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Background

Research evidence indicates that adolescents and young adults (AYA) living with HIV often have poorer treatment and clinical outcomes compared with older adults however, reasons for poorer outcomes among AYA are not well understood. As shown in Table 1, virological suppression is associated with being over the age of 29 years (86% vs. 91%, $p<0.001$). Achievement and maintenance of virological suppression is the final stage in the HIV Cascade of Care, originally espoused by Gardner et al. (Figure 1). This spectrum of engagement in care represents an important framework for surveillance and evaluation for HIV treatment. This cascade lays out the roadmap to achievement of virology suppression with each step representing numerous opportunities to engage with clients and to assist them in successfully moving to the next step. **The aim of this study is to assess and compare time to virological suppression following combination antiretroviral therapy (cART) initiation among AYA (18-29 years) and older adults and to explore factors associated with virological suppression among AYA.**

Figure 1: HIV Cascade of Care (based on Gardner et al, 2011)



Methods

Participants are HIV-positive individuals from the Canadian Observational Cohort Collaboration (CANOC), 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 September 30, 2011. Virologic suppression was defined as time to the first of at least two consecutive viral load measurements <50 HIV-1 RNA copies/ at least 30 days apart. Life tables and Kaplan-Meier curves were used to estimate probabilities of virologic suppression. Univariate and multivariable [Accelerated Failure Time] models explored factors associated with virologic suppression among AYA aged 18-29 compared with older adults >30 years. Final multivariate models were selected using an exploratory model selection process based on Akaike Information Criterion (AIC) and Type III p-values. A two-sided P-value below 0.05 was considered statistically significant. All analyses were performed using SAS software (version 9.3).

Results

A total of 8471 individuals were included in this analysis. 1,168 (13.8%) of individuals were ≤ 29 years old at the time of cART initiation. Among AYA (median age=27), 1,007 (86%) had ever experienced virologic suppression compared with 6670 (91%) of older adults ($p<0.001$). 71% of AYA compared with 78% of older adults suppressed within the first year of cART initiation ($p<0.001$). In adjusted analyses among AYA, those who suppressed were more likely to be male (Adjusted Hazard Ratio [aHR]: 1.68, 95% CI=1.44-1.95, $p<0.001$), to have started cART in later calendar years (aHR=2.46, CI: 2.08-2.92, $p<0.001$) and were less likely to have a history of IDU (aHR: 0.46, 95% CI=0.38-0.55, $p<0.001$), to have started cART on an unboosted protease inhibitor (aHR: 0.55, CI=0.43-0.70, $p<0.001$), and less likely to be living in Ontario (aHR= 0.86, CI: 0.74-1.0, $p=0.043$).

Discussion

- AYA are less likely than older adults to achieve virological suppression.
- Over a quarter of AYA are not achieving virological suppression within the first year of treatment.
- Not achieving virological suppression was associated with gender, drug use, era of cART initiation and the province of residence.
- Disparities in virologic responses between men and women are likely largely influenced by context; and have been found to be related to socioeconomic and psychosocial rather than biological ones, which may be the case with our cohort of young people.
- The link between drug use and poor suppression is well established. AYA with a history of drug use may be managing competing priorities such as housing, food security, and active addictions which may impede optimal access to care and adherence to cART, resulting in a need for increased supportive services to help them prioritize their health.
- As illustrated by our data, the era in which a person initiated cART has an effect on clinic outcomes. Virological suppression is more likely among individuals who initiated cART in calendar years 2008-2011. Since 2000, regimens have been improving and new drugs have been introduced that reduce dosing frequency, pill burden, and the level of toxicity, and also with improving degrees of efficacy, tolerability and convenience
- As illustrated in Figures 2-5, factors such as gender, drug use behaviours and the era of cART initiation must be considered while also treating the individual's HIV disease.
- AYA are an important to engage with in order for TasP to be successful. Multi-faceted care such as women-centered programming, establishment of maximally assisted therapy programs, and innovation ways to re-engage in care for those individuals who have dropped out is needed to optimize both individual health and Treatment as Prevention (TasP).

Figure 2: Probability of achieving virological suppression by age

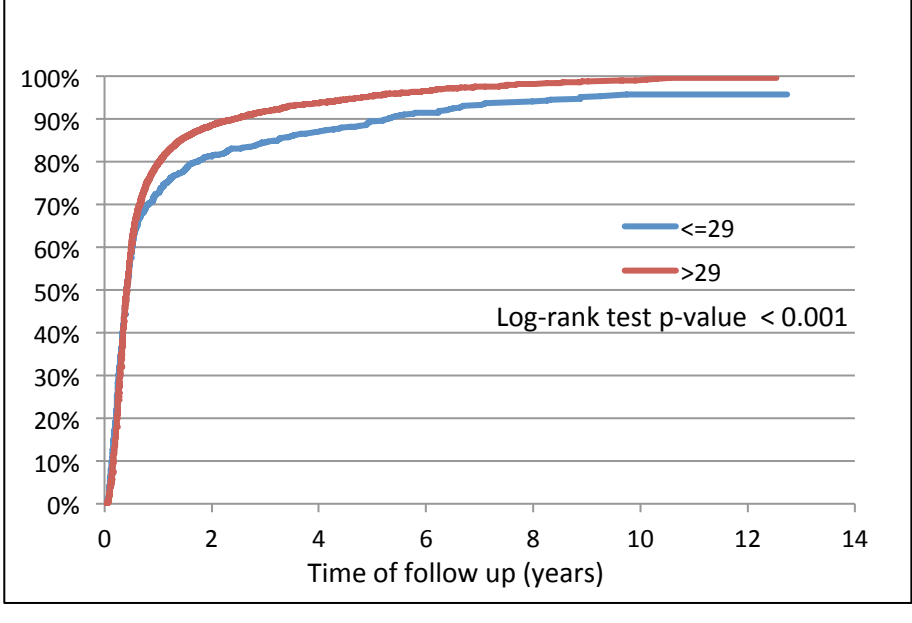


Figure 3: Probability of achieving VL suppression by gender among AYA

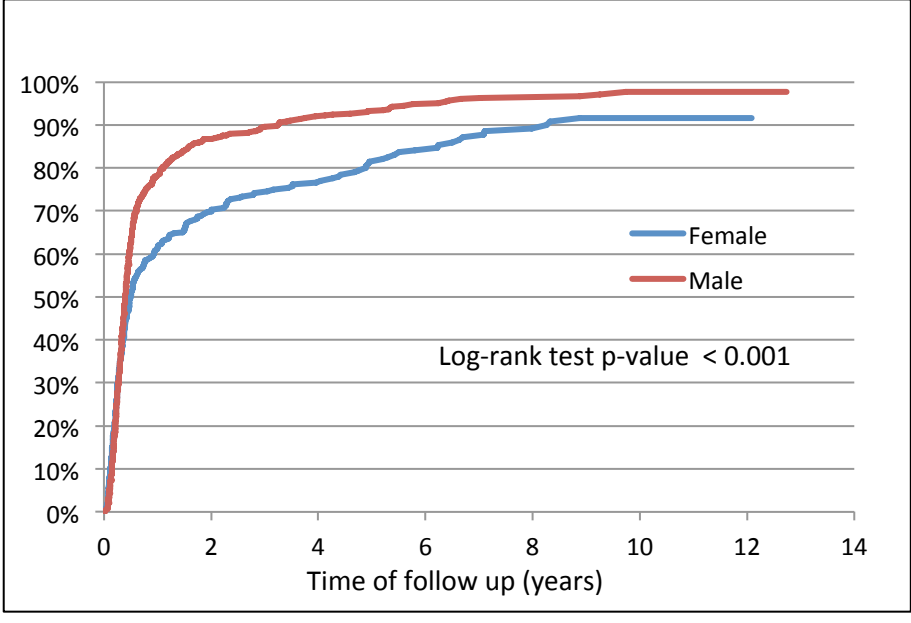


Table 1: Virological suppression stratified by age in CANOC, n = 8471

Variable	Age at first ARV initiation (years)		P-value
	<= 29 (N=1168) N (%)	> 29 (N=7303) N (%)	
Gender			
Male	795 (68)	6117 (84)	<0.001
Province			
BC	470 (40)	3441 (47)	<0.001
ON	451 (39)	2410 (33)	
QC	247 (21)	1452 (20)	
Aboriginal			
Yes	66 (6)	340 (5)	0.124
HIV risk MSM			
Yes	424 (36)	2702 (37)	0.502
HIV risk IDU			
Yes	234 (20)	1650 (23)	0.012
Hepatitis C			
Co-infected	241 (21)	1866 (26)	0.001
Baseline ADI			
At least one before/on first cART date	101 (9)	1164 (16)	<0.001
Era of ART initiation			
2000-2003	284 (24)	1907 (26)	<0.001
2004-2007	340 (29)	2452 (34)	
2008-2011	544 (47)	2944 (40)	
Virological suppression ever			
Yes	1007 (86)	6670 (91)	<0.001
Classes of ARVs in first regimen			
NNRTI	540 (46)	3460 (47)	<0.001
Unboosted PI	121 (10)	384 (5)	
Boosted PI	430 (37)	2979 (41)	
Other	77 (7)	480 (7)	
Third drug in ARV regimen			
Nevirapine	127 (11)	719 (10)	<0.001
Efavirenz	411 (35)	2657 (36)	
Lopinavir	181 (15)	1261 (17)	
Atazanavir	250 (21)	1619 (22)	
Nelfinavir	87 (7)	253 (3)	
Other	112 (10)	794 (11)	
Age at first ARV initiation (years)	27 (24-28)	42 (36-48)	<0.001
Baseline CD4 (cells/mm3)	256 (160-360)	210 (116-310)	<0.001
Baseline VL (Log10 copies/mL)	5 (4-5)	5 (4-5)	<0.001
Time to virological suppression (months)	5 (3-12)	5 (3-9)	0.747
Follow up time (years)	4 (2-8)	5 (3-8)	<0.001

Table 2: Factors associated virological suppression among CANOC participants ≤ 29 years, n=1168

	Unadjusted		Adjusted	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Gender				
Female	1.00 (-)	<0.001	1.00 (-)	<0.001
Male	2.03 (1.77, 2.33)		1.68 (1.44, 1.95)	
HIV risk IDU				
No	1.00 (-)	<0.001	1.00 (-)	<0.001
Yes	0.38 (0.32, 0.45)		0.46 (0.38, 0.55)	
Unknown	0.84 (0.71, 0.99)		0.89 (0.75, 1.06)	
Aboriginal			-	
Not aboriginal	1.00 (-)	<0.001		
Aboriginal	0.47 (0.35, 0.62)			
Unknown/Missing	1.13 (1.00, 1.29)			
Baseline ADI			-	
No ADI ever	1.00 (-)	0.087		
None before or on FARVDT	1.01 (0.76, 1.35)			
At least one before or on FARVDT	0.78 (0.55, 1.11)			
Baseline CD4 cell counts (cells/mm3)			-	
<200	1.00 (-)	<0.001		
≥ 200	1.2 (1.05, 1.37)			
Classes of ARVs in first regimen				
NNRTI	1.00 (-)	<0.001	1.00 (-)	<0.001
Unboosted PI	0.49 (0.4, 0.61)		0.55 (0.43, 0.70)	
Boosted PI	1.1 (0.96, 1.26)		0.89 (0.77, 1.03)	
Other	1.03 (0.79, 1.33)		1.08 (0.83, 1.41)	
Era of ART initiation				
2000-2003	1.00 (-)	<0.001	1.00 (-)	<0.001
2004-2007	1.82 (1.53, 2.16)		1.69 (1.42, 2.02)	
2008-2011	3.43 (2.93, 4.02)		2.46 (2.08, 2.92)	
Province				
BC	1.00 (-)	<0.001	1.00 (-)	0.043
ON	1.38 (1.2, 1.58)		0.86 (0.74, 1.00)	
QC	1.71 (1.45, 2.01)		1.03 (0.86, 1.24)	
Baseline viral load (Log10 copies/mL)	0.82 (0.74, 0.90)	<0.001	0.72 (0.65, 0.80)	<0.001

Table 3: The probability of virological suppression by months and age

Time (months)	Age		P-value
	<=29	>29	
6	0.58 (0.56, 0.61)	0.6 (0.59, 0.61)	0.517
12	0.73 (0.7, 0.75)	0.8 (0.79, 0.81)	<0.001
18	0.78 (0.76, 0.81)	0.86 (0.85, 0.86)	<0.001
24	0.81 (0.79, 0.83)	0.89 (0.88, 0.89)	<0.001

Figure 4: Probability among AYA of achieving virological suppression by IDU status

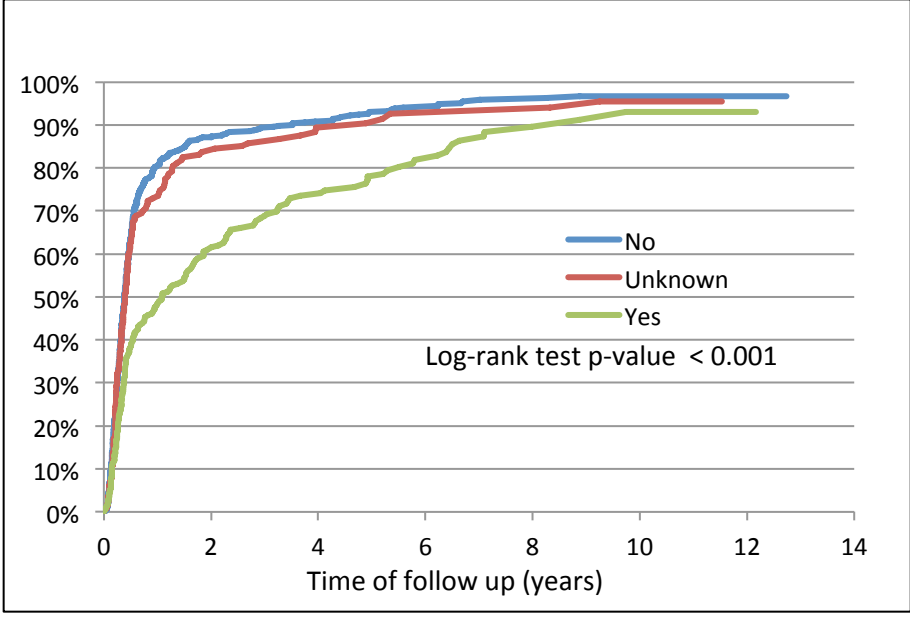
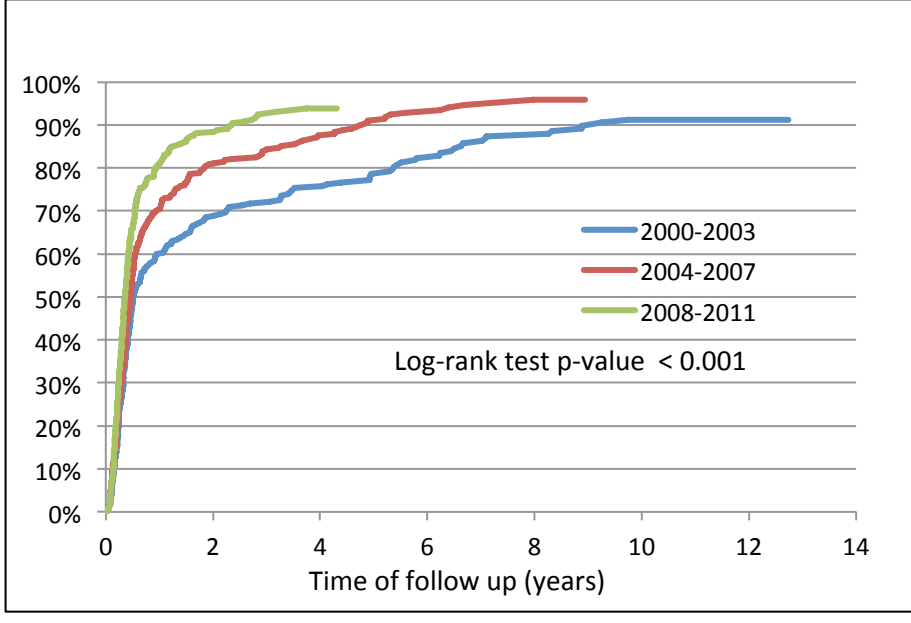


Figure 5: Probability among AYA of achieving virological suppression by era of cART initiation



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