A province-wide HIV initiative to accelerate initiation of treatment-as-prevention and virologic suppression in British Columbia, Canada: a population-based cohort study

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Abstract

Background: In 2010, HIV treatment as prevention (TasP), encompassing widespread HIV testing and immediate initiation of free antiretroviral treatment (ART), was piloted under the Seek and Treat for Optimal Prevention of HIV/AIDS initiative (STOP) in British Columbia, Canada. We compared the time from HIV diagnosis to treatment initiation, and from treatment initiation to first virologic suppression, before (2005–2009) and after (2010–2016) the implementation of STOP.

Methods: In this population-based cohort study, we used longitudinal data of all people living with an HIV diagnosis in BC from 1996 to 2017. We included those aged 18 years or older who had never received ART and had received an HIV diagnosis in the 2005–2016 period. We defined the virologic suppression date as the first date of at least 2 consecutive test results within 4 months with a viral load of less than 200 copies/mL. Negative binomial regression models assessed the effect of STOP on the time to ART initiation and suppression, adjusting for confounders. All p values were 2-sided, and we set the significance level at 0.05.

Results: Participants who received an HIV diagnosis before STOP (n = 1601) were statistically different from those with a diagnosis after STOP (n = 1700); 81% versus 84% were men (p = 0.0187), 30% versus 15% had ever injected drugs (p < 0.0001), and 27% versus 49% had 350 CD4 cells/μL or more at diagnosis (p < 0.0001). The STOP initiative was associated with a 64% shorter time from diagnosis to treatment (adjusted mean ratio 0.36, 95% confidence interval [CI] 0.34–0.39) and a 21% shorter time from treatment to suppression (adjusted mean ratio 0.79, 95% CI 0.73–0.85).

Interpretation: In a population with universal health coverage, a TasP intervention was associated with shorter times from HIV diagnosis to treatment initiation, and from treatment initiation to viral suppression. Our results show accelerating progress toward the United Nations' 90-90-90 target of people with HIV who have a diagnosis, those who are on antiretroviral therapy and those who are virologically suppressed, and support the global expansion of TasP to accelerate the control of HIV/AIDS.

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 rates among people living with HIV/AIDS,[1–3] ART has also been shown to reduce the incidence of HIV cases in a population.[4,5] This evidence 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 death, as well as the spread of HIV.[6–8] The success of TasP for HIV transmission relies on the ART-led suppression of HIV replication, resulting in sustained undetectable viral load in bodily fluids and a risk of sexual transmission of HIV that is effectively zero — referred to as "undetectable = untransmissible" (U=U).[9,10]

To achieve the goal of ending AIDS as a pandemic by 2030, the United Nations Joint AIDS Programs (UNAIDS) proposed the TasP-based 90-90-90 target, whereby at least 90% of people living with HIV have a diagnosis, 90% of people with an HIV diagnosis are treated with ART and 90% of ART-treated people living with HIV are virologically suppressed by 2020.[11] Meeting the 90-90-90 target would result in a substantial decrease in AIDS-related morbidity and mortality rates and new HIV infections within a decade.[12,13] The global progress toward the 90-90-90 target has been encouraging, despite political, fiscal and programmatic challenges.[14–18]

In British Columbia, Canada, TasP was piloted in 2010 and subsequently expanded across the province under the publicly funded Seek and Treat for Optimal Prevention of HIV/AIDS initiative (STOP). The STOP initiative 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 a ratio of 84-85-93,[20] and 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, we aimed to assess the population-level impact of a TasP intervention in accelerating the progression toward the UNAIDS 90-90-90 target by comparing the time from HIV diagnosis to ART initiation, and, among those who achieved suppression, the time from ART initiation to virologic suppression, before and after the implementation of STOP (2005–2009 and 2010–2016, respectively). To evaluate whether STOP affected various population subgroups equally, we further stratified analyses of both outcomes by demographic and clinical characteristics.

Methods

Study design and setting

We conducted a retrospective population-based cohort study using a province-wide HIV clinical registry and administrative health data in BC. The BC Centre for Excellence in HIV/AIDS Drug Treatment Program has been responsible for ART distribution in the province since 1992.[22] Antiretroviral therapy and routine laboratory monitoring (including plasma viral load and CD4 cell counts) are free of charge for all people living with HIV. BC's HIV therapeutic guidelines provide guidance for ART eligibility, including minimum CD4 thresholds to initiate ART, which have evolved from 200 cells/μL before 2008 to 350 cells/μL in 2008 and 500 cells/μL in 2010.[23] Since 2012, ART has been prescribed regardless of CD4 count. The recommended first-line ART regimens in these guidelines have also evolved.[23] Credited with faster virologic suppression and reduced drug resistance,[24,25] integrase strand-transfer inhibitor–based ART has been available in BC as a first-line therapy option since 2011 for raltegravir, 2013 for elvitegravir and 2014 for dolutegravir.

The STOP initiative was piloted on Feb. 4, 2010, in 2 major urban areas where more than 50% of people living with HIV in BC resided and with the highest HIV-related mortality rates.[19] During this pilot phase, STOP supportive services were also available to people living with HIV from all over BC who sought care in these urban areas, making STOP readily available to at least 80% of the BC population. The expansion of STOP and its relevant infrastructure to the rest of the province occurred shortly after the pilot began and was completed on Apr. 1, 2013. In this study, we chose the start of the pilot phase, which was the official implementation date of the STOP initiative, as the beginning of our post-STOP period.

Participants

Eligible participants included adults (aged ≥ 18 yr) living with HIV who were diagnosed in BC between Jan. 1, 2005, and Dec. 31, 2016, and who initiated ART for the first time through the Drug Treatment Program. Limiting the HIV diagnosis period to 2005 to 2016 allowed for a balanced number of participants who received their HIV diagnosis before and after the implementation of STOP. The date of the latest available data linkages from the STOP cohort for our study was Mar. 31, 2017.

Data sources

We obtained individual-level longitudinal data of all people living with HIV in BC who received their HIV diagnosis between April 1996 and March 2017 from the STOP population-based cohort.[26] The cohort was constructed by linking the Drug Treatment Program's clinical registry[22] and various provincial administrative data sets[26–31] that provided demographic, clinical, laboratory, health care utilization and treatment information. Relevant data stewards performed the linkages by matching individuals' personal provincial health numbers, which were provided at birth or through immigration. The aforementioned data linkages and corresponding data capture are detailed in Appendix 1, Appendix Table 1, available at www.cmajopen.ca/content/10/1/E27/suppl/DC1).

Outcomes and exposures

Our outcomes were time from HIV diagnosis to ART initiation and from ART initiation to first virologic suppression. Our exposures were the eras of HIV diagnosis and ART initiation, 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 plasma viral load, an HIV-related hospitalization, 3 HIV-related physician visits, an AIDS-defining illness, or ART dispensation, as previously validated.[32] AIDS-defining illnesses included indicator diseases specified by the BC Centre for Disease Control,[33] and are outlined in Appendix 1, Appendix Table 2. We obtained the ART initiation date from the Drug Treatment Program.

We defined the virologic suppression date as the first instance of at least 2 consecutive test results within 4 months with a plasma viral load of less than 200 copies/mL, a conservative definition that we selected by taking into account the quantification range of plasma viral load assays during our study period. We excluded people living with HIV with less than 4 months of follow-up upon ART initiation who were therefore unable to meet the virologic suppression definition, and those who did not achieve suppression during the study period from the analysis of time from treatment to virologic suppression.

Confounders

We investigated the following potential confounders, selected based on relevance and availability of data: gender (women, men), age (< 30, 30–39, 40–49, ≥ 50 yr), health authority 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 risk group for HIV acquisition (gay, bisexual and other men who have sex with men; people who have ever injected drugs; heterosexual or other; unknown).

We collected age, health authority of residence and CD4 count at time of diagnosis and at time of ART initiation. For analysis of the time from treatment to viral suppression, we also assessed additional treatment-related potential confounders, measured at ART initiation, namely plasma viral load (continuous in $\log_{10}$ copies/mL) and first-line ART class (non-nucleoside reverse transcriptase inhibitor, protease inhibitor, integrase strand-transfer inhibitor, integrase strand-transfer inhibitor combined with non-nucleoside reverse transcriptase inhibitor and/or protease inhibitor, other). We used the CD4 count closest to (within a year before) the diagnosis and ART initiation dates, respectively. If unavailable, we chose the closest CD4 count measured within 3 months after these dates. We applied similar criteria when establishing plasma viral load at ART initiation. To accommodate differential quantification limits across monitoring assays for viral load,[34] we categorized all values of less than 50 copies/mL as 49 copies/mL and values over 100 000 copies/mL as 100 010 copies/mL.

Statistical analysis

We explored the annual trends (2005–2016) in time from diagnosis to treatment, and from treatment to viral suppression. We also evaluated the distribution of the 2 outcomes pre- and post-STOP, across gender, age, health authority 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 from diagnosis to treatment, and from treatment to viral suppression, adjusted for confounders.

We compared categorical variables using the Fisher exact test or χ^2 test, and compared continuous variables using the Kruskal–Wallis test.[35] We modelled the overdispersed time from diagnosis to treatment and from treatment to viral suppression using a negative binomial regression model.[36] Starting with a full model, we gradually omitted confounding variables until the change in the coefficient for the main explanatory variable was 5% or more.[37] We modelled time from diagnosis to treatment and from treatment to viral suppression in days, although for descriptive purposes and ease of reading, we converted these to months. All p values are 2-sided, and we set the significance level at 0.05. We performed analyses in SAS version 9.4 and R version 3.6.0.

Ethics approval

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 BC's *Freedom of Information and Protection of Privacy Act*.

Results

Of the 3301 eligible people in BC living with HIV who received their diagnosis in 2005–2016, 2719 (82%) were men, 1906 (58%) were aged 30 to 49 years old, 1831 (55%) were white, 1690 (51%) were residents of the Vancouver Coastal health authority, 1259 (38%) had a CD4 count of less than 350 cells/µL at diagnosis, and 1359 (41%) were part of the risk group of gay, bisexual and other men who have sex with men (Table 1). Those diagnosed pre- (n = 1601, 49%) and post-STOP (n = 1700, 51%) were significantly different in all demographic and clinical characteristics except for ethnicity.

Of the 2979 (90%) people living with HIV who achieved viral suppression, those who initiated ART pre- (n = 998, 34%) and post-STOP (n = 1981, 66%) were statistically significantly different on all characteristics except gender, ethnicity and health authority of residence. Of the 322 (10%) people living with HIV who were excluded from the analysis of time from treatment to viral suppression, 114 did not have the required minimum 4 months of follow-up, and 208 did not achieve suppression within the study period (median follow-up 2 [25th, 75th percentile (Q1, Q3) 1, 3] mo v. median follow-up 22 [Q1 8, Q3 43], mo respectively).

Time from HIV diagnosis to treatment initiation

The median time from HIV diagnosis to ART initiation declined from 23 (Q1 4, Q3 47) months in 2005 to 1 (Q1 1, Q3 2) month in 2016 (Figure 1). The decline in time from diagnosis to treatment before and after STOP was statistically significant across all population subgroups (Appendix 2, available at www.cmajopen.ca/content/10/1/E27/suppl/DC1). Additionally, the gaps in time from diagnosis to treatment across age, CD4 count and HIV acquisition risk groups narrowed after the implementation of STOP. For instance, before STOP, the median time from diagnosis to treatment among people younger than 30 years old was 20 months longer than those aged 50 years and older. After STOP, people living with HIV across all age groups initiated ART within a median of 2 months. After adjusting for CD4 count at diagnosis, the time from diagnosis to treatment was, on average, 64% shorter after STOP (adjusted mean ratio 0.36, 95% confidence interval [CI] 0.34–0.39) than before STOP.

Time from treatment initiation to viral suppression

The annual median time from treatment to viral suppression declined from 4 (Q1 2, Q3 6) months in 2005 to 1 (Q1 1, Q3 3) month in 2016; people who initiated ART in 2007 to 2013 achieved suppression within a steady median of 3 months (Figure 1). The decline in time from treatment to viral suppression before and after STOP was statistically significant, except among women, residents of the Northern health authority and those initiating ART with 200 to 349 CD4 cells/µL (Appendix 2). After the initiation of STOP, residents of the Northern health authority and people who had ever injected drugs had the longest median

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

Characteristic	No. (%) of participants† n = 3301	Time Dx-Tx			Time Tx-Vx		
		No. (%) of participants pre-STOP† n = 1601	No. (%) of participants post-STOP† n = 1700	p value	No. (%) of participants pre-STOP† n = 998	No. (%) of participants post-STOP† n = 1981	p value
Age, yr‡				0.0005			< 0.0001
< 30	719 (21.8)	320 (20.0)	399 (23.5)		126 (12.6)	421 (21.3)	
30–39	977 (29.6)	488 (30.5)	489 (28.8)		302 (30.3)	575 (29)	
40–49	929 (28.1)	493 (30.8)	436 (25.6)		323 (32.4)	560 (28.3)	
≥ 50	676 (20.5)	300 (18.7)	376 (22.1)		247 (24.7)	425 (21.5)	
Gender				0.0187			0.5013
Women	582 (17.6)	308 (19.2)	274 (16.1)		175 (17.5)	328 (16.6)	
Men	2719 (82.4)	1293 (80.8)	1426 (83.9)		823 (82.5)	1653 (83.4)	
Ethnicity				0.0626			0.0662
White	1831 (55.5)	893 (55.8)	938 (55.2)		581 (58.2)	1074 (54.2)	
Non-white	921 (27.9)	422 (26.4)	499 (29.4)		251 (25.2)	574 (29.0)	
Unknown	549 (16.6)	286 (17.9)	263 (15.5)		166 (16.6)	333 (16.8)	
Health authority‡				0.0138			0.6474
Fraser	787 (23.8)	348 (21.7)	439 (25.8)		240 (24.0)	496 (25.0)	
Interior	215 (6.5)	104 (6.5)	111 (6.5)		59 (5.9)	121 (6.1)	
Northern	190 (5.8)	99 (6.2)	91 (5.4)		50 (5.0)	100 (5.0)	
Vancouver Coastal	1690 (51.2)	824 (51.5)	866 (50.9)		536 (53.7)	1038 (52.4)	
Vancouver Island	366 (11.1)	192 (12.0)	174 (10.2)		109 (10.9)	207 (10.4)	
Unknown	53 (1.6)	34 (2.1)	19 (1.1)		< 5	19 (1.0)	
CD4 count, cells/µL‡				< 0.0001			< 0.0001
≥ 350	1259 (38.1)	427 (27)	832 (49)		192 (19.2)	1022 (51.6)	
200–349	530 (16.1)	225 (14)	305 (18)		336 (33.7)	463 (23.4)	
< 200	724 (21.9)	340 (21)	384 (23)		461 (46.2)	482 (24.3)	
Not measured	788 (23.9)	609 (38)	179 (11)		9 (0.9)	14 (0.7)	
HIV acquisition risk group				< 0.0001			< 0.0001
gbMSM	1359 (41.2)	562 (35)	797 (47)		357 (35.8)	913 (46.1)	
PWID	733 (22.2)	474 (30)	259 (15)		276 (27.7)	351 (17.7)	
Heterosexual or other	834 (25.3)	382 (24)	452 (27)		259 (26.0)	488 (24.6)	
Unknown	375 (11.4)	183 (11)	192 (11)		106 (10.6)	229 (11.6)	
Suppressed eventually				0.0329			NA§
No	322 (9.8)	138 (8.6)	184 (10.8)		NA§	NA§	
Yes	2979 (90.3)	1463 (91.4)	1516 (89.2)		NA§	NA§	
First-line ART class¶				NA¶			< 0.0001
INSTI	NA¶	NA¶	NA¶		5 (0.5)	365 (18.4)	
NNRTI	NA¶	NA¶	NA¶		405 (40.6)	675 (34.1)	
PI	NA¶	NA¶	NA¶		584 (58.5)	852 (43.0)	
INSTI + PI, INSTI + NNRTI, or INSTI + PI + NNRTI	NA¶	NA¶	NA¶		< 5	82 (4.1)	
Other	NA¶	NA¶	NA¶		0 (0)	7 (0.4)	
Viral load, log$_{10}$ copies/mL, median (Q1, Q3)¶	NA¶	NA¶	NA¶	NA¶	4.92 (4.40, 5.00)	4.78 (4.24, 5.00)	< 0.0001

Note: ART = antiretroviral treatment; gbMSM = gay, bisexual and other men who have sex with men; INSTI = integrase strand-transfer inhibitor; NA = not applicable; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PWID = people with history of injection drug use; Q1 = 25th percentile; Q3 = 75th percentile; STOP = Seek and Treat for Optimal Prevention of HIV/AIDS initiative; time Dx-Tx = time from HIV diagnosis to ART initiation; time Tx-Vx = time from ART initiation to viral suppression.
*For time Dx-Tx analysis, CD4 count was the only selected confounder; for time Tx-Vx analysis, selected confounders included health authority, CD4 count, HIV acquisition risk group and ART type.
†Unless indicated otherwise.
‡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.
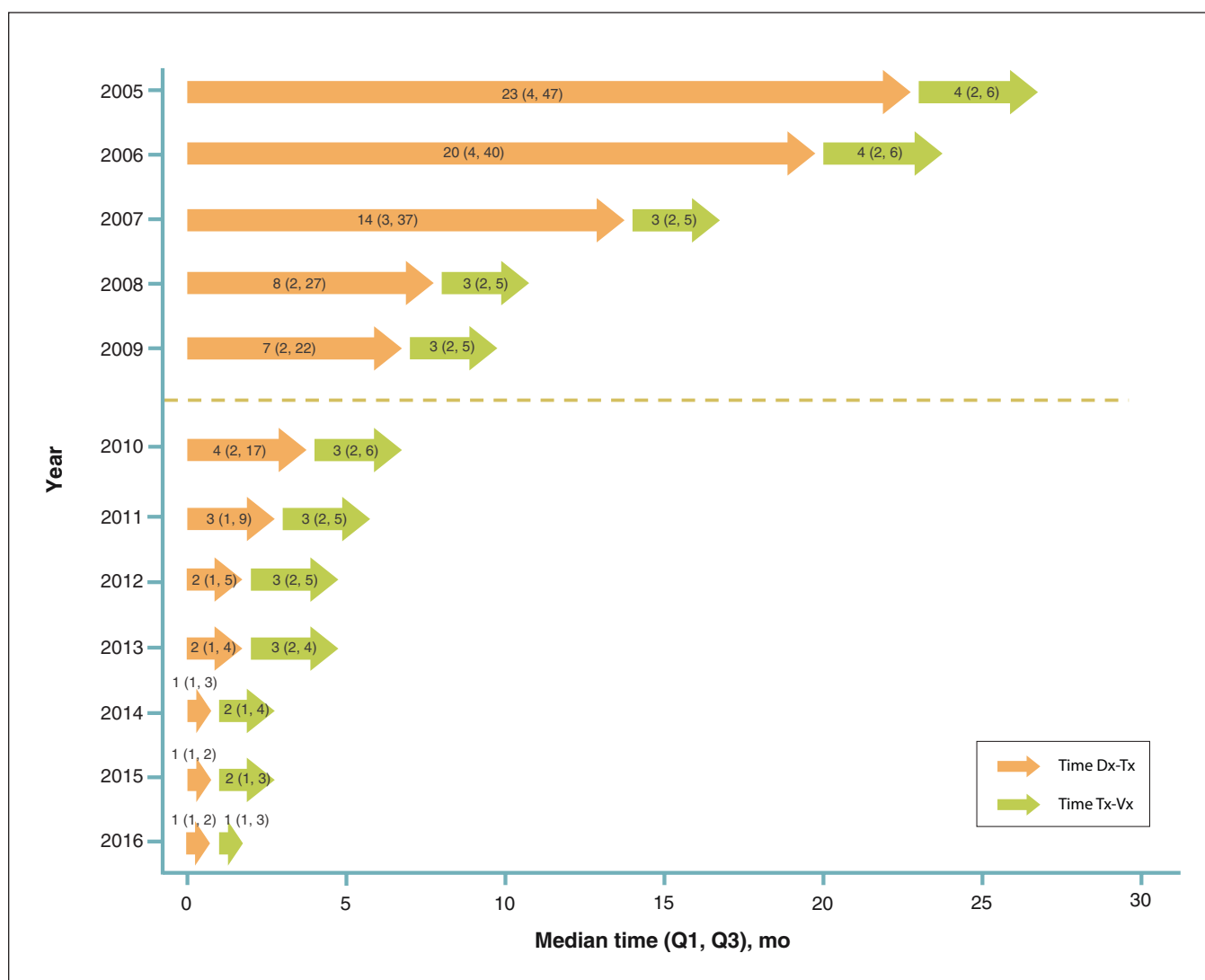¶Variables were measured only at the time of ART initiation.

Figure 1: The distribution of time from HIV diagnosis to initiation of antiretroviral treatment (time Dx-Tx) and from HIV treatment initiation to viral suppression (time Tx-Vx) among people living with HIV in British Columbia from 2005 to 2016. Time is in months, presented as median, with 25th and 75th percentiles (Q1, Q3). The dotted line represents the implementation date of the Seek and Treat for Optimal Prevention of HIV/ AIDS initiative on Feb. 4, 2010.

time from treatment to viral suppression at 4 (Q1 2, Q3 9) months. On average, after adjusting for health authority of residence, CD4 count at ART initiation, HIV acquisition risk group and type of first-line ART, STOP was associated with a 21% shorter time from treatment initiation to viral suppression (adjusted mean ratio 0.79, 95% CI 0.73–0.85).

Interpretation

Within our universal health care setting, a TasP intervention was strongly associated with earlier ART initiation and shorter time to virologic suppression. Even when adjusted for changes in ART eligibility, first-line ART preferences and other confounders, the TasP intervention implemented in BC was associated with a 64% shorter time from diagnosis to treatment and a 21% shorter time from treatment to suppression.

Observational studies from the Netherlands, South Korea, Thailand and New York City also reported a significant decrease in time from HIV diagnosis to treatment initiation in the 2012 to 2015 period,[38–41] when international guidelines began to recommend rapid ART initiation independent of CD4 count.[42–46] By 2015, however, 75% of people living with HIV in BC initiated ART within 2 months of their diagnosis, compared with 6 months, as noted in the other observational studies.[38–41] Although the independent impact of STOP in accelerating time from HIV diagnosis to treatment 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 1 in 7 people living with HIV in BC, particularly those who were older, were heterosexual, had ever injected drugs and resided

in the Northern health authority.[47] 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 times from treatment initiation to viral suppression.[48,49] Others reported faster suppression from the time of diagnosis,[50–56] which can be driven by shorter time from diagnosis to treatment or from treatment to viral suppression. In 2016, BC's combined median time from diagnosis to suppression was up to 2 months faster than that observed in several US jurisdictions.[54,55] Although our annual trends signalled that regimens using integrase strand-transfer inhibitors likely contributed to the faster decline in time from treatment to viral suppression, 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.[57,58] This assertion 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.[59–61] Our study showed BC's remarkable progress on rapid viral suppression by 2016, but further studies should investigate how the COVID-19 pandemic may affect this progress. Interrupted health care access, medication disruption and psychological stress from self-isolation and income loss are among additional challenges faced by people living with HIV during this pandemic, threatening progress on the control of HIV/AIDS.[62–65] Our study indicated potential disparities in the impact of STOP on early ART initiation across gender and health authority of residence. Further studies should explore specific barriers that may prevent population subgroups, such as women and residents of the Northern health authority, from receiving the full benefits of STOP.

Limitations

Administrative health data are susceptible to coding errors. We thus used validated case-finding algorithms, specifically developed to ascertain HIV diagnosis dates in administrative data sets. Our lack of granular data on ethnicity limited our ability to assess ethnic disparities in our outcomes fully. However, a recent study found no difference in HIV treatment outcomes between Indigenous and non-Indigenous people living with HIV who injected drugs in BC.[66]

We were able to assess only the overall impact of STOP, and not the individual impact of STOP's various supportive services. We did not distinguish STOP's pilot and full roll-out phases, and thus our findings represented the overall impact of the implementation of STOP initiative. Our data availability and structure rendered us unable to evaluate smaller time intervals. Consequently, although we found strong associations between STOP and faster ART initiation and virologic suppression, we were unable to separate the role of STOP and the role of time (i.e., other management and policy changes). A small proportion (2%–24%) of data on CD4 count, HIV acquisition risk group, health authority and ethnicity were unknown or unmeasured, which may minimally affect our findings.

People who recently received an HIV diagnosis may have achieved virologic suppression after the administrative censoring date of Mar. 31, 2017, and were thus excluded from the analysis of time from treatment initiation to viral suppression. Given the high suppression rates, the impact of this administrative censoring on our findings should be minimal. Our data were limited to this administrative censoring date. Nevertheless, given that ART eligibility has not changed between 2017 and the present, our findings remain valuable in elucidating STOP's contribution in optimizing the HIV care continuum.

Conclusion

Our large population-based study offers empirical evidence of the impact of a TasP intervention in accelerating the progress of BC toward the UNAIDS 90–90–90 target, in that the intervention was strongly associated with earlier ART initiation and shorter time to virologic suppression. These findings support the continued expansion of sustainable and equitable TasP-based policy and programmatic efforts that target underserved and hard-to-reach populations as key tools to reduce AIDS-related morbidity and mortality rates, as well as HIV transmission rates further, and thus alleviate the overall global burden of HIV/AIDS.

References

1. Hogg RS, Heath KV, Yip B, et al. Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. *JAMA* 1998; 279:450-4.
2. Murphy EL, Collier AC, Kalish LA, et al.; Viral Activation Transfusion Study Investigators. Highly active antiretroviral therapy decreases mortality and morbidity in patients with advanced HIV disease. *Ann Intern Med* 2001;135:17-26.
3. 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;372:293-9.
4. Porco TC, Martin JN, Page-Shafer KA, et al. Decline in HIV infectivity following the introduction of highly active antiretroviral therapy. *AIDS* 2004;18:81-8.
5. Donnell D, Baeten JM, Kiarie J, et al.; Partners in Prevention HSV/HIV Transmission Study Team. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 2010;375:2092-8.
6. Montaner JSG, Hogg R, Wood E, et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* 2006;368:531-6.
7. Montaner JSG. Treatment as prevention: a double hat-trick. *Lancet* 2011; 378:208-9.
8. Granich RM, Gilks CF, Dye C, et al. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009;373:48-57.
9. The Lancet Hiv. U=U taking off in 2017. *Lancet HIV* 2017;4:e475.
10. Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection undetectable equals untransmittable. *JAMA* 2019;321:451-2.
11. 90-90-90: treatment for all. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS). Available: https://www.unaids.org/sites/default/files/media_asset/90-90-90_en.pdf (accessed 2020 Nov. 1).
12. Granich RM, Gilks CF, Dye C, et al. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009;373:48-57.
13. Stover J, Hallett TB, Wu Z, et al.; New Prevention Technology Study Group. How can we get close to zero? The potential contribution of biomedical prevention and the investment framework towards an effective response to HIV. *PLoS One* 2014;9:e111956.
14. Yombi JC, Mertes H. Treatment as prevention for HIV infection: current data, challenges, and global perspectives. *AIDS Rev* 2018;20:131-40.
15. Brault MA, Spiegelman D, Abdool Karim SS, et al. Integrating and interpreting findings from the latest treatment as prevention trials. *Curr HIV/AIDS Rep* 2020;17:249-58.
16. Zuniga JM. UNAIDS 90-90-90: opportunity in every difficulty. *J Int Assoc Provid AIDS Care* 2018;17:2325958218809075.
17. Ending AIDS: progress towards the 90-90-90 targets. Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2017.

18. Duncombe C, Ravishankar S, Zuniga JM. Fast-track cities: striving to end urban HIV epidemics by 2030. *Curr Opin HIV AIDS* 2019;14:503-8.

19. About STOP HIV/AIDS. Seek and Treat for Optimal HIV Prevention of HIV/AIDS (STOP HIV/AIDS). Available: https://stophivaids.ca/about/ (accessed 2020 Nov. 1)

20. Lima VD, Brumme ZL, Brumme C, et al.; STOP HIV/AIDS Study Group. The impact of treatment as prevention on the HIV epidemic in British Columbia, Canada. *Curr HIV/AIDS Rep* 2020;17:77-87.

21. B.C. marks record achievements in effort to end AIDS [news release]. Victoria: British Columbia Ministry of Health; 2020 Dec. 1. Available: https://archive.news.gov.bc.ca/releases/news_releases_2020-2024/2020HLTH0062-001988.htm (accessed 2020 Dec. 1).

22. Drug Treatment Program. Vancouver: B.C. Centre for Excellence in HIV/AIDS. Available: bccfe.ca/drug-treatment-program (accessed 2018 Apr. 24).

23. BC Centre for Excellence in HIV/AIDSop. Therapeutic guidelines: antiretroviral (ARV) treatment of adult HIV infection. Vancouver: B.C. Centre for Excellence in HIV/AIDS; 2019, updated June 2020. Available: bccfe.ca/sites/default/files/uploads/Guidelines/2020_06_30-BC-CfE_Adult_ARV_Therapeutic_Guidelines.pdf (accessed 2019 Jan. 10).

24. Patel DA, Snedecor SJ, Tang WY, 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* 2014;9:e105653.

25. Kamelian K, Lepik KJ, Chau W, 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* 2019;6:ofz060.

26. Heath K, Samji H, Nosyk B, et al.; STOP HIV/AIDS Study Group. Cohort profile: seek and treat for the optimal prevention of HIV/AIDS in British Columbia (STOP HIV/AIDS BC). *Int J Epidemiol* 2014;43:1073-81.

27. Medical services plan (MSP) payment information file; consolidation file (MSP Registration & Premium Billing); Home & Community Care (continuing care); mental health; PharmaNet. Data Extract. MOH. Victoria: British Columbia Ministry of Health; 2016. Available: https://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/data-access-health-data-central (accessed 2020 Nov. 1).

28. Canadian Institute of Health Information. Discharge abstract database (hospital separations). Data Extract. MOH. Victoria: British Columbia Ministry of Health; 2016. Available: https://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/data-access-health-data-central (accessed 2020 Nov. 1).

29. British Columbia Centre for Disease Control Public Health Laboratory. HIV laboratory testing datasets (tests: ELISA, Western blot, NAAT, p24, culture). Clinical Prevention Services, British Columbia Centre for Disease Control. Data Extract. Victoria: British Columbia Ministry of Health; 2016. Available: http://www.bccdc.ca/about/accountability/data-access-requests/public-health-data (accessed 2020 Nov. 1).

30. British Columbia Centre for Disease Control. HIV/AIDS Information System (HAISYS). Clinical Prevention Services, British Columbia Centre for Disease Control. Data Extract. Victoria: British Columbia Ministry of Health; 2016. Available: http://www.bccdc.ca/about/accountability/data-access-requests/public-health-data (accessed 2020 Nov. 1).

31. British Columbia Vital Statistics Agency. Vital statistics. Data Extract. Victoria: British Columbia Ministry of Health; 2016. Available: https://www2.gov.bc.ca/gov/content/health/conducting-health-research-evaluation/data-access-health-data-central (accessed 2020 Nov. 1).

32. Nosyk B, Colley G, Yip B, et al.; STOP HIV/AIDS Study Group. Application and validation of case-finding algorithms for identifying individuals with human immunodeficiency virus from administrative data in British Columbia, Canada. *PLoS One* 2013;8:e54416.

33. Acquired Immune Deficiency Syndrome (AIDS) case report form. Vancouver: BC Centre for Disease Control; 2013. Available: www.bccdc.ca/resource-gallery/Documents/Communicable-Disease-Manual/Chapter%205%20-%20STI/AIDSsurveillanceCRF_2013_Final.pdf (accessed 2021 July 16).

34. 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;51:3-6.

35. McDonald JH. *Handbook of biologial statistics*. 2nd ed. Baltimore: Sparky House Publishing; 2009.

36. Khorana AA, Tullio K, Elson P, et al. Time to initial cancer treatment in the United States and association with survival over time: an observational study. *PLoS One* 2019;14:e0213209.

37. Lima VD, Geller J, Bangsberg DR, et al. The effect of adherence on the association between depressive symptoms and mortality among HIV-infected individuals first initiating HAART. *AIDS* 2007;21:1175-83.

38. Robertson MM, Braunstein SL, Hoover DR, et al. Timeliness of human immunodeficiency virus diagnosis and antiretroviral treatment initiation in the era of universal testing and treatment. *J Infect Dis* 2019;220:648-56.

39. Boender TS, Smit C, Van Sighem A, et al.; ATHENA national observational HIV cohort. AIDS Therapy Evaluation in the Netherlands (ATHENA) national observational HIV cohort: cohort profile. *BMJ Open* 2018;8:e022516.

40. Kim YJ, Kim SW, Kwon KT, 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* 2019;34:e239.

41. Teeraananchai S, Kerr SJ, Khananuraksa P, et al. 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* 2020;23(Suppl 5):e25574.

42. Eholié SP, Badje A, Kouame GM, et al. Antiretroviral treatment regardless of CD4 count: the universal answer to a contextual question. *AIDS Res Ther* 2016;13:27.

43. *Guideline on when to start antiretroviral pre-exposure prophylaxis for HIV*. Geneva: World Health Organization; 2015. Available: https://apps.who.int/iris/bitstream/handle/10665/186275/9789241509565_eng.pdf (accessed 2020 Nov. 4).

44. *EACS Guidelines version 8.2, January 2017*. Brussels (Belgium): European AIDS Clinical Society (EACS); 2017. Available: https://www.eacsociety.org/files/guidelines_8.2-english.pdf (accessed 2020 Nov. 4).

45. Panel on Antiretroviral Guidelines for Adults and Adolescents. *Guidelines for the use of antiretroviral agents in adults and adolescents with HIV*. Rockville (MD): National Institutes of Health; updated 2021 Aug. 16. Available: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf (accessed 2020 Nov. 4).

46. Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA Panel. *JAMA* 2018;320:379-96.

47. Nanditha NGA, St-Jean M, Tafessu H, et al. Missed opportunities for earlier diagnosis of HIV in British Columbia, Canada: a retrospective cohort study. *PLoS One* 2019;14:e0214012.

48. Nance RM, Delaney JAC, Simoni JM, et al. HIV viral suppression trends over time among HIV-infected patients receiving care in the United States, 1997 to 2015: a cohort study. *Ann Intern Med* 2018;169:376-84.

49. Bacon O, Chin J, Cohen SE, 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* 2021;73:e122-8.

50. Toren KG, Buskin SE, Dombrowski JC, et al. Time from HIV diagnosis to viral load suppression: 2007–2013. *Sex Transm Dis* 2016;43:34-40.

51. Medland NA, Nicholson S, Chow EPF, et al. Time from HIV infection to virological suppression: dramatic fall from 2007 to 2016. *AIDS* 2017;31:2377-85.

52. Colasanti J, Sumitani J, Mehta CC, 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* 2018;5:ofy104.

53. Wilton J, Liu J, Sullivan A, et al.; Ontario HIV Epidemiology and Surveillance Initiative. Trends in HIV care cascade engagement among diagnosed people living with HIV in Ontario, Canada: a retrospective, population-based cohort study. *PLoS One* 2019;14:e0210096.

54. Doshi RK, Li J, Dorsey K, et al. Earlier diagnoses and faster treatment of HIV in the District of Columbia: HIV surveillance analysis, 2006–2016. *AIDS Care* 2019;31:1476-83.

55. Crepaz N, Song R, Lyss S, et al. Trends in time from HIV diagnosis to first viral suppression following revised US HIV treatment guidelines, 2012–2017. *J Acquir Immune Defic Syndr* 2020;85:46-50.

56. 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. *J Acquir Immune Defic Syndr* 2015;70:529-37.

57. Xia Q, Coeytaux K, Braunstein SL, et al. 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* 2019;219:851-5.

58. Dombrowski JC, Baeten JM. It's time to make the time to viral suppression after HIV diagnosis a metric of HIV care success. *J Infect Dis* 2019;219:845-7.

59. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000;133:21-30.

60. Arnsten JH, Demas PA, Grant RW, et al. Impact of active drug use on antiretroviral therapy adherence and viral suppression in HIV-infected drug users. *J Gen Intern Med* 2002;17:377-81.

61. Chander G, Himelhoch S, Fleishman JA, et al. HAART receipt and viral suppression among HIV-infected patients with co-occurring mental illness and illicit drug use. *AIDS Care* 2009;21:655-63.

62. Sun S, Hou J, Chen Y, et al. Challenges to HIV care and psychological health during the COVID-19 pandemic among people living with HIV in China. *AIDS Behav* 2020;24:2764-5.

63. Jiang H, Zhou Y, Tang W. Maintaining HIV care during the COVID-19 pandemic. *Lancet HIV* 2020;7:e308-9.

64. Ridgway JP, Schmitt J, Friedman E, et al. HIV care continuum and COVID-19 outcomes among people living with HIV during the COVID-19 pandemic, Chicago, IL. *AIDS Behav* 2020;24:2770-2.

65. Kowalska JD, Skrzat-Klapaczyńska A, Bursa D, et al.; ECEE Network Group. HIV care in times of the COVID-19 crisis: Where are we now in central and eastern Europe? *Int J Infect Dis* 2020;96:311-4.

66. Milloy M-J, King A, Kerr T, 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* 2016;19:20617.