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Treatment Interruptions Common Among Adolescents and Young Adults Living with HIV in Canada

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Background

In the current clinical landscape of Treatment as Prevention (TasP), the main focus is to have all persons living with HIV on treatment and support them to achieve virological suppression. Trends among adolescents and young adults (AYA) show AYA are facing on-going challenges with adherence to combination antiretroviral therapy (cART). Although AYA may initiate treatment in a timely manner, evidence suggests they do not always adhere to their prescribed medication and are more likely to experience treatment interruptions (TIs). Incomplete adherence and TIs often result in viral rebound and are associated with treatment failure, HIV resistance, suboptimal clinical outcomes and increased potential of HIV transmission. Given that AYA comprise nearly one-quarter of all HIV-positive Canadians and are reported to have poorer clinical outcomes than among adults, AYA are a priority demographic for research and intervention.

In order to better understand treatment interruptions among AYA, this study seeks to assess and compare treatment interruptions among AYA (18-29 years) and older adults and explore factors associated with treatment interruptions among AYA

Methods

Participants are HIV-positive individuals from the Canadian Observational Cohort (CANOC) Collaboration, a multi-site Canadian cohort of antiretroviral-naïve patients initiating cART on/after 1 January 2000. This analysis was limited to CANOC participants who initiated cART during the period January 1, 2000 to December 31, 2011**. A treatment interruption was defined as a gap in treatment >90 consecutive days during the follow-up time**. Life tables and Kaplan-Meier curves were used to estimate probabilities of treatment interruptions. Univariate and multivariate [Cox Proportional Hazards] models explored factors associated with treatment interruptions among AYA aged 18-29 compared with older adults >30 years. An exploratory model selection process based on Akaike Information Criterion (AIC) and Type III p-values was conducted to find factors that were significantly associated with the outcome. These two criteria balanced the model choice by finding the best exploratory model and, at the same time, selecting a model with the best goodness-of-fit statistic. A two-sided P-value below 0.05 was considered statistically significant. All analyses were performed using SAS software (version 9.3).

Results

8582 people living with HIV were included in this analysis, with 1182 (13.8%) aged 18-29 (AYA). AYA were more likely than older adults to experience treatment interruptions (29% vs. 20%, p<0.001). **Table 1** illustrates differences between AYA and older adults. Approximately 31% of AYA were female, 6% identify as Aboriginal, 37% identify as MSM, 20% report a history of injection drug use (IDU), 21% are coinfected with Hepatitis C, 9% had a baseline AIDS-defining illness (ADI), and 47% of AYA initiated cART between 2008 and 2011. Almost half (47%) of AYA initiated cART on an NNRTI based regimen with almost 75% starting with a baseline CD4 count lower than 350 cells/mm^3). The time to first treatment interruption among AYA was 7 (3-21) months compared with 13 (4-31) months among older adults. In adjusted analyses (**Table 2**), factors associated with TIs among AYA were being female (adjusted hazard ratio [AHR]: 1.79; 95% confidence interval [CI]: 1.41-2.26, p<0.001), self-identifying as Aboriginal (AHR: 1.52; 95% CI:1.02-2.26, p<0.010), and having a history of IDU (AHR: 2.22; 95% CI: 1.68-2.94, p<0.001).

Discussion

- AYA disproportionally experienced treatment interruptions compared to adults over the study period. Despite access to universal, free-of-charge health care and cART availability, a quarter of AYA were not remaining on treatment.
- Young women, Aboriginal youth and those with a history of injection drug use are especially at risk for treatment interruptions.
- Young women are at greater risk for TIs than young men. Research evidence suggests that this difference is due to competing priorities such as childcare, employment and housing, each of which affects one's ability to remain on medications as directed. Women are also more likely to suffer from depressive symptoms which may also inhibit their ability to adhere to and take cART as prescribed.
- Recent research indicates that people who inject drugs can achieve optimal adherence and suppression even in the context of ongoing drug use, which suggests that social-structural forces play a role in mediating the relationship between injection drug use and HIV treatment outcomes. Tailored support programs can assist AYA who use drugs with retention in care.
- Aboriginal AYA living with HIV report social stigma and discrimination, which may complicate access to HIV care. Many report a lack of culturally appropriate services where they can discuss their treatment in confidence and access holistic care.
- Individualized care plans developed in collaboration with the patient that factor in not only HIV management but also culturally relevant holistic services that treat interconnected health issues such as addiction and/or trauma can increase feelings of support and levels of comfort communicating with health providers which may result in improved retention in treatment.

Table 1: CANOC participants stratified by age (n= 8582)

Variable	≤ 29 (N=1182)	> 29 (N=7400)	P-value
	N (%)	N (%)	
Gender			
Male	812 (69)	6212 (84)	<0.001
Female	370 (31)	1188 (16)	
Province			
BC	475 (40)	3528 (48)	<0.001
ON	453 (38)	2401 (32)	
QC	254 (21)	1471 (20)	
Ethnicity			
Caucasian	297 (25)	2073 (28)	<0.001
Black	139 (12)	613 (8)	
Aboriginal	66 (6)	355(5)	
Other	105 (9)	545 (7)	
Unknown/Missing	575 (49)	3814 (52)	
HIV risk MSM			
Yes	433 (37)	2726 (37)	0.590
HIV risk IDU			
Yes	238 (20)	1680 (23)	0.007
Hepatitis C			
Coinfected	244 (21)	1901 (26)	<0.001
Baseline AIDS-defining illness			
At least one before first	105 (9)	1202 (16)	<0.001
Era of ART initiation			
2000-2003	289 (24)	1954 (26)	<0.001
2004-2007	339 (29)	2501 (34)	
2008-2011	554 (47)	2945(40)	
Classes of ARVs in first regimen			
NNRTI	550 (47)	3442 (47)	<0.001
Unboosted PI	117 (10)	391 (5)	
Boosted PI	436 (37)	3033 (41)	
Other	79 (7)	534 (7)	
Third drug in ARV regimen			
Nevirapine	128 (11)	728 (10)	0.244
Efavirenz	414 (35)	2649 (36)	
Lopinavir	171 (14)	1203 (16)	
Atazanavir	235 (20)	1500 (20)	
Other	234 (20)	1320 (18)	
Baseline CD4 (cells/ mm3)			
< 200	404 (34)	3456 (47)	<0.001
200-350	466 (39)	2698 (36)	
> 350	312 (26)	1246 (17)	
Treatment interruption (ever)			
Yes	338 (29)	1503 (20)	<0.001
Age at first ARV initiation (years)	27 (24-28)	42 (36-48)	<0.001
Baseline CD4 (cells/ mm3)	252 (160-360)	210 (110-305)	<0.001
Baseline VL (Log10 copies/mL)	5 (4-5)	5 (4-5)	<0.001
Time to first treatment interruption (months)	32 (13-59)	44 (19-78)	<0.001
Follow up time (years)	4 (2-7)	5 (3-8)	<0.001

Table 2: Factors associated with treatment interruptions among CANOC participants ≤ 29 years, n=1168

	Unadjusted		Adjusted	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Gender				
Male	1.00 (-)	<0.001	1.00 (-)	<0.001
Female	2.7(2.18, 3.34)		1.79(1.41, 2.26)	
Province				
BC	1.00 (-)	<0.001	1.00 (-)	<0.001
ON	0.42(0.33, 0.54)		0.61(0.45, 0.82)	
QC	0.36(0.26, 0.5)		0.39(0.27, 0.56)	
Ethnicity				
Caucasian	1.00 (-)	<0.001	1.00 (-)	0.010
Black	1.28(0.89, 1.83)		1.42(0.95, 2.11)	
Aboriginal	3.66(2.52, 5.3)		1.52(1.02, 2.26)	
Other	0.58(0.34, 0.98)		0.65(0.39, 1.11)	
Unknown/Missing	1.07(0.82, 1.4)		1.38(1.02, 1.86)	
HIV risk IDU				
No	1.00 (-)	<0.001	1.00 (-)	<0.001
Yes	3.3(2.62, 4.16)		2.22(1.68, 2.94)	
Unknown	0.88(0.63, 1.23)		0.77(0.53, 1.13)	
Era of ART initiation				
2000-2003	1.00 (-)	<0.001	1.00 (-)	0.008
2004-2007	0.66(0.51, 0.84)		0.83(0.62, 1.12)	
2008-2011	0.31(0.23, 0.41)		0.52(0.34, 0.79)	
Classes of ARVs in first regimen			Not selected	
NNRTI	1.00 (-)	<0.001		
Unboosted PI	2.13(1.58, 2.88)			
Boosted PI	1.04(0.81, 1.33)			
Other	0.8(0.48, 1.32)			

Figure 1: Probability of treatment interruption by Age

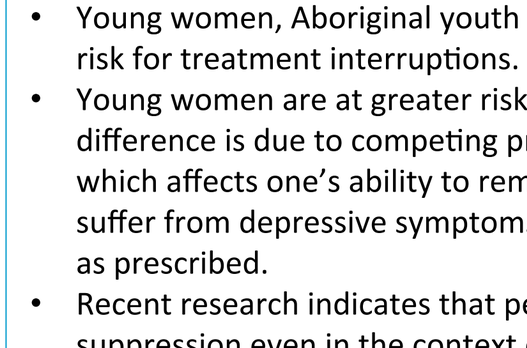


Figure 2: Probability of treatment interruption by Gender

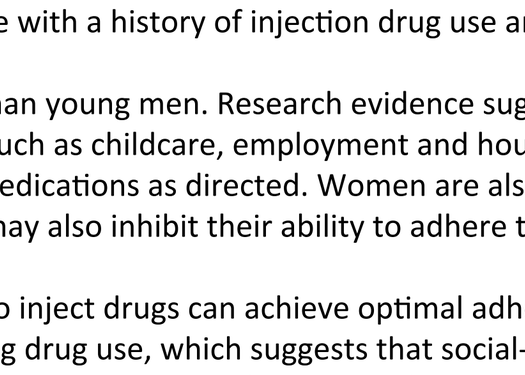


Figure 3: Probability of treatment interruption by Ethnicity

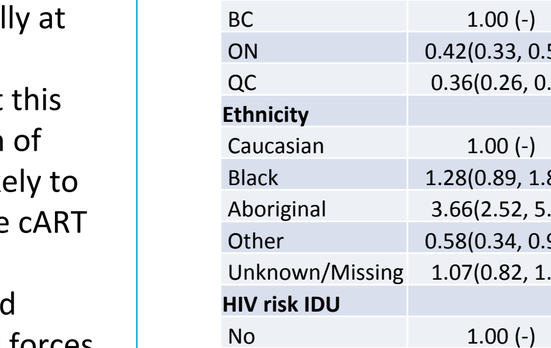
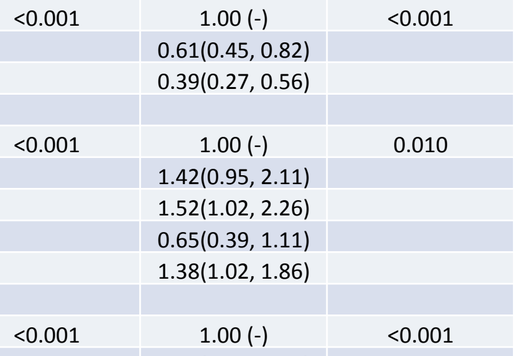


Figure 4: Probability of treatment interruption by IDU



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