Time since last negative HIV test among men who have sex with men and people who use injection drugs in British Columbia, 2006-2011

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ABSTRACT

OBJECTIVES: Canadian surveys of men who have sex with men (MSM) and people using injection drugs (IDU) demonstrate that most have tested for HIV at least once, but that half or fewer have done so in the previous year. To better inform targeted HIV testing guidelines for these populations, we derived estimates of inter-test interval (ITI) for persons newly diagnosed with HIV in British Columbia (BC) between 2006 and 2011, and assessed variables associated with longer ITI among MSM and IDU.

METHODS: Provincial HIV case report and testing data were linked by deterministic and probabilistic matching (based on unique personal health number, name, and date of birth). ITI was defined as time from last recorded negative to first positive HIV result; those with ITI ≤ 30 days were excluded.

RESULTS: Of 2,004 eligible individuals, 1,116 (55.7%) had a recorded negative HIV test result in the previous ten years. Overall median ITI was 20 months with a skewed distribution (inter-quartile range 8-46); median ITI was 15 months for MSM and 21 months for IDU with 41.2% and 33.1% testing in the past year, respectively. Longer ITI was associated with older age for both groups, and among MSM with residence outside Vancouver and not known to have an HIV-positive partner.

CONCLUSIONS: These findings highlight potential missed opportunities for earlier detection of HIV and prevention of secondary transmission among newly diagnosed MSM and IDU, and provide evidence to inform recommendations for HIV test frequency and testing strategies for these populations in BC.

KEY WORDS: HIV; British Columbia; homosexuality, male; substance abuse, intravenous; testing

La traduction du résumé se trouve à la fin de l'article.

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Early identification of HIV infection and engagement in HIV care and treatment has individual clinical benefit through reduction of morbidity and mortality, as well as population benefit through behaviour change following diagnosis and taking effective antiretroviral therapy (i.e., treatment as prevention).^{1,2} Strategies to increase testing and reduce undiagnosed HIV infections are a key component of *seek, test and treat* approaches to HIV prevention and the first step of the cascade of HIV care.^{3,4} In 2009, the province of British Columbia (BC) implemented STOP HIV/AIDS, a seek, test and treat approach to HIV prevention focused on two regions of the province (Vancouver, Prince George) in which expansion of HIV testing was a key strategy.⁵

Increasing frequency of HIV testing may improve rates of early diagnosis and treatment (leading to improved clinical outcomes), prevent secondary infections, and be cost-effective.⁶⁻¹⁰ Canadian surveys of gay, bisexual, and other men who have sex with men (MSM) and people who use injection drugs (IDU) demonstrate that most have tested at least once, but that half or fewer have done so in the previous year.^{11,12} In a recent Vancouver survey among MSM with undiagnosed HIV infection, 71% had previously tested for HIV (50% in the previous two years).¹³ Models suggest that increasing test frequency among MSM already engaged in testing is more effective at reducing

undiagnosed infections and preventing secondary infections than testing untested individuals.^{8,14} Globally, test frequency recommendations for MSM and IDU vary (annually to every 3 to 6 months), typically based on expert opinion.^{15,16} HIV testing recommendations recently released by the Public Health Agency of Canada recommend that individuals involved in high-risk practices be screened for HIV at least annually, with more frequent testing for some individuals (including MSM with multiple or anonymous partners, or who have sex in conjunction with illicit drug use).¹⁷ However, these guidelines also acknowledge that there is insufficient evidence to provide recommendations for the exact frequency of HIV testing given the multitude of possible scenarios and client characteristics.

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Table 1. Time from last negative to first positive HIV test (inter-test interval) among individuals diagnosed with HIV in BC, by selected characteristics, 2006-2011

Category		Diagnoses		Previous negative test		Inter-test interval (months)		% ITI		
		N	n	%		Median	IQR	≤3 mos	≤6 mos	≤12 mos
Total (BC)		2004	1116	55.7		20	(8, 46)	6.1	16.9	35.4
Year of diagnosis	2006	359	203	56.5		16	(7, 33)	5.4	21.2	37.9
	2007	389	215	55.3		20	(9, 45)	7.4	15.8	35.3
	2008	341	178	52.2		23	(10, 48)	3.4	12.9	29.8
	2009	334	170	50.9		26	(11, 50)	2.4	7.6	27.1
	2010	294	179	60.9		22	(9, 51)	6.1	15.6	34.1
	2011	287	171	59.6		14*	(5, 38)	11.7	28.1	48
Gender †	Female	391	233	59.6		22	(10, 47)	2.6	14.2	30
	Male	1609	879	54.6		20	(8, 45)	7.1	17.7	36.7
Age at diagnosis (years)†	15-24	174	112	64.4		10	(6, 19)	8.9	26.8	55.4
	25-29	272	169	62.1		19	(8, 38)	5.3	18.9	40.2
	30-39	591	352	59.6		18	(7, 42)	7.1	18.5	38.4
	40-59	850	446	52.5		27	(11, 54)	4.7	12.8	26.7
	≥60	109	36	33.0*		31	(9, 53)	8.3	13.9	27.8
Ethnicity	Aboriginal	302	203	67.2		22	(9, 47)	4.4	15.8	35.5
	Caucasian	1155	688	59.6		20	(8, 44)	6.4	16.7	35.2
	Other	547	225	41.1*		21	(8, 49)	6.7	18.7	36
Residence	Vancouver	1083	632	58.4		16	(7, 39)	7.3	19.9	39.7
	Other	921	484	52.6*		24*	(10, 52)	4.5	13	29.8
Exposure group †‡	Heterosexual - IR	276	117	42.4		32	(12, 65)	6	14.5	25.6
	Heterosexual - NIR	195	68	34.9		33	(14, 68)	1.5	10.3	17.6
	IDU	444	323	72.7		21	(9, 46)	2.8	13.6	33.1
	MSM	973	580	59.6*		15*	(7, 37)	8.3	20.3	41.2
HIV-positive partner	Yes	390	241	61.8		17	(6, 43)	9.5	24.9	42.3
	No	1614	875	54.2*		21*	(9, 46)	5.1	14.7	33.5
Test option†	Nominal	1506	871	57.8		20	(8, 46)	6.5	18	36.1
	Non-nominal	284	144	50.7*		17*	(8, 35)	4.9	15.3	37.5
Stage of infection at diagnosis	Acute	129	105	81.4		7	(3, 15)	20	45.7	68.6
	Other	1632	942	57.7		21	(9, 44)	2.9	4.3	10.1
	Advanced	243	69	28.4*		60*	(37, 84)	4.8	14.6	33.5

Note: IR = identified risk, NIR = no identified risk, IDU = persons who use injection drugs, MSM = men who have sex with men. Advanced HIV disease is defined as having an AIDS case report ≤12 months after diagnosis.

* $p < 0.05$ (across covariate category) examining % with previous negative HIV test by chi-square test (test for trend used for age) and inter-test interval (log-transformed) by univariate logistic regression.

† Unknown or other responses excluded.

‡ Individuals with >1 reported exposure category were assigned to the first category in the following hierarchy: 1. MSM, 2. IDU, 3. Heterosexual-IR, 4. Heterosexual-NIR.

Knowledge of the previous testing behaviour of newly diagnosed individuals may better inform recommendations for testing frequency in these key groups, such as assessing the time between last-known negative and first positive HIV tests, or inter-test interval (ITI).¹⁸

We examined ITI among persons newly diagnosed with HIV in BC, focusing on MSM and IDU, as key populations affected by HIV in our province and populations for whom test frequency recommendations are often tailored. To do this, we used provincial HIV surveillance and laboratory testing data to describe previous history of testing and ITI among new HIV diagnoses and to identify factors associated with longer ITI among MSM and IDU.

METHODS

We calculated ITI as the time between the dates of the last recorded negative test (in the ten years prior to diagnosis) and first reactive test leading to a confirmed HIV diagnosis. Surveillance records for individuals with a confirmed new diagnosis of HIV in BC (based on provincial case definitions¹⁹) between January 2006 and December 2011 were linked to laboratory HIV testing data from the Public Health Microbiology & Reference Laboratory (>90% of HIV tests in BC) through deterministic (unique personal health number) and probabilistic

matching (name and birthdate). The date of last negative test was taken from either laboratory or surveillance data (the latter if ≥30 days after last laboratory test, to capture later self-reported negative tests such as rapid or out-of-province testing). Based on clinical opinion, we excluded individuals with ITI ≤30 days as we considered the negative test to possibly be related to the same testing episode (e.g., repeat testing after a risk event).

To understand the potential impact of targeted testing strategies on existing testing patterns, we calculated the proportion of individuals having an ITI ≤3, ≤6, and ≤12 months, and used linear regression to identify variables associated with longer ITI for MSM and IDU separately (who constituted 71% of all cases during this period). We considered the following potentially associated with ITI: diagnosis year, gender, age, ethnicity (Caucasian, Aboriginal, other), region (Vancouver residence, other), known HIV positive partner, test reporting option (whether individual chose to be reported to public health non-nominally without identifiers, or nominally) and stage of infection at diagnosis (acute, advanced, other). Acute HIV infection was defined as detection of HIV DNA or RNA by nucleic acid amplification testing, or detection of p24 antigen with confirmation by neutralization assay in the absence of a confirmed antibody response. Advanced stage of infection was defined as having an AIDS diagnosis within 12 months of being diagnosed with HIV.

Figure 1. Distribution of inter-test interval by exposure category, BC, 2006-2011

The proportion of individuals with a previous negative test was compared across covariates using a two-sided Chi-square test ($p < 0.05$ considered statistically significant). ITI was log-transformed to ensure normality, and univariate and multivariable linear regression modeling was conducted to evaluate correlates of ITI. Stage of infection was considered a potential outcome of ITI and excluded from multivariable analysis. Variables were individually removed from a full model to examine the effects of confounding, and a final model was selected based on Akaike Information Criterion. Analysis was conducted using R version 2.11.1 (2010-05-31).

Ethics approval was not required as this study was consistent with the public health mandates of the BC Centre for Disease Control and the Provincial Public Health Microbiology & Reference Laboratory.

RESULTS

During the study period, there were 2,023 new HIV diagnoses in BC, of which 19 (0.9%) were excluded for ITI ≤ 30 days. Of the remainder, 1,116/2,004 (55.7%) had a recorded negative test, including 59.6% (580/973) of MSM and 72.7% (323/444) of IDU. All variables, with the exception of gender and year of diagnosis, were significantly associated with having a previous negative HIV test (Table 1).

The distribution of ITI was highly skewed for all groups, with an overall median ITI of 20 months [inter-quartile range (IQR) 8-45] (Figure 1, Table 1). Overall in BC, we observed significant differences ($p < 0.05$) in median ITI by year of diagnosis (with the lowest median ITI in 2011), and significantly lower ITI among Vancouver residents, individuals with a known HIV-positive partner, and individuals testing non-nominally. We also found a significant trend for median ITI by age, with higher ITI at older ages.

ITI differed significantly by exposure group ($p < 0.05$); median ITI was lowest for MSM at 15 months [IQR 7-37], with 8%, 20%,

and 41% having a last negative test within 3, 6, and 12 months prior to diagnosis, respectively. For IDU, the corresponding values were median 21 months [IQR 9-46] and 3%, 14%, and 33%, respectively. Among MSM (Table 2a), on univariate analysis longer ITI was significantly associated with older age, residence outside of Vancouver, not having a known HIV-positive partner, and non-acute stage of HIV infection at diagnosis. Older age, residence outside Vancouver, and not having a known HIV-positive partner were significant on full multivariable analysis (following exclusion of stage of infection), and were selected into the final MSM model. For IDU, longer ITI was associated with earlier year of diagnosis, older age, and advanced HIV disease at diagnosis. On full multivariable analysis (excluding stage of infection), only older age remained significant (Table 2b); age and region of residence were selected into the final IDU model.

DISCUSSION

We evaluated ITI for newly diagnosed individuals in BC between 2006 and 2011 and found an overall median ITI of 20 months [IQR 8-46 months], and that ITI was highly skewed across all categories. ITI differed by exposure category and was lowest among MSM and IDU at median 15 [IQR 7-37] and 21 months [IQR 9-46], respectively. Fewer than half of newly diagnosed MSM and IDU had an ITI < 1 year, and more frequent testing as per typical recommendations (i.e., at 3- and 6-month intervals) in these high-risk MSM and IDU appeared low. In multivariable analysis, we found longer ITI among both MSM and IDU was associated with older age, and among MSM with residence outside Vancouver and not being known to have an HIV-positive partner.

Using ITI as a metric for monitoring HIV testing patterns appears only recently in the published literature,¹⁸ and there are few published reports to which we can appropriately compare our findings among persons newly diagnosed with HIV. We identified three similar studies which have used HIV surveillance

Table 2. Effects of case attributes on interval between first positive and last negative test results among persons newly diagnosed with HIV in British Columbia, 2006-2011

a. Men who have sex with men (N=580)		n (%)	Univariate		Multivariable (full)*		Multivariable (final)	
			β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Year (continuous)	2006	91 (16)	-0.02	0.56	-0.01	0.67	–	
	2007	95 (16)	(-0.07, 0.04)		(-0.06, 0.04)			
	2008	97 (17)						
	2009	79 (14)						
	2010	105 (18)						
	2011	113 (19)						
Age (years) (continuous)*			0.02	<0.001	0.02	<0.001	0.02	<0.001
			(0.01, 0.03)		(0.01, 0.03)		(0.01, 0.03)	
	15-24	59 (10)						
	25-29	100 (17)						
	30-39	192 (33)						
	40-59	213 (37)						
Ethnicity	≥60	16 (3)						
	Caucasian	415 (72)	REFERENT		REFERENT		–	
	Aboriginal	29 (5)	-0.01	0.98	0.02	0.91		
			(-0.42, 0.41)		(-0.39, 0.44)			
	Other	136 (23)	-0.09	0.43	-0.05	0.64		
			(-0.30, 0.13)		(-0.28, 0.17)			
Residence	Vancouver	427 (74)	REFERENT		REFERENT		REFERENT	
	Other	153 (26)	0.34	<0.001	0.38	<0.001	0.35	<0.001
HIV-positive partner	No	451 (78)	(0.14, 0.54)		(0.17, 0.59)		(0.16, 0.55)	
	Yes	129 (22)	REFERENT	0.01	REFERENT	0.01	REFERENT	0.01
Testing option*	Non-nominal	90 (16)	-0.27		-0.30		-0.28	
	Nominal	448 (77)	(-0.48, -0.05)		(-0.53, -0.08)		(-0.49, -0.07)	
Stage of infection at diagnosis			REFERENT		REFERENT		–	
	Acute	75 (13)	0.01	0.96	0.01	0.96		
	Advanced	23 (4)	(-0.25, 0.26)		(-0.24, 0.26)			
	Other	482 (83)	REFERENT		Excluded †		Excluded †	
			2.11	<0.001				
			(1.62, 2.59)					
			0.82	<0.001				
			(0.57, 1.08)					
b. Persons who use injection drugs (N=323)		n (%)	Univariate		Multivariable (full)*		Multivariable (final)	
			β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Year (continuous)			0.08	0.03	0.06	0.13	–	
			(0.01, 0.15)		(-0.02, 0.13)			
	2006	85 (26)						
	2007	95 (29)						
	2008	42 (13)						
	2009	46 (14)						
Age (years) (continuous)*	2010	33 (10)						
	2011	22 (7)						
			0.03	<0.001	0.03	<0.001	0.02	<0.001
			(0.02, 0.04)		(0.01, 0.04)		(0.02, 0.04)	
	15-24	36 (11)						
	25-29	43 (13)						
Gender*	30-39	96 (30)						
	40-59	145 (45)						
	≥60	3 (1)						
	Female	136 (42)	REFERENT		REFERENT		–	
	Male	185 (58)	0.20	0.08	0.10	0.44		
			(-0.02, 0.43)		(-0.20, 0.28)			
Ethnicity	Caucasian	176 (54)	REFERENT		REFERENT		–	
	Aboriginal	109 (34)	-0.07	0.55	0.15	0.27		
			(-0.32, 0.17)		(-0.17, 0.35)			
	Other	38 (12)	0.17	0.34	0.34	0.08		
Residence			(-0.18, 0.53)		(-0.05, 0.66)			
	Vancouver	119 (37)	REFERENT		REFERENT		REFERENT	
HIV-positive partner	Other	204 (63)	0.06	0.63	0.04	0.73	0.03	0.77
			(-0.17, 0.29)		(-0.19, 0.26)		(-0.19, 0.25)	
Testing option*	No	267 (83)	REFERENT		REFERENT		–	
	Yes	56 (17)	0.003	0.98	0.11	0.47		
Stage of infection at diagnosis			(-0.29, 0.30)		(-0.22, 0.37)			
	Non-nominal	32 (10)	REFERENT		REFERENT		–	
Testing option*	Nominal	262 (81)	0.29	0.12	0.14	0.46		
			(-0.08, 0.66)		(-0.25, 0.52)			
	Acute	17 (5)	REFERENT		Excluded †		Excluded †	
	Advanced	25 (8)	1.49	<0.001				
Other			(0.88, 2.09)					
			0.90	<0.001				
			(0.42, 1.38)					

Note: Restricted to individuals with previous negative HIV test ≥30 days and <10 years prior to HIV diagnosis.

* Unknown or other categories excluded.

† Stage of infection at diagnosis excluded from multivariable analysis as considered a potential outcome of ITI.

data for a defined geographic area to calculate inter-test interval for individuals newly diagnosed with HIV. An analysis of testing patterns among youth newly diagnosed with HIV in the United States between 2005 and 2008 found similar rates of prior negative HIV testing compared to youth in our study (54% among 13-19 yrs, 68% among 20-24 yrs vs. 64% among 15-24 year olds in BC) and having an ITI ≤ 12 months (64% among 13-19 yrs, 54% among 20-24 yrs vs. 55% among 15-24 year olds in BC).²⁰ A recent report using HIV surveillance data from Seattle/King County in Washington, USA found among MSM diagnosed with HIV between 2004-2010 a median ITI of 12 months, with 13% and 49% having an ITI ≤ 3 and ≤ 12 months, respectively; no temporal trend was detected.²¹ A second report, also using HIV surveillance data from Seattle/King County for all individuals diagnosed with HIV between 2005-2009, found a median ITI of 13 months overall.¹⁸ These differences in median ITI from those in our study may be related to geographic differences in the populations studied, such as population density, access to testing, or testing campaigns. Similar factors may explain why we have demonstrated in our study differences in ITI for individuals residing in Vancouver compared to those residing in other parts of BC.

This analysis suggests that individuals with the highest risk for HIV infection (as demonstrated by their new HIV diagnosis) may benefit from more frequent testing as this may reduce ITI and lead to earlier HIV diagnosis. Initiatives to increase HIV testing frequency among MSM and IDU populations in BC may have an impact in this regard, particularly for older individuals and non-Vancouver residents. In consideration of this analysis, the STOP HIV/AIDS Initiative endorsed recommendations for annual HIV testing among MSM and IDU, with more frequent testing (every 3 months) for individuals at higher risk. While developing recommendations for clinicians and programs is important, achieving increased frequency of HIV testing requires a comprehensive approach. Expanding routine offer of HIV testing in health care settings may contribute by providing more frequent testing opportunities for all exposure groups, including MSM and IDU.²² Expansion of targeted testing strategies and programs may be particularly important for MSM in BC, who in 2011 comprised 57% and 46% of incident and prevalent infections, respectively, and where new HIV diagnoses per year remain elevated (in contrast to recent declining trends among IDU).^{19,23,24} Expansion of established interventions such as low-threshold models of testing, HIV testing as part of STI care, and rapid HIV testing, as well as new interventions such as texting testing reminders or internet-based testing, should be considered.²⁵⁻²⁷

We recognize that there are limitations of this analysis due to the use of administrative data (surveillance and laboratory data). The proportion of individuals not having a documented previous negative test may be due to inability to link surveillance and laboratory data as tests or case reports may contain partial identifiers, due to non-nominal testing or reporting. Rapid testing has been increasingly available since 2010 and is not captured in provincial laboratory data (although representing <5% of total tests). For these reasons, we may have misclassified individuals based on prior test history, excluding previously-tested individuals from the analysis, or over-estimated ITI for

some individuals. However, a strength of our study is our ability to include laboratory data and self-reported prior negative tests, as this is consistently documented in surveillance data during public health follow-up. This may explain why we found a more consistent association between ITI and stage of disease at diagnosis than a recently published study which relied on surveillance data only; although we also recognize discrepancies within our data in this regard (e.g., as some individuals with advanced HIV disease at diagnosis were identified as having a recent negative HIV test).¹⁸ We are also unable to describe ITI among individuals with a negative HIV test in BC overall and by exposure category, and as such we are unable to compare ITI between HIV-negative and newly diagnosed individuals in total or among MSM and IDU. However, describing ITI among newly diagnosed MSM and IDU is most relevant as these represent individuals at highest risk of infection (by virtue of a new HIV diagnosis).

We conclude that there is room for improvement in the frequency of HIV testing (as reflected by ITI) among key populations such as MSM and IDU in BC. Continued implementation and expansion of strategies to increase both overall HIV testing and test frequency among MSM and IDU are being pursued in BC, with expansion of the STOP HIV/AIDS program provincially in 2013. We note encouragingly that the overall ITI for the province decreased in 2011, and that more recent year of diagnosis was significantly associated with lower ITI among IDU. However, no reduction in ITI was observed among MSM, who comprise the majority of new HIV diagnoses in BC. As seek, test and treat approaches expand in BC as well as elsewhere, our findings suggest that ITI may be a useful indicator for monitoring the success of entry into the diagnosis, engagement and treatment cascade of HIV care.³

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RÉSUMÉ

OBJECTIFS : Les enquêtes canadiennes auprès des hommes ayant des relations sexuelles avec des hommes (HARSAH) et des utilisateurs et utilisatrices de drogue par injection (UDI) montrent que la plupart de ces personnes ont subi un test de dépistage du VIH au moins une fois, mais que moins de la moitié l'ont fait au cours de l'année précédente. Pour mieux éclairer les lignes directrices de dépistage du VIH ciblant ces populations, nous avons calculé des estimations de l'intervalle inter-dépistage (IIT) pour les personnes ayant nouvellement reçu un diagnostic de VIH en Colombie-Britannique entre 2006 et 2011, et évalué les variables associées à un IIT plus long chez les HARSAH et les UDI.

MÉTHODE : Les exposés de cas de VIH et les données de dépistage de la province ont été maillés par appariement déterministe et probabiliste (d'après le numéro d'assurance-maladie, le nom et la date de naissance). Nous avons défini l'IIT comme étant le temps écoulé entre le dernier résultat négatif et le premier résultat positif enregistré pour le VIH; les personnes dont l'IIT était ≤ 30 jours ont été exclues.

RÉSULTATS : Sur les 2 004 personnes admissibles, 1 116 (55,7 %) avaient eu un résultat négatif enregistré au test de dépistage du VIH au cours des 10 années précédentes. Globalement, l'IIT médian était de 20 mois, avec une distribution asymétrique (écart interquartile de 8-46); l'IIT médian était de 15 mois pour les HARSAH et de 21 mois pour les UDI; 41,2 % et 33,1 % des sujets avaient été dépistés au cours de l'année précédente, respectivement. Un IIT plus long était associé à un âge plus avancé dans les deux groupes, et parmi les HARSAH, au fait de résider à l'extérieur de Vancouver et de ne pas avoir de partenaire séropositif pour le VIH connu.

CONCLUSIONS : Ces constatations soulignent qu'il pourrait y avoir des occasions manquées de détecter le VIH plus tôt et d'en prévenir la transmission secondaire parmi les HARSAH et les UDI nouvellement diagnostiqués; les données probantes de l'étude peuvent éclairer les recommandations sur la fréquence et les stratégies de dépistage du VIH dans ces populations en Colombie-Britannique.

MOTS CLÉS : VIH; Colombie-Britannique; homosexualité masculine; toxicomanie intraveineuse; dépistage