM transmission among genetically linked individuals.
- This study also found that local epidemics are likely sustained by regional human migration.
- These findings provide a framework for prioritization and allocation of treatment and prevention resources.

Fig.4. Key role of local transmission in the spread of the HIV epidemic in the Caribbean.

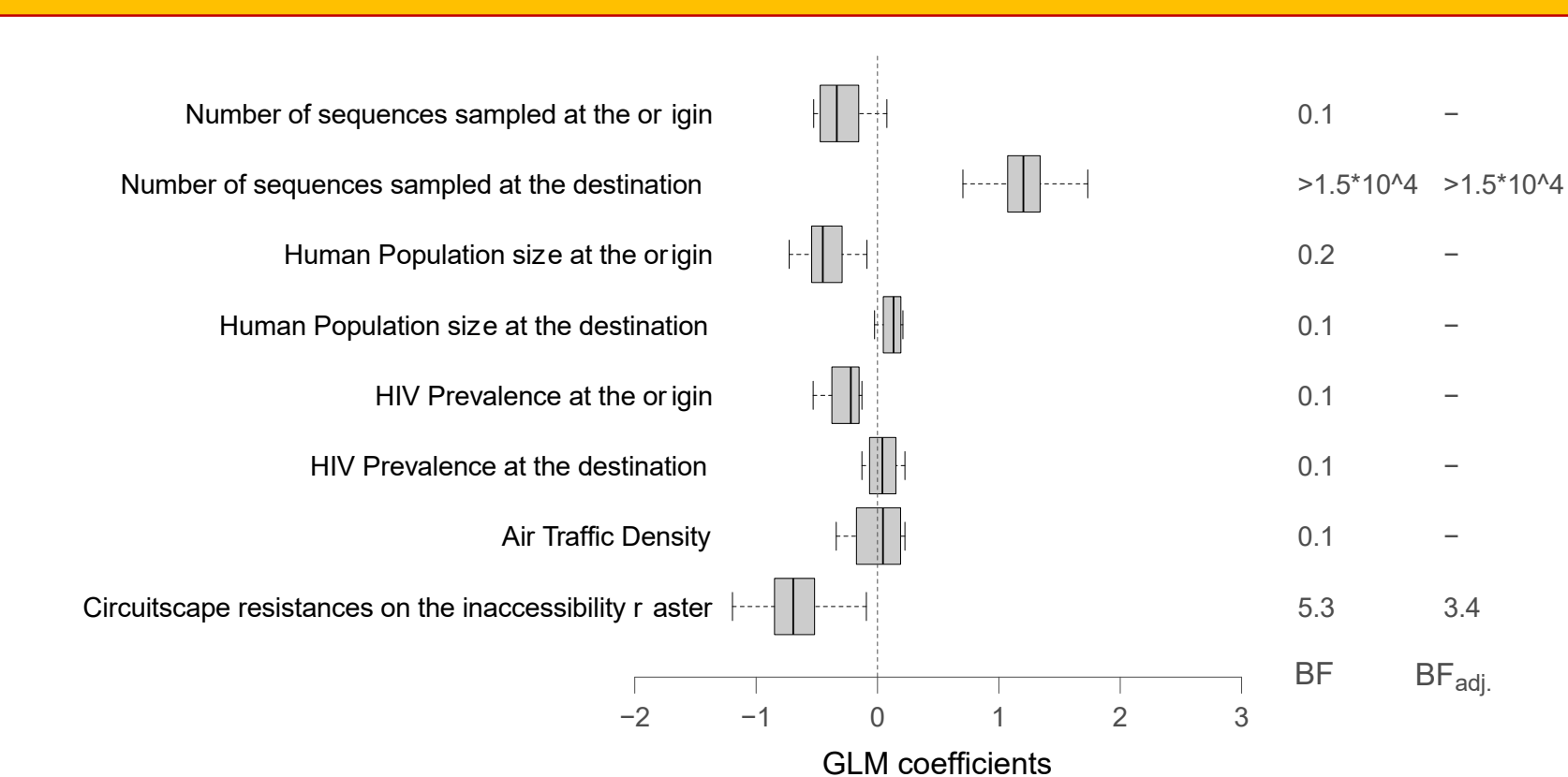


Fig 4. Box plots of the GLM coefficients for all tested predictors. Bayes factors (BF) support for inclusion of each predictor in the model is indicated in red on the right. Inaccessibility among administrative areas were computed using an algorithm based on circuit theory implemented in the program Circuitscape 4.0.5 [6].