

## SPECIAL REPORT

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# ADVANCED HIV DISEASE AT THE TIME OF HIV DIAGNOSIS IN BRITISH COLUMBIA

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1995 TO 2008

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## TABLE OF CONTENTS

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EXECUTIVE SUMMARY .....	3
INTRODUCTION .....	4
METHODS .....	4
1. Data Sources .....	4
2. Case Definition .....	5
3. Analyses .....	5
4. Ethics .....	6
RESULTS .....	6
DISCUSSION .....	7
LIMITATIONS .....	8
SUMMARY .....	9
REFERENCES .....	16

## EXECUTIVE SUMMARY

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### Background

- As a result of delayed access to HIV treatment and care, clinical management is more challenging and health outcomes are compromised among individuals with Advanced HIV Disease (AHD) at the time of HIV diagnosis. At a population level, this group is important for HIV prevention and control because opportunities to reduce onward transmission of HIV have been delayed.

### Objective

- To describe the proportion and characteristics of persons with AHD at the time of HIV diagnosis in BC.
- To examine multivariate factors associated with AHD in BC.

### Methods

- We used HIV and AIDS surveillance data to describe the characteristics of individuals with AHD at the time of HIV diagnosis, from 1 January 1995 to 31 December 2008.
- Multivariate logistic regression was used to evaluate factors associated with AHD at the time of HIV diagnosis from 1 January 2004 to 31 December 2008.
- AHD was defined as individuals with an AIDS case report received within one year of a new HIV diagnosis. For regression analyses, we expanded our definition of AHD to include individuals with a first CD4+ cell count of less than 200 cells/mm<sup>3</sup>, regardless of whether an AIDS case report was filed (data available from 2004 onwards).

### Key Findings

- From 1995 to 2008, the overall proportion of individuals with AHD at HIV diagnosis was 9% and the annual proportion varied over time (7-14%, from 28 to 67 cases per year).
- Using the expanded definition, the overall proportion with AHD from 2004 to 2008 was 17%, and was relatively stable over this recent time period (from 60 to 75 cases per year).
- Most people (76%) with AHD at the time of diagnosis had identified risk factors for HIV infection.
- Multivariate analyses found that AHD was significantly more likely among males, older age groups, persons with no identified risk factors other than heterosexual exposure, individuals who tested nominally for HIV, those who had never previously tested for HIV, and people who did not report having an HIV-positive partner.

### Conclusions

- In BC, the overall proportion of persons diagnosed with HIV at an advanced stage has remained relatively stable over time and is lower than reported in other jurisdictions.
- A high proportion of persons with AHD had identified risk factors; however, the findings suggest that individuals at perceived lower risk of infection may be more likely to have AHD. Strategies to expand HIV testing that consider both of these groups may reduce the proportion of individuals with AHD at the time of HIV diagnosis in BC.

## INTRODUCTION

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Understanding HIV trends at a population level is critical to inform policy and programming related to HIV prevention and treatment. As testing for HIV can occur at any time after HIV infection, some individuals at the time of diagnosis with HIV have advanced HIV disease (AHD), which is often defined as having an AIDS case report within one year of their first positive HIV test.[1] An expanded definition has considered those who had a CD4<sup>+</sup> T cell count less than 200cells/mm<sup>3</sup> at the time of HIV diagnosis to have AHD, regardless of whether an AIDS case report was filed.[1] Definitions of AHD vary by jurisdiction and setting, making international population-based comparisons difficult. Studies in North America and the United Kingdom where AHD was defined as a CD4<sup>+</sup> T cell count less than 200cells/mm<sup>3</sup> at the time of HIV diagnosis have reported the proportion of persons with AHD from 24 to 43%.[2]

Individuals with AHD at diagnosis present challenges to clinical care and experience a higher burden of HIV-related complications compared to those who are tested and treated at an earlier stage of HIV infection. Due to the delay in initiating highly active antiretroviral therapy (HAART), persons with AHD have greater rates of hospitalization, opportunistic infection and mortality.[3,4] Medical costs for individuals with AHD are higher, and treatment is typically more complex among those who initiate HAART at a late stage of HIV infection.[4-6]

From a public health perspective, persons with AHD at diagnosis represent an important group for HIV prevention and control. As a result of persistent undiagnosed HIV infection, opportunities to reduce secondary transmission of HIV have been missed. Earlier awareness of HIV status could lead to an earlier reduction in risk behaviours [7] and initiation of antiretroviral therapy which reduces the likelihood of transmission by decreasing HIV viral load.[8]

In British Columbia (BC), HIV and AIDS surveillance has been in place for more than two decades. AIDS cases have been reportable since 1986 and HIV officially became reportable in 2003 (although comprehensive data on new positive HIV tests in BC has been available since 1986). Using provincial HIV and AIDS surveillance data, this analysis examines trends in AHD among persons diagnosed with HIV in BC and describes multivariate factors associated with AHD.

## METHODS

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### 1. Data Sources

Information on individuals newly diagnosed with HIV in BC was extracted from the HIV/AIDS Information System (HAISYS), which contains provincial HIV and AIDS case report data. As part of routine surveillance, HIV and AIDS case reports are linked through a unique patient identifier by means of direct and probabilistic linkage; this process is subsequently verified by manual review. Information on individuals diagnosed with AIDS was obtained from case reports that are forwarded to the BCCDC from a care provider that has diagnosed an individual with an AIDS-defining illness (ADI). Additionally, AIDS cases are identified through biannual reports to the BCCDC from Drug Treatment Program data at the BC Centre for Excellence in HIV/AIDS. For more

information on HIV and AIDS case report data, see the Technical Appendix of the Annual Surveillance Report for HIV and Sexually Transmitted Infections 2009 (pg. 58).[9]

For this analysis, we identified individuals with a new positive HIV test from 1 January 1995 to 31 December 2008 from HAISYS. We also used HIV test data from the Provincial Public Health Microbiology and Reference Laboratory (PPHRL) to describe previous HIV testing among individuals newly diagnosed with HIV. Multiple HIV test results for the same individual were identified and linked using direct and probabilistic linkage so that the full HIV testing history could be examined for each person. A de-identified dataset was prepared for analysis from these data sources.

## 2. Case Definition

*Standard Definition:* Our case definition of AHD, consistent with that used by the CDC,[1] was an individual with a documented AIDS case report within one year of a new HIV diagnosis in HAISYS (based on date of receipt of positive specimen by PPHRL and the date of the AIDS case report). This standard definition is used to describe AHD in the 2009 BCCDC Annual HIV/AIDS Surveillance Report (page 50).[9] We applied this definition to analyses of all new HIV diagnoses from 1 January 1995 – 31 December 2008.

*Expanded Definition:* For multivariate regression, we included cases with a CD4<sup>+</sup> T cell count less than 200 cells/mm<sup>3</sup> at the time of diagnosis in the definition for AHD (regardless of whether they had an AIDS case report or not). This definition has been used elsewhere.[2] This variable was based on information collected by designated public health nurses during follow-up of individuals with a first positive HIV test and refers to the first documented CD4<sup>+</sup> T cell count on the HIV case report form (which is typically submitted up to six months after the date of first positive HIV test). As this data was first collected in late 2003, we examined AHD using the expanded definition for HIV diagnoses from 1 January 2004 – 31 December 2008.

## 3. Analyses

Initially, we examined trends in AHD (as per the standard definition) among persons newly diagnosed with HIV from 1 January 1995 to 31 December 2008. The number and proportion of persons with AHD was assessed by sex, age, Health Authority, ethnicity, and exposure category.

To determine Health Authority, clients' place of residence at the time of the diagnostic HIV test was used. If the residence was not available, we ascribed health authority based on the address of the clinic or physician who submitted the HIV test. Exposure category was assigned based on the standard hierarchy used for surveillance, but for the purpose of this analysis, regrouping of individual categories differed from routine surveillance reports. Exposure categories were as follows: Men who have sex with men (MSM) including MSM who use injection drugs (MSM-IDU); IDU; Heterosexual with identified risks (including sex trade workers [STW], patrons of STW, and persons reporting a partner who was STW, IDU, HIV-positive, or from an HIV-endemic country); Heterosexual with no identified risks; Other (includes recipients of blood/blood products,

occupational or perinatal exposure, persons born in an HIV-endemic country if sexual orientation could not be determined); Unknown/NIR (unknown or no identified risk).

Subsequently, we conducted multivariate logistic regression to explore factors associated with AHD. The following explanatory variables were used, based on a review of literature and availability of data in HAISYS:

- Sex
- Age group (<15, 15-24, 25-34, 35-44, 45-54, ≥55)
- Health Authority
- Ethnicity (Caucasian, Asian/South Asian, Black, Aboriginal, Hispanic, Other/Mixed [including Arab and West Asian])
- Exposure category (as described above)
- Tested nominally for HIV (yes vs no)
- Partner known to be HIV positive (yes vs no)
- Repeat tester (yes vs no, based on HIV test history previous to first positive HIV test)

Analyses were carried out in SAS version 9.2 (SAS Institute Inc., Cary, NC, USA). We calculated crude odds ratios (OR) and 95% confidence intervals (95% CI) in bivariate analysis, and selected variables associated with AHD at  $p < 0.10$  for multivariate regression. Variables independently associated with AHD at  $p < 0.05$  following backward selection were retained in the final model, from which adjusted odds ratios (AOR) were obtained.

#### 4. Ethics

Ethics approval was not required as this analysis was conducted as part of routine provincial surveillance for HIV/AIDS.

## RESULTS

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Overall, 6,374 persons were newly diagnosed with HIV in BC from 1995 to 2008, of which 585 (9%) had AHD (as per the standard definition) at the time of diagnosis. The annual number and proportion varied from 28 to 67 and 7% to 14%, respectively (Figure 1). Table 1 shows the number and proportion of persons with AHD over time by sex, age, Health Authority, ethnicity and exposure category. The proportion with AHD was consistently higher among males and in older age groups, and fluctuated over time in other categories.

Among 1,939 persons newly diagnosed with HIV in BC from January 1, 2004 to December 31, 2008, we identified 322 (17%) who had AHD at the time of diagnosis using the expanded definition. The annual number of persons with AHD was relatively stable over this recent time period and varied from 60 to 75 (14% to 22% of persons diagnosed with HIV per year; Figure 2). The majority (76%) of individuals with AHD at the time of diagnosis during this time period had identifiable risk factors (i.e., MSM, IDU, or heterosexual with identified risk factors; Figure 3).

Table 2 shows the proportion of individuals with AHD (expanded definition) at HIV diagnosis from 2004–2008 by study variable, including results of bivariate and multivariate analyses. The proportion with AHD differed significantly by sex, age group, Health Authority, exposure category, nominal HIV testing, testing history and HIV status of partners. A higher proportion of males (18%) had AHD at HIV diagnosis compared to females (11%), and the proportion with AHD increased with age. Overall, when examining risk factors among persons with AHD, most (246 of 322; 76%) were MSM, IDU or heterosexual with identified risk factors. However, by exposure category, the proportion with AHD was greatest among persons with no risk factors other than heterosexual sexual activity (33%), and among those in categories other than MSM, IDU or heterosexual (33%). Additionally, a substantial proportion of persons who were tested nominally for HIV, who were diagnosed with HIV on their first test (not known to be repeat testers), or who reported not having an HIV-positive partner were found to have AHD (18%, 24% and 19%, respectively). There were no significant differences in AHD by ethnicity, and this variable was not included in multiple regression.

In multivariate analysis, factors that remained significantly associated with AHD at time of HIV diagnosis (AOR [95% CI]) were older age (35–44 years, AOR: 3.92 [1.84–8.33], 45–54 years, AOR: 4.28 [1.98–9.25], ≥55 years, AOR: 5.74 [2.58–12.77]), being male (1.57 [1.05–2.35]), having no risk factors other than heterosexual exposure (2.15 [1.39–3.32]), having risk factors other than MSM, IDU or heterosexual exposure (2.51 [1.28–4.92]), testing nominally for HIV (1.73 [1.25–2.40]), having no previous known HIV test (2.52 [1.98–3.35]) and not having an HIV-positive partner (2.11 [1.41–3.16]).

## DISCUSSION

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The proportion of individuals with AHD at the time of HIV diagnosis in BC has remained relatively stable over time and in recent years. In recent years (2004 – 2008), this proportion was 10% according to the standard AHD definition used in routine surveillance reports at BCCDC. By broadening the case definition to include individuals with a CD4<sup>+</sup> T-cell count less than 200 cells/mm<sup>3</sup> regardless of whether an AIDS case report was completed within one year of HIV diagnosis, the proportion of persons with AHD increased to 17% for the same time period. This is lower than estimates in settings outside of Canada where the expanded definition for AHD was used.[2] Elsewhere in Canada, a study in Northern Alberta found 28% of new HIV cases from 1998–2008 had CD4<sup>+</sup> T-cell count less than 200 cells/mm<sup>3</sup> at the time of diagnosis.[10]

Multiple factors likely contribute to delays in diagnosis of HIV that lead to AHD, including provider testing practices, testing availability and accessibility, and characteristics of individuals who seek HIV testing in BC. We found several characteristics independently associated with AHD in multivariate analysis, including age, having with no identified risk factors other than heterosexual exposure, having not previously tested for HIV, and not reporting a HIV-positive partner. These characteristics may indicate individuals who may be (or are perceived to be) at lower risk for HIV infection, and as a result may not have been motivated to seek earlier HIV testing. These findings may also be related to provider perceptions of an individual's risk: based on these characteristics

providers may not have offered HIV testing, or may not have elicited information on risk factors during HIV testing or follow-up.

Other studies have associated AHD with older age, immigration, heterosexual transmission and unknown risk factors, suggesting that at least in part, individuals with AHD tend to be those at lower perceived risk of HIV infection.[2] A study comparing early and late HIV testers in 16 sites in the United States from 2000 to 2003 found that those who tested for HIV at a later stage of infection were significantly less likely to test anonymously.[1] This is consistent with our finding that individuals who tested nominally were more likely to have AHD at the time of HIV diagnosis. The association between nominal HIV testing and AHD may be related to a perception of low risk for HIV among nominal testers (i.e., that non-nominal HIV testing may be chosen or offered to individuals at a perceived higher risk for HIV).

In multivariate modeling, we did not find significant differences in AHD by health region. While AHD varied significantly by health region in bivariate analysis, this association no longer remained after adjusting for other variables. This is likely explained by regional differences in client demographics, populations at risk, HIV testing patterns and HIV prevalence. In this analysis health region could be considered a proxy for several factors associated with AHD and already accounted for in the model, such as exposure category, sex and age. In particular, we found that the proportion of persons who were diagnosed with HIV on their first test (i.e. not previously tested for HIV) varied by health region. As this variable was a strong predictor of AHD, health region did not remain independently associated.

Testing for HIV in BC is widely available, with over 180,000 tests conducted annually. HIV testing is typically offered or promoted to individuals and populations who are perceived to have a higher risk of HIV infection.[11] Targeted strategies to encourage earlier testing in these groups include expansion of HIV testing to non-medical or outreach settings, increasing the frequency of testing, point of care testing, partner notification programs, peer or community-led projects to encourage testing, and promotion of HIV testing at the time of testing for other STI. As we found the majority of individuals with AHD in BC (76%) to have an identifiable risk factor for HIV infection, expanding these targeted approaches to HIV testing may have a substantial impact on reducing the proportion of individuals with AHD in BC. However, as the findings suggest that AHD is more likely among individuals diagnosed with HIV who are at perceived lower risk of infection (e.g., who have no identified risk factors), other strategies may need to be considered that expand testing on a broader population basis. For example, in order to improve the timeliness of diagnosis of HIV in the United States it is recommended that all adults be routinely tested for HIV in health care settings where the prevalence of undiagnosed infection is 0.1% or greater.[12]

## LIMITATIONS

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There are limitations of this analysis that warrant acknowledgement, primarily related to possible misclassification. Although we used both direct and probabilistic linkage methods in this study, errors in matching records may have occurred, and as a result we may have underestimated the number of repeat testers or persons with HIV to whom an AIDS case report was linked. We may



have also underestimated the number of individuals with AHD as AIDS case reporting is passive and likely under-represents the true number of AIDS cases each year, and as information on first CD4<sup>+</sup> T-cell count is not documented for all new HIV diagnoses. By restricting the multivariate analysis to more recent years where data quality is better, the potential for these errors was minimized to the extent possible. Finally, our results may have been influenced by social desirability bias as a history of risk factors for HIV may not be elicited from individuals during public health follow-up.

Monitoring AHD is influenced by a number of factors. In particular, the proportion of persons with AHD is sensitive to the absolute number of persons newly diagnosed with HIV and this needs to be considered when interpreting trends in proportion of persons with AHD. While the absolute number of persons with AHD has remained relatively stable, total HIV diagnoses have fluctuated over time and by health region, making interpretation of proportions more challenging. Regional estimates of AHD are particularly difficult to interpret due to underlying heterogeneity at the population level. Persons with AHD represent those who sought HIV testing, tested HIV-positive, were reported to the provincial HIV surveillance system, and had an AIDS case report within one year of HIV diagnosis or CD4<sup>+</sup> test results at the time of public health follow-up. Therefore, estimates of AHD are influenced by regional differences in populations at risk for HIV and HIV test uptake, as well as completeness and timeliness of case reporting. Furthermore, rates of AHD within populations at increased risk for HIV are difficult to determine because denominator data for these groups are unavailable.

There are several opportunities to examine AHD further using existing surveillance data. Information on reason for HIV testing and place of testing (e.g., GP, hospital, public health clinics) may increase our understanding of the characteristics of people with AHD. To explore missed opportunities for HIV testing, additional data linkages could assess health service utilization among people with AHD prior to HIV diagnosis (e.g., physician or emergency room visits, or previous STI testing). Linkage of provincial HIV surveillance data to clinical information indicative of HIV care (CD4<sup>+</sup> cell count, viral loads) may also enhance our ability to identify individuals with AHD.

## SUMMARY

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The overall proportion of persons diagnosed with HIV at an advanced stage has remained relatively stable in BC. In multivariate analysis, AHD was more likely among males, older age groups, persons with no identified risk factors other than heterosexual exposure, individuals who tested nominally for HIV, those who had never previously tested for HIV, and people who did not report having an HIV-positive partner. However, among people with AHD, we found a high proportion of MSM, IDU and heterosexuals with known HIV risk factors. These findings may indicate continued barriers to timely HIV testing within these groups – such as motivation for testing, HIV stigma or poor access to testing services. Strategies to expand HIV testing that promote increased and earlier uptake of HIV testing within these different groups may help to reduce the number of people with AHD in BC.

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Figure 1. Number and proportion of persons with Advanced HIV Disease (AHD, standard definition) at the time of HIV diagnosis, BC, 1995 – 2008

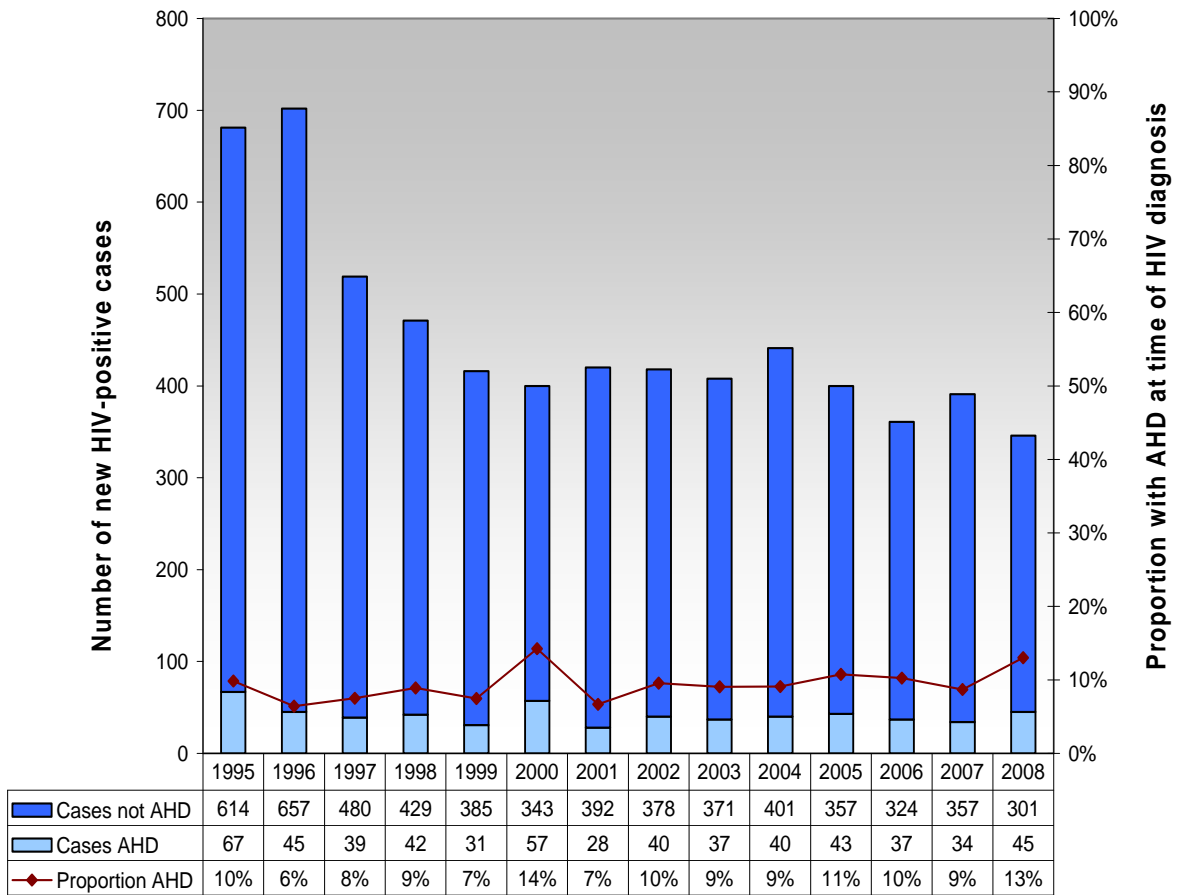
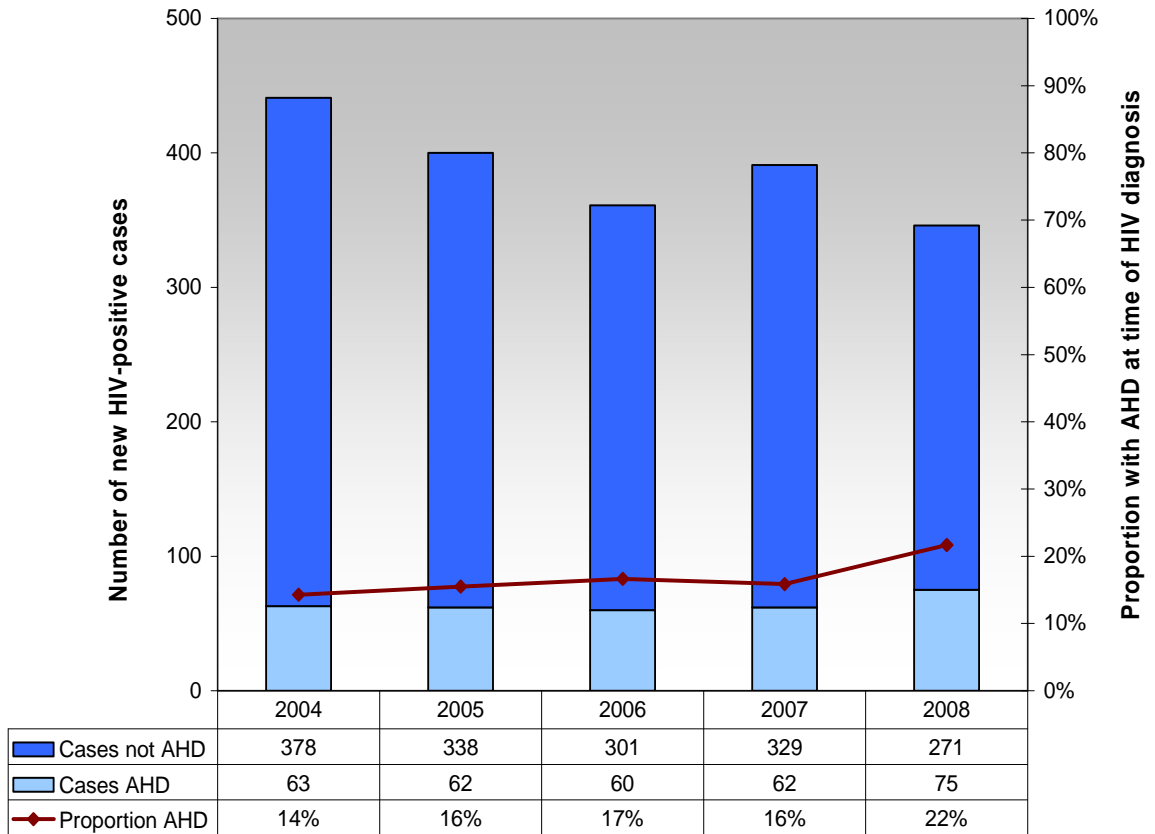
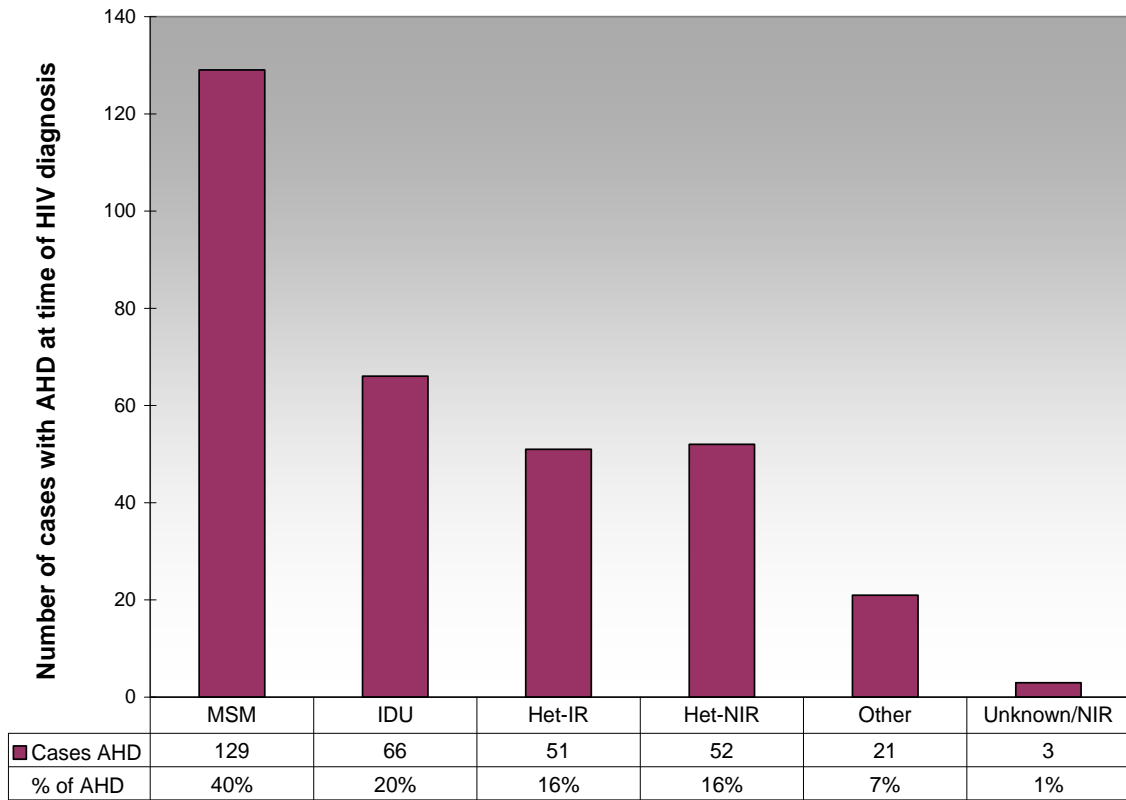


Figure 2. Number and proportion of persons with Advanced HIV Disease (AHD, expanded definition) at the time of HIV diagnosis, BC, 2004 – 2008



**Figure 3. Number and proportion of persons with Advanced HIV Disease (AHD, expanded definition) at the time of HIV diagnosis in BC, by exposure category, 2004 – 2008**



**Table 1. Number and proportion of new HIV-positive cases with Advanced HIV Disease (AHD, standard definition) at time of HIV diagnosis in BC, 1995 – 2008**

Characteristic	1995-2003		2004		2005		2006		2007		2008	
	Cases	AHD %	Cases	AHD %	Cases	AHD %	Cases	AHD %	Cases	AHD %	Cases	AHD %
<b>Total</b>	4,435	386	441	40	400	43	361	37	391	34	346	45
<b>Sex</b>												
Male	3,453	338	336	36	322	38	289	32	303	31	287	38
Female	949	47	105	4	77	5	72	5	85	3	59	7
<b>Age group</b>												
<15	52	8	4	0	1	0	3	0	0	0	3	1
15-24	370	5	34	1	30	0	38	0	38	1	25	0
25-34	1,552	95	101	5	95	3	101	6	112	1	95	6
35-44	1,569	140	164	11	144	16	112	13	136	15	106	14
45-54	640	85	98	16	98	16	59	7	71	11	77	10
≥55	252	53	40	7	32	8	48	11	34	6	40	14
<b>Health Authority</b>												
Vancouver Coastal	2,665	187	212	20	213	22	188	20	209	16	187	25
Fraser	955	98	109	12	88	16	72	5	81	7	69	7
Interior	239	33	19	2	20	3	17	3	17	3	26	7
Northern	93	10	26	3	28	1	29	2	28	3	24	1
Vancouver Island	458	55	71	3	45	1	51	7	53	4	39	5
<b>Ethnicity</b>												
Caucasian	2,681	243	296	23	264	31	227	22	243	21	188	31
Asian/South Asian	253	28	25	6	33	3	27	0	29	3	39	5
Black	165	16	19	4	17	1	15	3	10	1	17	2
Aboriginal	704	40	70	4	60	5	55	5	63	4	44	4
Hispanic	126	13	11	0	16	2	15	4	19	0	24	1
Other/Mixed	17	2	6	1	2	0	4	1	6	1	9	0
<b>Exposure category</b>												
MSM	1,427	170	187	14	181	18	160	12	173	12	181	25
IDU	1,767	87	138	7	124	6	113	6	118	6	59	2
Het-IR	224	56	58	7	53	6	44	9	47	7	50	7
Het-NIR	550	38	38	7	26	7	25	6	40	5	30	8
Other	84	19	16	5	12	6	17	4	10	4	9	1
Unknown/NIR	383	16	4	0	4	0	2	0	3	0	17	2

Note: MSM = Men who have sex with men, IDU = People who use Injection Drugs, Het = Heterosexual, IR = Identified Risk, NIR = No Identified Risk

**Table 2. Bivariate and multivariate analyses of factors associated with Advanced HIV Disease (AHD, expanded definition) at time of HIV diagnosis in BC, 2004 to 2008**

Characteristic	AHD/Total Cases	% AHD	OR	95% CI	AOR	95% CI
<b>Sex</b>						
Male	277/1,537	18%	1.73	[1.23, 2.41]	1.57	[1.05, 2.35]
Female	45/398	11%	1.00		1.00	
<b>Age</b>						
< 15	1/11	9%	1.96	[0.78, 3.69]	0.61	[0.06, 5.94]
15-24	8/165	5%	1.00	Referent	1.00	
25-34	40/504	8%	1.69	[0.78, 3.69]	1.49	[0.68, 3.30]
35-44	118/662	18%	4.26	[2.04, 8.90]	3.92	[1.84, 8.33]
45-54	93/403	23%	5.89	[2.79, 12.43]	4.28	[1.98, 9.25]
≥ 55	62/194	32%	9.22	[4.26, 19.94]	5.74	[2.58, 12.77]
<b>Health Authority</b>						
Vancouver Coastal	162/1,009	16%	1.00	Referent	----	----
Fraser Health	74/419	18%	1.12	[0.83, 1.52]	----	----
Interior Health	29/99	29%	2.17	[1.36, 3.45]	----	----
Northern Health	21/135	16%	0.96	[0.59, 1.58]	----	----
Vancouver Island	34/259	13%	0.79	[0.53, 1.18]	----	----
<b>Ethnicity</b>						
Caucasian	203/1,218	17%	1.00	Referent	----	----
Asian/South Asian	29/153	19%	1.17	[0.76, 1.80]	----	----
Black	16/78	21%	1.29	[0.73, 2.28]	----	----
Aboriginal	41/292	14%	0.82	[0.57, 1.17]	----	----
Hispanic	13/85	15%	0.90	[0.49, 1.66]	----	----
Other/Mixed	4/27	15%	0.87	[0.30, 2.54]	----	----
<b>Exposure category</b>						
MSM	129/882	15%	1.00	Referent	1.00	
IDU	66/552	12%	0.79	[0.58, 1.09]	0.99	[0.69, 1.43]
Het-IR	51/252	20%	1.48	[1.03, 2.12]	1.46	[0.96, 2.24]
Het-NIR	52/159	33%	2.84	[1.94, 4.15]	2.15	[1.39, 3.32]
Other	21/64	33%	2.85	[1.64, 4.96]	2.51	[1.28, 4.92]
Unknown/NIR	3/30	10%	0.65	[0.19, 2.17]	0.42	[0.05, 3.56]
<b>Tested nominally for HIV</b>						
Yes	261/1,422	18%	1.68	[1.25, 2.27]	1.73	[1.25, 2.40]
No	61/517	12%	1.00		1.00	
<b>Repeat tester</b>						
Yes	96/984	10%	1.00		1.00	
No	226/955	24%	2.87	[2.22, 3.71]	2.52	[1.89, 3.35]
<b>Partner HIV-positive</b>						
Yes	34/422	8%	1.00		1.00	
No	288/1,517	19%	2.67	[1.84, 3.88]	2.11	[1.41, 3.16]

Note: OR = Odds Ratio, CI = Confidence Interval, AOR = Adjusted Odds Ratio, MSM = Men who have sex with men, IDU = People who use Injection Drugs, Het = Heterosexual, IR = Identified Risk, NIR = No Identified Risk

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