Faculty of Medicine | UNIVERSITY OF MANITOBA

B.Sc.(Med)Program
Office of the Associate Dean, Research

Student Name: Adam Erickson **Date:** 8/8/14

Project Title: Substance Use and its Impact on Care Outcomes among HIV-Infected Individuals in Manitoba

Primary Supervisor Name: Dr. Yoav Keynan

Department: Medical Microbiology

SUMMARY: (no more than 250 words single spaced)

BACKGROUND: The high prevalence of substance use among HIV-infected individuals creates numerous challenges to patient care. This study was undertaken in order to understand the impact of substance use on care outcomes for HIV-infected persons in Manitoba. METHODS: Clinical records of 564 HIV-infected individuals in care at the Health Sciences Centre in Winnipeg, Manitoba were reviewed. Clinical data was extracted from patient charts for substance users (illicit substance users, alcohol abusers, and chronic users of opioids or benzodiazepines) and non-users. RESULTS: Among HIV-infected individuals in Manitoba, 38% were substance users with overrepresentation by Aboriginals, females, young adults, and residents of Winnipeg's core areas. Opioids and benzodiazepines were the most commonly used substances with the majority of substance users having used multiple classes of substances in their lifetime. Substance users were more likely than non-users to have missed clinic appointments. Among substance users, missed appointments were more common among those who self-identified as Aboriginal, females, young adults, residents of Winnipeg's core areas, heterosexuals, and those who had abused alcohol or cocaine/crack. Substance use also affected the prescription of antiretroviral medications and was associated with liver damage. DISCUSSION: Substance use is common among HIV-infected individuals in Manitoba, with important health-related implications arising from the use and/or misuse of potentially harmful substances. The negative impact of substance use on engagement in care and health outcomes has important implications on clinical care which must be addressed by targeted patient recruitment, the use of harm reduction and patient-centred care.

Adam Erickson Digitally signed by Adam Erickson DN: cn=Adam Erickson, o=University of Manitoba, ou, email=erickso9@myumanitoba.ca, c=CA Date: 2014.08.07 15:38:20 -05'00'

Student Signature

Yoav Keynan Digitally signed by Yoav Keynan DN: cn=Yoav Keynan, o=University of Manitoba, ou, email=keynany@yahoo.com, c=CA Date: 2014.08.08 09:39:39 -05'00'

Supervisor Signature

ACKNOWLEDGEMENTS:

I gratefully acknowledge the support by one or more of the following sponsors;

H.T. Thorlakson Foundation
Dean, Faculty of Medicine
Manitoba Health Research Council
Manitoba Institute of Child Health
Kidney Foundation of Manitoba
Leukemia and Lymphoma Society of Canada
CancerCare Manitoba
Manitoba Medical Service Foundation
Associate Dean (Research), Faculty of Medicine
Heart and Stroke Foundation
Health Sciences Centre Research Foundation
Other: Alan Klass Memorial Health Equity Program

INTRODUCTION & BACKGROUND

Acquired immunodeficiency syndrome (AIDS) has been a worldwide epidemic since the early 1980's[1]. AIDS is caused by human immunodeficiency virus (HIV), a retrovirus spread through sexual intercourse, the transfer of blood or blood products, and from breastfeeding[1]. HIV infects CD4 cells, a type of T-helper cell involved in the adaptive immune response against environmental pathogens[1]. The resulting immune system destruction increases the susceptibility to infection and disease for HIV-infected persons.

An estimated 71,300 people were infected with HIV in Canada by the end of 2011, with roughly one quarter of those being unaware of their infection[2]. Manitoba has some of the highest rates of HIV per capita in Canada with more than 1,100 people currently enrolled in care[2,3]. HIV transmission is driven by heterosexual intercourse in Manitoba followed by homosexual sex between men and injection drug use[3]. Aboriginal populations infected with HIV are overrepresented in Canada, and especially in Manitoba where the infection rate is 3.6 times higher than the general population[2,3].

The harmful effects of concurrent substance use and HIV infection are well established. Substance use is defined as the inappropriate consumption of medicines, drugs, or other materials including prescription and over the counter drugs, street drugs, alcohol and tobacco[4]. Although substance use and abuse are not mutually inclusive, substance use is the foundation for substance abuse and therefore encompasses substance abuse in its definition. When compared to HIV-infected non-users, HIV-infected substance users are less likely to adhere to treatments and are more likely to have worse health outcomes, leading to increased comorbidity and mortality[5,6]. Liver disease is the most common non-HIV-related cause of death in HIV-infected persons, with substance users being at increased risk of developing liver disease due to hepatitis C co-infection and alcohol-related liver damage[8-10]. Still, HIV-infected substance users can attain improved health outcomes when effectively treated with antiretroviral therapy[5].

Although much is known about HIV in Manitoba, there is little knowledge about the substance use patterns and the impact of substance use among the HIV-infected population in Manitoba. Therefore, a chart review of patients enrolled in care in the Manitoba HIV Program (MHP) at Winnipeg's Health Sciences Centre (HSC) was conducted in order to characterize the substance use patterns and the effect of substance use on several parameters of HIV-infection including presentation to and engagement in care, comorbidity, and clinical outcome.

MATERIALS & METHODS

Study Design

We conducted a retrospective chart review of all HIV-positive patients enrolled in care in the MHP, HSC site in Manitoba, Canada. All patients enrolled in care at HSC during the initiation of the chart review were included in the study. Substance use in this study was defined as the use of an illicit substance at least one time, the daily consumption of prescription benzodiazepines or opioids for four or more consecutive months, or having a history of alcohol abuse or addiction. This study was conducted between June, 2013 and July, 2014 and was approved by the institutional Human Research Ethics Board at the University of Manitoba.

Data Collection

From June to August, 2013, a data extraction tool was used to obtain demographic information, substance use history, HIV CD4 counts and viral loads, sexual orientation, and medical and psychiatric comorbidities from substance users. Geographic location was obtained by recording the first three digits of each participant's postal code and mapping them to geographical areas within Manitoba and north-western Ontario with subsequent grouping into "urban core" (Winnipeg's Downtown and Point Douglas communities) or "non-urban core" (all other areas of Winnipeg, rural Manitoba and north-western Ontario). Data dating back to each participant's presentation to the HIV clinic at HSC was extracted from each individual clinic chart. For non-substance users, demographic information, geographic location, and CD4 counts at presentation were obtained from the clinic charts. The number of attended and missed appointments was obtained directly from the HIV clinic at HSC for all participants using records from January 1, 2012 to August 15, 2013.

During June and July, 2014, each participant's current antiretroviral prescription and most recent lab values were extracted from patient charts for both substance users and non-users.

Analysis

Socio-demographic and clinical parameters for substance users and non-users were analyzed using chi-square tests of association and Kruskal-Wallis tests, where appropriate. Following the initial analysis, the study cohort was subset to include only substance users with the main variables of interest being types of substance used. An expanded set of socio-demographic and clinical characteristics were then compared between those who had missed clinic appointments and those who had not using chi-square tests of association or analysis of variance, where appropriate. With the exception of the substance use variables, all variables significantly associated with the outcome at the $p < 0.20$ level were included in multivariate analyses. Bivariate analyses using chi-square tests of association were performed for the analysis of viral load suppression for substance users and for the analysis of prescribed antiretroviral regimen and laboratory values for the entire HIV cohort.

RESULTS

The clinic charts of all 564 HIV-infected individuals enrolled in care in the MHP at HSC were examined. Of the 564 study participants, 215 (38%) were substance users. All study participants were 18 years of age or older at the time of chart review. A comparison of socio-demographic and clinical characteristics between substance users and non-users is presented in Table 1. Females, individuals who self-identified as Aboriginal, patients between 18-39 years of age, and individuals living in the core areas of Winnipeg were significantly more likely to use substances. Substance users were more likely than non-users to have missed at least one clinic appointment. No difference was found in CD4 count at the time of presentation to care between substance users and non-users.

The most commonly used substances included opioids, benzodiazepines, alcohol and cocaine/crack at 74%, 60%, 51% and 39% of substance users, respectively. Ongoing substance use was reported by 94% of substance users at the time of chart review, with 73% of users having used multiple classes of substances in their lifetime. Eighty-six percent of all substance users had used at least one substance daily, with 68% of those being attributable to non-medically prescribed usage. Medical prescriptions for opioids and benzodiazepines accounted for the entire substance use of 18% of the substance users studied.

The association between missing clinic appointments and several clinical parameters for substance users is presented in Table 2. Bivariate analysis showed that substance users who were female, Aboriginal, between 18-39 years of age, living in the core areas of Winnipeg, and heterosexual were significantly more likely to have missed at least one clinic appointment. Alcohol and cocaine/crack abusers were also more likely to miss clinic appointments than substance users who had no documented history of alcohol or cocaine/crack abuse. Multivariate analysis showed that substance users who were Aboriginal (AOR 3.33, 95% CI 1.39-7.97), adults younger than 40 years of age (AOR 0.34, 95% CI 0.12-0.95 for ages 40-49; AOR 0.15, 95% CI 0.05-0.45 for ages 50+) or heterosexual (AOR 0.34, 95% CI 0.11-0.99 for homosexuals & bisexuals; AOR 0.25, 95% CI 0.09-0.71 for those of unknown sexual orientation) were highly likely of missing clinic appointments.

The relationship between clinical parameters and a substance users' likelihood of suppressing their HIV viral load at least one time since their presentation to the HIV clinic is presented in Table 3. Seventy-nine percent of substance users recorded suppression of their HIV viral load at least one time. Substance users who self-identified as Aboriginal or were between 18-39 years of age were significantly less likely than non-Aboriginal and older individuals to have ever suppressed their HIV viral load.

A summary of the antiretroviral regimens prescribed at the time of chart review for substance users and non-users is shown in Table 4. Substance users were significantly more likely to have been prescribed for a protease inhibitor while non-substance users were more likely to have been prescribed a non-nucleoside reverse transcriptase inhibitor (NNRTI) or integrase strand transfer inhibitor (ISTI). There was no difference in prescriptions for nucleoside/nucleotide reverse transcriptase inhibitors (NRTI) between substance users and non-users. Fifty-three percent of substance users on therapy anecdotally claimed to be less than 95% adherent to their antiretroviral regimen.

The most recent laboratory values for substance users and non-users, organized into standard cut-off values are presented in Table 5. No difference in creatinine was found between substance users and non-users. However, substance users were significantly more likely to have elevated liver enzymes while non-users were more likely to have elevated total cholesterol and apolipoprotein B. Non-users were also more likely to have abnormally low phosphate compared to substance users. The prevalence of diabetes in the HIV cohort was 12.4%, though no difference was found between substance users and non-users.

DISCUSSION

This study is the first to describe the substance use patterns among HIV-infected individuals in Manitoba. Thirty-eight percent of HIV-infected individuals in care at HSC use substances with an overrepresentation among Aboriginals, females, young adults, and those residing in Winnipeg's core areas. Substance users were more likely to miss clinic appointments than non-substance users with Aboriginal substance users being at the highest risk of missing scheduled clinic appointments. Substance users were also more likely to be prescribed a protease inhibitor and have liver damage as indicated by elevated liver enzymes. The risk factors identified for HIV-infected substance users can be used to target engagement strategies towards specific populations in Manitoba in order to improve engagement in care and clinical outcomes for individuals at higher risk of using substances.

The association between substance use and HIV is well documented. Injection drug use accounts for a significant proportion of HIV-infections in Manitoba, while non-injection drug and alcohol use can result in high risk behaviours leading to the transmission of HIV and increased comorbidity[3,11]. There is evidence to suggest that substance use is a predictor of a more rapid HIV disease progression regardless of adherence to antiretroviral therapy[12]. In the context of this study, the analysis suggests that substance use is associated with female gender, residence in the core downtown area, and Aboriginal ethnicity, which may represent the vulnerability to adverse health outcomes for these populations in general. These factors act together to decrease engagement in care, resulting in HIV progression, comorbidity and mortality[13].

In consistency with previous studies, nearly 40% of adults receiving care for HIV in Manitoba use substances other than cannabis, though the prevalence of substance use and dependence in the Canadian general population is significantly lower[14,15]. Alcohol is the most widely abused substance in the Manitoba general population, though other drugs including solvents, cannabis, cocaine and opioids are commonly reported[16]. The disparity between substances used in the general population and HIV-infected individuals may be partially due to the availability of prescription drug information through the Drug Program Information Network (DPIN) in comparison to the self-reporting of alcohol or illicit substance use, leading to underreporting of the usage of alcohol and other non-prescription substances. Thus the observation of higher rates of alcohol and cocaine usage among individuals that miss appointments may be underestimated. In contrast to opioid or benzodiazepines where replacement therapy or harm reduction strategies are applied, the effect of alcohol and cocaine on engagement in care needs to be further investigated.

With poor medication adherence among HIV-infected substance users there is no surprise that a higher number of protease inhibitors were prescribed to substance users due to their reduced susceptibility to resistance when compared to other antiretroviral medications[6,17]. However, protease inhibitors may carry a worse side-effect profile than the other classes of antiretroviral medications, leading to adverse health outcomes[18]. Alcohol-related liver disease and chronic viral hepatitis may play a significant role in the elevation of liver enzymes seen in substance users. The mechanism of hypercholesterolemia and elevated apolipoprotein B in non-substance users is unclear. Medication-induced lipodystrophy is a major complication of antiretroviral therapy, especially with the use of protease inhibitors[19]. However, the effects of lipodystrophy may be reduced in substance users due to poor dietary intake, resulting in less hypercholesterolemia in the substance using cohort but creating further challenges to patient care[20].

Drug use and substance use disorders are well known barriers to healthcare. Many substance users are reluctant to receive healthcare treatment or procrastinate in seeking medical treatment, regardless of their health status[21]. The abuse of alcohol and cocaine/crack was associated with decreased engagement in care for HIV-infected patients in Manitoba, an association not seen with opioids and benzodiazepines. This may be in part due to harm reduction strategies available for opioid and benzodiazepine abuse. Still, the ability to administer adequate harm reduction is complicated by the fact that nearly three-quarters of substance users abuse multiple classes of substances.

Although the abuse of prescription drugs has emerged as a serious concern in Canada, harm reduction is an important and effective tool for engaging individuals in healthcare and working to improve healthcare outcomes. HIV education has also been found to be an effective tool for engaging patients in the healthcare system and improving health outcomes[13]. We know

that the effective treatment of substance use disorders improves HIV treatment outcomes, including access to and retention in care programs[11]. Therefore, a comprehensive, multidisciplinary, patient-centred approach to care with the utilization of cognitive behavioural therapy, pharmacotherapy and patient education must be utilized in order to engage patients in care and improve health outcomes for HIV-infected individuals[22,23].

This study examined 564 of the roughly 1100 HIV-infected individuals in Manitoba and may not be representative of the entire HIV population in Manitoba as only one clinical site was studied. The retrospective nature of this study limited the collected data to what had been recorded in private patient charts, leading to potential underreporting of substance use, comorbidities, and other aspects of care. The nature of the study also made it unclear as to which of the participants were using multiple classes of substances simultaneously or independently. Furthermore, the criteria for 'substance use' in this study were not exclusively based off of a standardized definition of substance use due to limitations of the patient charts. More specifically, the DPIN in the patient charts often-times only displayed a four-month prescription history, which is why a consecutive four-month history of opioid or benzodiazepine usage was classified as substance use in this study. We recognize that some study participants on chronic opioids or benzodiazepines have legitimate medical requirements for the medications; however, several patients had anecdotally claimed to be abusing medically prescribed opioids and benzodiazepines, and so their use was included in the definition of substance use in this study.

REFERENCES

1. HIV/AIDS. National Institute of Allergy and Infectious Disease website. http://www.niaid.nih.gov/topics/hivaids/understanding/Pages/Default.aspx. Accessed July 28, 2014.

2. Public Health Agency of Canada. Summary: Estimates of HIV Prevalence and Incidence in Canada, 2011. 2012; 1-7.

3. Manitoba HIV program update 2011. 2011; 1-8.

4. Miller-Keane, O'Toole MT. Miller-Keane Encyclopedia & Dictionary of Medicine, Nursing & Allied Health (Elsevier Inc., ed. 7, 2003).

5. Altice FL, Izaman AK, Soriano VV, et al. Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. Lancet 2010; 376: 367-87.

6. Gonzalez A, Barinas J, O'Cleirigh C. Substance use: Impact on adherence and HIV medical treatment. Curr HIV/AIDS Rep 2011; 8: 223-34.

7. Malta M, Strathdee SA, Magnanini MM, et al. Adherence to antiretroviral therapy for human immunodeficiency virus/acquired immune deficiency syndrome among drug users: A systematic review. Addiction 2008; 103: 1242-57.

8. The Data Collection on Adverse Events of Anti-HIV drugs (D:A:D) Study Group. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D study. AIDS 2010; 24: 1537-1548.

9. Klein RS. Trends related to Aging and Co-Occurring Disorders in HIV-Infected Drug Users. Substance Use & Misuse 2011; 46: 233-244.

10. Muga R, Sanvisens A, Fuster D, Tor J, Martinez E, Pérez-Hoyos S, Muñoz A. Unhealthy Alcohol Use, HIV Infection and Risk of Liver Fibrosis in Drug Users with Hepatitis C. PLOS One 2012; 7(10): e46810.

11. Meyer JP, Althoff AL, Altice FL. Optimizing Care for HIV-Infected People Who Use Drugs: Evidence-Based Approaches to Overcoming Healthcare Disparities. Clinical Infectious Diseases 2013; 57: 1309-17.

12. Carrico AW. Substance use and HIV disease progression in the HAART era: Implications for the primary prevention of HIV. Life Sciences 2011; 88: 940-7.

13. Jones D, Cook R, Rodriguez A, Waldrop-Valverde D. Personal HIV Knowledge, Appointment Adherence and HIV Outcomes. AIDS and Behaviour 2013; 17: 242-249.

14. Bing EG, Burnam MA, Longshore D, et al. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. General Psychiatry 2001; 8: 721-8.

15. Tjepkema M. Alcohol and illicit drug dependence. Statistics Canada Supplement to Health Reports 2004; 15: 9-19.

16. Canadian Community Epidemiology Network on Drug Use, Winnipeg Site Network Team. CCENDU 2009/2010 Winnipeg Report. 2011; 1-73.

17. Andreoni M, Perno CF. Positioning of HIV-protease inhibitors in clinical practice. European Review for Medical and Pharmacological Sciences 2012; 16: 10-18.

18. AIDS Info: U.S. Department of Health and Human Services. Side Effects of Anti-HIV Medications. 2005; 1-14.

19. Guaraldi G, Stentarelli C, Zona S, Santoro A. HIV-Associated Lipodystrophy: Impact of Antiretroviral Therapy. Drugs 2013; 73: 1431-1450.

20. Hendricks KM, Erzen HD, Wanke CA, Tang AM. Nutrition issues in the HIV-infected injection drug user: findings from the nutrition for healthy living cohort. The Journal of the American College of Nutrition 2010; 29: 136-43.

21. McCoy CB, Metsch LR, Chitwood DD, et al. Drug Use and Barriers to Use of Health Care Services. Substance Use & Misuse 2001; 36: 789-806.

22. McHugh RK, Hearon BA, Otto MW. Cognitive Behavioural Therapy for Substance Use Disorders. Psychiatry Clinics of North America 2010; 33: 511-25.

23. Bruce RD, Kresina TF, McCance-Katz EF. Medication-assisted treatment and HIV/AIDS: aspects in treating HIV-infected drug users. AIDS 2010; 24: 331-40.

24. The Medical Council of Canada. Clinical Laboratory Tests: Normal Values. http://apps.mcc.ca/Objectives_Online/objectives.pl?lang=english&loc=values. Published March 3, 2013. Accessed August 5, 2014.

25. Royal College of Physicians and Surgeons of Canada. Clinical Laboratory Tests - Normal Values. http://www.royalcollege.ca/portal/page/portal/rc/common/documents/exams/normal_values_e.pdf. Published 2010. Accessed August 5, 2014.

TABLES

Table 1. Socio-demographic and clinical characteristics between substance users and non-users among 564 HIV-infected individuals.

	Non-Substance User No. (%)	Substance User No. (%)	Total No. (%)	P[a]
Age Group				< 0.0001
18-39	101 (28.9)	91 (42.3)	192 (34.0)	
40-49	115 (33.0)	81 (37.7)	196 (34.8)	
50+	133 (38.1)	43 (20.0)	176 (31.2)	
Sex				0.019
Male	240 (68.8)	127 (59.1)	367 (65.1)	
Female	109 (31.2)	88 (40.9)	197 (34.9)	
Aboriginal*				< 0.0001
Non-Aboriginal	283 (81.1)	63 (29.3)	346 (61.3)	
Aboriginal	66 (18.9)	152 (70.7)	218 (38.7)	
Geography				0.004
Non-urban core	222 (63.6)	110 (51.2)	332 (58.9)	
Urban core	127 (36.4)	105 (48.8)	232 (41.1)	
≥ 1 Missed Appointment				< 0.0001
No	177 (50.7)	49 (22.8)	226 (40.1)	
Yes	172 (49.3)	166 (77.2)	338 (59.9)	
CD4 at Presentation				0.897
≤ 200	121 (34.7)	72 (33.6)	193 (34.3)	
201-350	81 (23.2)	50 (23.4)	131 (23.3)	
351-500	68 (19.5)	47 (22.0)	115 (20.4)	
501+	79 (22.6)	45 (21.0)	124 (22.0)	
CD4 [Mean (IQR)][b]	327 (118-480)	349 (143-470)	335 (129-473)	0.614

[a]Unless otherwise noted, p-values are from chi-square tests of association
[b]Based on Kruskal-Wallis test
*Aboriginal status determined by self-identification and includes First Nation, Inuit and Métis

Table 2. The results of chi-square analysis and a logistic regression model examining the association between clinical characteristics and missing clinic appointments among 215 HIV-infected substance users.

	No Missed Appointments No. (%)	Missed Appointments No. (%)	Total No. (%)	AOR (95% CI)	P*
Age Group					< 0.0001
18-39	8 (16.3)	83 (50.0)	91 (42.3)	Ref (--)	
40-49	20 (40.8)	61 (36.7)	81 (37.7)	0.34 (0.12-0.95)	0.039
50+	21 (42.9)	22 (13.3)	42 (20.0)	0.15 (0.05-0.45)	0.001
Sex					0.003
Male	38 (77.6)	89 (53.6)	127 (59.1)	Ref (--)	
Female	11 (22.4)	77 (46.4)	88 (40.9)	0.89 (0.34-2.35)	0.821
Aboriginal					< 0.0001
Non-Aboriginal	30 (61.2)	33 (19.9)	63 (29.3)	Ref (--)	
Aboriginal	19 (38.8)	133 (80.1)	152 (70.7)	3.33 (1.39-7.97)	0.007
Geography					0.004
Non-urban core	34 (69.4)	76 (45.8)	110 (51.2)	Ref (--)	
Urban core	15 (30.6)	90 (54.2)	105 (48.8)	2.22 (0.99-5.00)	0.052
Sexual Orientation					< 0.0001
Heterosexual	25 (51.0)	134 (80.7)	159 (74.0)	Ref (--)	
Homosexual/bisexual	13 (26.5)	16 (9.6)	29 (13.5)	0.34 (0.11-0.99)	0.048
Unknown	11 (22.4)	16 (9.6)	27 (12.6)	0.25 (0.09-0.71)	0.010
CD4 at Presentation					0.576
≤ 200	18 (37.5)	54 (32.5)	72 (33.6)		
201-500	19 (39.6)	78 (47.0)	97 (45.3)		
501+	11 (22.9)	34 (20.5)	45 (21.0)		
Opioid Use					0.166
Yes	32 (65.3)	125 (75.3)	157 (73.0)	1.55 (0.64-3.75)	0.324
Benzodiazepine Use					0.293
Yes	26 (53.1)	102 (61.4)	128 (59.5)	1.50 (0.67-3.39)	0.497
Alcohol Use					0.009
Yes	17 (34.7)	93 (56.0)	110 (51.2)	1.33 (0.58-3.06)	0.207
Cocaine/Crack Use					0.002
Yes	10 (20.4)	74 (44.6)	84 (39.1)	1.77 (0.73-4.32)	0.275

AOR: Adjusted odds ratio

*P-values in alignment with row headings are from chi-square analysis while p-values adjacent to adjusted odds ratios are from logistic regression analysis

Table 3. Effect of socio-demographic parameters and missing clinic appointments on achieving viral load (VL) suppression at least one time among 215 substance users.

	Suppressed VL No. (%)	Did Not Suppress VL No. (%)	Total No. (%)	P
Age Group				0.002
18-39	63 (37.1)	28 (62.2)	91 (42.3)	
40-49	71 (41.8)	10 (22.2)	81 (37.7)	
50+	36 (21.2)	7 (15.6)	43 (20.0)	
Sex				0.379
Male	103 (60.6)	24 (53.3)	127 (59.1)	
Female	67 (39.4)	21 (46.7)	88 (40.9)	
Aboriginal				0.008
Non-Aboriginal	57 (33.5)	6 (13.3)	63 (29.3)	
Aboriginal	113 (66.5)	39 (86.7)	152 (70.7)	
Geography				0.095
Non-urban core	82 (48.2)	28 (62.2)	110 (51.2)	
Urban core	88 (51.8)	17 (37.8)	105 (48.8)	
≥ 1 Missed Appointment				0.919
No	39 (22.9)	10 (22.2)	49 (22.8)	
Yes	131 (77.1)	35 (77.8)	166 (77.2)	

Table 4. Antiretroviral prescriptions by class between substance users and non-users among 564 HIV-infected individuals.

	Non-Substance User No. (%)	Substance User No. (%)	Total No. (%)	P
NRTI				0.0810
Yes	311 (89.1)	201 (93.5)	512 (90.8)	
No	38 (10.9)	14 (6.5)	52 (9.2)	
Protease Inhibitor				< 0.0001
Yes	201 (57.6)	171 (79.5)	372 (66.0)	
No	148 (42.4)	44 (20.5)	192 (34.0)	
NNRTI				< 0.0001
Yes	107 (30.7)	30 (14.0)	137 (24.3)	
No	242 (69.3)	185 (86.0)	427 (75.7)	
ISTI				0.0126
Yes	46 (13.2)	14 (6.5)	60 (10.6)	
No	303 (86.8)	201 (93.5)	504 (89.4)	
Antiretroviral Therapy				0.4894
Yes	328 (94.0)	205 (95.3)	533 (94.5)	
No	21 (6.0)	10 (4.7)	31 (5.5)	

NRTI: nucleoside/nucleotide reverse transcriptase inhibitor
NNRTI: non-nucleoside reverse transcriptase inhibitor
ISTI: integrase strand transfer inhibitor

Table 5. A comparison of standard cut-off laboratory values between substance users and non-users among 564 HIV-infected individuals. Laboratory values were obtained from the Medical Council of Canada and Royal College of Physicians and Surgeons of Canada[24,25].

	Non-Substance User No. (%)	Substance User No. (%)	Total No. (%)	P
Creatinine				0.6140
≤ 110 µmol/L	320 (93.6)	196 (92.5)	516 (93.1)	
> 110 µmol/L	22 (6.4)	16 (7.5)	38 (6.9)	
AST				< 0.0001
≤ 40 U/L	315 (90.3)	163 (76.5)	478 (85.1)	
> 40 U/L	34 (9.7)	50 (23.5)	84 (14.9)	
ALT				< 0.0001
≤ 35 U/L	281 (80.5)	135 (63.4)	416 (74.0)	
> 35 U/L	68 (19.5)	78 (36.6)	146 (26.0)	
ALP				0.0131
≤ 126 U/L	303 (86.8)	168 (78.9)	471 (83.8)	
> 126 U/L	46 (13.2)	45 (21.1)	91 (16.2)	
GGT				< 0.0001
≤ 40 U/L	218 (63.0)	91 (43.1)	309 (55.5)	
> 40 U/L	128 (37.0)	120 (56.9)	248 (44.5)	
Cholesterol				0.0499
< 5.2 mmol/L	189 (67.3)	113 (76.4)	302 (70.4)	
≥ 5.2 mmol/L	92 (32.7)	35 (23.6)	127 (29.6)	
Apolipoprotein B				0.0024
< 1.25 mmol/L	231 (87.2)	150 (96.2)	381 (90.5)	
≥ 1.25 mmol/L	34 (12.8)	6 (3.8)	40 (9.5)	
Phosphate				0.0105
< 0.80 mmol/L	51 (15.6)	16 (8.0)	67 (12.7)	
≥ 0.80 mmol/L	276 (84.4)	185 (92.0)	461 (87.3)	
Diabetes				0.7294
Type 1	0 (0.0)	2 (0.9)	70 (12.4)	
Type 2	42 (12.0)	26 (12.1)		
No	307 (88.0)	187 (87.0)	494 (87.6)	

AST: aspartate transaminase
ALT: alanine transaminase
ALP: alkaline phosphatase
GGT: gamma-glutamyl transferase