Phylodynamic Method of Identifying HIV-1 Transmission Foci in British Columbia

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Background

- Identifying areas that are at a high risk for ongoing HIV transmission is critical for prioritization of limited public health resources to support people living with HIV and prevent new cases.
- Despite advancements in testing and treating, foci of high transmission remain, even in developed countries.
- Since transmission of HIV to a new host is equivalent to the formation of a new lineage, diversification rates inferred from viral phylogenetic trees can serve as estimates for transmission rates.
- By combining patients' diversification rates, viral load measurements, and geographic data, we built a predictive model to identify areas with high HIV-1 incidence that are expected to experience ongoing transmission.

Methods

We applied this method to 1,685 HIV-1 sequences from 1,188 anonymized patients living in British Columbia, Canada between 2008 and 2013. The data were split into three 2-year time intervals in order to build three approximate maximum likelihood phylogenetic trees using FastTree2.1 from which the diversification rates were calculated (**Figure 2**). The diversification rate (DR) for each tip is the reciprocal sum of its branch lengths from root to tip, weighted by the distance of the branch from the root. To maintain patient confidentiality, census tracts were merged with proximate census tracts until no fewer than five patients resided in that polygon in any time interval for a final 57 merged census tract polygons. Longitudinal summary statistics were generated for merged census tracts of patient residence. HIV incidence in each merged census tract was estimated using the date of patients' first viral load measurement. Mean age, proportion male, and other risk factors were also estimated for each merged census tract. A predictive multiple linear regression model was trained using data from the 2008-2009 time interval. The model was then tested on the subsequent time intervals (2010-2011, 2012-2013) by comparing each merged census tract's predicted HIV incidence rank with its observed HIV incidence rank. Ethical approval for this study was granted by the Providence Health Care/ University of British Columbia Research Ethics Board.

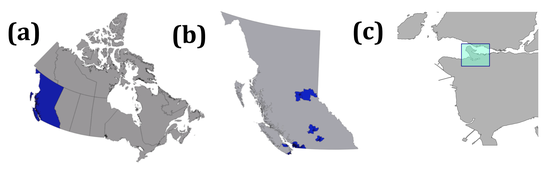

Figure 1. The study area is based in **(a)** British Columbia (BC), Canada and includes **(b)** all census tracts. **(c)** Subsequent maps depict downtown Vancouver.

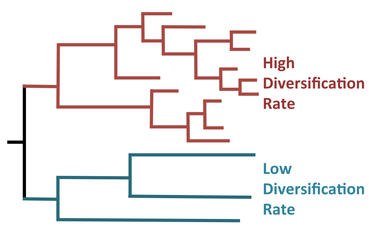

Figure 2. The diversification rate for each tip on a viral phylogenetic tree estimates the between-host transmission rate based on weighted branch lengths.

Results

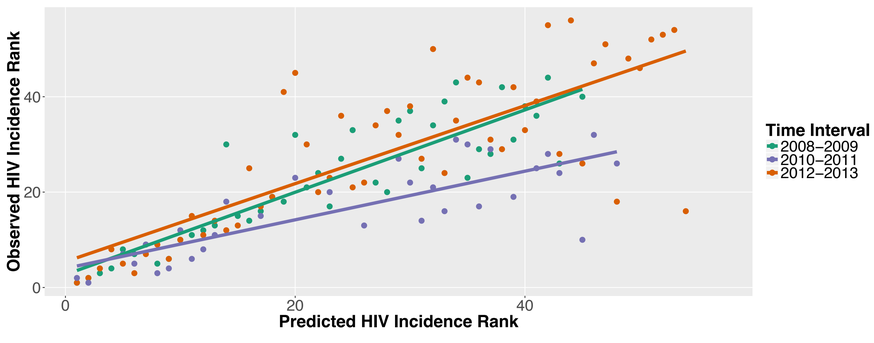

Figure 3. A predictive spatial regression model was fit using log10(diversification rate), and log10(viral load) to predict cumulative HIV incidence. The 2008-2009 time interval was used to train the model and then the data was tested on the subsequent time intervals (2010-2011, 2012-2013). The predicted rank, where 1 is the highest incidence in the time interval, was compared to the observed rank for each merged census tract's cumulative incidence. The predictive fit was evaluated for each time interval separately: R^2= 0.64 for 2008-2009, R^2=0.62 for 2008-2009, and R^2=0.80 for 2012-2013.

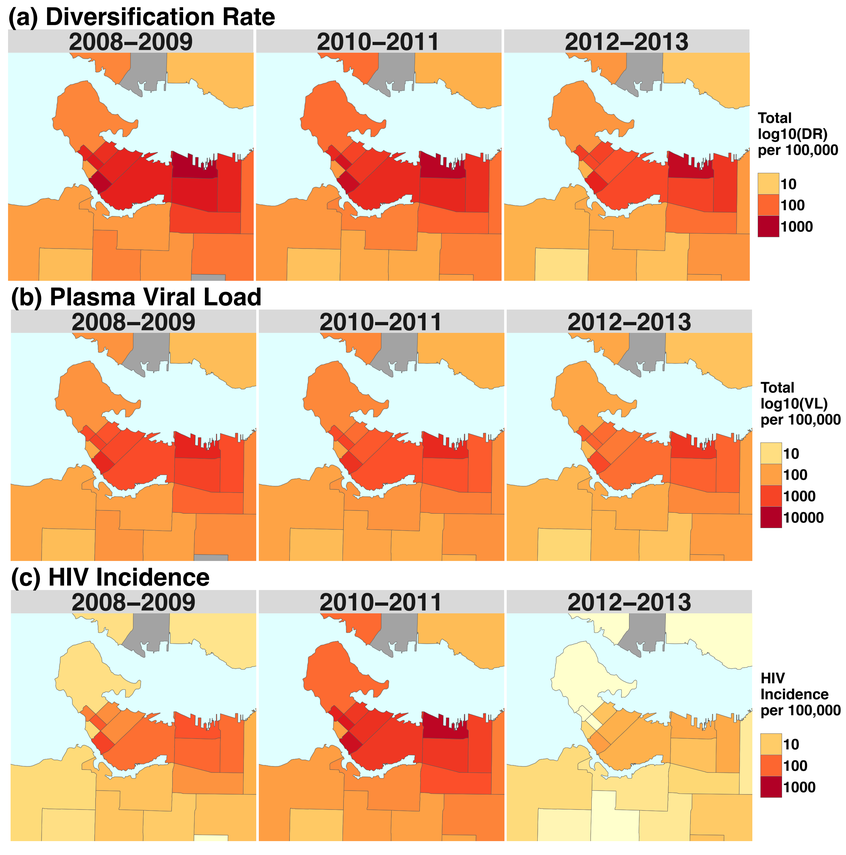

Figure 4.The spatial and temporal distributions of **(a)** diversification rate, **(b)** plasma viral load, and **(c)** HIV incidence in downtown Vancouver are log normal across all time intervals at the merged census tract level. **(a)** The diversification rate shown is the sum of the $\log_{10}$ (diversification rate) across all patients residing in each merged census tract, normalized to the entire merged census tract population as measured in the most recent census. **(b)** The plasma viral load is the sum of the $\log_{10}$ (plasma viral load) across all patients residing in each merged census tract, normalized to the entire merged census tract population as measured in the most recent census. **(c)** The HIV cumulative incidence is the sum of all individuals with a first detectable viral load (>10^2) in BC within each 2-year time period, normalized to the entire merged census tract population as measured in the most recent census. The plasma viral load and diversification rate for each patient in each time interval correspond to the earliest detectable viral load and available sequence in the time interval.

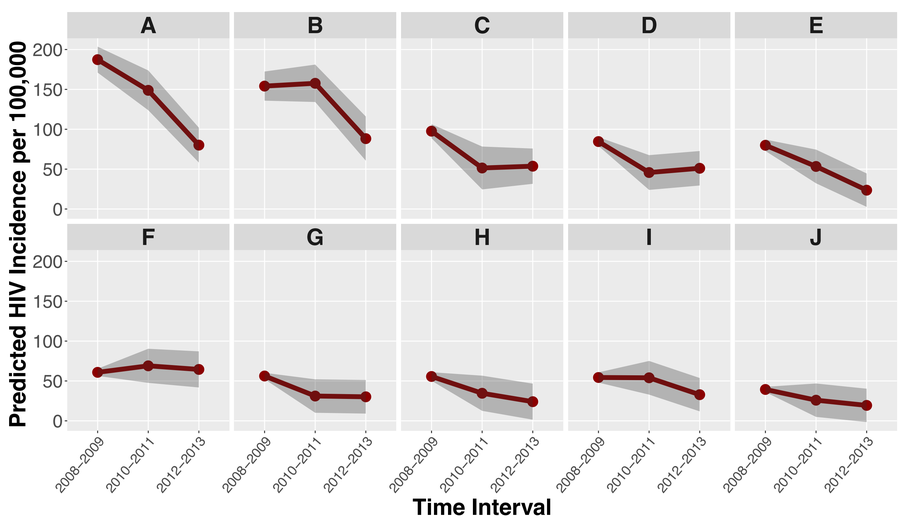

Figure 5. The predicted cumulative HIV incidence over time for the merged census tracts **A-J** with the top 10 predicted values in 2010-2011. Shaded regions indicate the 95% predictive interval. Predicted incidence decreased from 2008-2009 to 2012-2013 in nearly all merged census tracts.

Conclusions

- Areas that are home to people living with HIV who have simultaneously high viral load and HIV transmission rates, as measured by phylogenetic diversification rate, have high cumulative HIV incidence.
- By aggregating data by patients' census tract of residence, studies of the temporal and spatial distribution of phylogenetic and clinical traits of HIV can identify areas at risk of ongoing transmission.
- Phylogenetic data can complement traditional epidemiological data by providing insight into temporally-informed between-host evolution.
- Foci of high HIV-1 transmission remain active in developed countries that approach the 90-90-90 target.

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