Characterizing HIV Antiretroviral Therapy Interruption and Resulting Disease Progression Using Population-Level Data in British Columbia, 1996–2015

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Background

- Suboptimal retention is among the biggest challenges to realize the full benefits of combination antiretroviral therapy (ART).
- In British Columbia (BC), Canada, despite progress over time, gaps exist at each stage of the HIV cascade including achieving suppressed plasma viral load (pVL), underscoring the pressing need to optimize ART continuation.
- We aimed to describe ART interruption patterns and identify determinants of disease progression while off ART in BC.

Methods

- We used population-level data on ART utilization and laboratory testing among individuals who were antiretroviral naïve at age ≥19 years and initiated ART between 1996 and 2015 in BC.
- The study cohort was followed in a unique environment characterized by universal medical care, including free in- and outpatient care, laboratory monitoring, and antiretroviral drugs.
- ART interruption was defined as a minimum 90-day gap between the prescription refill date and the date when previously dispensed medications were expected to be finished.
- First, we evaluated the proportion of individuals interrupting ART during follow-up and compared their characteristics to those remaining on ART.
- Second, we examined the number of first and subsequent interruption episodes by calendar year and, the proportion of individuals who received at least 1 CD4/pVL test while off ART.
- Third, a 4-state continuous-time Markov model was implemented to identify determinants of disease progression during individuals' first ART interruption episode.
- Disease progression was measured according to CD4-based state transitions (cells/μL: ≥500 to 200–499; 200–499 to <200; ≥500 to death; 200–499 to death; and <200 to death).

Table 1. Characteristics at ART Initiation of 8110 Individuals Who Initiated ART in BC, by ART Interruption 1996–2015.

	Ever interrupted ART	Never interrupted ART
Characteristics (N(%)/Median [IQR])	(N=3129)	(N=4981)
Age, years	**38.2 [32.2, 44.8]**	**42.4 [34.9, 49.7]**
Male	**2342 (74.8)**	**4294 (86.2)**
Caucasian		
Yes	1841 (58.8)	3072 (61.7)
No	792 (25.3)	1057 (21.2)
Unknown	496 (15.9)	852 (17.1)
Aboriginal ethnicity		
Yes	**617 (19.7)**	**405 (8.1)**
No	2016 (64.4)	3724 (74.8)
Unknown	496 (15.9)	852 (17.1)
People who inject drugs		
Yes	**1595 (51.0)**	**1056 (21.2)**
No	1034 (33.0)	2595 (52.1)
Unknown	500 (16.0)	1330 (26.7)
CD4 <200 cells/mm^3 [a]		
Yes	1162 (37.1)	1776 (35.7)
No	1675 (53.5)	2838 (57.0)
Unknown	292 (9.3)	367 (7.4)
HIV drug resistance [b]	277 (8.9)	428 (8.6)
Hepatitis C positive		
Yes	**1724 (55.1)**	**1260 (25.3)**
No	1200 (38.4)	3276 (65.8)
Unknown	205 (6.6)	445 (8.9)
Modern regimen [c]	**1611 (51.5)**	**4089 (82.1)**
Calendar year		
1996-2003	**1678 (53.6)**	**884 (17.7)**
2004-2007	607 (19.4)	1015 (20.4)
2008-2011	598 (19.1)	1584 (31.8)
2012-2015	246 (7.9)	1498 (30.1)
Follow-up years	8.0 [4.3, 13.5]	4.4 [1.5, 7.9]

Results

- Among 8110 individuals initiating ART, 3129 **(38.6%) interrupted ART** over a median of 8-year follow-up (interquartile range [IQR], 4.3–13.5 years).
- Individuals interrupting ART were younger at ART initiation and were more likely to be aboriginal, people who inject drugs and hepatitis C positive, compared with individuals remaining on ART (**Table 1**).
- Those interrupting ART had a median of 1 interruption (IQR, 1.0–3.0), with **the first interruption occurring 12.8 months** (IQR, 4.0–36.1) **after ART initiation, lasting for 7.5 months** (IQR, 4.1–20.3).
- The absolute number of individuals interrupting ART remained high over time (**Figure 1**).
- A large proportion of individuals remained in HIV monitoring care after their first ART interruption (**Figure 1**).
- In the multivariable analysis, age, historical pVL, and ART regimen changes prior to interruption were associated with increased hazard of CD4 decline and death (**Figure 2**).

Figure 1. Longitudinal trends of ART interruption and individuals' retention to HIV care (N=3129).

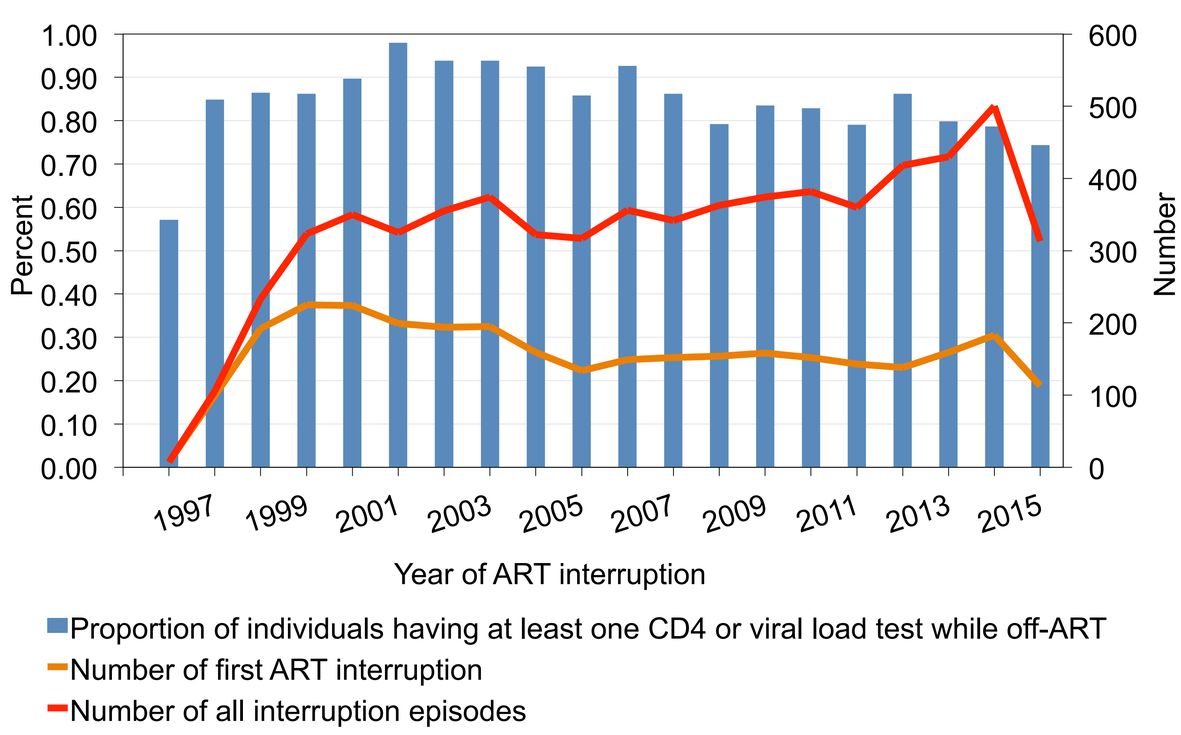
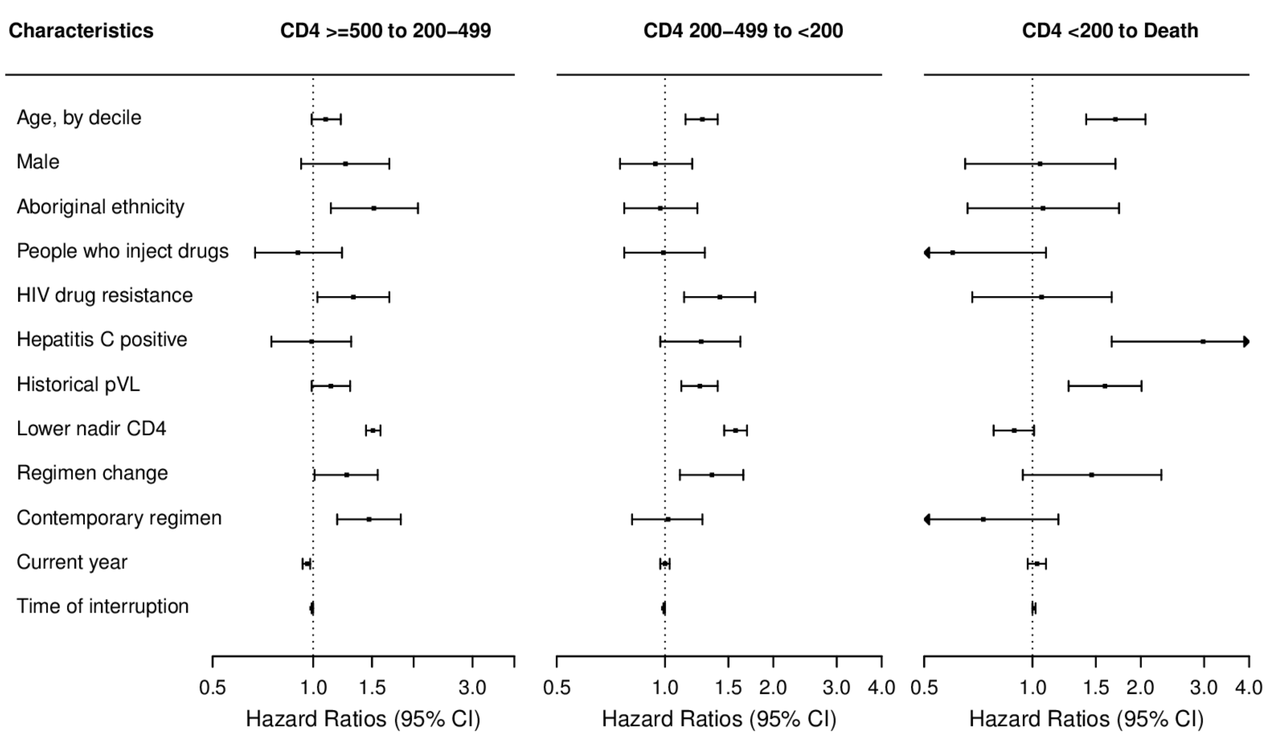


Figure 2. Adjusted hazard ratios associated with disease progression during the first ART interruption episode among 2212 individuals.



Conclusions

- Our results demonstrate that ART interruptions are common even in a high-resource setting with universal free access to HIV care.
- Despite observed improvement over time, further efforts are needed to promote ART re-engagement and may consider prioritizing individuals with older age, higher levels of historical pVL, and prior ART regimen change experience.

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