The impact of a province-wide HIV Treatment-as-Prevention-based initiative in accelerating progress towards the United Nations' 90-90-90 target: A population-based cohort study in British Columbia, Canada

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Author's contribution

Concept and design: NGAN, VDL; Acquisition, analysis, or interpretation of data: XD, HMT, ML, VDL; Drafting of the manuscript: NGAN, VDL; Critical revision of the manuscript for important intellectual content: NGAN, XD, HMT, ML, RB, JSGM, VDL; Administrative,

technical, or material support: RB, JSGM, VDL. All authors (NGAN, XD, HMT, ML, RB, JSGM, VDL) have read and approved the final manuscript. XD and HMT contributed equally to this work.

Abstract

Background: In British Columbia (BC), Canada, "HIV Treatment as Prevention" (TasP), encompassing widespread HIV testing and immediate initiation of free ART, was piloted in 2010 under the Seek and Treat for Optimal Prevention of HIV/AIDS initiative (STOP). We compared the time from HIV diagnosis to antiretroviral therapy (ART) initiation, and from ART initiation to first virologic suppression before and after the implementation of STOP.

Methods: This population-based cohort study used longitudinal data of all diagnosed people living with HIV (PLWH) in BC. Eligible PLWH were ≥18 years old, ART naïve, and newly diagnosed in BC during 2005-2016. Virologic suppression date was the first of ≥2 consecutive viral load measures <200 copies/mL within four months. Negative binomial regression models assessed the effect of STOP on the time from diagnosis to ART initiation, and from ART initiation to suppression, adjusting for confounders.

Results: PLWH diagnosed before (N=1601) and after STOP (N=1700) were significantly different: 81% vs. 84% were men, 30% vs. 15% ever injected drugs, and 27% vs. 49% had ≥350 CD4 cells/μL at diagnosis. STOP was associated with a 65% shorter time from diagnosis to treatment (adjusted mean ratio: 0.35 [95%CI: 0.32-0.38]) and a 22% shorter time from treatment to suppression (adjusted mean ratio: 0.78 [95%CI: 0.72-0.85]).

Interpretation: In a population with universal health coverage, a TasP-based intervention was associated with accelerating progress towards the United Nations' 90-90-90 target. Our results

support the global expansion of TasP to accelerate the control of HIV/AIDS, as currently recommended by the United Nations.

Keywords: HIV; continuum of care; treatment as prevention; health service; 90-90-90 target

Introduction

The personal and public health benefits of early initiation of antiretroviral treatment (ART) are well documented (1–5). In addition to decreasing morbidity and mortality among people living with HIV/AIDS (PLWH) (1–3), ART has also been shown to reduce HIV incident cases in a population (4,5). The latter led to the conception of "HIV Treatment as Prevention" (TasP), the scaling-up of testing followed by the immediate initiation of ART, as a strategy for reducing AIDS-related morbidity and mortality and, simultaneously, the spread of HIV (6–8). The success of TasP on HIV transmission relies on the ART-led suppression of HIV replication, resulting in sustained undetectable viral load in bodily fluids and an effectively zero risk of sexual transmission of HIV - referred to as "undetectable=untransmissible" (U=U) (9,10).

To achieve the "End of AIDS as Pandemic" goal by 2030, the United Nations Joint AIDS Programs (UNAIDS) proposed the TasP based 90-90-90 Target constituting at least 90% PLWH diagnosed, 90% diagnosed PLWH on ART and 90% ART-treated PLWH virologically suppressed by 2020 (11). Meeting the 90-90-90 Target would yield in a dramatic decrease in AIDS-related morbidity and mortality and HIV new infections within a decade (12,13). The global progress towards the 90-90-90 Target has been encouraging despite political, fiscal and programmatic challenges (14–18). In British Columbia (BC), Canada, TasP was piloted in 2010 and subsequently expanded province-wide under the publicly-funded Seek and Treat for Optimal Prevention of HIV/AIDS initiative (STOP HIV/AIDS; hereinafter referred to as STOP). STOP used TasP as a framework to address the HIV care continuum including widespread HIV testing, immediate ART initiation, public health follow-ups for care interruptions, and targeted community outreach (19). By 2016, BC achieved 84-85-93 (20); by December 2020, BC surpassed the 90-90-90 Target (21).

Evidence-based strategies that improve HIV clinical outcomes in a timely manner are needed to inform future prevention and care efforts. As such, this study aimed to assess the population-level impact of a TasP-based intervention in accelerating the progression towards the UNAIDS 90-90-90 Target by comparing: (1) the time from HIV diagnosis to ART initiation, and (2) the time from ART initiation to virologic suppression, before and after the implementation of STOP (2005-2009 and 2010-2016, respectively). To examine whether STOP affected various population subgroups equally, analyses of both outcomes were further stratified by demographic and clinical characteristics.

Methods

Study setting

The BC Centre for Excellence in HIV/AIDS Drug Treatment Program (DTP) has been responsible for ART distribution in BC since 1992 (22). ART and routine laboratory monitoring (including plasma viral load [pVL] and CD4 cell counts) are free-of-charge for all PLWH. BC's HIV therapeutic guidelines advise ART eligibility (23), with the minimum CD4 count to initiate ART evolving from 200 cells/μL before 2008 to 350 cells/μL in 2008 and 500 cells/μL in 2010. Since 2012, ART is prescribed regardless of CD4 count. The recommended first-line ART regimens have also evolved. Credited with faster virologic suppression and reduced drug resistance (24,25), integrase strand-transfer inhibitor-based (INSTI) ART has been available in BC as a first-line therapy option since 2011 for raltegravir, 2013 for elvitegravir, and 2014 for dolutegravir.

Study design

In this population-based cohort study, eligible participants included ART-naïve PLWH aged ≥18 years, who were diagnosed between January 1, 2005 and December 31, 2016, and initiated ART for the first time through the DTP. Longitudinal individual-level data on PLWH in BC were obtained from the STOP population-based cohort through linkages between the DTP clinical registry (22), and various provincial administrative datasets containing health information (26–31). The cohort has been described elsewhere (26).

Outcomes and exposures

Our outcomes were time from HIV diagnosis to ART initiation (time Dx-Tx) and from ART initiation to first virologic suppression (time Tx-Vx). Our exposures were HIV diagnosis and ART

initiation eras, each grouped into pre-STOP (2005-2009) and post-STOP (2010-2016). Diagnosis date was the first instance of a positive HIV antigen/antibody test, a detectable pVL, an HIV-related hospitalization, three HIV-related physician visits, an AIDS-defining illness, or ART dispensation (32). ART initiation date was obtained from the DTP. Virologic suppression date was the first instance of ≥2 consecutive pVLs <200 copies/mL within four months. PLWH with <4 months of follow-up upon ART initiation, hence unable to meet the above virologic suppression definition, and those who did not achieve suppression during the study period were excluded from the time Tx-Vx analysis.

Potential confounders

The following potential confounders were investigated: gender (female, male), age (<30, 30–39, 40–49, ≥50 years), health authority (HA) of residence (Fraser, Interior, Northern, Vancouver Coastal, Vancouver Island, unknown), CD4 count (<200, 200–349, ≥350 cells/mm3, unmeasured), ethnicity (White, non-White, unknown), and HIV acquisition risk group (gay, bisexual, and other men who have sex with men [gbMSM], people who have ever injected drugs [PWID], heterosexual/other, unknown). Note that age, HA of residence and CD4 count were measured at diagnosis and ART initiation for time Dx-Tx and Tx-Vx analyses, respectively. For Tx-Vx analysis, additional treatment-related potential confounders, measured at ART initiation, were also assessed: pVL (continuous in log10 copies/mL) and first-ART class (non-nucleoside reverse transcriptase inhibitor [NNRTI], protease inhibitor [PI], INSTI, INSTI combined with NNRTI and/or PI, others).

Of note, Vancouver Coastal HA cares for >50% of BC's PLWH, while Northern is one of the most remote HAs. CD4 count was the closest measure within a year before diagnosis and ART

initiation dates, respectively. If unavailable, the closest CD4 count measured within three months after these dates was chosen. Similar criteria were applied when establishing pVL at ART initiation. To accommodate differential quantification limits across pVL monitoring assays (33), values <50 copies/mL received the value 49 copies/mL and values >100,000 copies/mL received the value 100,010 copies/mL.

Statistical approach

We explored the annual trends in time Dx-Tx and time Tx-Vx during 2005-2016. We also examined the distribution of the two outcomes pre- and post-STOP, across gender, age, HA of residence, CD4 count, ethnicity, and HIV acquisition risk groups to account for population subgroup differences. Lastly, we estimated the relative effects of STOP on time Dx-Tx and time Tx-Vx, adjusted for confounders.

Categorical variables were compared using the Fisher's exact test or Chi-squared test, and continuous variables were compared using the Kruskal Wallis test (34). We modelled the overdispersed time Dx-Tx and time Tx-Vx (i.e., as the number of months, respectively) using a negative binomial regression model (35). Starting with a full model, confounding variables were gradually omitted until the change in the coefficient for the main explanatory variable was ≥5% (36). All p-values are two-sided, and the significance level was set at 0.05. Analyses were performed in SAS version 9.4 (SAS, Cary North CA, USA) and R© version 3.6.0 (R Core Team, Vienna, Austria).

Ethics

Linkage and usage of administrative databases were approved and performed by data stewards in each collaborating agency and facilitated by the BC Ministry of Health. The University of British Columbia Ethics Review Committee at the St. Paul's Hospital site provided ethics approval for this study (H18-02208). This study was conducted using strictly anonymized laboratory and administrative databases, and thus informed consent was not required. This study complies with the BC's Freedom of Information and Protection of Privacy Act.

Results

Study population

Of the 3301 eligible PLWH diagnosed in BC during 2005-2016, 82% were male, 58% 30-49 years old, 55% White, 51% Vancouver Coastal HA residents, 38% diagnosed with <350 CD4 cells/μL, 41% gbMSM (Table 1). Those diagnosed pre- and post-STOP (N=1601 [49%] vs. 1700 [51%]) were significantly different in demographic and clinical characteristics except for ethnicity. Of the 2979 PLWH (90%) who achieved suppression, those who initiated ART pre- and post-STOP (N=998 [34%] vs. 1981 [66%]) were significantly different except in gender, ethnicity and HA of residence.

Time Dx-Tx

The median time Dx-Tx substantially declined from 23 months ([25th, 75th percentile [Q1, Q3]: 4, 47) in 2005 to one month (Q1, Q3: 1, 2) in 2016 (Figure 1). The decline in time Dx-Tx pre- and post-STOP was statistically significant across all population subgroups (Figure 2). Additionally, post-STOP, the previously observed gaps in time Dx-Tx across age, CD4 count and HIV acquisition risk groups have narrowed. For instance, pre-STOP, the median time Dx-Tx among those <30 years old was 20 months longer than those ≥50 years old. Post-STOP, PLWH across age groups initiated ART within a median of two months. Adjusted for confounder CD4 count at diagnosis, time Dx-Tx was on average 65% shorter (adjusted mean ratio: 0.35 [95% confidence interval: 0.32-0.38]) post-STOP.

Time Tx-Vx

Annual median time Tx-Vx declined from four months (Q1, Q3: 2, 6) in 2005 to one month (Q1, Q3: 1, 3) in 2016, with PLWH initiating ART during 2007-2013 achieving suppression within a steady median of three months (Figure 1). The decline in time Tx-Vx pre- and post-STOP was statistically significant, except among females, Northern HA residents and those initiating ART with 200-349 CD4 cells/μL (Figure 2). Post-STOP, Northern HA residents and PWID experienced the longest median time Tx-Vx (4 months [Q1, Q3: 2, 9], respectively). On average, adjusted for confounders HA of residence, CD4 count at ART initiation, HIV acquisition risk and type of first ART, STOP was associated with 22% shorter time Tx-Vx (adjusted mean ratio: 0.78 [95% confidence interval: 0.72-0.85]).

Interpretation

Within our universal healthcare setting, a TasP-based intervention was strongly associated with earlier ART initiation and shorter time to virologic suppression, even when changes in ART eligibility and first-line ART preferences were adjusted for. Observational studies from the Netherlands, South Korea, Thailand and New York City also reported a significant decrease in time Dx-Tx during 2012-2015 (37–40), when international guidelines began to recommend CD4-count-independent rapid ART initiation (41–45). By 2015-2016, however, 75% of PLWH in BC initiated ART within two months of their diagnosis, compared to 6 months in the aforementioned jurisdictions (37–40).

While the independent impact of STOP's in accelerating time Dx-Tx in BC was evident, the full public benefit of early ART to reduce transmission risk requires a decline in another more complex time component, namely time from infection to diagnosis. Delayed HIV diagnosis has previously been observed in one in seven BC's PLWH, particularly those who were older, heterosexual, PWID and residing in Northern HA (46). This reality argues for targeted interventions to improve HIV screening among the identified populations.

During our study period, other North American cohort studies also reported shorter time Tx-Vx (47,48). Others reported faster suppression from the time of diagnosis (49–55), which can be driven by shorter time Dx-Tx and/or time Tx-Vx. In 2016, BC's combined median time from diagnosis to suppression was up to two months faster than the observations in several United States jurisdictions (53,54). While our annual trends signalled that INSTI-based regimens likely contributed to the faster decline in time Tx-Vx, our multivariable model corroborated the independent impact of STOP.

In the present U=U era, a shortened time to achieve suppression is a critical measure of HIV care success (56,57). This contention urges population-wide improvements in key risk factors of virologic suppression, such as removing barriers to ART adherence, reducing substance use and managing mental health disorders (58–60). While our study demonstrates BC's remarkable progress on rapid viral suppression by 2016, further studies should investigate how the coronavirus disease pandemic may affect this progress. Interrupted healthcare access, medication disruption, and psychological stress from self-isolation and income loss are among additional challenges faced by PLWH during this pandemic, threatening progress on the control of HIV/AIDS (61–64).

Limitations

First, administrative health data are susceptible to coding errors. We thus used validated case-finding algorithms specifically developed to ascertain HIV diagnosis dates in administrative datasets. Second, our lack of granular ethnicity data limited our ability to fully assess ethnic disparities in our outcomes. However, a recent study found no difference in HIV treatment outcomes between indigenous and non-indigenous PWID in BC (65). Lastly, those recently diagnosed may achieve virologic suppression after the administrative censoring date of March 31, 2017, and were thus excluded from the time Tx-Vx analysis. Given the high suppression rates, the impact of this administrative censoring on our findings should be minimal.

Conclusion

Our large population-based study offers empirical evidence of the impact of a TasP-based intervention in accelerating the progress of BC towards the UNAIDS' 90-90-90 target. These findings support the continued expansion of sustainable and equitable TasP-based policy and

programmatic efforts, targeting underserved and hard-to-reach populations, as key tools to further reduce AIDS-related morbidity and mortality, as well as HIV transmission, and thus alleviate the overall global burden of HIV/AIDS.

Acknowledgement

We would like to thank all the participants included within STOP HIV/AIDS, the British Columbia Centre for Excellence in HIV/AIDS, the BC Ministry of Health, and the institutional data stewards for granting access to the data.

Competing interests

JSGM has received institutional grants from Gilead Sciences and Merck. All other authors declare no competing interests.

Funding

This work was supported by the following sources of funding: JSGM's Treatment as Prevention (TasP) research, paid to his institution, has received support from the Public Health Agency of Canada, and the British Columbia Ministry of Health. VDL is funded by grants from the Canadian Institutes of Health Research (PJT-148595 and PJT-156147), and the Canadian Foundation for AIDS Research (CANFAR Innovation Grant – 30-101). NGAN is supported by Canadian Institutes of Health Research Canada Graduate Student – Master's Award and the University of British Columbia's Four-Year Doctoral Fellowship. The sponsors had no role in the design, data collection, data analysis, data interpretation, or writing of the report.

Disclaimer

The sponsors had no role in the design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility to submit for publication. All inferences, opinions, and conclusions drawn in this

manuscript are those of the authors, and do not reflect the opinions or policies of the Data Steward(s).

Meeting

Preliminary results were presented by NGAN at the 23rd International Workshop on HIV and Hepatitis Observational Databases in Athens, Greece on March 28-30, 2019.

Data statement

The British Columbia Centre for Excellence in HIV/AIDS (BC-CfE) is prohibited from making individual-level data available publicly due to provisions in our service contracts, institutional policy, and ethical requirements. In order to facilitate research, we make such data available via data access requests. Some BC-CfE data is not available externally due to prohibitions in service contracts with our funders or data providers. Institutional policies stipulate that all external data requests require collaboration with a BC-CfE researcher. For more information or to make a request, please contact Mark Helberg, Senior Director, Internal and External Relations, and Strategic Development: mhelberg@bccfe.ca. The underlying analytical codes are available from the authors on request.

References

1. Hogg RS, Heath KV, Yip B, Craib KJ, O'Shaughnessy MV, Schechter MT, et al. Improved Survival Among HIV-Infected Individuals Following Initiation of Antiretroviral Therapy. J Am Med Assoc. 1998;279(6):450–4.
2. Murphy EL, Collier AC, Kalish LA, Assmann SF, Para MF, Flanigan TP, et al. Highly active antiretroviral therapy decreases mortality and morbidity in patients with advanced HIV disease. Ann Intern Med. 2001 Jul 3;135(1):17–26.
3. The Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. Lancet. 2008 Jul 26;372(9635):293–9.
4. Porco TC, Martin JN, Page-Shafer KA, Cheng A, Charlebois E, Grant RM, et al. Decline in HIV infectivity following the introduction of highly active antiretroviral therapy. AIDS [Internet]. 2004 [cited 2020 Oct 30];18(1):81. Available from: /pmc/articles/PMC2442908/?report=abstract
5. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. Lancet. 2010 Jun 12;375(9731):2092–8.
6. Montaner JS, Hogg R, Wood E, Kerr T, Tyndall M, Levy AR, et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic [Internet]. Vol. 368, Lancet. Elsevier Limited; 2006 [cited 2020 Oct 30]. p. 531–6. Available from: http://www.thelancet.com/article/S0140673606691629/fulltext
7. Montaner JSG. Treatment as prevention--a double hat-trick. Lancet [Internet]. 2011 [cited 2020 Oct 30];378(9787):208–9. Available from:

https://pubmed.ncbi.nlm.nih.gov/21763923/

8. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet. 2009 Jan 3;373(9657):48–57.

9. The Lancet HIV. U=U taking off in 2017 [Internet]. Vol. 4, The Lancet HIV. Elsevier Ltd; 2017 [cited 2020 Nov 1]. p. e475. Available from: http://programme.ias2017.

10. Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection undetectable equals untransmittable [Internet]. Vol. 321, JAMA - Journal of the American Medical Association. American Medical Association; 2019 [cited 2020 Nov 1]. p. 451–2. Available from: https://jamanetwork.com/journals/jama/fullarticle/2720997

11. The Joint United Nations Programme on HIV and AIDS (UNAIDS). 90-90-90: An ambitious treatment target to help end the AIDS epidemic. 2020.

12. Granich RM, Gilks CF, Dye C, De Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet [Internet]. 2009 Jan 3 [cited 2020 Oct 15];373(9657):48–57. Available from: https://pubmed.ncbi.nlm.nih.gov/19038438/

13. Stover J, Hallett TB, Wu Z, Warren M, Gopalappa C, Pretorius C, et al. How Can We Get Close to Zero? The Potential Contribution of Biomedical Prevention and the Investment Framework towards an Effective Response to HIV. Tang JW, editor. PLoS One [Internet]. 2014 Nov 5 [cited 2021 Mar 4];9(11):e111956. Available from: https://dx.plos.org/10.1371/journal.pone.0111956

14. Yombi JC, Mertes H. Treatment as prevention for HIV infection: Current data, challenges, and global perspectives. AIDS Rev [Internet]. 2018 Jul 1 [cited 2020 Nov 1];20(3):131–

40. Available from: https://pubmed.ncbi.nlm.nih.gov/30264827/

15. Brault MA, Spiegelman D, Abdool Karim SS, Vermund SH. Integrating and Interpreting Findings from the Latest Treatment as Prevention Trials. Curr HIV/AIDS Rep. 2020;17(3):249–58.

16. Zuniga JM. UNAIDS 90-90-90—Opportunity in Every Difficulty [Internet]. Vol. 17, Journal of the International Association of Providers of AIDS Care. SAGE Publications Inc.; 2018 [cited 2020 Nov 1]. p. 232595821880907. Available from: http://journals.sagepub.com/doi/10.1177/2325958218809075

17. The Joint United Nations Programme on HIV and AIDS (UNAIDS). Ending AIDS: Progress towards the 90-90-90 targets. 2017.

18. Duncombe C, Ravishankar S, Zuniga JM. Fast-Track Cities: Striving to end urban HIV epidemics by 2030. Curr Opin HIV AIDS. 2019;14(6):503–8.

19. Seek and Treat for Optimal HIV Prevention of HIV/AIDS. STOP HIV/AIDS [Internet]. 2019 [cited 2020 Nov 1]. Available from: http://stophivaids.ca/about/

20. Lima VD, Brumme ZL, Brumme C, Sereda P, Krajden M, Wong J, et al. The Impact of Treatment as Prevention on the HIV Epidemic in British Columbia, Canada. Curr HIV/AIDS Rep [Internet]. 2020 [cited 2020 Mar 9]; Available from: https://doi.org/10.1007/s11904-020-00482-6

21. BC Ministry of Health, BC Centre for Excellence in HIV/AIDS. News Release: B.C. marks record achievements in effort to end AIDS [Internet]. 2020. Available from: https://archive.news.gov.bc.ca/releases/news_releases_2020-2024/2020HLTH0062-001988.htm

22. British Columbia Centre for Excellence in HIV/AIDS (BCCfE). Drug Treatment Program

[Internet]. 2019 [cited 2018 Apr 24]. Available from: http://www.cfenet.ubc.ca/drug-treatment-program%0Ahttp://www.cfenet.ubc.ca/research/laboratory-program

23. BC Centre for Excellence in HIV/AIDSop. Therapeutic Guidelines Antiretroviral (ARV) Treatment of Adult HIV Infection [Internet]. 2019 [cited 2019 Jan 10]. Available from: http://cfenet.ubc.ca/sites/default/files/uploads/Guidelines/BC-CfE-Adult-ARV-Therapeutic-Guidelines_2020-01-16.pdf

24. Patel DA, Snedecor SJ, Tang WY, Sudharshan L, Lim JW, Cuffe R, et al. 48-Week Efficacy and Safety of Dolutegravir Relative to Commonly Used Third Agents in Treatment-Naive HIV-1–Infected Patients: A Systematic Review and Network Meta-Analysis. PLoS One [Internet]. 2014 [cited 2020 Oct 21];9(9). Available from: /pmc/articles/PMC4154896/?report=abstract

25. Kamelian K, Lepik KJ, Chau W, Yip B, Zhang WW, Lima VD, et al. Prevalence of human immunodeficiency virus-1 integrase strand transfer inhibitor resistance in British Columbia, Canada between 2009 and 2016: A longitudinal analysis. Open Forum Infect Dis [Internet]. 2019 Mar 1 [cited 2020 Oct 30];6(3). Available from: /pmc/articles/PMC6419991/?report=abstract

26. Heath K, Samji H, Nosyk B, Colley G, Gilbert M, Hogg RS, et al. Cohort profile: Seek and treat for the optimal prevention of HIV/AIDS in British Columbia (STOP HIV/AIDS BC). Int J Epidemiol. 2014;43(4):1073–81.

27. British Columbia Ministry of Health [creator]. Medical services plan (MSP) payment information file; consolidation file (MSP Registration & Premium Billing); Home & Community Care (continuing care); mental health; PharmaNet. British Columbia Ministry of Health [publisher]. Data Extract. MOH (2016).

28. Canadian Institute of Health Information [creator]. Discharge abstract database (hospital separations). British Columbia Ministry of Health [publisher]. Data Extract. MOH (2016) [Internet]. Available from: https://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/data-access-health-data-central

29. British Columbia Centre for Disease Control Public Health Laboratory [creator]. HIV laboratory testing datasets (tests: ELISA, Western blot, NAAT, p24, culture). Clinical Prevention Services, British Columbia Centre for Disease Control. British Columbia Ministry of Health [publisher]. Data Extract. MOH (2016) [Internet]. Available from: http://www.bccdc.ca/about/accountability/data-access-requests/public-health-data

30. British Columbia Centre for Disease Control [creator]. HIV/AIDS Information System (HAISYS). Clinical Prevention Services, British Columbia Centre for Disease Control. British Columbia Ministry of Health [publisher]. Data Extract. MOH (2016) [Internet]. Available from: http://www.bccdc.ca/about/accountability/data-access-requests/public-health-data

31. British Columbia Vital Statistics Agency [creator]. Vital Statistics. British Columbia Ministry of Health [publisher]. Data Extract. MOH (2016) [Internet]. Available from: https://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/data-access-health-data-central

32. Nosyk B, Colley G, Yip B, Chan K, Heath K, Lima VD, et al. Application and validation of case-finding algorithms for identifying individuals with human immunodeficiency virus from administrative data in British Columbia, Canada. PLoS One [Internet]. 2013 [cited 2018 May 29];8(1):e54416. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23382898

33. Lima V, Harrigan R, Montaner JSG. Increased reporting of detectable plasma hiv-1 rna levels at the critical threshold of 50 copies per milliliter with the taqman assay in comparison to the amplicor assay. J Acquir Immune Defic Syndr. 2009;51(1):3–6.

34. McDonald JH. Handbook of Biologial Statistics. 2nd ed. Baltimore: Sparky House Publishing; 2009.

35. Khorana AA, Tullio K, Elson P, Pennell NA, Grobmyer SR, Kalady MF, et al. Time to initial cancer treatment in the United States and association with survival over time: An observational study. PLoS One [Internet]. 2019 Mar 1 [cited 2020 Nov 24];14(3). Available from: https://pubmed.ncbi.nlm.nih.gov/30822350/

36. Lima VD, Geller J, Bangsberg DR, Patterson TL, Daniel M, Kerr T, et al. The effect of adherence on the association between depressive symptoms and mortality among HIV-infected individuals first initiating HAART. AIDS [Internet]. 2007 May 31 [cited 2018 Jun 21];21(9):1175–83. Available from: https://insights.ovid.com/crossref?an=00002030-200705310-00011

37. Robertson MM, Braunstein SL, Hoover DR, Li S, Nash D. Timeliness of Human Immunodeficiency Virus Diagnosis and Antiretroviral Treatment Initiation in the Era of Universal Testing and Treatment. J Infect Dis [Internet]. 2020 Jan 1 [cited 2020 Nov 4];221(1):648–56. Available from: https://www.researchwithrutgers.com/en/publications/timeliness-of-human-immunodeficiency-virus-diagnosis-and-antiretr

38. Boender TS, Smit C, Van Sighem A, Bezemer D, Ester CJ, Zaheri S, et al. AIDS Therapy Evaluation in the Netherlands (ATHENA) national observational HIV cohort: Cohort profile. BMJ Open [Internet]. 2018 [cited 2020 Nov 3];8(9). Available from:

https://pubmed.ncbi.nlm.nih.gov/30249631/

39. Kim YJ, Kim SW, Kwon KT, Chang HH, Kim S Il, Kim YJ, et al. Significance of increased rapid treatment from HIV diagnosis to the first antiretroviral therapy in the recent 20 years and its implications: The Korea HIV/AIDS cohort study. J Korean Med Sci [Internet]. 2019 Oct 1 [cited 2020 Nov 3];34(38):1–6. Available from: /pmc/articles/PMC6776834/?report=abstract

40. Teeraananchai S, Kerr SJ, Khananuraksa P, Ruxrungtham K, Puthanakit T. Rapid antiretroviral initiation among Thai youth living with HIV in the National AIDS programme in the era of treatment at any CD4 cell count: a national registry database study. J Int AIDS Soc [Internet]. 2020 Sep 1 [cited 2020 Nov 3];23(S5). Available from: /pmc/articles/PMC7459169/?report=abstract

41. Eholié SP, Badje A, Kouame GM, N'takpe JB, Moh R, Danel C, et al. Antiretroviral treatment regardless of CD4 count: The universal answer to a contextual question [Internet]. Vol. 13, AIDS Research and Therapy. BioMed Central Ltd.; 2016 [cited 2020 Nov 4]. p. 27. Available from: /pmc/articles/PMC4960900/?report=abstract

42. World Health Organization. Guideline on when to start antiretroviral pre-exposure prophylaxis for HIV guidelines [Internet]. 2015 [cited 2020 Nov 4]. Available from: https://apps.who.int/iris/bitstream/handle/10665/186275/9789241509565_eng.pdf

43. European AIDS Clinical Society. EACS Guidelines version 8.2, January 2017 [Internet]. 2017 [cited 2020 Nov 4]. Available from: https://www.eacsociety.org/files/guidelines_8.2-english.pdf

44. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV [Internet]. 2019 [cited 2020

Nov 4]. Available from: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf

45. Saag MS, Benson CA, Gandhi RT, Hoy JF, Landovitz RJ, Mugavero MJ, et al. Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults 2018 Recommendations of the International Antiviral Society-USA Panel Clinical Review & Education JAMA | Special Communication Downloaded From: by a University of Alabama-Birmingham User on 07/24/2018. JAMA. 2018;320(4):379–96.

46. Nanditha NGA, St-Jean M, Tafessu H, Guillemi SA, Hull MW, Lu M, et al. Missed opportunities for earlier diagnosis of HIV in British Columbia, Canada: A retrospective cohort study. Sued O, editor. PLoS One [Internet]. 2019 Mar 21 [cited 2019 May 10];14(3):e0214012. Available from: http://dx.plos.org/10.1371/journal.pone.0214012

47. Nance RM, Chris Delaney JA, Simoni JM, Wilson IB, Mayer KH, Whitney BM, et al. HIV viral suppression trends over time among HIV-infected patients receiving care in the United States, 1997 to 2015 a cohort study [Internet]. Vol. 169, Annals of Internal Medicine. American College of Physicians; 2018 [cited 2020 Nov 12]. p. 376–84. Available from: /pmc/articles/PMC6388406/?report=abstract

48. Bacon O, Chin J, Cohen SE, Hessol NA, Sachdev D, Coffey S, et al. Decreased Time From Human Immunodeficiency Virus Diagnosis to Care, Antiretroviral Therapy Initiation, and Virologic Suppression during the Citywide RAPID Initiative in San Francisco. Clin Infect Dis [Internet]. 2020 May 25 [cited 2020 Nov 12]; Available from: https://pubmed.ncbi.nlm.nih.gov/32449916/

49. Toren KG, Buskin SE, Dombrowski JC, Cassels SL, Golden MR. Time From HIV

Diagnosis to Viral Load Suppression: 2007-2013. [cited 2020 Nov 16]; Available from: http://www.stdjournal.com

50. Medland NA, Nicholson S, Chow EPF, Read TRH, Bradshaw CS, Denham I, et al. Time from HIV infection to virological suppression: Dramatic fall from 2007 to 2016 [Internet]. Vol. 31, AIDS. Lippincott Williams and Wilkins; 2017 [cited 2020 Nov 12]. p. 2377–85. Available from: https://pubmed.ncbi.nlm.nih.gov/28857828/

51. Colasanti J, Sumitani J, Christina Mehta C, Zhang Y, Nguyen ML, Del Rio C, et al. Implementation of a rapid entry program decreases time to viral suppression among vulnerable persons living with HIV in the southern United States. Open Forum Infect Dis [Internet]. 2018 Jun 1 [cited 2020 Nov 12];5(6). Available from: https://academic.oup.com/ofid/article/5/6/ofy104/5046229

52. Wilton J, Liu J, Sullivan A, Rachlis B, Marchand-Austin A, Giles M, et al. Trends in HIV care cascade engagement among diagnosed people living with HIV in Ontario, Canada: A retrospective, population-based cohort study. PLoS One [Internet]. 2019 Jan 1 [cited 2020 Nov 12];14(1). Available from: /pmc/articles/PMC6319701/?report=abstract

53. Doshi RK, Li J, Dorsey K, Allston A, Kharfen M. Earlier diagnoses and faster treatment of HIV in the District of Columbia: HIV surveillance analysis, 2006–2016. AIDS Care - Psychol Socio-Medical Asp AIDS/HIV [Internet]. 2019 Dec 2 [cited 2020 Nov 12];31(12):1476–83. Available from: https://pubmed.ncbi.nlm.nih.gov/30897926/

54. Crepaz N, Song R, Lyss S, Hall HI. Trends in Time From HIV Diagnosis to First Viral Suppression Following Revised US HIV Treatment Guidelines, 2012-2017. J Acquir Immune Defic Syndr [Internet]. 2020 Sep 1 [cited 2020 Nov 12];85(1):46–50. Available from: https://pubmed.ncbi.nlm.nih.gov/32379083/

55. Schwarcz S, Hsu LC, Scheer S. Disparities and trends in viral suppression during a transition to a "test and treat" approach to the HIV epidemic, San Francisco, 2008-2012. In: Journal of Acquired Immune Deficiency Syndromes [Internet]. Lippincott Williams and Wilkins; 2015 [cited 2020 Nov 12]. p. 529–37. Available from: https://pubmed.ncbi.nlm.nih.gov/26569177/

56. Xia Q, Coeytaux K, Braunstein SL, Torian L V., Daskalakis DC. Proposing a new indicator for the National Human Immunodeficiency Virus/AIDS strategy: Percentage of newly diagnosed persons achieving viral suppression within 3 months of diagnosis. J Infect Dis [Internet]. 2019 Feb 23 [cited 2020 Nov 13];219(6):851–5. Available from: https://pubmed.ncbi.nlm.nih.gov/30304520/

57. Dombrowski JC, Baeten JM. It's time to make the time to viral suppression after HIV diagnosis a metric of HIV care success [Internet]. Vol. 219, Journal of Infectious Diseases. Oxford University Press; 2019 [cited 2020 Nov 12]. p. 845–7. Available from: https://www.preventionaccess.org/.

58. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med [Internet]. 2000 Jul 4 [cited 2020 Nov 16];133(1):21–30. Available from: https://pubmed.ncbi.nlm.nih.gov/10877736/

59. Arnsten JH, Demas PA, Grant RW, Gourevitch MN, Farzadegan H, Howard AA, et al. Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. J Gen Intern Med [Internet]. 2002 [cited 2020 Nov 16];17(5):377–81. Available from: https://pubmed.ncbi.nlm.nih.gov/12047736/

60. Chander G, Himelhoch S, Fleishman JA, Hellinger J, Gaist P, Moore RD, et al. HAART

receipt and viral suppression among HIV-infected patients with co-occurring mental illness and illicit drug use. AIDS Care [Internet]. 2009 May 14 [cited 2020 Nov 16];21(5):655–63. Available from: https://www.tandfonline.com/doi/full/10.1080/09540120802459762

61. Sun S, Hou J, Chen Y, Lu Y, Brown · Larry, Operario D. Challenges to HIV Care and Psychological Health During the COVID-19 Pandemic Among People Living with HIV in China. AIDS Behav [Internet]. 1234;24:2764–5. Available from: https://doi.org/10.1007/s10461-020-02903-4

62. Jiang H, Zhou Y, Tang W. Maintaining HIV care during the COVID-19 pandemic [Internet]. Vol. 7, The Lancet HIV. Elsevier Ltd; 2020 [cited 2020 Nov 17]. p. e308–9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7239666/

63. Ridgway JP, Schmitt J, Friedman E, Taylor M, Devlin S, McNulty M, et al. HIV Care Continuum and COVID-19 Outcomes Among People Living with HIV During the COVID-19 Pandemic, Chicago, IL [Internet]. Vol. 24, AIDS and Behavior. Springer; 2020 [cited 2020 Nov 17]. p. 2770–2. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7203502/

64. Kowalska JD, Skrzat-Klapaczyńska A, Bursa D, Balayan T, Begovac J, Chkhartishvili N, et al. HIV care in times of the COVID-19 crisis — Where are we now in Central and Eastern Europe? Int J Infect Dis [Internet]. 2020 Jul 1 [cited 2020 Nov 17];96:311–4. Available from: https://doi.org/10.1016/j.ijid.2020.05.013

65. Milloy MJ, Alexandra K, Thomas K, Evan A, Hasina S, Silvia G, et al. Improvements in HIV treatment outcomes among indigenous and non-indigenous people who use illicit drugs in a Canadian setting. J Int AIDS Soc [Internet]. 2016 Apr 18 [cited 2020 Dec

21];19(1). Available from: https://pubmed.ncbi.nlm.nih.gov/27094914/

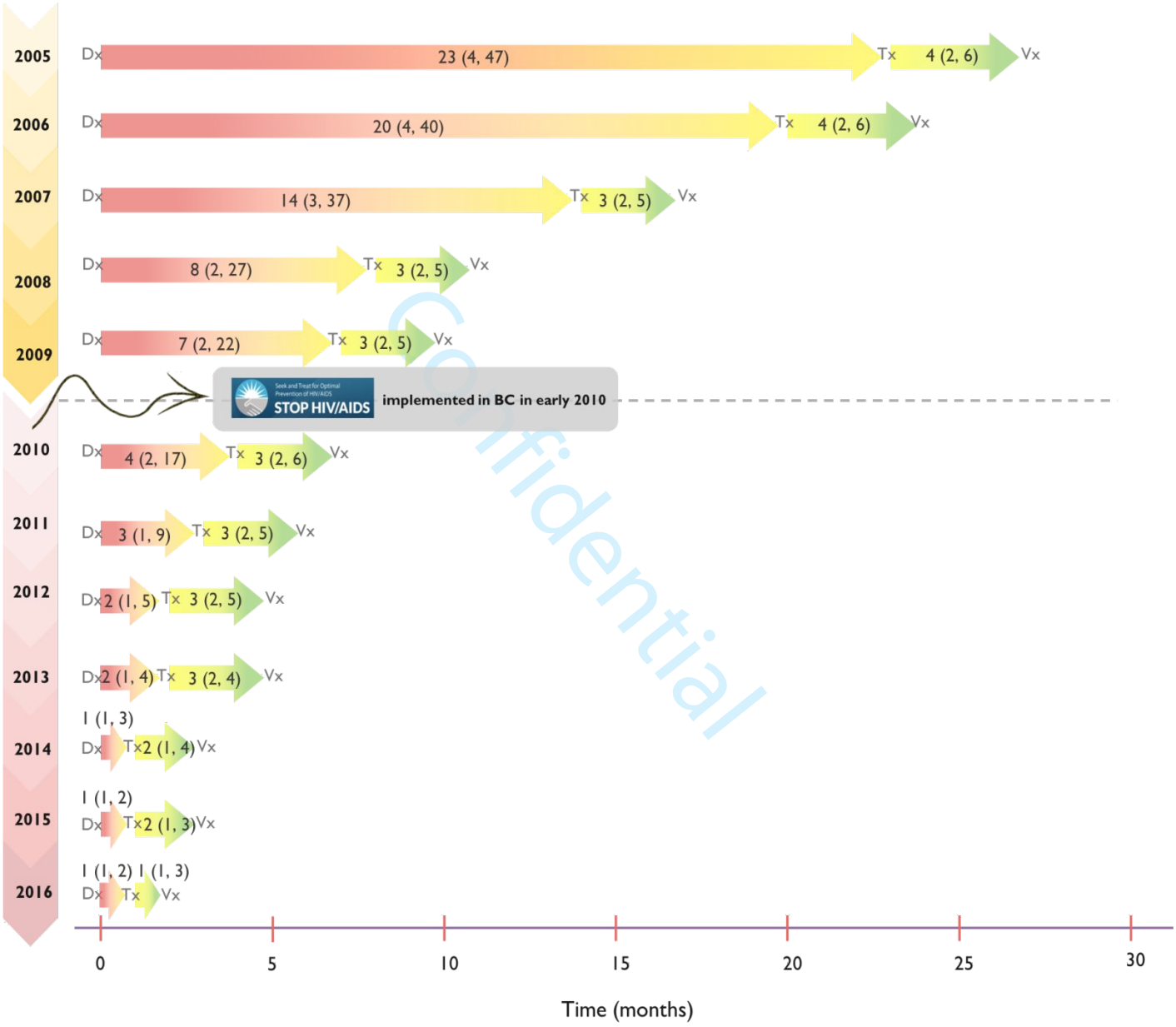
Table 1. Characteristics of people living with HIV in British Columbia from 2005-2016 included in the study and in each analysis.

Sociodemographic and clinical factors		Overall *N=3301*	Time Dx-Tx analysis *N=3301* Pre-STOP HIV/AIDS *N=1601*	Time Dx-Tx analysis *N=3301* Post STOP HIV/AIDS *N=1700*	p-value	Time Tx-Vx analysis *N=2979* Pre-STOP HIV/AIDS *N=998*	Time Tx-Vx analysis *N=2979* Post STOP HIV/AIDS *N=1981*	p-value
		N (%)	N (%)	N (%)		N (%)	N (%)	
Age† (years)	< 30	719 (22)	320 (45)	399 (55)	0.0005	126 (23)	421 (77)	<0.0001
	30-39	977 (30)	488 (50)	489 (50)		302 (34)	575 (66)	
	40-49	929 (28)	493 (53)	436 (47)		323 (37)	560 (63)	
	≥ 50	676 (20)	300 (44)	376 (56)		247 (37)	425 (63)	
Gender	Female	582 (18)	308 (53)	274 (47)	0.0187	175 (35)	328 (65)	0.5013
	Male	2719 (82)	1293 (48)	1426 (52)		823 (33)	1653 (67)	
Ethnicity	White	1831 (55)	893 (49)	938 (51)	0.0626	581 (35)	1074 (65)	0.0662
	Non-White	921 (28)	422 (46)	499 (54)		251 (30)	574 (70)	
	Unknown	549 (17)	286 (52)	263 (48)		166 (33)	333 (67)	
Health authority†	Fraser	787 (24)	348 (44)	439 (56)	0.0138	240 (33)	496 (67)	0.6474
	Interior	215 (7)	104 (48)	111 (52)		59 (33)	121 (67)	
	Northern	190 (6)	99 (52)	91 (48)		50 (33)	100 (67)	
	Vancouver Coastal	1690 (51)	824 (49)	866 (51)		536 (34)	1038 (66)	
	Vancouver Island	366 (11)	192 (52)	174 (48)		109 (34)	207 (66)	
	Unknown	53 (2)	34 (64)	19 (36)		<5 (17)	19 (83)	
CD4 count† (cells/μL)	≥350	1259 (38)	427 (34)	832 (66)	<0.0001	192 (16)	1022 (84)	<0.0001
	200-349	530 (16)	225 (42)	305 (58)		336 (42)	463 (58)	
	<200	724 (22)	340 (47)	384 (53)		461 (49)	482 (51)	
	Not measured	788 (24)	609 (77)	179 (23)		9 (39)	14 (61)	
HIV acquisition risk	gbMSM	1359 (41)	562 (41)	797 (59)	<0.0001	357 (28)	913 (72)	<0.0001
	PWID	733 (22)	474 (65)	259 (35)		276 (44)	351 (56)	
	Heterosexual/Other	834 (25)	382 (46)	452 (54)		259 (35)	488 (65)	
	Unknown	375 (11)	183 (49)	192 (51)		106 (32)	229 (68)	

Suppressed eventually	No	322 (10)	138 (43)	184 (57)	0.0329	*Not applicable*‡		
	Yes	2979 (90)	1463 (49)	1516 (51)				
ART type†	INSTI	*Not applicable*§		*Not applicable*§		5 (1)	365 (99)	<0.0001
	NNRTI					405 (38)	675 (63)	
	PI					584 (41)	852 (59)	
	INSTI + (PI and/or NNRTI)					<5 (5)	82 (95)	
	Other					0 (0)	7 (100)	
Viral load†	Median (Q1, Q3) in log10 copies/mL	*Not applicable*§		*Not applicable*§		4.92 (4.40, 5.00)	4.78 (4.24, 5.00)	<0.0001

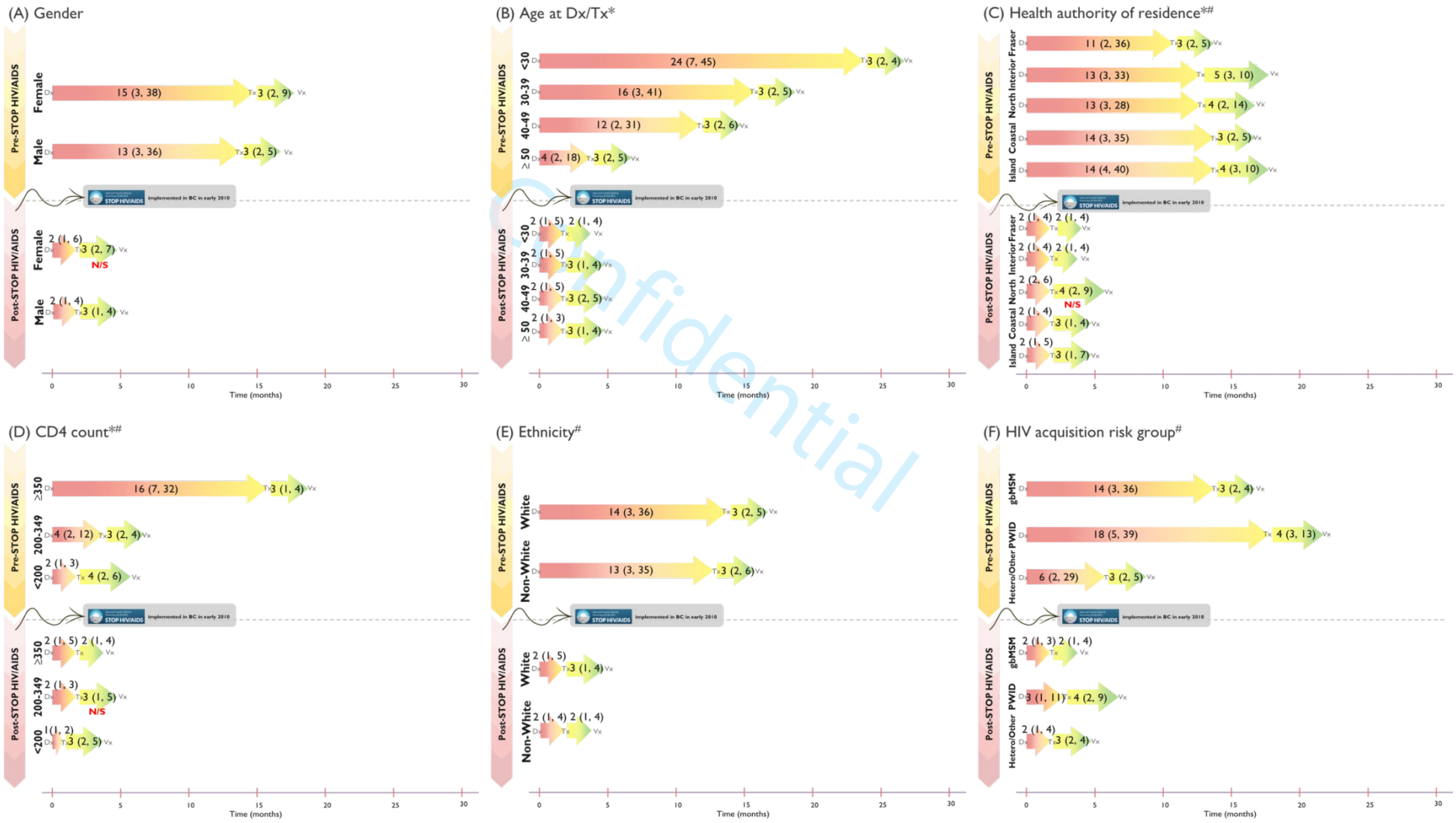
Note: Q1-Q3: 25th-75th percentiles; Time Dx-Tx: time from HIV diagnosis to ART initiation; Time Tx-Vx: time from ART initiation to viral suppression; gbMSM: gay, bisexual and other men who have sex with men; PWID: people with history of injection drug use; †: Variables were measured at the time of HIV diagnosis (for overall and time Dx-Tx analysis) or at ART initiation (for time Tx-Vx analysis); ‡: All participants in time Tx-Vx analysis were virologically suppressed; §: Variables were only measured at the time of ART initiation. For time Dx-Tx analysis, CD4 count was the only selected as confounder; for time Tx-Vx analysis, selected confounders included health authority, CD4 count, HIV acquisition risk and ART type.

Figure 1. The distribution of time from HIV diagnosis to ART initiation and from HIV ART initiation to viral suppression (measured in months) among people living with HIV in British Columbia from 2005-2016.



Note: Dx: HIV diagnosis; Tx: ART initiation; Vx: viral suppression. PLWH: people living with HIV

Figure 2. The distribution of time from HIV diagnosis to ART initiation and from ART initiation to viral suppression (measured in months) before and after STOP HIV/AIDS roll-out, stratified by selected demographic and clinical characteristics.



Note: Dx: HIV diagnosis; Tx: ART initiation; Vx: Viral suppression; North: Northern Health Authority; Coastal: Vancouver Coastal; Island: Vancouver Island. *Age, CD4 level and health authority of residence were measured at HIV diagnosis for time Dx-Tx and at ART initiation for the Tx-Vx, respectively. #Analyses for the unknown group is not shown. Time is in months, presented as median (25th percentile, 75th percentile). N/S: The difference in time before and after STOP HIV/AIDS was NOT statistically significant (p-value>0.05).