Differential reductions in HIV clusters' effective reproductive ratio following population level interventions in British Columbia, Canada

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Background

- Phylogenetic analyses of viral genetic sequences offer a means of evaluating the impact of interventions on epidemic dynamics within subpopulations.
- Key HIV interventions in British Columbia (BC), Canada.
  - 1996: highly active antiretroviral therapy (HAART)
  - 2006: Treatment as Prevention (TasP), HAART free-of-cost for any CD4 count
  - 2017: Targeted-PrEP (T-PrEP) for individuals at highest risk
  - 2018: PrEP available free-of-cost (rapid uptake with ~5700 clients at end of 2019)
- We applied Bayesian phylodynamic modelling to test the hypothesis that declines in cluster-specific effective reproductive ratio (R_e) in the largest HIV phylogenetic clusters would follow the wide-scale availability of HAART and PrEP

Methods

- 37,304 HIV partial pol sequences from 9,848 people living with HIV in BC in the Drug Treatment Program between 1996 and Feb 2019 => 100 ~max. likelihood phylogenies.
- Identified clusters with at least 5 individuals with pairwise patristic distance <0.02 subs/site supported by >90% of phylogenies (methodology as in Poon *et al.* 2015).
- Focused on the four largest clusters in Feb 2019: two predominantly included people who inject drugs (PWID), two were primarily men who have sex with men (MSM).

Table 1. Characteristics of the four largest phylogenetic clusters in BC in Feb 2019.

Cluster size	Predom	MSM	PWID	HET	Male	Female	Trans	Median birth year	Median year first VL
108	MSM	64	10	7	91	0	0	1980	2013
114	PWID	6	93	50	79	28	2	1962	1999
136	MSM	76	14	8	128	0	0	1979	2013
333	PWID	15	250	120	194	121	2	1965	2002

- Analyzed each cluster in birth-death skyline serial model in BEAST2 (Stadler *et al*. 2013) to evaluate temporal changes in R_e in relation to the availability of HAART and PrEP.
- R_e = transmission rate / (host recovery/death rate + sampling rate)
- Specified a relaxed uncorrelated LN clock, strict priors for the period of infectiousness (with a rate shift in 1996), 20 equally-spaced intervals for R_e.
- Ran MCMC for 500M steps with states logged every 10,000 steps. Used Tracer to confirm convergence (ESS>200) after 10% burn-in.

Results

Table 2. The true cluster sizes (including individuals outside the BC cohort) were estimated using the inferred sampling proportion in 2018.

Observed cluster size	Mean sampling proportion	Estimated cluster size Feb 2019
108	0.127	850
114	0.184	620
136	0.317	429
333	0.091	3,659

Results

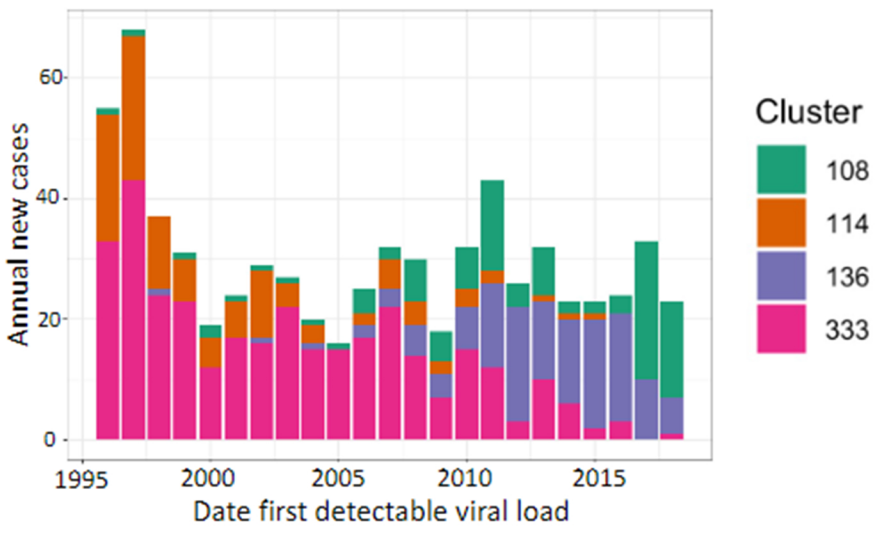

Figure 1. New cases added to the four largest phylogenetic clusters between 1995 and 2019, estimated by the date of first detectable plasma viral load.

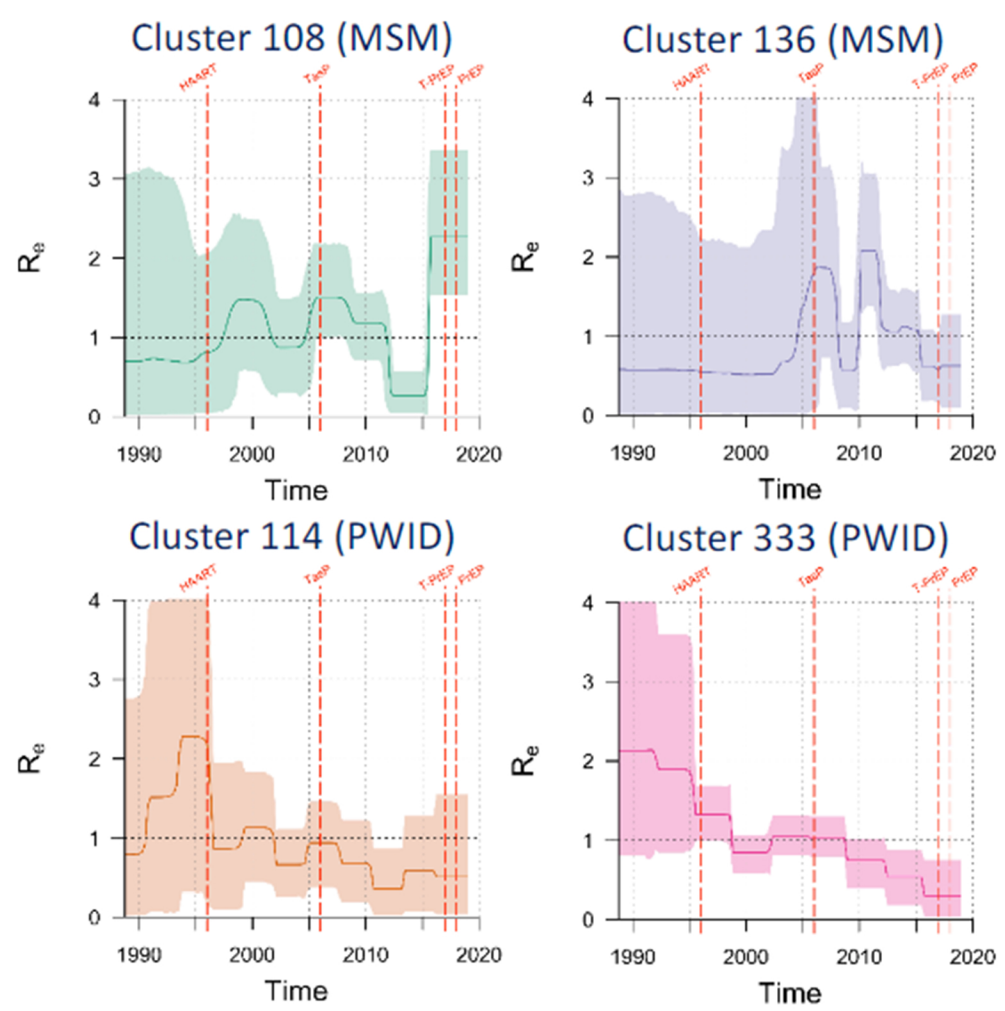

Figure 2. The effective reproductive ratio (R_e) over time for the four largest phylogenetic clusters in relation to the availability of HAART, TasP, T-PrEP, and PrEP.

- PWID clusters "114" and "333" grew most rapidly in mid-1990s, attaining maximum R_e >2, then declined steadily since the availability of HAART, with R_e<1.0 since ~2010.
- R_e of MSM cluster "136" has declined since its peak in 2012 at 2.3 (1.4-3.3), with R_e<1.0 since 2015.
- In contrast, growth of MSM cluster "108" peaked in early 2019 with R_e=2.5 (1.8-3.5), after availability of PrEP.

Conclusions

- Transmission dynamics within HIV phylogenetic clusters in BC varied amid widespread availability of PrEP, illuminating subpopulations in need of enhanced connection with treatment and prevention services.
- In light of non-identifiability of birth-death-sampling models for serially-sampled trees (Louca *et al.* 2021), need to ensure robust priors for removal and sampling rates and validate estimates using an alternative model strategy.

References

Poon, A. F. Y. et al. The Impact of Clinical, Demographic and Risk Factors on Rates of HIV Transmission: A Population-based Phylogenetic Analysis in British Columbia, Canada. J INFECT DIS 211, 926–935 (2015).

Stadler, T. et al. Birth–death skyline plot reveals temporal changes of epidemic spread in HIV and hepatitis C virus (HCV). PNAS (2013). doi:10.1073/pnas.1207965110.

Louca et al. Fundamental identifiability limits in molecular epidemiology. Molecular Biology and Evolution. (2021). doi: 10.1093/molbev/msab149

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