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MOPED743

IAS 2015 vancouver, canada

Predictors of viral suppression and rebound among HIV-positive gay, bisexual, and other men who have sex with men in a large multi-site Canadian cohort

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Background

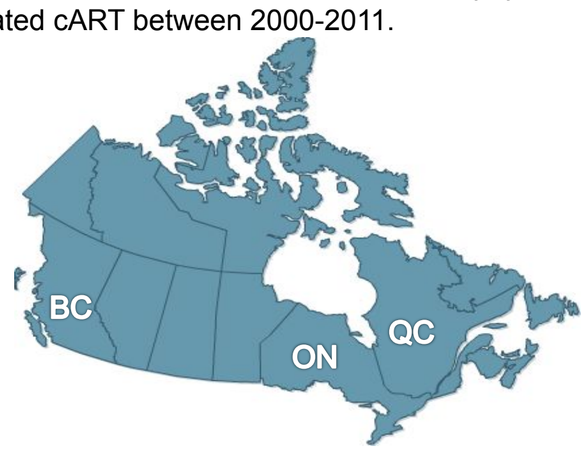
Gay, bisexual, and other men who have sex with men (MSM) represent the largest HIV transmission category in Canada. While many risk factors for HIV seroconversion among MSM have been explored, there are limited pan-provincial data regarding HIV treatment outcomes after initiation of combination antiretroviral therapy (cART) among this population. Both viral suppression and subsequent experiences of viral rebound are important clinical predictors of long-term health and HIV transmission risk. Additionally, the new UNAIDS objective that 90% of people receiving cART have viral suppression by 2020 provides a timely and pertinent framework for assessing where Canadian MSM on cART stand with regard to this ambitious HIV treatment and prevention target.

We aim to identify and describe socio-demographic and clinical correlates of viral suppression and rebound among MSM in order to inform treatment and retention strategies specific to this population.

Methods

Design: Retrospective, observational cohort.

Participants: Treatment naïve MSM from the Canadian Observational Cohort (CANOC) Collaboration, a multi-site cohort of HIV-positive adults from Canada's three most populous provinces, who initiated cART between 2000-2011.



Data Collection: Data extraction of demographic, laboratory and clinical variables is performed at the data centres of the eight participating cohort studies and submitted annually to the BC Centre for Excellence in HIV/AIDS in Vancouver for data pooling, cleaning and analysis.

Analysis: Demographic and clinical characteristics at treatment initiation (baseline) were summarized using frequencies and proportions for categorical variables and medians and interquartile ranges (Q1-Q3) for continuous variables. Univariate and multivariable accelerated failure time models were used to assess **time to viral suppression** (≥2 consecutive measures <50 copies/mL, ≥30 days apart within 1 year following treatment initiation) and **time to viral rebound** (≥2 consecutive measures >200 copies/mL, ≥30 days apart after achieving suppression), and key socio-demographic and clinical correlates were identified.

Results

Table 1: Demographic and clinical characteristics by suppression status (n = 3,180)*

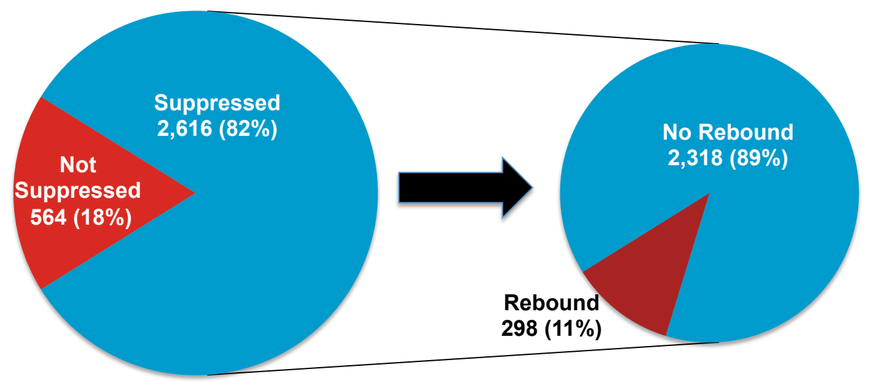
Characteristic	Total (%)	Suppressed within 1 year, n (%) or median (Q1-Q3)		p-value
		No (n = 564)	Yes (n = 2,616)	
Province				
British Columbia	935 (29)	191 (34)	744 (28)	0.036
Ontario	1138 (36)	191 (34)	947 (36)	
Quebec	1107 (35)	182 (32)	925 (35)	
Age at ART initiation (years)	40 (33-46)	38 (33-44)	40 (34-46)	0.002
Era of ART initiation				
2000-2003	746 (23)	161 (29)	585 (22)	0.002
2004-2007	966 (30)	145 (26)	821 (31)	
2008-2012	1468 (46)	258 (46)	1210 (46)	
Initial 3rd ARV Class				
NNRTI	1422 (45)	200 (35)	1222 (47)	< 0.001
Unboosted PI	135 (4)	40 (7)	95 (4)	
Boosted PI	1347 (42)	261 (46)	1086 (42)	
Other	276 (9)	63 (11)	213 (8)	
IDU history				
No	2854 (90)	475 (84)	2379 (91)	< 0.001
Yes	259 (8)	70(12)	189 (7)	
Unknown	67 (2)	19 (3)	48 (2)	
Hepatitis C status				
Negative	2694 (85)	455 (81)	2239 (86)	0.009
Positive	352 (11)	82 (15)	270 (10)	
Unknown	134 (4)	27 (5)	107 (4)	
Viral load tests/year				
<3	643 (20)	129 (23)	514 (20)	< 0.001
3-4	1666 (52)	213 (38)	1453 (56)	
5-6	394 (12)	66 (12)	328 (13)	
>6	477 (15)	156 (28)	321 (12)	
Baseline viral load (log_{10} copies/mL)	4.95 (4.48-5.00)	5.00 (4.69-5.00)	4.91 (4.44-5.00)	< 0.001
Baseline CD4 count (cells/mm^3)	237 (130-340)	220 (110-347)	240 (140-340)	0.085

*Percentages may not equal 100% as a result of rounding.
ARV = antiretroviral, IDU = injection drug use, NNRTI = non-nucleoside reverse transcriptase inhibitor, PI = protease inhibitor

Results (continued)

Figure 1: Proportion of suppression and rebound outcomes experienced among participants

Of 3,180 participants initiating cART between 2000-2012, 2,616 achieved **viral suppression** within one year of cART initiation. The median time to suppression was 4 months (Q1-Q3: 3-6 months)



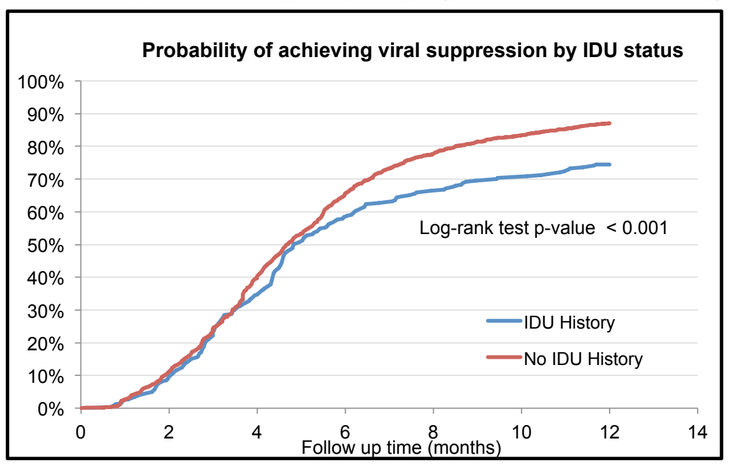
Among participants achieving viral suppression, 298 experienced **viral rebound** in a median time of 22 months (Q1-Q3: 11-39 months)

Table 2: Adjusted multivariable results* for viral suppression (n = 3,180)

Factor	Adjusted HR (95% CI)	p-value
Era of ART initiation		
2000-03	1.00	< 0.001
2004-07	1.27 (1.14-1.42)	
2008-12	1.26 (1.14-1.40)	
Baseline age (per 10 year increment)	1.05 (1.01-1.09)	0.017
IDU History (yes vs. no)	0.75 (0.65-0.87)	< 0.001
Viral load tests per year		
<3	1.00	< 0.001
3-4	1.19 (1.07-1.31)	
5-6	1.14 (0.99-1.31)	
>6	0.91 (0.79-1.05)	
Initial 3rd ARV class		
NNRTI	1.00	< 0.001
Unboosted PI	0.65 (0.53-0.81)	
Boosted PI	0.81 (0.74-0.88)	
Other	0.98 (0.84-1.13)	
Baseline viral load (per log10 copies/mL)	0.65 (0.60-0.70)	< 0.001

*Weibull distribution. Goodness of fit was assessed with a log-log survival plot

Figures 2 and 3: Kaplan Meier curves for time to viral suppression (n=3,180) by IDU status and age



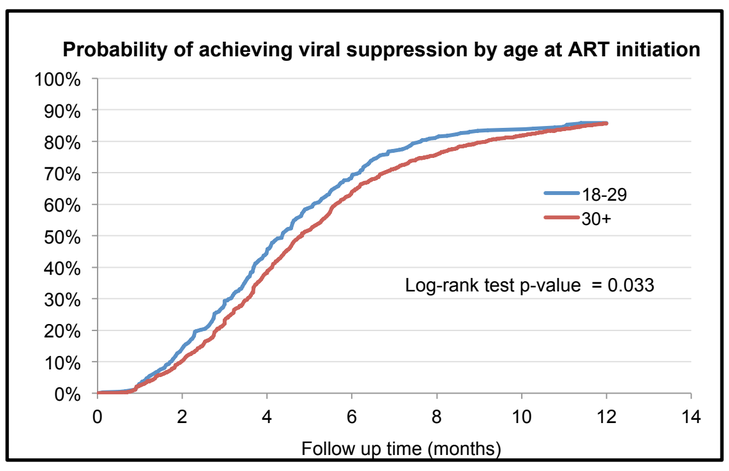
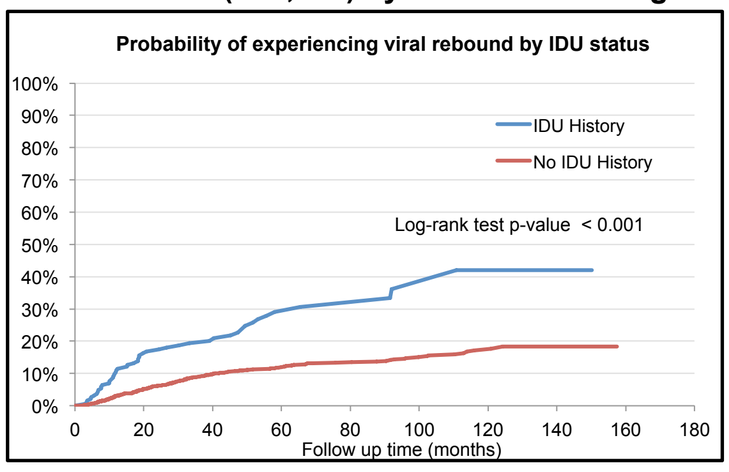


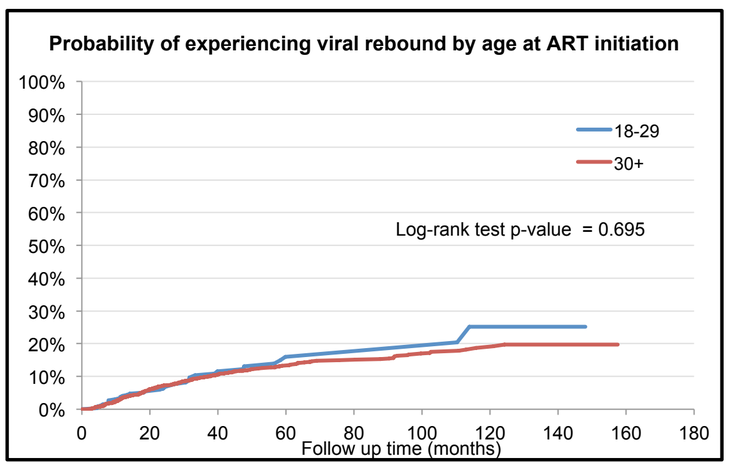
Table 3: Adjusted multivariable results* for viral rebound (n = 2,616)

Factor	Adjusted HR (95% CI)	p-value
Era of ART initiation		
2000-03	1.00	< 0.001
2004-07	0.60 (0.46-0.79)	
2008-12	0.29 (0.20-0.43)	
Province		
British Columbia	1.00	0.003
Ontario	0.63 (0.46-0.86)	
Quebec	0.59 (0.43-0.82)	
Baseline age (per 10 year increment)	0.70 (0.61-0.80)	< 0.001
IDU History (yes vs. no)	2.28 (1.64-3.17)	< 0.001
Viral load tests per year		
<3	1.00	< 0.001
3-4	0.97 (0.70-1.33)	
5-6	1.26 (0.80-1.98)	
>6	2.54 (1.62-3.97)	
Initial 3rd ARV class		
NNRTI	1.00	0.090
Unboosted PI	1.46 (0.89-2.39)	
Boosted PI	1.12 (0.85-1.46)	
Other	1.62 (1.07-2.45)	
Baseline CD4 count (per 100 cells/mm^3)	1.13 (1.04-1.22)	0.002

Exponential distribution. Goodness of fit was assessed with a log survival plot.

Figures 4 and 5: Kaplan Meier curves for time to viral rebound (n=2,616) by IDU status and age





Limitations

Data only represent 3 provinces and may not be generalizable to all HIV-positive individuals in Canada.

Data from Ontario and Quebec are based on a selection of clinics, whereas BC data represent the entire sample of HIV-positive people on antiretroviral therapy in the province.

2,547 participants had to be excluded from the analysis because of missing or unknown MSM data.

Conclusions

We found that 82% of MSM living in BC, Ontario, and Quebec achieved viral suppression within a median of 4 months of initiating treatment, and of these MSM, 11% subsequently experienced a viral rebound within a median time of 22 months from the time they suppressed.

MSM in Canada nearly meet the UNAIDS proposed target that 90% of individuals starting cART will have viral suppression.

Our finding that younger MSM and those with a history of IDU are at greater risk of poor treatment outcomes reinforces the importance of prioritizing appropriately tailored case management interventions to avoid future treatment failure among Canadian MSM.

Acknowledgements

We would like to thank all of the participants for allowing their information to be a part of the CANOC Collaboration. The CANOC Centre is supported by the Canadian Institutes of Health Research (CIHR) and the CIHR Canadian HIV Trials Network (CTN 242). ANB and TA are supported by CIHR New Investigator Awards. AC is supported through a CANOC Centre Scholar Award. CC is supported through an Applied HIV Research Chair from the OHTN. MBK is supported by a Chercheur National Award from the Fonds de recherche du Québec-Santé (FRQ-S). MRL receives salary support from CIHR. JSGM is supported by an Avant-Garde Award from the National Institute on Drug Abuse, National Institutes of Health. SP is supported by a Study Abroad Studentship from the Leverhulme Trust. JR is supported through an OHTN Chair in Biostatistics.

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