HIV cases averted in phylogenetic clusters via pre-exposure prophylaxis in British Columbia, Canada

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BACKGROUND

- Monitoring HIV phylogenetic cluster growth informs evaluations of public health interventions' effectiveness.
- Pre-exposure prophylaxis (PrEP) effectively prevents HIV acquisition and is a key pillar for ending the epidemic.
- In British Columbia (BC), Canada, PrEP has been provided free of charge since 2018, but there have been disparities in eligibility and potential barriers to access and adherence, as PrEP options have not been equally evaluated or proven as effective in all populations.
- We hypothesized that widespread PrEP availability in BC since 2018 has averted new HIV cases heterogeneously across phylogenetic clusters, with more cases averted in clusters comprising mostly gay, bisexual, and other men who have sex with men (gbMSM), compared to people who inject drugs (PWID).

METHODS

- Data obtained February 9, 2023 for **10,740 participants in the BC Centre for Excellence Drug Treatment Program**
- Aligned **42,043 HIV partial pol sequences** individuals to the HXB2 ref. with minimap2[1]; masked codons of known surveillance drug resistance mutations (Stanford HIVdb[2])
- **100 bootstrap approx. maximum likelihood phylogenetic trees** inferred in FastTree2.1[3], outgroup rooted to oldest subtype B sequence in the data (other outgroups compared)
- **Identified phylogenetic clusters** with 5 or more members with pairwise tree distance less than 0.02 subs/site in >90% of bootstraps[4]
- **Calculated growth rates and effective reproduction numbers (Re) using line list new diagnoses over time in EpiEstim**[5] for i) all BC, ii) key risk populations, and iii) actively growing clusters (new case since 2018)
  - Gamma-distributed serial interval with mean 0.5, 1, or 2 yr; stdev 0.25, 0.5, or 1 yr (shown: m=1, sd=0.5, smooth k=1)
- **Compared periods before and after PrEP availability:**
  - Jan 2016-Dec 2017: Preceding PrEP availability
  - Jan 2018-Feb 2020: Following PrEP, before COVID-19
  - Mar 2020-Feb 2022: With PrEP, during COVID-19
- **Counterfactual estimation of cases averted via PrEP** for actively growing phylogenetic clusters:
  1) Calculated growth rates and Re preceding PrEP
  2) Fit deterministic (shown) and stochastic branching processes to each cluster to estimate expected cases without PrEP
  3) Averted cases = expected (w/o PrEP) – observed (w/ PrEP)

References: 1. Li, H. (2018) https://doi.org/10.1093/bioinformatics/bty191. 2. Bennett, D. E., et al. (2009) https://doi.org/10.1371/journal.pone.0004724 3. Price, M. N., et al. (2010). https://doi.org/10.1371/journal.pone.0009490
4. Poon, A., et al. (2016). https://doi.org/10.1016/s2352-3018(16)00046-1 5. Cori, A., et al. (2013). https://doi.org/10.1093/aje/kwt133

Widespread availability of PrEP in British Columbia, Canada since January 2018 averted 2-4 new HIV cases per month in large, gbMSM-predominant phylogenetic clusters

RESULTS

Reduction of effective reproduction number (Re) in gbMSM population following PrEP availability

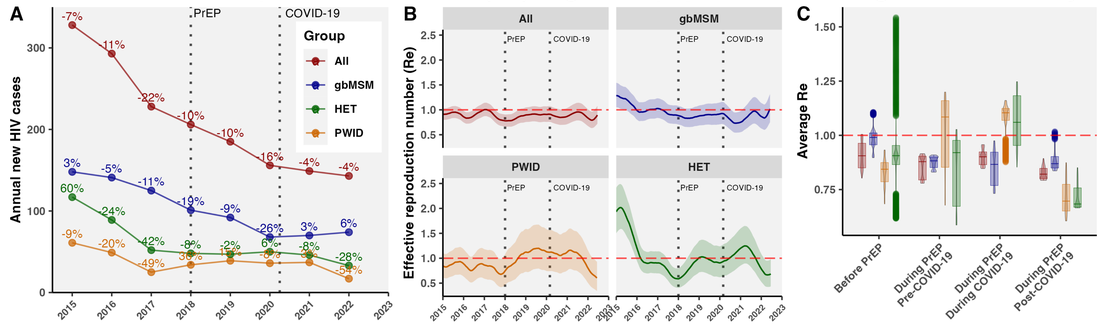


Fig. 1. HIV epidemiological dynamics of British Columbia from 2015 to 2023 in the context of PrEP. **A)** Annual new HIV cases (based on first ART date) overall and in key risk groups, gbMSM (gay, bisexual, and other men who have sex with men), HET (heterosexual exposure), and PWID (people who inject drugs), annotated with annual percentage change. **B)** The effective reproduction number (Re) overall for British Columbia and in key risk groups. **C**) The piecewise average Re for periods before PrEP, during PrEP & before COVID-19, during PrEP & during COVID-19, and during PrEP and post-COVID-19.

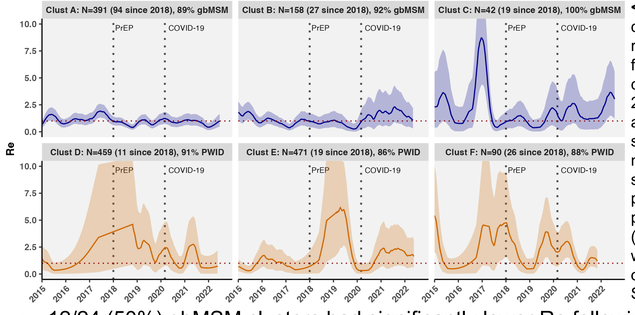
Previous PrEP use among newly diagnosed associated with higher odds of clustering

Table 1. Newly diagnosed HIV cases and number/percentage who joined phylogenetic clusters in BC overall from 2015 to end of 2022, and since PrEP availability in 2018, stratified by those with no previous PrEP exposure and those with previous PrEP dispensations. Sum/mean across 2018-2022 reported.

	Overall newly diagnosed				Newly diagnosed, no previous PrEP				Newly diagnosed, previous PrEP			
Year	N	N clustering	% clustering	N unique clusters	N	N clustering	% clustering	N unique clusters	N	N clustering	% clustering	N unique clusters
2015	256	140	54.7	48								
2016	252	121	48	45								
2017	183	103	56.3	43								
2018	174	94	54	40	173	93	53.8	40	1	1	100	1
2019	168	83	49.4	43	160	78	48.8	42	8	5	62.5	4
2020	127	83	65.4	30	121	78	64.5	30	6	5	83.3	5
2021	131	74	56.5	34	125	70	56	34	6	4	66.7	3
2022	124	67	54	24	106	52	49.1	24	18	15	83.3	7
Sum/Mean: 2018-2022					685	371	54.2	84	39	30	76.9	13

- In a binomial model of clustering adjusted for proportion gbMSM, age of first ARV, and baseline CD4 count, previous PrEP users had 2.6-times (95% CI: 1.2-6.4) higher odds of clustering compared to non-PrEP users

Differential expansion of actively growing HIV clusters following widespread PrEP availability



< Fig. 2. Phylogenetic cluster-level effective reproduction number for six of the largest clusters in BC from 2015 to 2022, annotated with cluster size in 2023, number of new cluster members since 2018, and the percentage of predominant risk group (also informs fill color, where blue is gbMSM, orange is PWID). Smoothed rates: k=90.

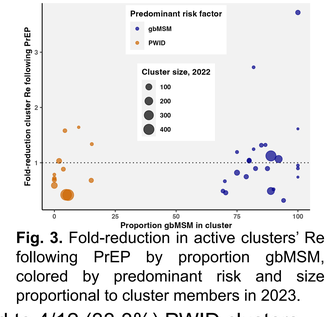


Fig. 3. Fold-reduction in active clusters' Re following PrEP by proportion gbMSM, colored by predominant risk and size proportional to cluster members in 2023.

- 12/24 (50%) gbMSM clusters had significantly lower Re following PrEP, compared to 4/12 (33.3%) PWID clusters
- During COVID-19, growth accelerated in clusters with a high proportion PWID and HET
- Since end of COVID-19, several gbMSM clusters are growing again after periods of Re<1

Cases averted via widespread PrEP availability have been primarily in large gbMSM-predominant clusters

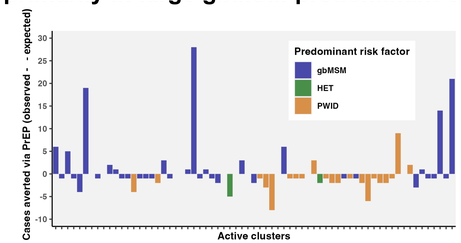


Fig. 4. Cases averted via PrEP in active phylogenetic clusters in BC between Jan. 2018 and Feb. 2020, colored by predominant risk group, were estimated as the difference in observed new cases from Jan. 2018 to Feb. 2020 and expected cases in the absence of PrEP. Expected cases were projected in clusters with deterministic simulations based on the mean cluster growth rate and cluster size preceding PrEP.

- We estimated PrEP averted 57-125 HIV cases from Jan. 2018 to Feb. 2020 (prior to COVID-19)
- Most averted cases concentrated in four clusters of young (median age first ART: 27-35), gbMSM (79-92%), and included previous PrEP users newly diagnosed (high PrEP awareness)
- Poisson model: fewer cases averted with lower % gbMSM, higher median age, higher % living in Vancouver Coastal Health Authority, and lower %new cases with previous PrEP exposure

CONCLUSIONS

- Modeling phylogenetic clusters' effective reproduction number dynamics revealed PrEP availability differentially reduced clusters' growth, but cumulatively may have averted a total of 57-125 new HIV cases from Jan. 2018 to Mar. 2020 (2.2-4.8 per month) in BC.
- These results highlight the success of the PrEP program in averting new HIV cases, emphasizing priority clusters and sociodemographic groups meriting prioritized treatment and prevention resources, including PrEP.
- Combining phylogenetics and counterfactual models is a pragmatic approach to inform public health policy.

Acknowledgements

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