

**PSYCHOSOCIAL DETERMINANTS OF MAINTENANCE OF, AND  
ADHERENCE TO, ANTIRETROVIRAL THERAPY AMONG INJECTION  
DRUG USERS LIVING WITH HIV/AIDS**

**by**

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### Abstract

Antiretroviral therapy (ART) has dramatically affected the course of HIV disease, producing significant reductions in both AIDS-related morbidity and mortality. However, the excitement generated by this new approach has been tempered by concerns about adherence to these complex therapies. Using a sample of 244 participants derived from the Vancouver Injection Drug Users Study, this study examined the impact of self-efficacy, social support, incarceration, and frequent illicit drug use on maintenance of and adherence to ART among injection drug users. Variables that were negatively associated with ART maintenance included negative outcome expectations and incarceration. Variables that were associated positively with ART maintenance included efficacy expectations and self-regulatory efficacy. Negative outcome expectations were also associated negatively with ART adherence, while efficacy expectations were associated positively with ART adherence.

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## *Chapter I*

### **Introduction**

The AIDS epidemic is a global phenomenon affecting many lives as well as the development of countries throughout the world. In 1996, the medical management of HIV/AIDS changed dramatically. The advent of antiretroviral therapy (ART) has altered significantly the course of HIV disease, producing substantial reductions in both AIDS-related morbidity and mortality (Hammer et al., 1997; Hogg et al, 1999; Montaner et al.; 1998).

While ART has greatly improved clinical outcomes among persons living with HIV/AIDS, the excitement generated by this new approach to the medical management of HIV/AIDS has been tempered by concerns about adherence to these complex regimens (Altice & Friedland, 1998). ART has been described as the most rigorous and demanding oral treatment ever offered to a patient population (Rabkin & Chesney, 2000). Treatment often requires that patients take up to 10 pills three times a day, and medications are often taken at odd intervals and in accordance with strict dietary guidelines (Friedland & Williams, 1999). Exacerbating the challenges of daily adherence are the numerous side-effects that are commonly experienced by patients taking ART (Rabkin & Chesney, 2000).

When patients fail to adhere to ART, viral mutation and drug-resistant strains of HIV virus may develop, which in turn can render an entire class of drugs ineffective for these patients (Vanhove et al., 1996). The transmission of resistant virus may then also confer limitations in treatment options for those newly infected (Gray et al., 2001; Quinn et al., 2000). Given the individual and public health concerns related to

adherence to ART, researchers from various disciplines have begun investigating the nature of maintenance and adherence to ART, as well as various related adherence-promoting interventions (Chesney et al., 2000).

Among those most affected by HIV in recent years is the injection drug using community. The view from a population health perspective reveals a complex picture of poor health among injection drug users (IDU). The effects of drugs themselves, in addition to drug-using social networks, mental health issues, high rates of childhood abuse, homelessness, social marginalization, poverty, and unemployment all contribute to a drug users' ability or inability reduce risk and maintain health (Canadian HIV/AIDS Legal Network, 1999; Strathdee et al., 1997; Tyndall et al., 2001; Zolopa et al., 1994). The health of IDUs is complicated further by avoidance and erratic use of primary care services and over-reliance on emergency rooms and acute care hospitalizations (Palepu et al., 2001), patterns that have been well-documented since the 1960s (Jouria, Hensle, & Rose, 1967; Sapira, 1968). The complex health status of IDUs has raised serious concerns about the ability of HIV-positive IDUs to maintain and adhere to ART, as well as concerns regarding the potential of widespread transmission of drug resistant strains of HIV within injection drug using social networks. A consequence of these concerns is that HIV-positive IDUs have poorer access to ART compared to other HIV-positive persons in Canada, the United States and Europe (Carrieri et al., 1999; Celentano et al., 1998; Lucas et al., 2001; Strathdee et al., 1998;). In Vancouver, where ART is provided at no cost to patients, only 40% of eligible HIV-positive IDUs studied had received any antiretroviral therapy at a median duration of 11 months following first eligibility for treatment (Strathdee et al., 1998).

Although a significant amount of recent research has focused on issues of maintenance and adherence to ART, there are several gaps in the current literature. One significant limitation pertains to how adherence has been measured. Most measures rely on self-report, while many of the objective measures in use assess only a subset of adherence behaviour. As well, while many determinants of adherence have been identified, much of this type of research has relied on clinic-based samples of mixed HIV-positive populations, and unspecified measures of psychological variables. Little is known, for example, about specific determinants of ART maintenance and adherence among IDU. Studies have also failed to identify determinants of adherence that are amenable to intervention. Studies of actual adherence interventions have suffered from an array of methodological shortcomings, including inadequate experimental control, lack of standardized intervention techniques, and reliance on small sample sizes recruited from clinic-based populations.

In order to address better the challenges associated with ART maintenance and adherence, studies using community-based samples of specific HIV subpopulations are needed urgently. As well, there is a pressing need for research that examines clearly defined determinants that are relevant to adherence interventions. Given the unique characteristics of the HIV-positive injection drug using population, and the associated challenges of adherence confronting this population, research examining psychosocial determinants of ART maintenance and adherence is now of paramount importance.

Using a sample of 244 participants derived from the Vancouver Injection Drug Users Study, the study examined the impact of self-efficacy, social support, incarceration, and frequent illicit drug use on maintenance of, and adherence to, ART

among injection drug users. This study includes a review of the literature pertaining to HIV/AIDS, injection drug use, and adherence to ART. Also included is a description of the methods employed to collect and analyze the data used, the results of the analyses, and a discussion of the study findings, and the implications of these findings for research, theory and practice.

## *Chapter II*

### **Literature review**

#### *AIDS Through Two Decades*

It has been twenty years since American and European scientists first identified the acquired immune deficiency syndrome (AIDS) and the human immunodeficiency virus (HIV) that causes it. Since that time, a global epidemic has emerged and HIV/AIDS has become the world's fourth leading cause of death (UNAIDS, 2001). As the epidemic evolves and changes, it remains an international crisis that affects the health of tens of millions of individuals and threatens the social welfare of communities and the economic development of many of the world's poorest nations (Forsyth, 2000).

AIDS is a blood-borne disease that was identified and defined in 1981 by the US Center for Disease Control. However, evidence suggests the virus has been present in Africa since the late 1950s and that it first appeared in North America in the mid-1970's (BC Centre for Excellence in HIV/AIDS, 2001). In January 1983 AIDS became a reportable disease in British Columbia, and the first case of AIDS was reported one month later (BC Centre for Excellence in HIV/AIDS, 2001). While HIV-1 was identified in 1984, a second less pathogenic immunodeficiency virus, HIV-2, has since been identified and is known to be prevalent in western Africa.

AIDS is caused by the HIV retrovirus that infects and destroys lymphocytes and other cells that have CD4 receptors. CD4 lymphocytes are responsible for the coordination of immune system functioning. The transmission routes of the HIV virus are well known and include: specific types of sexual activity; sharing of used syringes; vertical transmission from mother to child during delivery; mother to child transmission

during breast-feeding; transfusions of blood, organ transplants or donated sperm; and occasionally through occupational exposure (e.g., needle sticks). The sharing of needles and vaginal and anal sex carry the highest risk for transmission (BC Centre for Excellence in HIV/AIDS, 2001). In order for infection occur, a source of infection (e.g., presence of HIV in blood, semen, vaginal fluid, or breast milk), a means of transmission, a susceptible host, an appropriate route of entry (e.g., mucosal membranes), and sufficient levels of virus are needed to establish infection (Canadian AIDS Society, 1999).

The most pronounced physiological effects of HIV disease occur in two ways. First, there is a progressive deterioration of the immune system functioning, which in turn leads to increased susceptibility to opportunistic infections caused primarily by viruses, bacteria, fungi, protozoa and various malignancies (Tobin, Chow, Bowmer, & Bally, 1993). Second, there is progressive deterioration of the nervous system, mental deterioration, seizures, and sensory and motor changes (Tobin, Chow, Bowmer, & Bally, 1993). The course of the disease varies greatly across individuals. However, most cases are characterized by long periods without debilitating symptoms, followed by unpredictable and intermittent episodes of severe illness, a gradual decline in physical functioning and death (Cunningham et al., 1996). Until recently, disease progression was indicated by CD4 cell counts. In 1995, however, a major scientific breakthrough occurred when a measure to quantify HIV RNA in plasma became commercially available (Rabkin & Chesney, 1999). Now, CD4 cell count along with the HIV RNA viral load assay serve as the best available measure of disease progression.

Shortly after AIDS was identified, it quickly became an invisible epidemic (Broadhead, 2001). This was due in part to the fact that the main group believed to be at risk was gay men. In fact, when AIDS was first identified in the United States, it was given the acronym GRID, which stood for gay related immune deficiency (Marshall, 1990). Many viewed the disease as a consequence of moral breaches, and political leaders who were reluctant to speak about it publicly also failed to implement appropriate public health policies. As Fife and Wright (2000) note, AIDS was quickly classified as a sexually transmitted disease, associated with deviant and immoral behaviour, and viewed as a contagious and dangerous threat to the community at large. By the mid-eighties, injection drug users (IDUs) and prostitutes were also identified as high-risk groups, and by the late eighties it became evident that heterosexuals were in fact the population at greatest risk for acquiring HIV infection. However, as Broadhead (2001) suggests, because the high-risk heterosexual population “consisted of impoverished persons of color living in the developing nations of Sub-Saharan Africa, their global marginality led to an equally marginalized response” (p. 1). As the AIDS epidemic has matured, it has become clear that HIV infection continues to be primarily a problem among the “excluded ones” (Mann, 1998, p. 275; cited in Broadhead, 2001); that is, people who were marginalized and discriminated against prior to AIDS epidemic. Accordingly, in the early 1990s, after years of focus on personal choices about lifestyles, AIDS prevention programs began targeting the social and economic context of people’s daily lives, including the conditions that shape sexual and drug-related behaviour (UNAIDS, 2001).

Prior to 1996, medical treatment offered little to persons living with HIV/AIDS. Monotherapy (e.g., AZT or another antiretroviral drug alone) was the treatment of choice, and while gains were often made following the initiation of therapy, patients typically endured debilitating side-effects, and treatment effects were limited due to relatively low potency of the available drugs (Collazos, Mayo, & Martinez, 1998). Benefits in terms of survival and quality of life were poor and drug resistant HIV strains emerged quickly (Collazos, Mayo, & Martinez, 1998). Between 1996 and 1997 a new class of drugs called protease inhibitors were developed, and since then, morbidity and mortality rates among persons living with AIDS in developed countries has declined drastically (Hogg, 1999; Palella, 1998; Revicki, 1999). Despite these developments, there are ongoing problems associated with equitable distribution of medications, and developing countries that are hardest hit from HIV/AIDS do not enjoy widespread access to these drugs (Elliot, 2000).

To date, the impact of the AIDS epidemic has exceeded all early predictions. In its recent AIDS epidemic update, the UNAIDS Joint United Nations Programme on HIV/AIDS (2002) reported that there are currently 42 million people living with HIV/AIDS in the world (see Table 1). This figure is 50% higher than what had been predicted by the World Health Organization's Programme on AIDS in 1991 (UNAIDS, 2000). In the year 2002, 5 million adults and children were newly infected with HIV, and an estimated 3.1 million people died from AIDS. In all parts of the world except North Africa, the Middle East, sub-Saharan Africa, and the Caribbean, there are more men infected with HIV than women. In countries hardest hit, AIDS stands to kill more than half of the adults before they finish caring for their children.

Table 1.

*UNAIDS/WHO Global summary of the HIV/AIDS epidemic December 2002*


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<b>Number of people living with HIV/AIDS Total</b>		<b>42 million</b>
	Adults	38.6 million
	Women	19.2 million
	Children under 15 years	3.2 million

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<b>People newly infected with HIV in 2002 Total</b>		<b>5 million</b>
	Adults	4.2 million
	Women	2 million
	Children under 15 years	800 000

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<b>AIDS deaths in 2002</b>	<b>Total</b>	<b>3.1 million</b>
	Adults	2.5 million
	Women	1.2 million
	Children under 15 years	610 000

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The course of the AIDS epidemic is changing in different ways throughout the world. For example, according to a recent UNAIDS AIDS epidemic update (December, 2000), during the year 2000, more new HIV infections were recorded in the Russian federation than in all previous years of the epidemic combined. At the end of 1999 the estimated number of adults and children living with HIV/AIDS in Eastern Europe and the Soviet Union was 420,000, and only one year later the figure was estimated at

approximately 700,000 (UNAIDS, 2000). The epidemic in this region is in large part fueled by injection drug use, with over 90% of new infections in the Russian Federation recently being attributed to injection drug use (UNAIDS, 2002). However, underlying harsh economic conditions should not be overlooked, as many people have turned to the sex trade to make money for drugs to relieve the pain of living (Forsyth, 2000).

For the first time in two decades, the epidemic in sub-Saharan Africa appeared to have stabilized with the addition of 3.8 million new infections in 2000 (UNAIDS, 2000). While these early signs are encouraging, it should be noted that this trend is likely a reflection of epidemic saturation rather than a triumph of prevention (UNAIDS, 2000). Sub-Saharan Africa remains the worst affected region with 29.4 million people living with HIV/AIDS (UNAIDS, 2002). In African countries, the primary mode of transmission continues to be heterosexual sex (Forsyth, 2000). UNAIDS (2000) has recently warned that the epidemic could again explode on the African continent if low seroprevalence countries such as Nigeria begin to witness rising infection rates.

Transmission in Latin America and the Caribbean is more complex and driven by a combination of sex between men, sex between men and women, and injection drug use (UNAIDS, 2000). At the end of 2002 there were an estimated 1.9 million adults and children living with HIV/AIDS in this region (UNAIDS, 2002). The Caribbean has the highest HIV prevalence rate outside of Africa largely because the main mode of transmission is heterosexual sex (UNAIDS, 2000).

In North America and Western Europe, prevention efforts appear to have stalled but not eradicated infection rates. In 2002 there were an estimated 30,000 new HIV infections in Western Europe and approximately 45,000 in North America (UNAIDS,

2002). In Western Europe an increasing proportion of new HIV infections are occurring through heterosexual sex, with younger, marginalized populations becoming increasingly at risk (UNAIDS, 2002). Also discouraging are indications that the rate of infections among young gay men are increasing for the first time in years (Schechter, 1998). This is partially a reflection of optimism resulting from recent advances in highly active antiretroviral therapies (ART) and an associated increase in risk-taking behaviour (Craib et al., 2001). Injection drug use continues to account for a substantial number of new HIV infections in the United States and Canada (Kerr & Palepu, 2001). However, HIV infection rates among injection drug users have been more stable in Western Europe, due in large part to the implementation of a range of harm reduction programs such as safe injection facilities and low threshold methadone maintenance programs (Fischer, Rehm, & Blitz-Miller, 2000).

A detailed breakdown of global HIV prevalence and modes of HIV transmission is provided in Table 2. It should be noted that these rates are based on estimates rather than exact figures. As UNAIDS notes: “Every time new estimates of HIV infections or AIDS deaths are released, questions are asked about the source and validity of the data, the methods used to arrive at estimates, and whether the figures reflect the ‘reality’ of the epidemic” (p. 7). Regardless of the exact accuracy of surveillance reports, it is clear that the AIDS epidemic is a global phenomenon affecting many lives as well as the development and well-being of countries throughout the world.

Table 2.

*Regional HIV/AIDS Statistics and Features, end of 2002(UNAIDS, 2002)*

Region	Adults and children living with HIV/AIDS	Adults and children newly infected	Adult prevalence rate (*)	Main mode of transmission
Sub-Saharan Africa	29.4 million	3.5 million	8.8%	Hetero
North Africa & Middle East	550 000	83 000	0.3%	Hetero, IDU
South & South-East Asia	6.0 million	700 000	0.6%	Hetero, IDU
East Asia & Pacific	1.2 million	270 000	0.1%	IDU, hetero, MSM
Latin America	1.5 million	150 000	0.6%	MSM, IDU, hetero
Caribbean	440 000	60 000	2.4%	Hetero, MSM
Eastern Europe & Central Asia	1.2 million	250 000	0.6%	IDU
Western Europe	570 000	30 000	0.3%	MSM, IDU
North America	980 000	45 000	0.6%	MSM, IDU, hetero
Australia & New Zealand	15 000	500	0.1%	MSM
TOTAL	42 million	5 million	1.2%	

\* The proportion of adults (15 to 49 years of age) living with HIV/AIDS in 2002, using 2002 population numbers.

# Hetero (heterosexual transmission), IDU (transmission through injecting drug use), MSM (sexual transmission among men who have sex with men).

### *Injection Drug Use and AIDS*

Injection drug use is associated with severe health and social consequences for drug users, their families, and communities. The view from a population health perspective reveals a complex picture of poor health among injection drug users (IDUs). The effects of the drugs themselves, in addition to drug-using social networks, mental health issues, high rates of childhood abuse, homelessness, social marginalization, poverty, and unemployment all contribute to drug users' ability or inability to reduce the behaviors that put them at risk (Canadian HIV/AIDS Legal Network, 1999; Strathdee et al., 1997; Tyndall et al., 2001; Zolopa et al., 1994). The health of IDUs is further complicated by avoidance and erratic use of primary care services and over-reliance on emergency rooms and acute care hospitalizations (Palepu et al., 2001), patterns that have been well-documented since the 1960s (Jouria, Hensle, & Rose, 1967; Sapira, 1968). As a result, throughout the developed world, and increasingly in developing nations, injection-related human immunodeficiency virus (HIV), hepatitis C (HCV) outbreaks, and overdose deaths have reached epidemic proportions (Crofts et al., 1998; Strathdee et al., 1997).

Approximately 100,000 Canadians inject drugs and almost one-third reside either in Toronto, Montreal or Vancouver (Federal, Provincial and Territorial Advisory Committee on Population Health [FTP Committee], 2001). High rates of disease, death, crime, and the accompanying costs are common drug-related harms experienced within Canada (Fischer, Rehm, & Blitz-Miller, 2000). In Canada, British Columbia has the highest number of fatal drug-related overdoses, approximately 4.7 per 100 000 population annually, and in recent years illicit drug use has been the leading cause of

death among adults 30 to 49 years of age (BC Vital Statistics Agency, 2000). The Vancouver Injection Drug Users' Study (VIDUS) is an open cohort of approximately 1500 injection drug users that began in 1996. Within VIDUS, overdose is the leading cause of death, accounting for 25% of all deaths among HIV positive participants, and 42% of all deaths among HIV negative participants (Tyndall, 2002). The incidence of non-fatal overdose among IDUs is also extremely high, as indicated by a recent study conducted by the BCCDC Street Nurse Program that found that 75% of participating IDUs reported having at least one non-fatal overdose in their lifetime (Gold et al., 2000). Morbidity associated with non-fatal overdose can be severe and include anoxic brain damage and organ failure (Donoghoe & Wodak, 1998).

The downstream effects of injection drug use were illustrated in a recent study of hospital utilization patterns of participants in VIDUS (Palepu et al., 2001). The authors found that over a 39-month period, 440 participants incurred 2763 emergency department visits and 210 participants accounted for 495 hospitalizations (Palepu et al., 2001). The most common reasons for emergency department attendance were soft-tissue infections, and other illicit-drug use problems such as overdose, drug intoxication, and withdrawal. Most hospital admissions were for bacterial infections related to drug injection and may have been preventable with sterile injection techniques (Kerr & Palepu, 2001).

The introduction of HIV into populations of IDUs has in many cities resulted in rapid spread of HIV (Des Jarlais et al., 1998). However, several cities have succeeded in maintaining low seroprevalence among drug injectors. Evidence from the WHO twelve-city study of drug injecting and HIV infection indicates that rapid spread is

associated with certain conditions, most notably when high numbers of HIV serodiscordant IDUs are sharing injecting equipment within a short period, and when these instances of sharing occur outside of established friendships (DesJarlais et al, 1998). In contrast, rapid spread of HIV can be averted if prevention efforts are initiated when seroprevalence is low, if prevention efforts include outreach activities that serve to foster relationships between IDU and health-care workers, and if sterile injecting equipment is widely distributed (Des Jarlais et al, 1998; Strathdee et al, 1998). Once HIV is established in IDU communities, IDU often become vectors to heterosexual and perinatal HIV transmission (Friedman et al., 1993).

Prior to 1993, injection drug users accounted for less than 3% of new HIV infections in Canada. In 1993-94, for the first time, IDUs outnumbered men who have sex with men among those testing newly positive for HIV. In British Columbia today, IDUs account for 38% of new HIV infections (Fischer et al., 2000), and injection drug users have recently accounted for 26% of all new HIV infections in Canada (FTP Committee, 2000). Accordingly, HIV prevalence rates among IDUs have soared throughout the past decade, increasing from approximately 5% in 1988 to 23 % in 1996-97 in Montreal, and from 4.8% in 1992-93 to 8.6% in 1997-98 in Toronto (Canadian HIV/AIDS Legal Network, 1999). The most dramatic increase, however, occurred in Vancouver, where HIV prevalence rose from 4% in 1992-93 to 40% in 2001 (Tyndall, 2001).

Risk behaviours among injection drug users are common and are associated with the spread of diseases such as HIV/AIDS and hepatitis C. These behaviours include, but are not limited to, the sharing of needles and other injection equipment

(e.g., filters, spoons, cookers) and unprotected sex (including unprotected commercial sex). Specific injection practices are also associated with transmission of HIV and hepatitis. Practices such as “flagging” (pulling the syringe plunger after insertion until blood appears as a means of ensuring that a vein has been hit), “booting” (injecting quickly), and “backloading” and “frontloading” (dispensing prepared drugs from one syringe to another as a means of sharing drugs) are all associated with higher risk for HIV transmission (Grund, 1991; Patterson, 1999). The sharing of injection equipment other than syringes, also known as “indirect sharing” (Patterson, 1999; p.11), is common and associated with the transmission of blood-borne diseases. During the course of injection IDUs will often share ‘cookers’ used to heat drugs (e.g., spoons, bottle caps) or ‘filters’ (e.g., small pieces of cotton or cigarette filters) that are used to filter out particles contained in the drug preparation. In order to avoid transmission of blood-borne diseases, IDUs must either use a sterile syringe or go through a lengthy cleaning process that involves filling a syringe with bleach three times (for 30 seconds) and then rinsing thoroughly with water. However, because injection in public spaces and confrontations with police are common, many IDUs do not have sufficient resources, time, or patience required to adhere to safe injection practices (Broadhead, Altice, Kerr, & Grund, 2002). In fact, one study that examined adherence to bleach-cleansing procedure found that a substantial number of IDUs did not perform all the steps of a previously taught method (McCoy & Rivers, 1994; cited in Patterson). This same study found that while some IDUs were cleaning their syringes properly, many failed to disinfect other injection equipment.

While needle exchange services are available in most Canadian cities, recent evidence suggests that limited coverage and high rates of injection have overwhelmed the protective effect of needle exchange (Wood et al., 2001). For example, Wood et al. (2001) recently reported that 28% of the VIDUS participants reported needle sharing during a previous six-month period. Also of concern was the finding that 20% of the HIV-positive IDUs in the VIDUS cohort also reported sharing needles in the last six months. Variables that were independently associated with needle sharing in the multivariate analysis included difficulty getting sterile needles, requiring help to inject drugs, frequent cocaine injection, and frequent heroin injection.

As the findings of Wood et al. (2001) suggest, the increasing use of injectable cocaine has also contributed to an escalation in risk behaviour and HIV transmission, as many cocaine users inject frequently, often up to twenty times per day. The relationship between frequent cocaine injection and HIV infection was demonstrated in a recent study by Tyndall et al. (in press). The investigators examined four levels of injection cocaine use: Level 0 (less than once a month); Level 1 (once a month to once a week); Level 2 (twice a week to 3 times a day); Level 3 (more than 3 times a day). The results indicated that injection cocaine use was strongly and independently associated with HIV infection in a dose-dependent fashion: Level 1 (adjusted relative risk ratio [aRR] = 1.9); Level 2 (aRR = 4.2); Level 3: (aRR = 7.2).

A variety of psychosocial factors and demographic characteristics among IDUs have also been found to be associated with HIV-related risk behaviour and HIV status. The Point Project in Vancouver (cited in Millar, 1998) found that the factors most commonly associated with HIV infection among IDUs are homelessness, unstable

housing, frequent injecting, history of sexual abuse, and depression. Recently, female and Aboriginal IDU in Vancouver have been found to be at elevated risk for HIV infection (Spittal et al., 2002; Craib et al., 2003). Another study of HIV seroprevalence among IDUs in Vancouver found that low education, unstable housing, commercial sex involvement, borrowing needles and injecting with others were among the factors most strongly associated with HIV-positive serostatus (Strathdee et al., 1997). Twenty-three percent of this cohort reported being paid for sex in the previous six months, including 32% of all HIV-positive subjects. Many of these individuals are accorded the designation 'strawberry', which is used to denote people who trade sex for drugs. It is not surprising that homelessness has been repeatedly identified as a predictor of HIV status, since homeless IDUs are difficult to reach with prevention messages and training (Susser & Miller, 1996). As well, homeless IDUs are less likely to have places to store sterile injecting equipment and therefore rely heavily on the sharing of used syringes (Broadhead et al., 2000).

In a study of the social determinants associated with needle sharing among IDUs in Vancouver, Strathdee et al. (1997) found that needle sharing was associated with frequent injection, polydrug use, and ever having experienced non-consensual sex. Although having a higher level of depression was also statistically significant in the final multivariate model, this variable was not retained due to problems of co-linearity. The results from this study also found that among females, those living with a male partner were four times more likely to have borrowed needles. Indeed, it is well known that female IDUs often depend on male partners for access to and administration of drugs (Patterson, 1999). While several studies have also reported associations between

mental illness, HIV status, and risk behaviour among IDUs (Patterson, 1999), questions concerning reverse causality and accuracy of diagnosis remain.

The health status and treatment of HIV-positive injection drug users is complicated by high rates of co-infection (Strathdee et al., 1997), low global quality of life (Kerr, Ibanez-Carrasco, & Walsh, 2000), and psychiatric co-morbidity (Rabkin et al., 1997). Although studies have found that IDU have higher rates of psychiatric disorders (including depression, anxiety, and schizophrenia) than the general population, methodological shortcomings in these studies have not allowed for even limited causal claims (Donoghue & Wodak, 1998). Cohort studies of IDUs in the United States and the Netherlands have found that death among HIV-positive IDUs is more often a cause of overdose, suicide, and liver failure than HIV (Palepu, 1999), and HIV-positive IDUs are known to have high rates of hospitalization and poorer HIV-related treatment outcomes when compared to other HIV populations such as men who have sex with men (Palepu et al., 1999). While considerable advances have recently been made in the pharmacological treatment of HIV/AIDS, there is cause to believe that certain characteristics of these treatments will render them non-applicable or ineffective for many IDUs. Identifying methods for increasing optimal uptake of antiretroviral therapy among IDUs is now a pressing issue for researchers and clinicians.

### *Antiretroviral therapy (ART)*

In recent years, substantial improvements have been made in the pharmacological treatment of HIV/AIDS. Prior to 1996, monotherapy (e.g., AZT or another nucleoside analogue reverse transcriptase inhibitor [NRTI] alone) was the

treatment of choice used to interfere with HIV-related production of DNA needed for cell replication. However, because HIV has an extremely short life cycle (approximately 10 billion particles are produced and destroyed daily), viral replication occurs quickly as does mutation (Kelly et al., 1998). Consequently, while monotherapy could temporarily slow viral replication, clinical benefits were short lived, and this treatment approach was quickly rendered ineffective due to the likelihood of drug resistance developing within weeks or months (Kelly et al., 1998, Rabkin & Chesney, 2000).

Understanding of the viral dynamics and pathogenesis of HIV increased greatly during the mid 1990s, and in 1995 a major breakthrough occurred with the development of a quantitative HIV RNA assay (Williams, 1999). Around this time it became clear that with the rapid production of HIV, its short cellular life, and its ability to mutate quickly, effective treatment would only occur if HIV quantity and replication could be reduced rapidly (Kelly et al., 1998). Between 1995 and 1997 a new class of HIV drugs called protease inhibitors (PIs) emerged. As Kelly et al. (1998) note, unlike NRTIs that interfere with HIV replication early in the cycle, PIs greatly reduce plasma viral load by blocking “the maturation of viral particles, virions, released by a mature HIV cell into the blood stream, an event that occurs late in the replication cycle” (p. 311). This in turn leads to reduced HIV viral load in the blood stream and reduced immune system deficiency (i.e., diminished CD4 cell counts and functioning).

The treatment guidelines now espoused in most developed nations indicate that optimal treatment for HIV involves a combination consisting of a protease inhibitor or a non-nucleoside analogue reverse transcriptase inhibitor (NNRTI) and two nucleoside

analogue reverse transcriptase inhibitors (NRTIs). This combination, referred to as antiretroviral therapy (ART), is highly effective in comparison to monotherapy as the combination of NRTIs/NNRTIs and PIs act to interfere with HIV replication in both early and late stages in the viral replication cycle (Kelly, 1998). This combination has led to significant reductions in morbidity and mortality as well as an enhanced quality of life for many HIV-positive individuals (Hogg, 1999; Palella, 1998). In fact, one commonly used indicator of successful treatment is an undetectable viral load within six months (O'Brien, 1998).

Current treatment guidelines in British Columbia state that ART should be offered to all HIV-positive individuals, regardless of symptoms, except those with a normal CD4 count ( $> 500/\text{mm}^3$ ) and a plasma viral load lower than 5,000 copies/mL (BC Centre for Excellence in HIV/AIDS, 2001). While there is controversy over when to initiate treatment, recent clinical evidence suggests that ART should be started before immunodeficiency develops (O'Brien, 1998; BC Centre for Excellence in HIV/AIDS, 2001). Most developed countries now adhere to the International AIDS Society - USA Panel recommendations set out in the Journal of the American Medical Association in January, 2000:

Table 3.

*BC Centre for Excellence ART Treatment Guidelines*

CD4+	Plasma HIV RNA level		
	<5000	5000-30,000	>30,000
<350	recommend	recommend	recommend
350-500	consider	recommend	recommend
>500	defer	consider	recommend

The BC Centre for Excellence in HIV/AIDS guidelines (2001) also suggest that a decision to start ART should be based on medical history, physical exam, and prognostic laboratory markers (i.e., CD4 cell count and plasma viral load). However, because clinical symptoms are exceptionally rare in individuals with normal CD4 counts and low viral loads, clinical criteria rarely factor into decisions to initiate treatment.

While there is much good news concerning recent developments in treatments for HIV/AIDS, there is also much to be concerned about. As Rabkin and Chesney (2000) state, “[c]ombination therapy for HIV illness is perhaps the most rigorous, demanding, and unforgiving of any outpatient oral treatment ever introduced” (p. 62). Treatment often requires that patients take up to 10 pills three times a day (Friedland & Williams, 1999). Medications also must often be taken in accordance with strict dietary guidelines and therefore can greatly interfere with lifestyle and secrecy concerning HIV

status. As well, complex combinations are also often taken throughout the day at several intervals (O'Brien, 1998). For example, a common ART combination includes indinavir sulfate (PI), zidovudine (NRTI), and lamivudine (NRTI). Indinavir is taken on an empty stomach every 8 hours and with 48 ounces of water daily, while zidovudine is taken five times daily, and lamivudine is taken twice daily (Kelly et al., 1998). Side-effects are common and include nausea, vomiting, fatigue, diarrhea, and more chronic problems such as peripheral neuropathy, oral numbness, and metallic taste (Rabkin & Chesney, 2000).

The most significant problem associated with ART in terms of individual treatment and public health is viral mutation and the resulting development of drug-resistant strains of HIV. Patients who take antiretroviral drugs intermittently or at reduced doses often experience suboptimal drug levels, thus increasing the chance of drug resistance and failure of therapy (Vanhove et al., 1996). Unfortunately, because HIV replicates at such a high rate, mutations occur often (O'Brien, 1998). In order for HIV to use human cells to reproduce, the genetic material of HIV must be converted from RNA to DNA during a process called "reverse transcription" (O'Brien, 1998, p. 11). During this process, mistakes (i.e., mutations) are sometimes made in the copying of the HIV genome, making new virus particles that are slightly different from the parent virus (O'Brien, 1998). While most of these mutations create disadvantage for the virus, some mutations will result in viral strains that can still reproduce in the presence of antiretrovirals (O'Brien, 1998; Kuritzkes, 2001). Furthermore, viral replication occurring in the presence of drug selection pressure will ultimately select for new viral variants that are drug-resistant (Friedland & Williams, 1999). When a specific failing

ART regimen is continued, an accumulation of mutations will occur, leading to greater cross-resistance to other members of the drug class (Kuritzkes, 2001). The transmission of resistant virus may then also confer limitations in treatment options for those newly infected (Gray et al., 2001; Quinn et al., 2000).

While considerable advances have been made in the treatment of HIV/AIDS, the difficulties associated with antiretroviral therapy, particularly the issue of drug-resistant viral strains, have raised important ethical and clinical questions concerning access and adherence to antiretroviral therapy. As in classic debates concerning individual rights versus utilitarian values, discussions concerning access to ART have involved weighing individual treatment benefits against public health interests. As in the case of the classic debate, there are no easy answers to these complex problems.

### *Adherence to Medical Treatment*

The problem of adherence is as old as medical treatment itself, and few issues are as equally common across the health field as adherence (Meichenbaum & Turk, 1987). In discussing adherence it is first important to acknowledge the concept of 'compliance'. These terms have in the past been used somewhat interchangeably, although the term adherence has recently been adopted in favour of compliance (Chesney et al., 2000). Compliance typically refers to the extent to which a patient obeys the advice and directives of a doctor, and implies a passive role on the part of the patient and an overly authoritative role for the doctor (Meichenbaum & Turk, 1987; DiMatteo & Friedman, 1982). Furthermore, "compliance" is viewed as value-laden and containing a directional bias that assumes that physician guidelines are accurate and that patient behaviour should be measured in accordance with these guidelines

(Chesney et al., 2000). Adherence, on the other hand, is less value-laden, suggests a more collaborative relationship between doctor and patient, and promotes a more comprehensive study of variables that affect adherence (e.g., medical regimen, context, etc.). Ironically, proponents of the term 'compliance' such as Haynes (1979) have argued that "unhealthy connotations [of compliance] ... keep ethical and social issues in compliance research and management up front where they belong" (cited in DiMatteo & DiNicola, 1982, p. 7).

To date, knowledge about adherence has been gained primarily from studies in the areas of treatment for diabetes, coronary artery disease, tuberculosis, and asthma (Friedland & Williams, 1999; Williams, 1999). According to Friedland & Williams (1999), four conclusions can be drawn from existing adherence literature: (1) rates of adherence affect treatment outcome (low adherence reduces efficacy and toxicity); (2) adherence to medication regimens is poor across populations and illnesses; (3) clinicians are not able to predict accurately who will and who will not adhere to medications; (4) clinicians tend to overestimate rates of adherence.

Adherence rates to medicine regimens across illness are disturbingly low. According to Meichenbaum and Turk (1987), adherence rates range from 4% to 92%, with a more typical range being 30% to 60%. It is important to note that there are also several forms of medication treatment nonadherence. A comprehensive list is provided by Meichenbaum & Turk (1987) and includes: "[f]ailure to fill prescriptions; [f]illing the prescription but failing to take the medication or taking only a portion of it; [n]ot following the frequency or dose instructions of the prescriptions; [t]aking medications not prescribed" (p. 30). Furthermore, in order to assess adherence, issues of access must

also be considered. Indeed, some authors argue that a “delay in seeking care” is in fact a form of nonadherence (Meichenbaum & Turk, 1987).

### *Measuring Adherence to Antiretroviral Therapy (ART)*

At present, the most commonly employed methods of measuring adherence to HIV medications include pill counts, electronic monitoring, pharmacy record reviews (e.g., prescription refills), and a variety of self-report measures (Miller & Hays, 2000). Although the measurement of medication adherence is of critical importance in clinical research, there is a surprising lack of rigorous study and validation of adherence measurement techniques (Liu et al., 2001; Steiner & Prochazka, 1997). Studies of adherence measures rely typically on limited assessment of criterion-related forms of validity such as predictive or concurrent validity (Crocker & Algina, 1986). In most cases, validation of an adherence measure is based on how well the measure predicts or correlates with virologic success. While this is undoubtedly of central importance and a most desired outcome, a correlation with or an accurate prediction of virologic outcome (e.g., viral suppression) provides only limited information about what is actually being measured in terms of adherence behaviour. As well, some have argued that virologic failure is an inadequate indicator of non-adherence, as several other factors (e.g., viral mutations, HIV viraemia at initiation of therapy, potency of the particular combination of therapy prescribed, individual differences in absorption, and interactions) may mediate virologic outcome (Miller & Hays, 2000; Murri, Ammassari, De Luca, Cingolani, & Antinori, 1999). Assessments of content validity (i.e., how well the measurement items represent the entire universe of items or domain being assessed) and construct validity (i.e., how well a measure reflects some underlying construct or

latent variable) are rare. As Hubley and Zumbo (1996) assert, “to properly judge the appropriateness, meaningfulness, and usefulness of an inference, one must have some evidence of what the test score means or represents” (p. 211).

The confusion surrounding what is actually being measured in adherence studies has been perpetuated by the use of the term ‘adherence’ to refer to a variety of distinct adherence behaviours. For example, measures of pharmacy prescription pick-ups, pillbox openings, and compliance with dietary guidelines are all said to be measuring adherence (Miller & Hays, 2000). However, in each case, only a small subset of adherence behaviour is measured. It has been well established that adherence to medications requires a series of distinct behaviours, beginning with picking up a prescription and ending with consumption of the medication. In the case of adherence to ART, full adherence requires refilling a prescription, correctly counting the medications to be taken, and ensuring that medications are taken at the right time of day and in accordance with dietary guidelines. Medication adherence also consists of a series of cognitive and behavioural tasks that includes both prospective and retrospective memory components (Parks & Kidder, 1996; Einstein & McDaniel, 1996), as patients must not only remember when to perform the adherence behaviour (e.g., the time to take one’s medications), but they also must remember what the behaviour consists of (e.g., which medications to take, how many medications to take).

As Messick has noted (cited in Hubley & Zumbo, 1996), validity addresses two major threats to inferences made from measures. The first threat, construct under-representation, refers to instances in which a measure fails to include important dimensions of the construct being measured. The second threat, construct-irrelevant

variance, results from three problems: “(a) the measure is too broad and contains excess reliable variance associated with other distinct constructs; (b) reliable variance that is due to the manner in which the measure is obtained (i.e., method variance); and (c) unreliable or error variance that is due to the manner in which the measure is obtained” (Hubley & Zumbo, 1996, p. 212). Given the tendency on the part of researchers to measure the complex phenomenon of medication adherence with one behavioural measure, it is likely that measures of adherence suffer, to varying degrees, from both construct under-representation and construct-irrelevant variance. That is, most fail to measure adequately certain aspects of adherence behaviour and simultaneously capture variance that is in fact related to adherence behaviours not under study. For example, an instance of construct under-representation may occur when subjects are asked to report the number of medications missed, but are not asked to report whether or not they have taken their medications in accordance with dietary guidelines. An instance of construct-irrelevant variance can occur when electronic monitoring is used to determine the number of times that a subject opened his or her pill box. While it is assumed that in these instances the subject has taken one dose of the medication after opening the pill box, studies have shown that subjects will at times open the pill box out of curiosity (Bangsberg, Hecht, Charlebois, Chesney, & Moss, 2001).

Measuring adherence to medications is no simple task, as each of the methods currently in use has its strengths and limitations, depending on the patient group, the medication and how it is dispensed, the associated pharmacokinetics, and anticipated clinical outcomes. Most past research in the area of adherence to antiretroviral therapy has relied on self-report (Chesney et al., 2000). While this method is subject to social

desirability and recall bias, and therefore likely to underestimate nonadherence, research has found this approach to be associated with viral load (Chesney et al., 2000). Likewise, while counting prescription refills may seem like a crude method that overestimates actual adherence, this approach has also repeatedly been found to be a robust predictor of HIV plasma viral load suppression (Strathdee et al., 1998; Low-Beer, 2000). The Adherence and Retention Working Group on the Outcomes Committee and the Pharmacology Committee of the National Institute of Allergy and Infectious Diseases AIDS Clinical Trial Group has stated that subjective (e.g., self-report) and more objective (e.g., MEMS) measures provide different and complementary data concerning adherence, and therefore it is wise to combine methods when assessing patient adherence (Williams, 1999).

### ***Factors associated with Adherence***

There are numerous factors that affect adherence. Haynes' (1976) review of the topic identified over 200 variables that have been studied in relation to adherence (cited in Meichenbaum & Turk, 1987). Many of these variables have also been studied in relation to adherence to antiretroviral therapy. More recent reviews indicate that these variables can be placed into six categories: (1) the illness, (2) characteristics of the regimen, (3) the clinical setting, (4) characteristics of the physician, (5) the relationship between the patient and physician, and (6) patient characteristics (Chesney et al., 2000; Friedland & Williams, 2000; Meichenbaum & Turk, 1987; Rabkin & Chesney, 1999; Williams, 1999).

### *The Illness*

Illness characteristics influence rates of adherence in several ways. Most notably, patients with short-term illnesses tend to be more adherent than patients with chronic illnesses (Meichenbaum & Turk, 1987). As well, patients are more likely to be adherent when symptomatic, and when symptoms are relieved quickly following treatment (Rabkin & Chesney; 1999; Williams, 1999). With these points considered, it is clear that the characteristics of HIV/AIDS make adherence to treatment challenging. HIV/AIDS is an unpredictable chronic illness, medications are frequently taken when patients are not symptomatic, and treatment rarely provides immediate relief. As well, the stigma associated with the disease may influence adherence (Friedland & Williams, 1999). Patients may be reluctant to seek care regularly, and taking numerous pills during meal times in the presence of co-workers and other acquaintances may be difficult for those concerned about the stigma associated with having HIV/AIDS. This point was illustrated in a cross-sectional study involving 133 HIV-positive patients when Gifford et al. (1999) found that 17% of patients skipped doses because they didn't want others to notice them taking their medications.

Illness severity has been found to be associated with adherence to antiretroviral therapy, although the results have been mixed in terms of the strength and direction of the association (Gao et al., 2000; Gifford et al., 2000; Patterson et al., 2000; Samet et al., 1992; Singh et al., 1999). Patterson et al. (2000) studied adherence to antiretroviral therapy among 99 HIV-positive patients and found that adherence was better among patients who had spent fewer days in hospital, and those without an opportunistic infection. In a study involving 72 HIV-positive patients in various stages of illness, Gao

et al. (2000) examined the relationship between disease severity, health beliefs, and medication adherence. The results indicated that adherence was highest among patients who previously had AIDS-related complications. Singh et al. (1996) examined adherence to monotherapy among 46 HIV-positive patients longitudinally and found that illness severity, as indicated by CD4 count and number of opportunistic infections, did not discriminate adherent from nonadherent patients. Gifford et al. (2000) also examined several HIV-specific health indicators, and the association between symptom bothersomeness and nonadherence was the only significant finding involving an illness/disease variable.

### ***The Medication Regimen***

The qualities of the medication regimen also affect rates of adherence. In general, patients are more likely to adhere to a medication regimen when it is simple, produces immediate relief, and does not produce side-effects (Friedland & Williams, 1999; Meichenbaum & Turk, 1987; Rabkin & Chesney, 1999). Again, the characteristics of antiretroviral therapy make adherence challenging. The regimens involve numerous pills that are taken at odd intervals according to strict dietary guidelines. As well, side-effects are common, and relief from treatment does not occur immediately.

Early studies of zidovudine by Chesney et al. (1995) demonstrated that adherence decreased as the number of pills taken increased. However, in a study of zidovudine and didanosine adherence, Singh et al. (1999) found that the total number of pills taken was highest among adherent patients. Likewise, Murphy, Wilson, Durako,

and Muenz (2000) studied adherence to antiretrovirals (double and triple combination therapy) among 161 HIV-positive adolescents and found that number of pills did not predict adherence.

Some of the discrepancy concerning the influence of pill quantity may be explained by other variables, including medication complexity and regimen/lifestyle fit. For example, in examining the influence of the number of doses per day, Patterson et al. (2000) found that twice-daily administration was associated with a significant improvement in adherence when compared with three-times/day administration. In examining the influence of the convenience of ART regimens, Gifford et al. (2000) found that while the number of pills taken per day did not predict adherence, the perceived fit between the regimen and the patient's lifestyle remained as one of two independent predictors of adherence in a final multivariate model.

There are many side-effects associated with ART. Among the more common side-effects are nausea, vomiting, fatigue, diarrhea, and more chronic problems such as peripheral neuropathy and oral numbness (Rabkin & Chesney, 1999). In a study of adherence to ART involving 164 HIV-positive injection drug users, Moatti et al. (2000) found that 28% of the cohort reported missing doses due to side-effects. Likewise, Gifford et al. (1999) found that 17% of 133 HIV-positive patients reported that they had skipped doses due to side-effects, and 18% skipped doses because they found the medications to be too toxic. In a qualitative study of adherence to ART among HIV-infected women, Johnston-Roberts and Mann (2000) found that side-effects were reported by participants as a main barrier to adherence.

### *The Clinical Setting*

ART has been administered in a variety of clinical settings, including doctors' offices, pharmacies, and community-based organizations (Williams, 1999). As well, innovative outreach services have been used to ensure adherence among more marginalized HIV populations (Williams, 1999). Evidence suggests that certain types of clinical settings and services are associated with improved adherence when compared with standard pharmacy dispensing methods (Stenzel, McKenzie, Mitty, & Flannigan, 2001; Moatti, 2000).

There is some preliminary evidence suggesting that administering ART in the context of opioid replacement treatments such as methadone and buprenorphine maintenance therapies may help improve adherence to antiretroviral therapy. Because most opioid maintenance therapy requires that patients make daily visits during the week for supervised consumption, ART administration can be easily integrated into this type of service. This point was illustrated by Moatti et al. (2000), who found that patients in buprenorphine maintenance treatment achieved higher levels of adherence (78%) compared to former injection drug users (65%).

Directly observed therapy (DOT) has been utilized successfully in clinics and through outreach services to increase adherence to tuberculosis treatments among marginalized populations (Stenzel et al., 2001). A key component of this type of therapy involves service providers observing patients while they take some or all of their medications. Findings generated from initial trials of directly observed therapy have indicated that this type of service is associated with improved adherence to ART

(Stenzel et al., 2001). Stenzel et al. (2001) provided thirty-seven patients with histories of poor adherence with DOT over a ten-month period. The results indicate that adherence improved for nonobserved doses, and that adherence was associated with significant decreases in HIV RNA levels. While these outcomes are encouraging, it seems that modifying the clinical setting leads to benefits (i.e., improved adherence) during the intervention period but not beyond it (Tuldra et al., 2000). Further study and development of these programs is needed to ensure benefit beyond the intervention period.

### ***Health-Care Provider and Provider-Patient Relationship Variables***

Health-care provider characteristics and provider-patient relationship variables have also been found to mediate patient adherence. While it is well known that physician attitudes greatly influence access to antiretroviral therapy, these attitudes are significantly shaped by judgements concerning patients' ability to comply with medical directives (Escaffre et al., 2000; Wainberg, 1996). Escaffre et al. (2000) studied physicians' beliefs concerning adherence to antiretroviral therapy among 196 HIV-positive injection drug users. The likelihood of being perceived adherent was highest for women, patients 30 years of age and over, patients with biological markers indicating a healthier status, and patients perceived to be free of injecting behaviour and not receiving methadone therapy. It is also well known that physicians tend to overestimate adherence (Meichenbaum & Turk, 1987), and this tendency has been found among physicians and nurses overseeing antiretroviral therapy (Escaffre et al., 2000, Patterson et al., 2000). For example, in a 6-month longitudinal study of adherence to antiretroviral therapy among 166 HIV-positive patients, Patterson et al.

(2000) found that physicians predicted adherence incorrectly for 41% of patients, while nurses predicted adherence incorrectly for 30% of patients.

Physicians play an important role in mediating various factors that affect adherence. For example, because the fit between the medication regimen and the patient's lifestyle greatly affect adherence, physicians play a critical role in recommending an appropriate ART combination (Rabkin & Chesney, 1999). As well, information and educational messages provided by the physician during the prescribing appointment can affect adherence as patients must fully understand a regimen before they can possibly adhere to it (Chesney, Morin, & Storr, 2000; Rabkin & Chesney, 1999). Health-care provider interventions in the post-prescription phase also affect how well patients sustain adherence and manage adverse events related to the medications (Rabkin & Chesney, 1999). Unfortunately, professional practice varies greatly across health-care providers and affects patient adherence to antiretroviral therapy (Bakken et al., 2000; Johnston-Roberts & Volberding, 1999). In a qualitative study of fifteen physicians who prescribe antiretrovirals, Johnston-Roberts and Volberding (1999) found that physician practices such as the length of time spent in communicating with patients about adherence in the pre- and post-prescription phases, the timing of the check-ins, and the content of communications varied dramatically.

The quality of the provider-patient relationship also affects adherence. As Meichenbaum & Turk (1987) point out, patients who are not satisfied with their health-care provider are more likely to reject medical advice. According to an early study by Whitcher-Alagna (1983), patient satisfaction is most often determined by the degree to which the patient's beliefs and expectations have been met (cited in Meichenbaum &

Turk, 1987). Bakken et al. (2000) studied the effects of provider-patient relationships on adherence among 707 non-hospitalized HIV-positive patients. The study included a newly developed Engagement with Health-care Provider Scale, which included 13 items (e.g., my provider: listens to me, cares about me, answers my questions, spends time with me, involves me in decisions). The results indicated that patients reporting higher levels of engagement with the provider were more likely to be adherent. Likewise, in a qualitative study of barriers and facilitators of adherence, Roberts (2000) found that professional support in the form of verbal advice, supervised antiretroviral dosing, and verbal/written information from community-based agencies facilitated adherence.

### ***Patient Characteristics***

A number of patient variables have been studied in relation to adherence to medications. Many of these same variables have been applied in studies of adherence to monotherapy for HIV/AIDS and ART. However, in most cases, efforts to identify stable 'patient' predictors of adherence have been met with only moderate success. Epidemiological investigators examining relationships between adherence and immutable demographic characteristics such as gender, age, and social class have failed to identify consistently significant associations (Chesney et al., 2000; Meichenbaum & Turk, 1987; Williams, 1999). For example, while some studies have found relationships between adherence and African-American race (Singh et al., 1996; Andersen, Bozzette, Shapiro, & St. Clair, 2000; Lucas, Cheever, Chaisson, & Moore, 2001), others have not (Broers, Morabia, & Hirschel, 1994; Bangsberg et al., 2000). However, there is need for continued investigation of the relationship between demographic characteristics and

adherence, as demographic characteristics have proved predictive in some circumstances (DiMatteo & DiNicola, 1982). Other patient characteristics that have been found to be associated with adherence include health beliefs, self-efficacy, social support, mental health status, and substance use (Meichenbaum & Turk, 1987; O'Leary, 1985; Singh et al., 1996; Rabkin & Chesney, 1999; Williams, 1999).

Patients' health beliefs and knowledge have been studied in various ways. Underlying the various models that address health beliefs is the assumption that an individual faced with constraints has preferences and must make choices to maximize benefits and minimize costs (Moatti & Souteyrand, 2000). The Health Belief Model is now the most commonly applied model of beliefs (Gao, Nau, Rosenbluth, Scott, & Woodward, 2000). This model asserts that adherence and other health-related behaviours are determined by one's beliefs concerning the severity of the illness, one's personal susceptibility, and one's evaluation of the costs and benefits of the recommended action (Moatti & Souteyrand, 2000; Freidland & Williams, 1999). Applications of this model in studies of adherence have failed to yield consistently significant associations. Past studies have found that attitudes about zidovudine (protease inhibitor) and beliefs concerning its efficacy were associated with adherence (Blumenfield, Milazzo, & Wormser, 1990). As well, Gao et al. (2000) examined the relationship between disease severity, health beliefs, and adherence to ART among 72 HIV-positive patients in varying stages of illness. The findings suggested that the most ill patients perceived a higher risk of complications if they did not take their medications. As well, perceived susceptibility-inaction beliefs (i.e., beliefs that the disease will worsen if the patient is nonadherent) were associated with adherence.

According to DiMatteo and DiNicola (1982), the relationship between health beliefs at the beginning of treatment and adherence at the end of treatment tends to be less robust than the association between health beliefs and concurrent adherence. As well, in several cross-sectional and longitudinal studies, health beliefs have failed to predict adherence to antiretroviral therapy (Andersen, Bozzette, Shapiro, & St. Clair, 2000; Gifford et al., 2000; Gordillo, del Amo, Soriano, & Gonzalez-Lahoz, 1999). To address these shortcomings, researchers have attempted recently to expand the model, and reformulations have included measures of the physician/patient relationship and self-efficacy (Williams, 1999). The Health Belief Model has also been criticized for merely reflecting “rationalization processes and work[ing] within an overly individualistic framework” (Chesney et al., 2000, p. 1603).

Self-efficacy theory has been applied widely in the field of behavioural medicine and shown to mediate the effects of health interventions (O’Leary, 1985). Various definitions of self-efficacy can be found throughout the vast writings on the topic. For example, in an early work, Bandura (1977) defined self-efficacy expectations as “the conviction that one can successfully execute the behavior required to produce the outcome” (p. 193). In a later work, Bandura (1989) defined self-efficacy beliefs as “people’s beliefs about their capabilities to exercise control over events that affect their lives” (p. 1175). Implicit in both definitions is the assumption of the self as competent and the world as structured and responsive (Skinner, 1996). In sum, self-efficacy theory describes in detail how “people process, weigh, and integrate diverse sources of information concerning their capability, and ... regulate their choice of behavior and effort expenditure accordingly” (Bandura, 1977, p. 212). The literature addressing the

application of self-efficacy theory in therapeutic interventions have shown that increases in domain-specific self-efficacy are associated with reductions in animal phobias (Bandura, 1977), pain in childbirth (Manning & Wright, 1983), and increased in social support and well-being (Major, 1980).

In contrast with classical behaviourism, self-efficacy theory suggests that self-efficacy is the common cognitive mechanism through which behaviour change occurs (Bandura, 1977). This common mechanism is rooted in perceived coping capabilities rather than global personality traits or instinctual motives. Self-efficacy beliefs determine individual choice of activities, coping efforts, how much effort an individual will expend, and how he or she will persist in the face of obstacles. These beliefs derive from a variety of sources, including performance accomplishments, vicarious experience, verbal persuasion, and the appraisal of physiological arousal. Each source consists of various modes of induction. For example, efficacy beliefs based on performance accomplishments may be induced from participant modelling, performance desensitization, performance exposure, or self-instructed performance.

Self-efficacy beliefs also differ in magnitude, generality, and strength. Magnitude refers to impact of efficacy beliefs across varying degrees of difficulty of a given task. For example, beliefs of moderate magnitude may exert a positive effect when a given task is set at a lower level of difficulty but not at a higher level of difficulty. Generality refers to the effect of efficacy beliefs across tasks. A belief low in generality will exert a positive effect on only a very specific task, whereas an expectation high in generality will have an impact across different tasks. Strength refers to how stable the efficacy belief is. Beliefs that are weak are easily extinguished when

confronted with failure, while strong beliefs will persist in the face of disconfirming experiences.

Another key distinction in self-efficacy theory is drawn between efficacy expectations and outcome expectations (Bandura, 1977). Outcome expectations refer to a person's belief that a given behaviour will produce a specific outcome. Efficacy expectations refer to a person's belief that he or she can execute the behaviour required to produce a specific outcome. As Bandura (1989) has noted, both outcome expectations and efficacy expectations affect performance motivation, and therefore, both should be considered in studies examining correlates of behavioural performance.

Self-efficacy is theorized to mediate adherence behaviours in several ways. Because self-assessments of efficacy determine choices, decisions to initiate or continue taking a medication will be in part mediated by self-efficacy. The amount of effort exerted in the face of challenges is also influenced by self-efficacy, and therefore, will affect individual persistence in the face of medication side-effects and intrusions on daily routines. Likewise, individual assessments of coping self-efficacy will also determine how well one copes with anxiety and other negative emotional states related to initiating complex regimens with adverse side-effects. Finally, self-regulatory efficacy will also mediate one's ability to avoid circumstances (e.g., substance use) that will compromise adherence behaviours.

Also central to self-efficacy theory is the concept of reciprocal causation (Bandura, 1989). Reciprocal causation refers to the interacting and mutually influencing effects of cognition, behavior, affect, biology, and the environment. According to this concept, individuals are not autonomous agents, and behaviour is not

influenced solely by the environment in a purely mechanistic fashion (Bandura, 1989). Human functioning and health is instead regarded as the product of the highly dynamic and complex effects of reciprocal causation (Bandura, 2001a).

To date, at least three studies of adherence to ART have examined self-efficacy and found to be a robust correlate of adherence (Gifford et al., 2000; Kalichman et al., 2001; Tuldra et al., 2001). For example, Gifford et al. (2000) examined predictors of adherence to ART among a mixed sample of 133 HIV-positive adults. After exploring the influence of HIV treatment knowledge and beliefs, psychological status, social environment and resources, and clinical health status, only self-efficacy and convenience of the medication regimen remained significant in the final multivariate model (Gifford et al., 2000). In a recent study of adherence among 72 women living with HIV/AIDS, Kalichman et al. (2001) examined the relevance of the Information-Motivation-Behavioral Skills Model on adherence. Measures included assessments of treatment information, motivation to take medications, and adherence self-efficacy. Structural modelling indicated that self-efficacy was the only variable that had a direct effect on treatment adherence, while treatment motivation to take medications had direct effects on self-efficacy and indirect effects on adherence. The direct and indirect effects of treatment information were not significant. In a controlled study of an intervention to improve adherence involving 116 HIV-positive patients, Tuldra et al. (2000) found that self-efficacy was strongly and independently associated with adherence.

While these initial studies of self-efficacy and adherence have produced what appear to be encouraging results, several methodological shortcomings and limitations

should be noted. First, the study by Tuldra et al. (2000) provided only a limited description of the self-efficacy variable under study. It appears that self-efficacy in this study was assessed by one question assessing the patient's "beliefs about his or her perceived capacity to follow treatment" (p. 222). This measure clearly fails to capture, in any sensitive way, the range of behaviours involved in adhering to ART. It has been noted previously that global measures of self-efficacy like the one used in the Tuldra et al. (2000) study are inadequate, as they tend to leave "much ambiguity about exactly what is being measured and the level of task and situational demands that must be managed" (Bandura, 2001b, p. 1). A proper assessment of self-efficacy requires that the measure be grounded in an informed conceptual analysis of all the factors governing the selected domain of functioning (Bandura, 2001b). It has been argued that self-efficacy is best conceptualized as a multidimensional construct, and that measures that are more task-specific will have greater predictive power within research studies (Choi, Fuqua, & Griffin, 2001). Patients in the Tuldra et al. (2000) study were asked to respond to the self-efficacy item using a five-point scale indicating how "sure" they were that they could follow treatment. In discussing the creation of self-efficacy scales, Bandura (1997) argued that 10-point scales (e.g., 0, 10, 20...100) are more sensitive and reliable than smaller Likert scales (e.g., five-point scales). This contention was validated in a recent study of response format in self-efficacy measurement. In comparing a six-point Likert scale with 0-100 scale, Parjares, Hartley, and Valiante (2001) found that the response format recommended by Bandura (1977) had stronger concurrent and predictive validity than the six-point Likert scale. The Tuldra et al. (2000) study also suffers from limitations pertaining to generalizability, as the study

involved a sample of various HIV-positive populations (e.g., 38% IDU, 38% men who have sex with men) that was derived exclusively from a hospital setting.

Similar weaknesses apply to the study by Gifford et al. (2000). The authors note that five items assessing “behavioral efficacy and outcome expectancy” (p. 387) used in the study were adapted from instruments created by Lorig (2000). There is no further description of the actual survey items, and a review of the document by Lorig (2000) revealed no items specific to efficacy and outcome expectations. This study also used a mixed sample (17% were IDU) derived exclusively from clinic settings. As is the case with the study by Tuldra et al. (2000), the small size of the sample did not permit any meaningful stratification. Given the obvious differences in the challenges faced by subpopulations, it is reasonable to expect that the relative impact of efficacy and outcome expectations on adherence may be very different for IDU than for gay males. The lack of a clear description of efficacy items measured is also problematic in terms of interpretation, as the domains of functioning related to adherence are not clearly defined. This in turn limits the usefulness of the findings in informing policies and programs that aim to increase adherence behaviours.

The study by Kalichman et al. (2001) is the only known study of adherence that includes a full description of the self-efficacy items being measured. Seven items were created and used to form a composite treatment adherence self-efficacy score. Six of the seven items begin with the phrase “stick to your medications...”. The items addressed the ability to “stick” to medication schedules, and the ability to stick to medications when side-effects are present, when daily routines change, when one is unwell, when one has to “eat at different times” (p. 64), and when medications interfere

“with your day” (p. 64). The last item asks people to rate the extent to which they feel they can continue treatment “even if your T-cells go down”. Subjects were asked to respond on a 10-point scale (0 = cannot do it at all, 10 = certain you can do it). While these items appear to address situations that can affect adherence, they do not capture a complete set of adherence behaviours. For example, the questions do not address the ability to refill prescriptions and the ability to remember how many pills to take. As well, many items appear to reflect dimensions of self-regulatory efficacy rather than adherence efficacy expectations, as many items ask the subject to rate how well they can stick to their medications under different challenging circumstances (e.g., in the event of side-effects). The study also has limited generalizability, as the study involved a sample consisting exclusively of women recruited from service organizations and medical clinics. The study also did not include information pertaining to injection drug use history or risk characteristics.

Collectively, the limitations of previous studies of adherence and self-efficacy indicate that there is a need for population-specific studies that use measures of self-efficacy that are sound from a psychometric perspective. In particular, future studies should involve measures that assess the full range of behaviours that are central to maintaining adherence to ART.

Social support has been widely studied and recognized as a potent determinant of health (Young, 1998). As Green (1993) notes, social support is “an ‘omnibus’ term referring to a metaconstruct relating to different aspects of social relationships” (p. 87), including: (1) the existence and quantity of social relationships; (2) the functional quality of these relationships; and (3) the perceived quality and adequacy of the support

(Green, 1993). The definitions given to social support are broad and numerous, and the lack of consensus concerning the definition of social support is reflected in its measurement (Green, 1993). Social support is believed to affect adherence behaviours both directly (e.g., encouragement, systemic cues, positive reinforcements) and indirectly (e.g., buffering variables that compromise adherence, including stress, anxiety, depression) through various mechanisms (Friedland, Renwick, & McColl, 1996; Singh et al., 1999), and several types of social support have been described (Green, 1996).

In some recent studies of adherence to ART, social support has emerged as a potent psychosocial determinant (Friedland & Williams, 1999). However, the results to date have been equivocal. In a recent study involving 138 HIV-positive patients (mixed race and transmission categories), Singh et al. (1999) assessed the influence of three types of social support on adherence to ART using the Social Support Questionnaire. Social support subtypes included: (1) tangible, instrumental, or practical support, defined as the provision of material aid, physical assistance or help during a crisis; (2) emotional support defined as provision of emotional comforting including nurturance, approval, and acceptance; (3) informational support defined as provision of advice, guidance, and information on various issues including the patient's illness (Singh et al., 1999). The results indicated that total satisfaction with one's social support, as well as tangible and informational social support, discriminated between adherent and nonadherent patients. Emotional support was not predictive of adherence (Singh et al., 1999). Gordillo, del Amo, Soriano, and Gonzalez-Lahoz (1999) assessed the impact of various sociodemographic and psychological factors on adherence,

including depression, anxiety, health beliefs, and social support (measure not specified). In a final multivariate model, depression and lack of social support were both associated with poor adherence. Subjects with good social support had adherence rates that were almost twice as high as subjects who lacked support. However, an observed interaction effect suggested that social support improves adherence for patients who are not depressed, but not for those that are (Gordillo et al., 1999). This finding suggests that depression mediates the effect of social support on adherence.

It is also important to note that some social interactions have adverse effects on health behaviour (Meichenbaum & Turk, 1987; Dimatteo & DiNicola, 1982). While these effects have not been studied in the context of adherence to ART, several studies have demonstrated the adverse effects of negative social networks on adherence to other medical regimens (Meichenbaum & Turk, 1987). This in turn has led investigators to develop methods for assessing both positive and negative influences of social networks (e.g., families) on adherence behaviours (Schafer, McCaul, & Glasgow, 1986). The negative impacts of social networks may be particularly pronounced for IDU. Previous research has also indicated that IDU tend to rely primarily on other IDU for social support (Stowe et al., 1993). While IDU are known to exercise concern for the health of others (McKeganey, Friedman, & Mesquita, 1998), it is possible that the people providing support to IDU are also the people with whom they inject drugs. It has also been shown previously that many of the “riskiest” of injecting practices (e.g., sharing syringes, assisted injection) have been found to be confined to relationships characterized by close social ties (Neaigus et al., 1994). Therefore, there is need for

future studies that examine the impact of social support on adherence among IDU-specific samples.

Other patient characteristics that have been found to be predictive of adherence behaviours include mental health status and substance use (Chesney, Morin, & Sherr, 2000; Rabkin & Chesney, 1999; Williams, 1999). For example, various investigators have examined the influence of mental health characteristics such as depression, anxiety, hopelessness, stress, and coping style on adherence to ART, however; the results have been inconsistent (Gifford et al., 2000; Gordillo, del Amo, Soriano, & Gonzalez-Lahoz, 1999; Patterson et al., 2000; Singh et al., 1999). For example, Gordillo et al. (2000) assessed the influence of depression and anxiety, among other variables, on adherence to ART among 211 HIV-positive patients. Depression was measured using the Beck's Depression Inventory (BDI) and was found to predict adherence regardless of level of social support. Anxiety was measured using the Hamilton Anxiety scores, and was not found to be predictive of adherence. Singh et al. (1996) followed 46 HIV-positive patients longitudinally for 12 months to assess determinants of adherence to mono and double combination antiretroviral therapy. Psychological status was assessed, along with other variables, using the BDI and the Profile of Moods States (POMS) scale. While the POMS depression subscale did discriminate adherent from nonadherent patients, the BDI and POMS anxiety subscale did not. The Gifford et al. (2000) study of adherence to ART included the variables of depression (measured by the BDI), self-efficacy, stress (measured by the Perceived Stress Scale), and health beliefs. In the final logistic model, only self-efficacy and perceived and lifestyle/regimen fit were associated with greater adherence. Singh and

colleagues have twice examined the influence of coping style on adherence to antiretroviral therapy (Singh et al., 1996; Singh et al., 1999). In the aforementioned longitudinal study involving 46 patients, coping as measured by the Ways of Coping Scale was found to discriminate adherent and nonadherent patients. In a later study involving 123 HIV-positive patients, Singh et al. (1999) assessed the influence of coping on adherence using the Billings and Moos Inventory of Coping with Illness Styles scale. While active-behavioural and problem-focused coping were associated with adherence, avoidant coping was associated with nonadherence. Emotion-focused coping and active cognitive coping were not in any way associated with adherence (Singh et al., 1999).

While there have been few studies of the influence of neuropsychological status on adherence to ART (Rabkin & Chesney, 1999), simply forgetting to take medications has been consistently identified as a reason for nonadherence (Friedland & Williams, Chesney, Morin, & Sherr, 2001). For example, Gifford et al. (2000) asked 133 HIV-positive individuals to indicate their agreement with items on a list of reasons for not taking their medications. Being “too busy” or “simply forgot” was mentioned most frequently (by 52% of patients). In a qualitative study involving 28 HIV-positive patients, Roberts (2000) found that forgetting to take medications was the most commonly mentioned barrier to adherence. The results suggested that medications were missed most often when they were not tied to daily routines.

Several authors have suggested that substance use compromises adherence to antiretroviral therapy (Rabkin & Chesney, 1999; Williams, 1999). However, there have only been a few studies that have examined the influence of substances other than

injectable cocaine and heroin on adherence to ART. Moatti et al. (2000) examined adherence to ART among 164 injection drug users, 32 of whom were receiving buprenorphine drug maintenance treatment. Results from a logistic regression analysis indicated that alcohol consumption and active drug use were associated with decreased adherence. More specifically, the risk of being nonadherent increased 20% with each additional 25 drinks consumed per month. However, it remains controversial whether or not injection drug use is predictive of adherence to antiretroviral therapy. Some studies have suggested that injection drug users were less likely to adhere to zidovudine therapy (Samet, 1992; Singh, 1996). When psychiatric comorbidity has been adjusted for, however, Ferrando et al. (1996) found no difference in adherence to AZT therapy between injection drug users and other subgroups. In a recent study of adherence to ART involving 123 HIV-positive patients, intravenous drug use was not associated with adherence in univariate or multivariate analyses (Singh et al., 1999). The discrepancy in results concerning the influence of intravenous drug use may in fact reflect methodological shortcomings. Many studies examining this variable do not distinguish former from active injection drug users (Lucas, Cheever, Chaisson, & Moore, 2001). However, in a recent study, Lucas et al. (2001) compared adherence and virologic outcomes among a prospective cohort of 764 HIV-positive patients. The results indicated that while former and non-drug users had similar adherence levels and virologic responses, active drug users had significantly lower adherence rates and poorer virologic responses. One obvious gap in the literature addressing the influence of illicit drug use on adherence concerns the intensity of drug use. Currently, the impact of different levels of illicit drug use on adherence is not known. Therefore, future

studies should include measures that assess not only the presence of illicit drug use, but also different levels of illicit drug use in terms of the amount of drugs used. As well, previous studies have not examined the impact of different types and forms of illicit drug use on adherence. Therefore, further work identifying the impact of different types of drugs (e.g., cocaine versus heroin) and routes of administration (e.g., smoking versus injecting) are needed.

### ***Access, Maintenance, and Adherence to ART among Injection Drug Users***

Although the treatment of HIV/AIDS has improved vastly through the use of antiretroviral therapy, recent evidence suggests there is considerable disparity among HIV populations in terms of uptake of these new treatments (Carrier et al., 2000; Mocroft et al., 2000; Strathdee et al., 1998). Problems associated with adherence and the drug-resistant viral strains have raised concerns regarding individual treatment outcome and public health. Given the complexity of typical ART regimens and the complex health and social circumstances associated with injection drug use, it is understandable that concerns related to access, maintenance, and adherence would be amplified in the context of treatment for injection drug users living with HIV/AIDS.

Despite ongoing disparity in access to ART, the treatment guidelines outlined by the Treatment Programme of the BC Centre for Excellence in HIV/AIDS (2001) suggest that access to ART should be equal among persons living with HIV/AIDS:

Every eligible patient should be offered antiretroviral therapy. The nature of the treatment and the need for strict adherence to the regimen will be discussed in detail with each patient. Patients should fully

understand the possible consequences of poor adherence to the regimen (i.e. treatment failure, viral resistance, cross resistance to other drugs and decreased treatment options). ... The ultimate decision of when and how to start treatment will vary between patients. This decision will be arrived at only following careful consideration of the available evidence and individual factors, jointly by the patient and the treating physician.

(p. 7)

HIV-positive IDUs do have a lower uptake of antiretroviral therapy compared to other HIV-positive persons in Canada, the United States, and Europe (Ferrando, Wall, Batki, Sorenson, & 1996; Muma, Ross, Parcel, & Pollard, 1995; Samet et al., 1995; Singh et al., 1996; Strathdee et al., 1998; Wall et al., 1995). In fact, the United States Center for Disease Control 1998 guidelines recommend withholding ART from IDUs until active drug use has ceased (cited in Moatti & Souteyrand, 2000). In Vancouver, where antiretroviral therapy is provided at no cost to patients, only 40% (71/177) of eligible HIV-positive IDUs recently studied had received any antiretroviral therapy at a median of 11 months following first eligibility for treatment (Strathdee et al., 1998). IDUs who were not on therapy were more likely to be women, of younger age and less likely to be enrolled in an addiction treatment program. Another study of access to ART found that patients not on therapy were more likely to have physicians with less HIV experience (Samet et al., 1995). A cross-sectional survey of 404 HIV-positive IDUs in Baltimore, Maryland found only 51% of IDU participants reported receiving antiretroviral therapy. Factors associated with failure to receive therapy included a lack of participation in an addiction treatment program and absence of a

usual source of primary care or health insurance (Muma et al., 1995). In a prospective European cohort of 6,645 patients with HIV, IDUs were significantly less likely to receive antiretroviral therapy at recruitment than homosexual men. The continued use of drugs has been found to lower the likelihood of antiretroviral prescription among US and French HIV-positive IDUs who had regular access to AIDS-specialized hospital care (Freeman, Rodriguez, & French, 1998; Singh et al., 1996; Wall et al., 1995). In the Swiss HIV Cohort Study, active IDUs who were not in addiction treatment programs and those who acquired HIV through injection drug use had a significantly higher risk of inadequate antiretroviral treatment (Mehta, Moore, & Graham, 1997). Similar findings have been found elsewhere despite documentation of good adherence to therapy in the context of ambulatory services in hospitals or addiction treatment programs (Carpenter et al., 1997; Heath et al., 1997).

Research to date has demonstrated that various factors mediate optimal uptake of ART among IDUs. For example, it has been found that insufficient training in the care of people living with addictions and negative attitudes towards IDUs among physicians are associated with poor uptake of ART (Carpenter et al., 1997). As well, many clinicians are concerned about patient adherence to complex regimens and the transmission of multidrug-resistant HIV (Holzemer et al, 1999; Roca, Gomez, & Arnedo, 1999). As a result physicians may not prescribe antiretroviral therapy or may defer therapy until the injection drug user is enrolled in an addiction treatment program.

Studies have found that IDUs tend to delay their acceptance of antiretrovirals, and one recent study reported a delay of approximately 9 months for triple combination antiretroviral therapy (Friedland & Williams, 1999; Proctor, Tesfa, & Tompkins, 1999).

Another recent study examined patient characteristics associated with access to ART and found that female gender, heroin use, and unstable housing were predictive of poor uptake, while current methadone maintenance was associated with increased odds of receiving ART (Palepu et al., 2001b). Lucas et al. (2000) examined ART utilization and adherence among a prospective cohort of 764 HIV-positive patients, 575 of whom were current or former injection drug users. The results indicated active drug use was strongly associated with a failure to use ART when compared with non-drug use. Also associated with a failure to utilize ART were: regular alcohol use, heroin use, cocaine use, and combined heroin and cocaine use, female sex, black race, and no prior opportunistic infections

There are few studies that have examined issues of ART maintenance and discontinuation among IDU. The findings of these studies indicate that many IDU who initiate ART do not maintain the therapy. For example, Demas et al. (1998) examined ART acceptance and adherence among 135 HIV-positive IDU participating in methadone maintenance treatment. At the time of data collection, only 50% of the study participants who had at some time initiated ART were still receiving treatment. Similarly, Palepu et al. (2001b) found that only half of the HIV-positive IDU participating in a study of ART adherence had remained on the treatment. While there is limited evidence about the relationship between injection drug use and ART maintenance, one study investigating ART discontinuation with a mixed sample of HIV-positive patients found injection drug use to be predictive of ART discontinuation (Roca et al., 1999). Unfortunately, the studies reporting rates of ART maintenance among IDU have tended to focus more identifying determinants of adherence but not

maintenance. There are currently no known studies of determinants of ART maintenance among IDU. Therefore, little is known about the characteristics or events that predict ART maintenance or discontinuation among IDU.

Unfortunately there are only a limited number of studies that specifically examine problems associated with adherence to ART among injection drug users living with HIV/AIDS. While various determinants of adherence to ART have been identified, most have been explored within studies involving mixed HIV populations. These studies have involved small samples, and consequently stratification according to drug use has not been possible.

Moatti et al. (2000) examined adherence to ART among 164 HIV-positive patients who were infected through injection drug use, 113 of whom were patients who had stopped injecting more than six months prior to data collection. Nonadherence was associated with “negative life events” (p. 153). The life events that contributed most significantly to nonadherence included major financial problems, and confrontations with the police. Alcohol consumption and younger age were also associated with nonadherence. Palepu et al. (2001) examined treatment interruption among 238 VIDUS participants and found that recent incarceration and binge drug use were associated with treatment interruptions. Consistent with the findings of Moatti et al. (2000), older IDUs were found to be less likely to interrupt therapy. In the Lucas et al. (2000) study involving 575 former or current injection drug users, the only variable among several demographic and clinical factors associated with nonadherence was active drug use. Presently, little is known about the effects of cognition and behaviour on adherence among IDU.

One factor that may influence greatly the maintenance of, and adherence to, antiretroviral therapy is incarceration. Despite the fact that high rates of incarceration have been observed among IDU (Tyndall et al., in press), this contextual factor has received little attention in the ART literature. Consequently, little is known about the effect of incarceration on ART maintenance and adherence. The only known study of adherence that included a measure of incarceration did find that recent incarceration was associated independently with ART treatment interruption (Palepu et al., 2001a). One study of ART adherence among HIV-positive prisoners reported high rates of ART discontinuation among the study participants (Altice, 2001), as 62% of the prisoners who had at one time initiated ART had since discontinued therapy. However, the predictors of maintenance and reasons for discontinuing ART were not assessed, and therefore the association between incarceration and ART maintenance was not characterized fully.

It has been pointed out that HIV-positive inmates often endure severe discrimination and threats to their safety, and therefore many choose to conceal their HIV status (deBruyn, 1998). This in turn may prompt prisoners to discontinue ART in order to avoid being identified as being HIV-positive, or in some cases prisoners may skip doses when they are unable to consume their medications in private. It has also been pointed out that the daily routine within prisons is rigid and unable to accommodate complex treatment needs (deBruyn, 1998). Given the previously noted association between adherence and lifestyle fit, it may be that the rigid routines within prisons serve to compromise adherence to ART. Given that incarceration remains a

dominant response to the problems of injection drug use (Kerr & O'Briain, 2002), the effect of incarceration on ART maintenance and adherence is worthy of further study.

### ***Conclusion***

As the AIDS epidemic evolves and changes, it remains an international crisis that affects the health of tens of millions of individuals, threatens the social welfare of communities, and constrains the economic development of many of the world's poorest nations. Throughout the world, among the most affected by HIV/AIDS are marginalized groups, including injection drug users. The complex health and social status of injection drug users renders them a unique HIV subpopulation with complex treatment needs.

While in recent years substantial improvements have been made in the pharmacological treatment of HIV/AIDS, serious individual and public health challenges associated with new antiretroviral therapies remain. Many HIV-affected populations do not have adequate access to these medications, and many discontinue ART prematurely. As well, when adherence to these complex regimens is compromised, clinical outcomes are suboptimal, and transmissible drug-resistant strains of HIV quickly develop. Given the chaotic lifestyle of injection drug users and the associated stigma imposed by society, maintaining and adhering to ART is uniquely challenging for IDU populations. Ensuring adequate treatment of HIV/AIDS among IDU is further complicated by high rates of incarceration among this population. HIV-related discrimination within prisons and the rigid routine of prison life may well compromise treatment efforts. However, little is known about the effects of this structural determinant on the treatment of HIV/AIDS.

While maintenance of and adherence to ART remain issues of paramount importance for HIV-positive IDU, there is currently a lack of evidence available to inform relevant policies and programs. Most studies focused on these issues have involved mixed clinic-based populations, and results concerning various predictors of adherence, including continued illicit drug use, have been equivocal. As well, while self-efficacy potentially could be a key determinant of ART maintenance and adherence, previous investigations of this construct have suffered considerably from methodological shortcomings and limited generalizability. Furthermore, a small number of studies have indicated that many IDU do discontinue ART while still eligible for the therapy. However, there are no known studies that identify predictors of ART maintenance or the reported reasons for discontinuation of treatment. Given the pressing challenges posed by HIV/AIDS and its treatment, there is an urgent need to identify determinants of ART maintenance and adherence among populations of HIV-positive injection drug users.

### **Hypotheses Investigated in this Study**

The aim of this study is to test specific hypotheses pertaining to ART maintenance and adherence among IDU. These hypotheses address topics that have not been examined adequately by previous studies. As well, there is evidence indicating that a substantial number of IDU do not maintain ART (i.e., discontinue treatment soon after starting). However, there is a lack of studies identifying determinants of maintenance, and therefore this study will seek to identify determinants of ART maintenance as well as adherence, and the self-reported reasons for discontinuing ART and missing doses of ART.

The first study hypothesis pertains to the association between incarceration and ART maintenance and adherence. The impact of incarceration on the pharmacological treatment of HIV/AIDS has not been fully characterized. However, given the high rates of HIV-related discrimination occurring within prisons, and the rigid routine of the prison environment, it is likely that maintenance of and adherence to ART could be compromised during periods of incarceration. Therefore, it is hypothesized that recent incarceration will be associated independently and negatively with ART maintenance and adherence.

The second study hypothesis concerns the association between outcome expectancies and ART maintenance and adherence. There are currently no known studies that have explored the impact of specific outcome expectancies on ART maintenance and adherence. However, the side-effects of ART are often experienced almost immediately following initiation of treatment, while clinical benefits are rarely noticeable in the short term. Consequently, many patients may start therapy, experience

side-effects, and discontinue therapy under the assumption that ART only makes one sicker. Therefore, it is hypothesized that negative outcome expectancies pertaining to ART will be associated independently and negatively with ART maintenance and adherence.

The third study hypothesis concerns efficacy expectations. Previous studies have found that efficacy expectations are associated with adherence to ART, although these studies have suffered from methodological shortcomings, and have typically involved mixed samples of HIV-infected subpopulations recruited from clinical settings. However, efficacy expectations affect choice, and therefore a decision to continue taking ART as prescribed will likely be influenced by efficacy expectations. The amount of effort exerted in the face of challenges is also affected by efficacy expectations, and therefore adherence efficacy expectations will also likely influence individual persistence in the face of medication side-effects and intrusions on daily routines. Therefore, it is hypothesized that high efficacy expectations pertaining to adherence will be associated independently and positively with ART maintenance and adherence.

The fourth study hypothesis concerns self-regulatory efficacy. There are no known studies that have explored the association between self-regulatory efficacy and ART maintenance and adherence. Self-regulatory efficacy has, however, been shown previously to affect the ability to overcome challenging circumstances that compromise behavioural performance. Therefore, it is hypothesized that high self-regulatory efficacy, as it pertains to overcoming challenges relevant to taking ART, will be associated independently and positively with ART maintenance and adherence.

The fifth study hypothesis concerns social support. Previous studies have found social support to be associated with adherence behaviours. However, there are no known studies that have examined the association between social support and ART maintenance and adherence among IDU populations. While IDU social networks may have some adverse effects on health, it is expected that the net effect of these networks on ART maintenance and adherence will be positive. Therefore, it is hypothesized that social support will be associated independently and positively with ART maintenance and adherence.

The sixth study hypothesis pertains to frequent drug use. Previous studies have produced equivocal findings concerning the impact of illicit drug use on ART adherence. There are currently no known studies that have examined the impact of intensity of illicit drug use on ART adherence. However, it is expected that high levels of illicit drug use will compromise daily routines and cognitive abilities relevant to adherence behaviours more so than lower levels of illicit drug use. Therefore, it is hypothesized that high levels of drug consumption will be associated independently and negatively with ART maintenance and adherence.

The seventh and final hypothesis concerns the co-joint effects of the aforementioned variables on ART maintenance and adherence. Previous studies have shown that adherence behaviour is predicted by a set of measurable demographic and psychosocial determinants. Therefore, it is hypothesized that recent incarceration, outcome expectations, efficacy expectations, self-regulatory efficacy, social support, and frequent illicit drug use will predict, collectively, ART maintenance and adherence in a multivariate fashion.

### Chapter III – Methods

This chapter describes the methods employed to collect and analyze the data used in this study. Included is a description of the data sources, study samples, measures, and procedures.

#### *Data Sources*

Two data sources were accessed for this study: the Vancouver Injection Drug Users Study (VIDUS), and the HIV/AIDS Drug Treatment Program (DTP). Both data sources are housed within the British Columbia Centre for Excellence in HIV/AIDS.

#### *The Vancouver Injection Drug Users Study (VIDUS)*

The Vancouver Injection Drug Users Study (VIDUS) is a closed prospective cohort of injection drug users. Beginning in May 1996, persons who had injected illicit drugs at least once in the previous month and resided in the Greater Vancouver region were recruited into VIDUS. The study team established a storefront office in the Downtown Eastside (DTES) of Vancouver where enrollment and follow-up interviews could be conducted. In this ongoing prospective cohort study of 1416 IDUs, the baseline HIV prevalence was approximately 25%, and 40% of participants are now HIV-positive (Tyndall et al, 2001). Seventy-eight percent of the cohort was hepatitis C positive at baseline, and 76% had been in jail at some time. The mean age for the cohort at baseline was 37 years (14-61), and the average length of time since first injection was 13 years (0.1 – 44). Approximately 65% of participants are Caucasian and 25% are of Aboriginal ancestry. Since the study's inception, 190 participants have died (41 of HIV/AIDS, 51 of an overdose, and 98 of other causes including hepatitis and suicides). The overall follow-up rate is 85%.

Most of the participants (82%) came to the VIDUS study office after having learned of the study through recruitment materials (e.g., posted flyers) or other participants. The remaining subjects were referred by the needle exchange program (5%), other storefront agencies (10%), and clinics (3%). For initial enrollment, evidence of recent injection drug use was determined by examining needle track marks. Informed consent was obtained from all participants at time of enrollment. Participants were informed of the nature of the study, potential benefits and harms, their role as a participant, and then were asked to sign a consent form. The consent provided permits linkages with hospital records, including information contained with the British Columbia Centre for Excellence's Drug Treatment Program. The VIDUS study has ethical approval from the University of British Columbia/Providence Health-care Office of Research Services.

After providing written consent, participants provide blood samples for HIV and HCV antibody testing, and undergo a lengthy interview-administered questionnaire at the baseline visit and semi-annually thereafter. Blood specimens reactive upon ELISA are confirmed by Western Blot. Participants are reimbursed \$20 for each study visit, at which time referrals are provided for universal medical care, HIV/AIDS care, available drug and alcohol treatment, and counselling. All survey instruments are administered by a trained interviewer in a private space within the VIDUS office. Detailed information is collected on demographics, drug use and sexual behaviours, types of and frequency of drugs used, incarceration, housing, methadone maintenance and the utilization of health services such as emergency department, clinics and hospitalization in the previous six months.

The present analysis was restricted to the follow-up periods occurring from December 1, 2001 to May 31, 2002 (VIDUS Follow-up #11), and June 1, 2002 to November 30, 2002 (VIDUS Follow-up #12). Participants included in this analysis either came to VIDUS office voluntarily to complete a follow-up survey or were invited to complete a follow-up survey by a VIDUS outreach worker. In instances where participants completed surveys in both follow-up periods, only data collected during follow-up 11 was included.

### ***The HIV/AIDS Drug Treatment Program***

The British Columbia Centre for Excellence in HIV/AIDS supports the province-wide HIV/AIDS Drug Treatment Program (DTP) that distributes antiretroviral agents at no cost to eligible HIV-infected individuals. The DTP distributes antiretroviral drugs based on specific guidelines generated by the Therapeutic Guidelines Committee (Montaner et al., 1996). In June 1996, the DTP adopted plasma viral load driven antiretroviral therapy guidelines, consistent with those put forward by the International AIDS Society-USA (Carpenter et al., 2000). In brief, individuals naïve to antiretroviral therapy with plasma viral load  $> 100,000$  copies/mL were offered triple drug regimens while those with plasma viral loads from 5,000 to 100,000 copies/mL were offered dual nucleoside therapy. In July of 1997 the guidelines were revised to recommend triple combination therapy for all antiretroviral naive individuals with plasma viral loads  $> 5,000$  copies/mL or CD4 counts  $< 500$  cells/mm<sup>3</sup>. The DTP recommends that viral load be monitored at baseline, at 4 weeks after the start of antiretroviral therapy and every 3 months thereafter. Plasma viral load is measured using the Amplicor HIV-1 Monitor manufactured by Roche Diagnostic System

(Branchburg, NJ). From 1986 to 2000, a total of 6,494 HIV-positive British Columbians received antiretroviral therapy. Of these, 5,508 have been enrolled in the DTP. There are currently over 2,700 program participants receiving antiretroviral therapy in British Columbia.

At time of patient enrollment physicians must complete a drug request enrollment form for patients who are HIV-positive and eligible for ART. The form acts as a legal prescription and compiles information on the HIV-positive applicant, the follow-up physician, past HIV-specific drug history, viral load, CD4 cell counts, and current medication requests. A qualified practitioner then reviews the form to ensure that it meets the DTP guidelines.

All ART medications are stored within a centralized pharmacy in St. Paul's Hospital (Vancouver). ART can be dispensed directly from the St. Paul's pharmacy or sent to another pharmacy. The DTP maintains detailed records of all medications that are dispensed. At the time of initial prescription refill, participants complete an enrollment survey and an informed consent form, and their physician completes a clinical staging form. Participant surveys and clinical staging forms are then completed annually. The surveys elicit information regarding socio-demographic information and are used to create profiles for participants. Patient adherence to ART is calculated using prescription refill data obtained from pharmacy refill records.

### *Samples*

The study sample was restricted initially to HIV-positive participants (n = 244) who completed VIDUS questionnaires during the follow-up periods from December 1, 2001 to May 31, 2002 (VIDUS Follow-up #11), and June 1, 2002 to November 30,

2002 (VIDUS Follow-up #12). For the purposes of this analysis, two subsamples were drawn from this initial sample.

#### ***ART Treatment Subsample***

For a first analysis examining determinants of ART maintenance, a subsample of all HIV-positive individuals who had taken or were currently taking ART was selected. In order to be eligible for inclusion in this subsample, participants had to self-report that they had taken ART at some point since becoming HIV positive. In total, 160 individuals were selected, of whom 91 were male, and 69 were female. The mean age for the subsample was 39 years (SD = 7.04), with participants ranging in age from 24 to 56 years.

#### ***ART Adherence Subsample***

For a second analysis examining determinants of adherence to ART, a subsample of all HIV-positive individuals who had pharmacy-based adherence scores for the past twelve months was selected. Only individuals with adherence scores greater than 0 were included to ensure that participants had been taking ART at some point during the past year. One individual who reported having been taken off ART by his doctor (i.e., structured drug holiday ordered due to drug interactions) was removed from the analysis. In total, 108 participants were included in this analysis, of whom 59 were male and 49 were female. The mean age for this subsample was 39 years (SD = 7.07), with participants ranging in age from 26 to 56 years.

## *Independent Measures*

### *The VIDUS Questionnaire*

VIDUS questionnaires #11 & #12 are virtually identical, take approximately 20 - 30 minutes to administer, and contain a range of questions that have been divided into the following sections: current demographics, injection drug use, non-injection drug use, police activity, incarceration, sexual activity, drug and alcohol treatment, violence, social issues. Next, a second part of the questionnaire is administered by a nurse and contains questions concerning current health status and practices, health-care utilization, and antiretroviral therapy. This second part of the questionnaire takes approximately 15 minutes to administer.

Socio-demographic characteristics taken from the VIDUS questionnaire and considered in then present analyses include: gender, age, ethnicity, education (greater than or less than a grade 10), employment, source of income, recent incarceration, sex trade involvement, unstable housing. Unstable housing was defined as living in a single room occupancy hotel, transitional living arrangements, or being homelessness, whereas stable housing was defined as living in an apartment or house. VIDUS participants are asked to disclose their drug use behaviours for the past six months. Drug use and related behavioural variables considered in the analyses included: heroin use, cocaine use, crack use, frequent heroin injection, frequent cocaine injection, frequent crack use, syringe borrowing and lending, requiring help injecting, bingeing, and accidental overdose. All questions use the previous six months as a reference period (e.g., “In the past six months, when you were using, which of the following drugs did you inject?”, “In the past six months have you lent your used rig to someone

else?"). As in previous work (Wood et al., 2002), persons who reported injecting cocaine or heroin once or more per day were defined as frequent cocaine and frequent heroin users respectively. Individuals smoking crack once or more daily were considered to be frequent crack users. Participants were also asked if they were currently on methadone maintenance therapy.

Variables pertaining to antiretroviral therapy (ART) that were included in this analysis were: ever on ART, currently taking ART, self-reported adherence, doses missed in the previous two weeks, and reasons for stopping ART. The question pertaining to doses missed asks participants to indicate whether they have missed more than two doses of antiretroviral therapy in the past two weeks. The question concerning the reasons why participants stopped taking medications included a list of possible responses that could be checked off. The responses choices were: out of area, fed-up, sick with side-effects, methadone interaction, in jail, stopped by doctor, stopped after pregnancy, and other (participants are asked to specify other reasons for stopping). Participants were asked to select all the reasons that applied to their situation.

For the purposes of this analysis 10 additional questions related to adherence self-efficacy were added to the current VIDUS questionnaire, as was a brief social support survey. These questions addressing adherence focused on reasons for missing doses of ART and adherence self-efficacy.

#### ***The Adherence Self-efficacy Measure (ASEM)***

A 10-item adherence self-efficacy measure was developed for use in this study. Items obtained from earlier studies of self-efficacy (Bandura, 1997; Lorig, 1996) were modified for use in the proposed project. As is common in the measurement of self-

efficacy, items were tailored to reflect the specific behaviours and skills under study (Bandura, 1997). Three separate dimensions related to self-efficacy and specific to ART adherence were included. Self-reported efficacy expectations were measured using 6 items that address participants' confidence in their ability to: remember to take medications, follow dietary guidelines, count medications, pick-up prescription refills, manage side-effects, arrange daily activities in order to follow their ART regimen. Two regulatory self-efficacy items were also added and addressed participants' confidence in their ability to take medications as prescribed (1) when using drugs and (2) when "dope sick" (i.e., in withdrawal from opiates). For all self-efficacy expectation and self-regulatory efficacy items, participants were asked to respond using a ten-point scale ranging from 0 to 100 (i.e., 0, 10, 20, 30...100), with 0 anchored as "Can't/Couldn't do it at all" and 100 anchored as "Certain can/Could do it". For the present study, self-efficacy item scores was added and divided by the total number of items to form a composite adherence self-efficacy score. The same method was be used to calculate a composite self-regulation score. Two outcome expectancy items assessing beliefs concerning the efficacy of ART were initially included. One item asked participants to rate the extent to which they believed taking ART would make them better. As well, in light of the many concerns HIV-positive individuals have about the side-effects associated with ART, the second item asked participants to indicate the extent to which they thought taking ART will make one sicker. Participants were asked to respond using a ten-point scale ranging from 0 to 100 (i.e., 0, 10, 20, 30...100), with 0 anchored as "Certain it will not happen", and 100 anchored as "Certain it will happen". The two outcome expectancy items were highly correlated, suggesting that

the two items may well be measuring a similar belief concerning the efficacy of ART. In light of the many studies indicating that the experience of side-effects is strongly associated with nonadherence (Chesney et al., 2000; Health et al., 2002), only the item pertaining to beliefs about ART making one sicker was retained in the present analyses. The internal consistency reliability of the ASEM was assessed using both study samples and found to be high ( $\alpha = 0.82$  for the ART Treatment Sample, and  $\alpha = 0.81$  for Adherence Sample).

***Adult AIDS Clinical Trials Group (AACTG) Adherence Instrument: Reasons for Missed Doses Subscale***

The Recruitment, Adherence and Retention Subcommittee of the Adult Outcomes Committee and the Patient Care Committee of the AACTG have developed a comprehensive adherence measure referred to as the AACTG Adherence Instrument (Chesney et al., 2000). The groups worked together to develop instruments that are easy to implement and well accepted by patients, clinicians, and researchers. The AACTG instrument includes a subscale that asks participants to indicate reasons for missing doses. Twelve reasons for missing doses are provided as possible responses to the question “how often have you missed taking your meds because” and include: “away from home”; “busy with other things”; “simply forgot”; “had a change in routine”; “fell asleep/slept through dose”; “had problems taking meds at specific times”; “felt ill or sick”; “wanted to avoid side-effects”; “felt depressed /overwhelmed”; “had too many pills to take”; “did not want others to notice me taking meds”; and “felt drug was too toxic/harmful”. Participants are asked to respond to each reason listed using a four-point response scale consisting of: “never”, “rarely”, “sometimes”, and “often”.

Although the AACTG instrument has not undergone psychometric validation, a recent feasibility study indicated that the instrument was easily implemented and acceptable to patients (Chesney et al., 2000). This subscale was included in the present analysis and ten new response items were added: “had a problem with a timer/alarm”; “housing/living situation changed”; “was at work”; “family responsibilities got in the way”; “changes on weekends got in the way”; “did not understand instructions”; “did not have access to food or water”; “did not have a safe or secure place to keep medications”; “lost my medications”; and “was too high”. Participants were also asked to specify any other reasons for missing doses.

For the present analysis, the response categories were recoded into a dichotomous response scale, with never and rarely = 0, and sometimes and often = 1. The mean response for each reason was used to calculate the proportion of participants indicating which reasons caused them to miss doses either “sometimes” or “often”.

#### ***The Medical Outcomes Study (MOS) Social Support Survey***

Self-reported social support was measured using the social support survey contained within the Medical Outcome Studies (MOS) questionnaire (Sherbourne & Stewart, 1991). The MOS Social Support Survey is a brief multidimensional self-report survey that was developed for patients with chronic illnesses, and includes 19 items that focus on perceived availability of functional support. Participants are asked to indicate how often specific types of support are available to them (e.g., “someone to help you if you were confined to a bed”). Response categories include: “never”, “sometimes”, “often”, “usually”, and “always”. The items are clustered in four subscales: emotional/informational support, tangible support, affectionate support, and positive

social interaction. Subscales and a total social support score can be transformed to produce scores ranging from 0 – 100. The MOS Social Support Survey underwent substantial psychometric validation with a sample of 2987 adults living with chronic illnesses (Sherbourne & Stewart, 1991). The results indicate that the measure has high internal-consistency reliability ( $\alpha = 0.97$ ), and the measure was found to be stable over a one-year interval (stability coefficient = 0.78). A test of convergent validity revealed that the survey items correlated positively with their respected subscale (item-scale correlations ranging from 0.72 – 0.90, all  $p < .05$ ). Tests of discriminate validity revealed that the instrument was negatively associated with a MOS measure of loneliness ( $r = -0.67$ ,  $p < 0.01$ ). The internal consistency reliability of the MOS Social Support Survey was assessed using both samples included in this study and was found to high ( $\alpha = 0.96$  for the ART Treatment Sample, and  $\alpha = 0.97$  for Adherence Sample). In the present study, the total social support score will be used in all analyses.

### ***Dependent Variables***

#### ***Self-reported ART Maintenance***

All participants responding to the VIDUS questionnaire were asked to indicate whether they had ever taken ART and if they are still on the therapy. Response choices to both questions included “yes”, “no”, or “unsure/can’t remember”.

#### ***Drug Treatment Programme (DTP) Pharmacy-based Adherence Measure***

As discussed earlier, all patients receiving ART in the province of British Columbia are registered with the B.C. Centre for Excellence’s Drug Treatment Programme (DTP). Included in the DTP is a record of all prescription refills picked up by patients. In order to calculate pharmacy-refill adherence, the number of days for

which medications are supplied are divided by the number of days for which medications are prescribed. The number of days supplied is determined by the number of prescription refills that are picked up by the patient. For the purposes of this analysis a data linkage was performed to obtain pharmacy-refill adherence for VIDUS participants included in this study. The one-year adherence period included the year prior to the date that each VIDUS participant completed his or her most recent follow-up survey. Adherence is expressed as percentage from 0 to 100 (number of days medications were supplied divided by number of days for which medications were prescribed). In the present analysis, the distribution of adherence scores was negatively skewed, with 32% of the sample having adherence scores of 100. Therefore, a cut-off of 95% adherence was used. This cut-off has been established in the adherence literature as being the level of adherence required to ensure suppression of HIV (Low-Beer, 2000).

### ***Procedure***

Both VIDUS and the DTP have ethical approval from the University of British Columbia/Providence Health-care Office of Research Ethics. For the present study, a waiver from further ethical review was obtained by the University of Victoria's Office of the Vice-President of research. In order to obtain data from VIDUS, a formal data request form listing all the aforementioned study variables was submitted to the Directors of VIDUS and the DTP. Once the request was approved, a computerized file containing all the requested VIDUS data was obtained from a VIDUS database manager. This file contained no identifying information. This database manager then forwarded the same file to a DTP database manager, along with accompanying VIDUS

identification numbers, participant names and birth dates. The DTP manager performed a linkage between the VIDUS data file and the DTP database. Pharmacy-refill records were obtained for all the VIDUS participants included in this study who had previously or were currently registered with the DTP. The pharmacy refill records were transformed into adherence scores, and then attached to file containing only VIDUS identification numbers. The file was sent back to the VIDUS database manager who then removed the VIDUS identification numbers and forwarded the file to the study investigator.

### ***Analytic Strategy***

The following analyses will involve the development of two statistical models. The first model will examine determinants of ART maintenance. Maintenance in this case refers to sustained use of ART, and is the opposite of discontinuation, which refers to the cessation of ART. The second model will examine determinants of ART adherence. Adherence in this case refers to the extent to which individuals picked-up new medications as prescribed. The ART maintenance analysis will include an examination of reported reasons for discontinuing ART, and the ART adherence analysis will include an examination of reported reasons for missing doses of ART. The proportion of participants reporting specific reasons for discontinuing ART and missing doses of ART will be presented. The same analytic strategies will be used to identify determinants of ART maintenance and ART adherence, and are described below in six steps.

The first step of the analysis will involve the use of descriptive statistics (e.g., raw counts, percentages, and means) to describe the demographic characteristics of the

population (e.g., age, ethnicity), rates of illicit drug use, risk behaviours, and methadone use. Also included, will be the mean scores and standard deviations for efficacy expectations, self-regulatory efficacy, outcome expectancies, and social support.

Following the presentation of the descriptive statistics (raw counts) for dependent variables, the second step of the analysis will include univariate analyses used to evaluate unadjusted associations between the dependent variables of interest and all independent variables. Associations between dichotomized variables will be analyzed using Pearson's Chi-square test, and associations between dichotomized and continuous variables will be analyzed using t-tests for independent samples. Unadjusted odds ratios will be examined as measure of the strength and direction of the observed associations. Variables found to be associated with the dependent variable at  $p \leq .05$  will be included in subsequent multiple regression analyses.

At the third step, a Pearson correlation matrix will be completed to examine the relationships among independent variables. Variables included in the study hypotheses, and those found to be associated with the dependent variable at the univariate level will be included.

At the fourth step, independent variables considered in the study hypotheses will be evaluated in pairs for potential interaction effects using fixed logistic regression models. In each model, the product of the variable pair (i.e., the interaction term) will be entered into a fixed model with its constituent variables entered on their own. When interaction terms are found to be associated significantly with the dependent variables of interest (at  $p \leq .05$ ), an analytic strategy used in previous studies will be employed to

interpret the observed interaction effects (Wood et al., 2002). First, an analysis will be undertaken in which the unadjusted odds ratio found for the entire sample above, will be compared to the odds ratios in analyses in which the study sample is stratified according to the variable that is expected to be the mediating variable in the interaction effect (e.g., the entire sample versus those incarcerated versus those not incarcerated). The strength and direction of the associations between the remaining variable (from the interaction term) and the outcome of interest (maintenance or adherence) will be compared in each case. Second, the interactions will be further described by building fixed models with indicator variables to represent the populations in which the interaction effect is being observed. Here, continuous variables will be dichotomized using a median split to create a “high” and “low” category for the variable. While dichotomizing continuous variables has some limitations, this technique has been previously used in order to estimate interaction effects (Wood et al. 2002). Four categories will then be created using all possible combinations (e.g., high-high, high-low, low-high, low-low). The category found to be associated most strongly with the dependent variable, in the stratified analysis above, will serve as the reference category (i.e., the “constant”) in the fixed model. All remaining categories will be examined in relation to the reference category to determine the influence of the variables across different strata (i.e., high-high, versus high-low, etc.).

The fifth step will involve the use of sequential logistic models to explore potential instances of confounding or collinearity among independent variables of interest. Variables speculated to be associated less strongly with the dependent variable of interest will be entered first in order to determine if the variable is associated

significantly with the dependent variable initially, and following the introduction of other independent variables. Variables that do not remain significantly associated with the dependent variable in the final step will not be considered in further logistic analyses.

The sixth and final step will involve use of fixed logistic regression models to identify variables associated independently with the dependent variables of interest. All independent variables and interaction terms found to be associated at the univariate level (at  $p < .05$ ) with the dependent variables of interest will be included in these analyses to determine the best fitting model.

## Chapter IV

### *Results*

This chapter will report the results of this study as they bear on two main research questions. The first analysis will examine determinants of antiretroviral therapy (ART) maintenance and will include a presentation of the reasons given for discontinuing ART. Maintenance refers to the sustained use of ART, and is the opposite of discontinuation, which refers to the cessation of ART. The second analysis will examine determinants of adherence to antiretroviral therapy and include a presentation of the reasons given for missing doses of ART. Adherence refers to extent to which individuals who have maintained ART have pick-up their medications as prescribed. Each analysis will include a presentation of descriptive characteristics of, and univariate associations between, independent and dependent variables. Next, a series of multiple regression analyses used to test the study hypotheses will be presented.

#### *Determinants of Antiretroviral Therapy (ART) Maintenance*

##### *Socio-demographic and Drug Use Variables*

The final sample included in this analysis involved 160 participants, of whom 91 (57%) were men and 69 (43%) were women. The mean age of the sample was 39 years (SD = 7.04), with ages ranging from 26 to 56 years. There was a high representation of Aboriginal participants in the sample, as 103 participants (64%) were Caucasian and 57 (36%) were of Aboriginal ancestry. Thirty-one participants (19%) reported having less than a grade 10 education, and 76 (48%) were living in unstable

housing at the time the survey was administered. Only 10 (6%) participants were employed, and 149 (93%) reported that they were receiving income assistance. The mean monthly income for the sample was \$1624 (SD = \$2722.31). Twenty (13%) participants reported that they had been incarcerated during the last six months. While only 21 (13%) participants reported having worked directly in the sex trade, 59 (37%) reported deriving some monthly income from the sex trade. A closer analysis revealed some gender differences with respect to sex trade involvement, with 20% of women and 7% of men reporting that they had sold sex for money in the previous 6 months. Twenty-five percent of women and 46% of men reported deriving some monthly income from the sex trade (i.e., from selling sex, or from secondary involvement such as “pimping” or renting space where sex is sold).

Participants in this sample also reported high levels of illicit drug use, although rates of risk behaviours varied. One hundred and nine (68%) participants reported smoking crack in the last six months, while 59 (37%) and 81 (51%) reported injecting heroin and cocaine respectively. Among these individuals, 49 (31%) reported smoking crack once or more daily, 27 (17%) reported injecting heroin once or more daily, and 33 (21%) reported injecting cocaine once or more daily. Only 4 participants reported borrowing a used syringe in the last six months, and 2 individuals reported lending a used syringe to another person. Nineteen participants (12%) reported that they required help when injecting, 29 (18%) reported that they had binged on drugs during the six months, and 3 participants reported that they had an accidental drug overdose. Seventy-eight participants (49%) reported that they were currently on methadone maintenance therapy.

*Efficacy Expectations, Self-regulatory Efficacy, Outcome Expectations*

The descriptive statistics for the efficacy expectation items scores are presented in Table 4. ASEM scores were missing for 24 (15%) participants in the ART Treatment Sample due to participant unwillingness to provide a response or interviewer error (e.g., failure to request that the participant complete the second portion of the VIDUS questionnaire pertaining to ART). Mean scores were calculated for the two groups (currently on ART versus discontinued ART) and used to replace all missing values. Adherence efficacy expectations were generally high for this sample. As indicated in Table 4, the mean total efficacy expectation score (with possible scores ranging from 0 to 100) for the sample was 80.03 (SD = 21.15). Scores pertaining to one's ability to manage side-effects were the lowest of the efficacy expectation scores for the sample (M = 70.55, SD = 30.23), and scores pertaining to one's ability to remember how many pills to take were highest (M = 87.61, SD = 22.81).

Table 4

*Descriptive Statistics for Self-Efficacy Expectation Items And Total Adherence Self-efficacy Scores for the ART Treatment Sample (n = 160)*

Efficacy Expectation Item	M	SD
Remember how many pills to take	87.61	22.81
Remember to pick up prescriptions	83.39	26.31
Obtain food to be taken with medications	82.86	25.25
Arrange daily activities to take medications	82.29	24.59
Remember to take medications at right time	72.91	27.81
Manage side-effects of medications	70.55	30.23
Total Adherence Self-efficacy Score	80.03	21.15

The descriptive statistics for self-regulatory efficacy and outcome expectation scores are presented in Table 5. As indicated, the mean outcome expectation score (with possible scores ranging from 0 to 100) for the sample was 57.04 (SD = 37.61), while the mean self-regulatory efficacy score (with possible scores ranging from 0 to 100) was 58.71 (SD = 34.67).

Table 5

*Descriptive Statistics for Self-regulatory Efficacy and Outcome Expectation Scores for the ART Treatment Sample (n = 160)*

	M	SD
Self-regulatory efficacy	58.71	34.67
Outcome Expectation	57.04	37.61

### ***Social Support***

The descriptive statistics for the MOS Social Support Survey scores are presented in Table 6. MOS Social Support scores were missing for 11 participants in the ART Adherence Sample for reasons noted above. Mean scores for were calculated for the two groups (currently on ART on versus discontinued ART) and used to replace all missing values. As indicated in Table 6, the mean total social support score (with possible scores ranging from 0 to 100) for the sample was 60.83 (SD = 33.51). Emotional/informational support scores were lowest for the sample (M = 58.77, SD = 33.99), and tangible support scores were the highest (M = 63.38, SD = 35.27).

Table 6

*Descriptive Statistics for Social Support Subscale and Total Social Support Scores for the ART Treatment Sample (n = 160)*

Efficacy Expectation Item	M	SD
Tangible Support	63.38	35.27
Positive Social Interaction	61.25	34.68
Affectionate Support	60.58	35.26
Emotional/Informational Support	58.77	33.99
Total Social Support	60.83	33.51

### *Univariate Analysis*

To examine associations between sociodemographic, drug use, risk behaviour variables and ART maintenance, a univariate analysis was undertaken to evaluate unadjusted associations between ART maintenance and the relevant co-variables. In total, 71 (44%) participants discontinued ART, and 89 (56%) remained on ART. Four variables (employment, syringe borrowing, lending, and accidental overdose) were excluded from further analysis due to small cell sizes. Associations between dicotomous variables were analyzed using Pearson's Chi-square test, and associations between dicotomous and continuous variables were analyzed using t-tests for independent samples.

The univariate analysis of associations between socio-demographic characteristics and ART maintenance is shown in Table 7. As shown here, older age was associated with ART maintenance (OR = 1.06, 95%CI: 1.01 – 1.11,  $p = .019$ ), and there was also a statistically significant association between stable housing status and ART maintenance (OR = 0.53, 95%CI: 0.28 – 0.99,  $p = .046$ ). There was no evidence indicating an association between ART maintenance and gender, ethnicity, and education.

Table 7

*Univariate Analyses of Socio-demographic Characteristics Stratified by  
ART Maintenance (n = 160)*

	<u>ART Maintenance</u>		OR	(95% CI)	p
	No (n = 71) n (%)	Yes (n = 89) n (%)			
Mean Age (range)	37 (24 – 55)	40 (26 – 56)	1.06	(1.01 – 1.11)	.019
Gender					
Male	41 (57.8)	50 (56.2)	1.06	(0.58 – 2.01)	.842
Female	30 (42.2)	39 (43.8)			
Ethnicity					
Caucasian	44 (61.9)	59 (66.3)	0.83	(0.43 – 1.58)	.571
Aboriginal	27 (38.1)	30 (33.7)			
Education (> grade 10)					
No	14 (19.7)	17 (19.1)	1.04	(0.47 – 2.28)	.922
Yes	57 (80.3)	72 (80.9)			
Housing					
Stable	31 (43.7)	53 (59.5)	0.53	(0.28 – 0.99)	.046
Unstable	40 (56.3)	36 (40.5)			

Table 8 displays the univariate analysis of associations between incarceration, illicit drug use, and ART maintenance. As shown here, recent incarceration was associated with ART discontinuation (OR = 0.22, 95%CI: 0.07 – 0.65,  $p = .003$ ). There was no evidence indicating an association between cocaine, heroin, or crack use and ART maintenance (all  $p > 0.05$ ).

Table 8

*Univariate Analyses of Recent Incarceration and Drug Use Stratified by  
ART Maintenance (n = 160)*

	<u>ART Maintenance</u>		OR	(95% CI)	p
	No (n = 71)	Yes (n = 89)			
	n (%)	n (%)			
<b>Recent Incarceration</b>					
No	56 (78.8)	84 (94.4)	0.22	(0.07 – 0.65)	.003
Yes	15 (21.2)	5 (5.6)			
<b>Cocaine use</b>					
No	30 (42.3)	49 (55.1)	0.59	(0.32 – 1.12)	.108
Yes	41 (57.5)	40 (44.9)			
<b>Heroin use</b>					
No	37 (52.1)	64 (71.9)	0.42	(0.22 – 1.18)	.078
Yes	34 (47.9)	25 (28.1)			
<b>Crack use</b>					
No	23 (32.4)	28 (31.5)	1.04	(0.53 – 2.03)	.901
Yes	48 (67.6)	61 (68.5)			

The univariate analysis of associations between frequent drug use and ART maintenance is displayed in Table 9. As indicated here, there was an association between frequent heroin use and ART discontinuation (OR = 0.27, 95%CI: 0.11 – 0.66,  $p = .003$ ). There was no evidence suggesting an association between frequent cocaine or crack use and ART maintenance (both  $p > 0.05$ ).

Table 9

*Univariate Analyses of Intensity of Drug Use Stratified by ART**Maintenance (n = 160)*

Illicit Drug	<u>ART Maintenance</u>		OR	(95% CI)	p
	No (n = 71) n (%)	Yes (n = 89) n (%)			
<b>Frequent Cocaine Use</b>					
< 1 per day	53 (74.6)	74 (83.1)	0.59	(0.27 – 1.29)	.187
≥ 1 per day	18 (25.4)	15 (16.9)			
<b>Frequent Heroin Use</b>					
< 1 per day	52 (73.2)	81 (91.0)	0.27	(0.11 – 0.66)	.003
≥ 1 per day	19 (26.8)	8 (9.0)			
<b>Frequent Crack Use</b>					
< 1 per day	49 (69.0)	62 (69.6)	0.97	(0.49 – 1.91)	.930
≥ 1 per day	22 (30.0)	27 (30.3)			

The univariate associations between ART maintenance and sex trade work, bingeing, requiring help injecting, and methadone use is shown in Table 10. As indicated here, there was no evidence of any association between ART maintenance and these variables ( $p > .05$ ).

Table 10

*Univariate Analyses of Sex Trade Involvement, Bingeing, Requiring Help Injecting, and Methadone Use Stratified by ART Maintenance (n = 160)*

	<u>ART Maintenance</u>		OR	(95% CI)	p
	No (n = 71)	Yes (n = 89)			
	n (%)	n (%)			
<b>Sex Trade Work</b>					
No	59 (83.1)	80 (89.9)	0.55	(0.22 – 1.39)	.206
Yes	12 (16.9)	9 (10.1)			
<b>Bingeing</b>					
No	56 (78.9)	75 (84.3)	0.69	(0.31 – 1.56)	.379
Yes	15 (21.1)	14 (15.7)			
<b>Requiring Help Injecting</b>					
No	61 (85.9)	80 (89.9)	0.68	(0.26 – 1.79)	.440
Yes	10 (14.1)	9 (10.1)			
<b>Methadone Use</b>					
No	41 (57.8)	41 (46.1)	1.60	(0.85 – 3.01)	.142
Yes	30 (42.2)	48 (53.9)			

The univariate analysis of associations between ART maintenance and efficacy expectations, self-regulatory efficacy, outcome expectation, and social support is shown in Table 11. As indicated, there was an association between efficacy expectations and ART maintenance ( $t = - 5.57, p < .001$ ), with higher efficacy expectations being associated with remaining on ART. An association between self-regulatory efficacy and ART maintenance was also found ( $t = - 4.15, p < .001$ ), with higher self-regulatory efficacy being associated with remaining on ART. There was also an observed association between outcome expectation and ART maintenance, with higher negative outcome expectations (i.e., ART will make one sicker) being negatively associated with remaining on ART ( $t = 7.25, p < .001$ ). There was no observed association between social support and ART maintenance ( $p > .05$ ).

Table 11

*Univariate Analyses of Efficacy Expectations, Self-regulatory Efficacy, Outcome Expectation, and Social Support Stratified by ART Maintenance (n = 160)*

	<u>ART Maintenance</u>		t	p
	No (n = 71)	Yes (n = 89)		
	M (SD)	M (SD)		
Efficacy Expectations	70.47 (19.6)	87.66 (19.2)	- 5.57	0.001*
Self-regulatory Efficacy	46.57 (31.4)	68.39 (34.3)	- 4.15	0.001*
Outcome Expectations	65.29 (32.9)	26.09 (34.8)	7.25	0.001*
Social Support	65.88 (31.4)	56.81 (34.7)	- 1.71	0.089

\* p < 0.001

A Pearson correlation matrix was completed to examine the relationships among independent variables. All variables found to be independently associated with ART maintenance in the previous univariate analysis ( $p < .05$ ) were included. One variable considered important in the study hypotheses, but not previously found to be significantly associated with ART maintenance, (i.e., social support) was also included. As indicated in Table 12, significant positive correlations were found between: efficacy expectations and self-regulatory efficacy ( $r = .45$ ,  $p < .01$ ) self-regulatory efficacy and age ( $r = .22$ ,  $p < .01$ ); recent incarceration and unstable housing ( $r = .17$ ,  $p < .05$ ).

Significant negative correlations were found between: efficacy expectations and frequent heroin use ( $r = -.31, p < .001$ ), age and frequent heroin use ( $r = -.31, p < .01$ ); efficacy expectations and recent incarceration ( $r = -.16, p < .05$ ); outcome expectation and age ( $r = -.18, p < .05$ ).

Table 12

Intercorrelations between Selected Independent Variables (n = 160)

	1	2	3	4	5	6	7	8
1. Efficacy expectations	-	.45**	-.15	.01	-.31**	-.16*	-.02	-.09
2. Self-regulatory efficacy		-	-.13	.12	-.14	-.04	.22**	.09
3. Outcome Expectation			-	.07	.13	.03	-.18*	.03
4. Social Support				-	.01	.05	-.21	.01
5. Frequent Heroin Use					-	.13	-.31**	.14
6. Recent Incarceration						-	-.08	.17*
7. Age							-	-.08
8. Unstable Housing								-

\*  $p < .05$  \*\* $p < .01$

### ***Multiple Regression Analysis***

All variables included in the study hypotheses and those variables found to be independently associated with ART maintenance at  $p < .05$  were included in subsequent multivariate regression analyses. For logistic models, efficacy expectations,

self-regulatory efficacy, and outcome expectation scores were transformed. Scores ranging from 0 to 100 were divided by 10 to reflect the original 10-step response scales, making adjusted odds ratios and 95% confidence intervals reflective of the expected change in adherence for each 10% increase on the respective response scales.

As a first step, independent variables considered in the study hypotheses were evaluated in pairs for potential interaction effects using fixed logistic regression models. ART maintenance was entered as the dependent variable of interest. In each model, the product of the variable pair was entered into a fixed model with its constituent variables. Significant interactions were found between efficacy expectations and frequent heroin use, and outcome expectation and recent incarceration.

The interaction effect involving efficacy expectations and frequent heroin use was first examined in a stratified analysis that considered frequent and non-frequent heroin users separately. Here, the association between efficacy expectations and maintaining ART was greater for non-frequent heroin users (OR = 1.82, 95%CI: 1.34 – 2.40,  $p < .001$ ) when compared to the entire sample (OR = 1.68, 95%CI: 1.34 – 2.11,  $p < .001$ ) and frequent heroin users (OR = 1.14, 95%CI: 0.79 – 1.64,  $p = .465$ ).

This interaction effect was then interpreted further through logistic regression analysis. The efficacy expectation variable was first transformed into a dichotomous variable using a median split. A fixed model with indicator variables representing the four categories was then constructed. The high efficacy expectation and frequent heroin use category served as the reference category, as this population was the most likely to remain on ART. As indicated in Table 13, in comparison to the reference category,

frequent heroin use in the high efficacy expectation strata did not affect the association between efficacy expectations and ART maintenance in a statistically detectable way (OR = 0.8, 95%CI: 0.09 – 7.92, p =.892). However, frequent heroin use did affect the association between efficacy expectations and ART maintenance in the low efficacy expectation strata, with the low efficacy expectation and frequent heroin indicator being the only category that differed significantly from the reference category (OR = 0.03, 95%CI: 0.01 – 0.15, p = .007). Although the difference was not statistically detectable, the effect of frequent heroin use in the high efficacy expectation strata was in the direction of increasing the likelihood of remaining on ART. However, in the low efficacy expectation strata, frequent heroin use decreased the likelihood of remaining on ART.

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Table 13

*Logistic Regression Analysis of Interactions between Efficacy Expectations and Frequent Heroin Use (n = 160)*

---

Median Efficacy Expectations	Heroin Use	AOR	(95% CI)	p
High	≥1 per day	1.00	--REF--	--REF--
High	<1 per day	0.86	(0.09 – 7.92)	.892
Low	< 1 per day	0.11	(0.01 – 1.01)	.052
Low	≥ 1 per day	0.03	(0.01 – 0.39)	.007

---

An interaction effect was also found between negative outcome expectation and recent incarceration, with the interaction term remaining significant in a logistic regression model that also considered outcome expectation and recent incarceration ( $p = .002$ ). This effect was first examined in a stratified analysis in which the association between ART maintenance was markedly different for those in jail (OR = 1.07, 95%CI: 0.83 – 1.38,  $p = .597$ ) in comparison to those out of jail (OR = 0.67, 95%CI: 0.60 – 0.77,  $p < .001$ ) or the entire sample (OR = 0.74, 95%CI: 0.67 – 0.82,  $p < .001$ ). Two contrasts were required to interpret the effect. In the first, the low negative outcome expectation and no recent incarceration category served as the reference category. As indicated in Table 14, all three interaction indicators were significantly different from the reference category ( $p < .001$ ), suggesting that outcome expectation does affect the association between incarceration and ART maintenance when recent incarceration has not occurred ( $p < .001$ ), with higher negative outcome expectation being associated with greater likelihood of ART discontinuation. In the lower half of Table 14, the high negative outcome expectation and recent incarceration category was used as the reference category. As indicated, outcome expectation did not affect the association between incarceration and ART maintenance when a recent incarceration had occurred ( $p = .796$ ).

Table 14

*Logistic Regression Analysis of Interactions between Recent Incarceration and Outcome Expectation*

Recent Incarceration	Median Outcome Expectation	AOR	(95% CI)	p
No	Low	1.00	--REF--	--REF--
No	High	0.04	(0.01 – 0.10)	.001*
Yes	Low	0.02	(0.01 – 0.14)	.001*
Yes	High	0.03	(0.01 – 0.13)	.001*
Yes	High	1.00	--REF--	--REF--
Yes	Low	0.76	(0.01 – 0.10)	.796
No	High	1.20	(0.29 – 4.95)	.778
No	Low	32.53	(6.50 – 126.72)	.001*

\* p > .001

Given the noted associations between efficacy expectations and self-regulatory efficacy, an additional sequential logistical model was used to explore the relative contribution of these variables in adjusted analyses, instances of confounding among these variables, and to evaluate which variables were independently associated with ART maintenance. Accordingly, the variable less strongly associated with ART

maintenance in previous univariate analysis (i.e., self-regulatory efficacy) was entered first. At the first step the model was significant ( $p < .001$ ), and accounted for approximately 10% of variance in ART maintenance. Self-regulatory efficacy was a significant predictor at the first step (OR = 1.21, 95%CI: 1.09 – 1.33,  $p > .001$ ). At the second step, the model was again significant ( $p < .001$ ) and accounted for 25% of variance. Efficacy expectations was a significant predictor (AOR = 1.57, 95%CI: 1.23 – 1.97,  $p < .001$ ). Self-regulatory efficacy remained marginally significant (AOR = 1.11, 95%CI: 0.99 – 1.24,  $p = .057$ ), suggesting partial confounding. However, because both variables remained significant in the model, albeit to varying degrees, both were retained in further regression analyses.

The final logistic model is presented in Table 15. Variables entered into the fixed model included: age, unstable housing, self-regulatory efficacy, efficacy expectations, frequent heroin use, a frequent heroin/efficacy expectation interaction term, outcome expectations, recent incarceration, and an outcome expectation/recent incarceration interaction term. The final model was significant ( $p < .001$ ), and accounted for 60.2% of variance. As indicated in Table 15, self-regulatory efficacy remained significant (AOR = 1.22, 95%CI: 1.03 – 1.44,  $p = .020$ ), as did efficacy expectations (AOR = 1.55, 95%CI: 1.17 – 2.06,  $p = .002$ ). Outcome expectations entered the model as significant at this step (AOR = 0.64, 95%CI: 0.54 – 0.74,  $p < .001$ ), as did recent incarceration (AOR = 0.03, 0.01 – 0.23,  $p = .001$ ). The outcome expectation/recent incarceration interaction term was also significant (AOR = 1.05, 95%CI: 1.01 – 1.08,  $p = .004$ ).

Table 15

*Logistic Regression Analysis of Factors Associated with ART Maintenance*

	AOR	(95% CI)	p
Self-regulatory Efficacy	1.22	(1.03 – 1.44)	.020
Efficacy Expectations	1.55	(1.17 – 2.06)	.002
Outcome Expectation	0.64	(0.54 – 0.74)	.001*
Recent Incarceration	0.03	(0.01 - 0.23)	.001

\* p &lt; .001

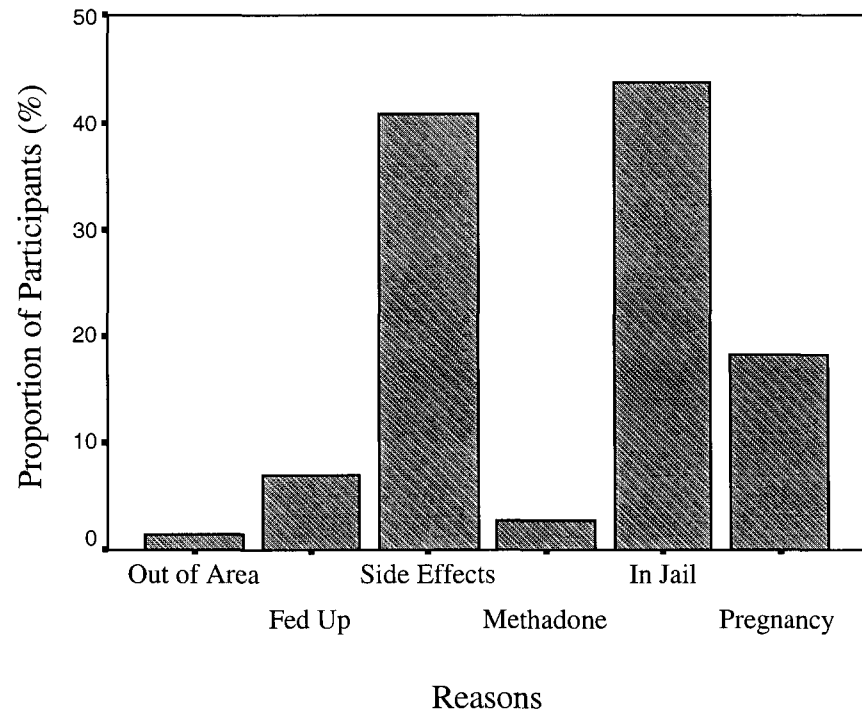
Note: Model was adjusted for interactions between efficacy expectations and frequent heroin use, and outcome expectation and recent incarceration.

***Reasons for Discontinuing ART***

To further examine ART discontinuation, reasons given for discontinuing ART were examined. As indicated in Figure 1, the most commonly cited reason for discontinuing ART was being in jail, with 43.7% of participants citing this reason. The second most commonly given reason for discontinuing ART was problems with side-effects, with 40.8% of participants citing this as a reason. Eighteen percent of participants said they discontinued ART after becoming pregnant. Less commonly cited reasons for discontinuing ART include being “fed up” (7%), “out of the area” (1.4%), and experiencing pharmacologic interaction with methadone (2.8%).

Figure 1

*Reasons for Discontinuing ART (n = 71)*



## *Determinants of Adherence to Antiretroviral Therapy (ART)*

### *Socio-demographic and Drug Use Variables*

The second sample included in this analysis involved 108 participants, of whom 59 (55%) were men and 49 (45%) were women. The mean age of the sample was 39 years (7.07), with ages ranging from 26 to 56 years. There was a high representation of Aboriginal participants in the sample, as 71 participants (66%) were Caucasian and 37 (34%) were of Aboriginal ancestry. Twenty-one participants (19%) reported having less than a grade 10 education, and 65 (60%) were living in unstable housing at the time the survey was administered. Only 9 (8%) participants were employed, and 102 (94%) reported that they were receiving income assistance. The mean monthly income for the sample was \$1622 (SD = \$2940). Seven (6%) participants reported that they had been incarcerated during the last six months, and while 11 (10%) participants reported working in the sex trade, 38 (35%) reported deriving some monthly income from the sex trade. A closer analysis again revealed some gender differences with respect to sex trade involvement, with 14% of women and 7% of men reporting having sold sex for drugs in the previous 6 months. Twenty-six percent of women and 42% of men reported deriving some monthly income from the sex trade (i.e., from selling sex, from secondary involvement such as “pimping” or renting space where sex is sold).

Participants in this sample also reported high levels of illicit drug use, although rates of related risk behaviours varied. Sixty-eight participants (63%) reported smoking crack in the last six months, while 32 (30%) and 52 (48%) reported injecting heroin and cocaine respectively. Among these individuals, 30 (28%) reported smoking crack once or more daily, 11 (10%) reported injecting heroin once or more daily, and 18 (17%)

reported injecting cocaine once or more daily. Only two participants reported borrowing a used syringe in the last six months, and one individual reported lending a used syringe to another person. Twelve participants (11%) reported that they required help when injecting, 18 (17%) reported that they had binged on drugs during the six months, and 3 participants reported that they had an accidental drug overdose. Fifty-nine participants (55%) reported that they were currently on methadone maintenance therapy.

***Efficacy Expectations, Self-regulatory Efficacy, Outcome Expectations***

The descriptive statistics for the efficacy expectation items scores are presented in Table 16. ASEM cores were missing for 14 participants in the ART Adherence Sample due to participant unwillingness to provide a response or interviewer error. All missing values were replaced with sample mean scores to maintain adequate sample size. Adherence efficacy expectations were generally high for this sample. As indicated in Table 16, the mean total adherence efficacy expectation score (with possible scores ranging from 0 to 100) for the sample was 85.36 (SD = 19.35). Efficacy expectations pertaining to one's ability to manage side-effects were lowest for this sample (M = 78.49, SD = 27.68), and expectations pertaining to one's ability to remember how many pills to take were highest (M = 92.11, SD = 19.90).

Table 16

*Descriptive Statistics for Self-Efficacy Expectation Items And Total Adherence Self-efficacy Scores for the ART Adherence Sample (n = 108)*

Efficacy Expectation Item	M	SD
Remember how many pills to take	92.11	19.90
Remember to pick up prescriptions	90.32	22.77
Arrange daily activities to take medications	85.81	23.65
Obtain food to be taken with medications	85.59	24.48
Remember to take medications at right time	79.84	24.75
Manage side-effects of medications	78.49	27.68
Total Adherence Self-efficacy Score	85.36	19.36

The descriptive statistics for self-regulatory efficacy and outcome expectation scores are presented in Table 17. As indicated there, the mean outcome expectation score (with possible scores ranging from 0 to 100) for the sample was 61.27 (SD = 38.89), while the mean self-regulatory efficacy score (with possible scores ranging from 0 to 100) was 65.15 (SD = 33.74).

Table 17

*Descriptive Statistics for Self-regulatory Efficacy and Outcome Expectation Scores for the ART Adherence Sample (n = 108)*

	M	SD
Self-regulatory Efficacy	65.15	33.74
Outcome Expectation	61.27	38.89

### ***Social Support***

The descriptive statistics for the MOS Social Support Survey scores are presented in Table 18. MOS Social Support scores were missing for 9 participants in the ART Adherence Sample for reasons noted above, and all missing values were replaced with sample mean scores. As indicated in Table 18, the mean total social support score (with possible scores ranging from 0 to 100) for the sample was 59.09 (SD = 26.75). Emotional/informational support scores were lowest among participants (M = 57.73, SD = 34.17), and tangible support scores were highest (M = 61.55, SD = 35.42).

Table 18

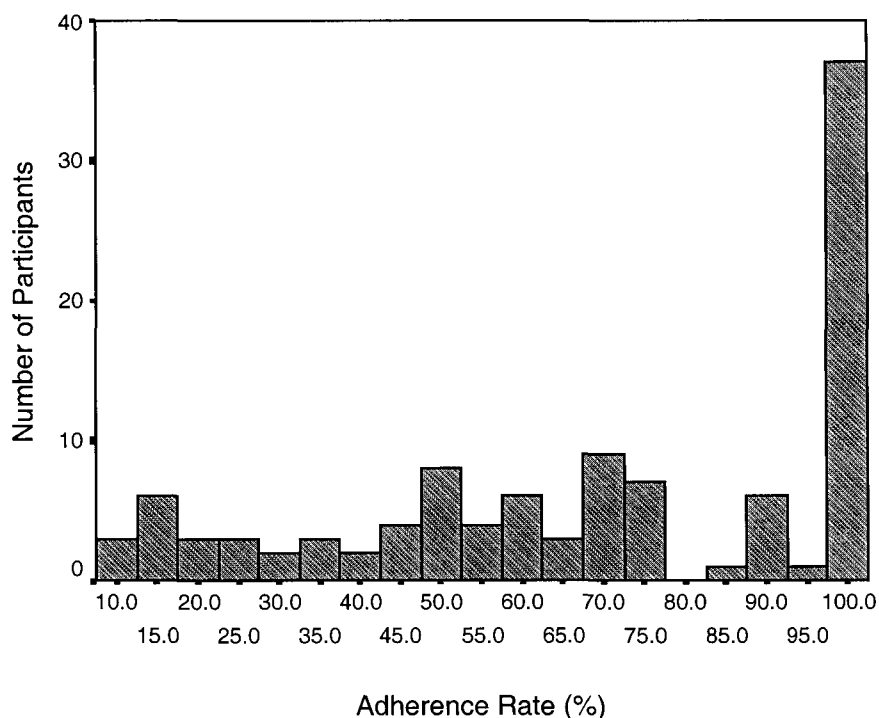
*Descriptive Statistics for Social Support Subscale and Total Scores for the ART Adherence Sample (n = 108)*

Efficacy Expectation Item	M	SD
Tangible Support	61.55	35.42
Affectionate Support	61.12	35.92
Positive Social Interaction	59.67	35.09
Emotional/Informational Support	57.73	34.17
Total Social Support	59.09	26.75

### ***Pharmacy-based Adherence***

Pharmacy-based adherence scores were generally quite high within the sample, with 32% of participants having an adherence score of 100 (i.e., they picked up 100% of all prescription refills). When considered as continuous variable, the mean adherence score was 68.46 (SD = 29.88), and the median score was 69.75. Figure 2 displays the distribution of adherence scores for ART Adherence Sample.

Figure 2

*Pharmacy-based Adherence Rates of ART Adherence Sample*

Given the non-normal distribution of adherence scores, with a natural break point at 95%, a dichotomous adherence variable was used in logistic regression analyses. The decision to use this dicotomy was based on the distribution of the data, shown above, as well as the substantial literature demonstrating that 95% adherence to ART may be required for several measures of clinical response (Low-Beer et al., 2000; Lucas et al., 2001). In total, 71 (65.7%) of participants had adherence scores less than 95%, and 37 (34.3 %) had scores of 95% or greater

***Univariate Analysis***

To examine associations between sociodemographic, drug use, risk behaviour, and adherence variables, a univariate analysis was undertaken to evaluate unadjusted associations between adherence and the relevant co-variates. Four variables

(employment, syringe borrowing, lending, and accidental overdose) were excluded from this analysis due to small cell sizes. Associations between dicotomous variables were analyzed using Pearson's Chi-square test, and associations between dicotomous and continuous variables were analyzed using t-tests for independent samples.

The univariate analysis of associations between socio-demographic characteristics and adherence is shown in Table 19. As shown here, there was no evidence indicating an association between adherence and gender, ethnicity, education, and unstable housing.

Table 19

*Univariate Analyses of Socio-demographic Characteristics Stratified by Adherence Rate*

	<u>Adherence Rate</u>		OR	(95% CI)	p
	< 95% (n = 71)	>95% (n = 37)			
	n (%)	n (%)			
<b>Gender</b>					
Male	40 (56.3)	19 (51.3)	1.22	(0.55 – 2.71)	.621
Female	31 (43.7)	18 (48.7)			
<b>Ethnicity</b>					
Caucasian	49 (69.1)	22 (59.5)	1.52	(0.66 – 3.47)	.321
Aboriginal	22 (30.9)	15 (40.5)			
<b>Education (&gt; grade 10)</b>					
No	14 (19.7)	7 (18.9)	1.05	(0.4 – 2.9)	.921
Yes	57 (80.3)	30 (81.1)			
<b>Housing</b>					
Stable	41 (57.7)	24 (64.9)	0.74	(0.33 – 1.68)	.473
Unstable	30 (42.3)	13 (35.1)			

Table 20 displays the univariate analysis of associations between incarceration, illicit drug use, and adherence. As shown here, evidence of an association was found between heroin use in the previous six months and adherence, with heroin use tending

to be associated with lower adherence. This association did not, however, meet conventional significance (OR = 0.43, 95% CI: 0.16 – 1.12,  $p = 0.078$ ). There was no evidence indicating an association between incarceration, cocaine use, or crack use and adherence (all  $p > 0.1$ ).

Table 20

*Univariate Analyses of Recent Incarceration and Drug Use Stratified by Adherence Rate*

	<u>Adherence Rate</u>		OR	(95% CI)	p
	< 95% (n = 71)	>95% (n = 37)			
	n (%)	n (%)			
<b>Recent Incarceration</b>					
No	67 (66.3)	34 (57.1)	1.47	(0.31 – 6.98)	.621
Yes	4 (43.7)	3 (42.9)			
<b>Cocaine use</b>					
No	33 (46.5)	23 (62.2)	0.53	(0.23 – 1.19)	.122
Yes	38 (53.5)	14 (37.8)			
<b>Heroin use</b>					
No	46 (64.7)	30 (81.1)	0.43	(0.16 – 1.12)	.078
Yes	25 (35.3)	7 (18.9)			
<b>Crack use</b>					
No	23 (32.3)	17 (45.9)	0.56	(0.25 – 1.27)	.166
Yes	48 (67.6)	20 (54.1)			

The univariate analysis of associations between frequent drug use and adherence is displayed in Table 21. As indicated here, there tended to be an association between frequent heroin use, with frequent heroin use being associated with lower adherence. However, this association also did not reach conventional significance (OR = 0.17, 95% CI: 0.21 – 1.37; p = 0.063). There was no evidence suggesting an association between frequent cocaine or crack use and adherence.

Table 21

*Univariate Analyses of Intensity of Drug Use Stratified by Adherence Rate*

Illicit Drug	<u>Adherence Rate</u>		OR	(95% CI)	p
	< 95% (n = 71)	>95% (n = 37)			
	n (%)	n (%)			
<b>Frequent Cocaine Use</b>					
< 1 per day	57 (80.5)	33 (62.0)	0.49	(0.15 – 1.62)	.238
≥ 1 per day	14 (19.5)	4 (38.0)			
<b>Frequent Heroin Use</b>					
< 1 per day	61 (80.5)	36 (62.0)	0.17	(0.21 – 1.37)	.063
≥ 1 per day	10 (19.5)	1 (38.0)			
<b>Frequent Crack Use</b>					
< 1 per day	50 (80.5)	28 (62.0)	0.76	(0.31 – 1.89)	.563
≥ 1 per day	21 (19.5)	9 (38.0)			

The univariate associations between adherence and sex trade work, bingeing, requiring help injecting, and methadone use is shown in Table 22. As indicated here, there was no evidence of any association between adherence and these variables.

Table 22

*Univariate Analyses of Sex Trade Involvement, Bingeing, Requiring Help Injecting, and Methadone Use Stratified by Adherence Rate*

	<u>Adherence Rate</u>		OR	(95% CI)	p
	< 95% (n = 71)	>95% (n = 37)			
	n (%)	n (%)			
<b>Sex Trade Work</b>					
No	63 (66.3)	34 (57.1)	0.69	(0.17 – 2.79)	.606
Yes	8 (43.7)	3 (42.9)			
<b>Bingeing</b>					
No	58 (46.5)	32 (62.2)	0.69	(0.23 – 2.13)	.526
Yes	13 (53.5)	5 (37.8)			
<b>Requiring Help Injecting</b>					
No	62 (64.7)	34 (81.1)	0.61	(0.15 – 2.39)	.473
Yes	9 (35.3)	3 (18.9)			
<b>Methadone Use</b>					
No	35 (32.3)	14 (45.9)	1.59	(0.71 – 3.59)	.256
Yes	36 (67.6)	23 (54.1)			

The univariate analysis of associations between adherence and efficacy expectations, self-regulatory efficacy, outcome expectation, and social support is shown in Table 23. As indicated, there was an association between efficacy expectations and adherence ( $t = -3.68$ ,  $p < 0.001$ ), with higher efficacy expectations being associated with greater adherence. An association between self-regulatory efficacy and adherence was also found, with higher self-regulatory efficacy being associated with greater adherence rates ( $t = -2.39$ ,  $p = 0.019$ ). There was also an observed association between outcome expectation and adherence, with higher negative outcome expectations (i.e., ART will make one sicker) being associated with lower adherence ( $t = 2.74$ ,  $p = 0.007$ ). There was no observed association between social support and adherence.

Table 23

*Univariate Analyses of Efficacy Expectations, Self-regulatory Efficacy, Outcome Expectation, and Social Support Stratified by Adherence Rate*

	<u>Adherence Rate</u>		t	p
	< 95% M (SD)	>95% M (SD)		
Efficacy Expectations	81.49 (21.8)	92.78 (10.0)	- 3.68	0.001*
Self-regulatory Efficacy	59.68 (33.8)	75.68 (32.3)	- 2.39	0.019
Outcome Expectations	44.17 (37.8)	23.22 (37.1)	2.74	0.007
Social Support	57.34 (26.5)	62.45 (27.2)	- 9.41	0.349

\*  $p < .001$

A Pearson correlation matrix was completed to examine the relationships between selected independent variables. All variables found to be independently associated with adherence in the previous univariate analysis ( $p < .05$ ) were included. Three variables considered important in the study hypotheses, but not previously found to be significantly associated with adherence, (i.e., recent incarceration, frequent heroin use, and social support) were also included. Adherence scores were entered as continuous raw scores. As indicated in Table 24, there was a significant positive correlation between efficacy expectations and self-regulatory efficacy ( $r = .38, p < .01$ ), and a significant negative correlation between efficacy expectations and frequent heroin use ( $r = -.28, p < .01$ ).

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Table 24

*Intercorrelations between Selected Independent Variables (n = 108)*

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	1	2	3	4	5	6
1. Efficacy expectations	-	.38**	-.09	-.28*	-.04	-.09
2. Self-regulatory efficacy		-	-.07	-.12	-.16	-.17
3. Outcome Expectations			-	.18	.15	-.07
4. Frequent Heroin Use				-	-.09	-.01
5. Recent Incarceration					-	.07
6. Social Support						-

---

\*  $p < .05$  \*\* $p < .01$

### ***Multiple Regression Analysis***

All variables included in the study hypotheses and those variables found to be independently associated with adherence at  $p < .05$  were included in subsequent multivariate regression analyses. For logistic models, efficacy expectations, self-regulatory efficacy, and outcome expectation scores were transformed. As above, scores ranging from 0 to 100 were divided by 10 to reflect the original 10-step response scales, making adjusted odds ratios and 95% confidence intervals reflective of the expected change in adherence for each 10% increase on the respective response scales.

As a first step, independent variables considered in the study hypotheses were evaluated in pairs for potential interaction effects using sequential logistic regression models. Adherence (<95% adherence vs. >95% adherence) was entered as the dependent variable of interest. In each model, the product of the variable pair was entered first as an interaction term, and was followed by each of the variables included in the pair (in separate blocks). Individual blocks were then examined to determine the contribution made to the model at each step. All interaction terms examined failed to reach statistical significance at  $p < .05$ .

Given the noted associations between efficacy expectations, self-regulatory efficacy, and outcome expectations, three additional sequential logistical models were used to explore potential confounding among these variables and to evaluate which variables were independently associated with adherence when adjusted for other psychological measures. Each model contained one pair of variables (e.g., efficacy expectations/self-regulatory efficacy, efficacy expectations/ outcome expectations, self-regulatory efficacy/outcome expectation). In order to explore the relative contribution

of these variables in adjusted analyses and instances of confounding, variables less strongly associated with adherence were entered first. In one model, self-regulatory efficacy was entered in a block ahead of efficacy expectations. The model was statistically significant at the first step ( $p = .016$ ), accounting for 7.3% of variance in adherence, with self-regulatory efficacy remaining a significant predictor (AOR = 1.17, 95%CI: 1.02 – 1.34,  $p = .022$ ). The model was statistically significant at the second step ( $p = .001$ ), accounting for 17.6% of variance in adherence, with efficacy expectations entering as a significant predictor (AOR = 1.83, 95%CI: 1.12 – 3.01,  $p = .016$ ). However, self-regulatory efficacy did not remain statistically at the second step after adjusted for efficacy expectations. (AOR = 1.09, 95%CI: 0.95 – 1.26,  $p = .204$ ). No other instances of confounding between independent variables were observed.

Inspection of distributions of self-regulatory efficacy and efficacy expectation scores suggested a high degree of colinearity between the variables, and the statistical association between variables was noted in earlier analyses. Together, these observations suggested that the association between self-regulatory efficacy and adherence observed in univariate analyses, was a result of partial confounding, and that efficacy expectations was the independent predictor of adherence. As a result, self-regulatory efficacy was not included in further multivariate analyses. Although frequent heroin use did not meet conventional significance at the univariate level ( $p = .06$ ), it was included in the final model due to its potential to adjust for residual confounding as a result of drug using behavior. As hypothesized, it was anticipated that frequent heroin use is a behavioural marker that may mediate efficacy expectations and outcome expectations.

The final logistic model is presented in Table 25. Variables entered in the fixed model included: frequent heroin use, efficacy expectations, outcome expectations. The final model was again significant and accounted for 22.4% of variance in adherence. As indicated in Table 25, efficacy-expectations were significantly associated with adherence (AOR = 1.74, 95%CI: 1.07 – 2.83, p = .025), as was outcome expectations (AOR = 0.87, 95%CI: 0.78 – 0.99, p = .036). Frequent heroin use was not significantly associated with adherence (AOR = 0.37, 95%CI: 0.04 - 3.35, p = .376).

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Table 25

*Logistic Regression Analysis of Factors Associated with Adherence*

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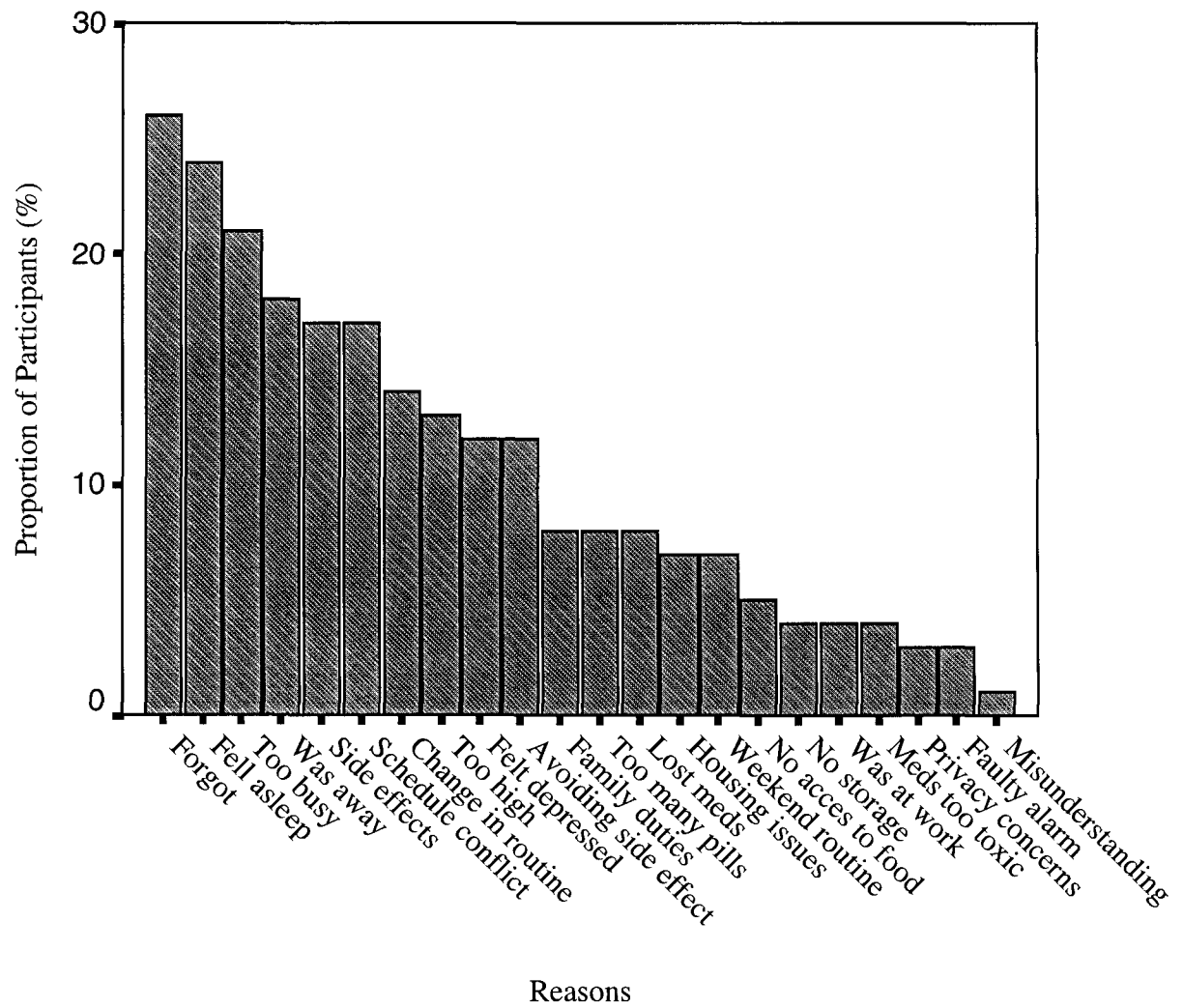
	AOR	(95% CI)	p
Efficacy Expectations	1.74	(1.07 – 2.83)	.025
Outcome Expectation	0.87	(0.78 – 0.99)	.036
Frequent Heroin Use	0.38	(0.04 - 3.35)	.376

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### *Reasons for Missing Doses*

To further explore issues of adherence to ART, participant ratings of reasons for missed doses were analyzed. Figure 3 shows the various reasons for missing doses, and the percentage of participants reporting that the reasons were “sometimes” or “often” a factor when they missed doses of ART. As indicated there, the most commonly cited reason for missing doses was “simply forgot”; with 27% of participants reporting that this sometimes or often was a reason for missing doses. Sleeping through doses was cited a reason for missing doses by 24% of participants, while being too “busy with other things” was reported by 21% of participants. Being away from home was reported as a reason for missing doses by 18% of participants, and 17% cited side-effects and problems with dose schedules as a problem. Fourteen percent of participants said they missed doses because of a change in routine and 13% said they missed doses because they were “too high”. Twelve percent of participants cited being too depressed and avoiding side-effects as reasons for missing doses. Less commonly cited reasons (cited by less than 10% of participants) included: “too many pills to take”; family responsibilities; lost medications; change on weekends; housing problems; access to food; no safe place to store medications; was at work; problem with an alarm; concerns about privacy (e.g., others noticing medication consumption); and toxicity. The least commonly cited reason for missing doses of ART was misunderstanding prescription instructions.

Figure 3

*Reasons for Missing Doses of ART*

## Chapter V

### General Discussion

This chapter will review the substantive findings of the study, and will begin with descriptive information concerning the dependent variables of interest, ART maintenance and adherence. Because these variables are related, the discussion will then examine the independent variables of interest and their relationship to the dependent variables. The chapter will also include a discussion of the limitations of the study, the implications of the findings for theory, practice, and future research.

#### *Summary and Integration of Results*

One substantive finding of this study is that discontinuation of ART was very common. Forty-four percent of the participants who initiated ART had discontinued treatment. This is consistent with the findings of Demas et al. (1998) and Palepu et al. (2001b) who found that only half of the HIV-positive IDU participating in studies of ART adherence had remained on the treatment. These high rates of discontinuation could be partially explained by the fact that the present and aforementioned studies involved samples consisting solely of IDU. For instance, one recent study investigating ART discontinuation with a mixed sample of HIV-positive patients found lower rates of discontinuation overall (32%), and that injection drug use was predictive of ART discontinuation (Roca et al., 1999).

Another substantive finding concerns the observed rates of pharmacy-based adherence. As in other studies of ART adherence, adherence scores in the present study tended to be quite high (Meichenbaum & Turk; Moatti et al., 2000), with a substantial number of participants (32%) having adherence scores of 100%. The high proportion of

participants with this level adherence is consistent with several other studies (Altice, 2001; Carrieri et al., 2001; Demas et al., 1998; Gifford et al., 2000) including those using pharmacy-based measures (Low-Beer et al., 2000). This high level of adherence may be partially explained by current prescribing practices. When ART is prescribed and dispensed, physicians, pharmacists and other care-providers emphasize greatly the importance of adherence and the likelihood of drug-resistant strains of HIV developing if patients fail to adhere. When these issues are presented simultaneously, the sum message to patients is that they should take all of their ART or none at all.

The other factor that may explain the rates of adherence is the method employed to measure adherence. Pharmacy-based adherence measures have been found to be predictive of virologic outcome and survival (Low-Beer, 2000; Wood et al., in press). However, like other adherence measures currently in use, this method measures only one aspect of adherence behaviour (Chesney et al., 2000; Friedland & Williams, 1999). Information concerning compliance to daily medication-quantity, medication-interval, and medication-diet adherence cannot be discerned from this form of measurement. Nevertheless, it is reasonable to assume that many individuals who pick up their prescriptions do not consume all their medications, and therefore this method may overestimate actual adherence. Evidence of this was found by Altice et al. (2001) who reported a strong correlation between a pharmacy-based measure of adherence and a more “subjective” measure of self-reported adherence – another method known to overestimate adherence (Lui et al., 2001). Comparisons of multiple methods of adherence have concluded that pharmacy-based adherence measurement tends to

produce higher adherence scores than other “objective” methods of adherence measurement such as pill counts and electronic monitoring systems (Lui et al., 2001).

The predictive validity associated with pharmacy-refill adherence is surprising. This rather narrow measure of adherence behaviour has produced relatively strong linear associations with virologic outcomes (Low-Beer, 2000). While the data presented here cannot be used to explain this relationship, it could be argued that there is considerable systematic error associated with pharmacy-based measures of adherence. It may be that this method consistently overestimates adherence across adherence strata. As for the issue of the level of pharmacy-based adherence required to suppress viral load, previous studies have suggested that greater than 95% adherence is required or the likelihood of achieving viral load suppression precipitously declines. However, it may be that these drugs are in fact much more potent than originally believed, and that lower levels of exposure may in fact be adequate for viral suppression.

Other substantive findings are related to the first study hypothesis, and concern the associations between recent incarceration, ART maintenance and adherence. Consistent with the first study hypothesis, being incarcerated was associated with discontinuing ART. This finding was further supported by participants' self-reported reasons for discontinuing ART, as 43% of those who had discontinued ART cited being in jail as a reason for discontinuing. This finding is also consistent with a previous study by Palepu et al. (2001b) who found that recent incarceration was associated with treatment interruption among IDU. As well, a recent study by Altice et al. (2001) examining acceptance and adherence to ART found that 62% of HIV-positive prisoners who had once been on ART had discontinued the therapy.

Recent incarceration was associated with ART discontinuation, however, there was no association between recent incarceration and adherence in the present study. This is inconsistent with the first study hypothesis that stated that recent incarceration would be associated with a failure to adhere to ART. While this appears to suggest that those who maintain ART in prison or following their incarceration are likely to adhere to ART, it is critical to note that the lack of an observed association between incarceration and ART adherence may be a reflection of small sample size, as only 7 individuals in the ART Adherence Sample reported having been incarcerated in the past six months.

The present study reveals only an association between incarceration in the past six months and ART discontinuation. Whether ART has been discontinued prior to, during, or following incarceration is unclear. However, given that jail was given as the most common reason for discontinuing ART, it is likely that ART is being discontinued while participants are in jail, not after they are released. Despite this finding, it has been reported that prison-based health-care programs go to great lengths to provide prisoners living with HIV/AIDS with optimal medical care (Jurgens, 1996). This is reinforced by the *Corrections and Conditional Release Act* requires that prisons provide inmates with essential health-care that conforms to professional standards (Jurgens, 1996). Consequently, there are several possible explanations for the observed finding.

One possible explanation may relate to the structure and routine of prisons that make continuing ART challenging. As de Bruyn (1998) has noted:

The regime that is stipulated for a particular combination of drugs  
– ingestion at specific intervals, with or without food – is not

followed in prison, because it does not fit in with the prison routine. Prisoners routinely miss medications when they go to court, when they are transferred, or when they are released; contingency plans that are customary to ensure that inmates with tuberculosis or diabetes receive their medication are, apparently, not made for prisoners with HIV/AIDS. (p. 71)

Given this explanation, it would be expected that incarceration would also be associated with nonadherence. However, while barriers in prison may make regular consumption of medications difficult, the method of adherence measurement used in the present study provides only an estimate of whether prescriptions have been picked up. Prison health-care services may be efficient at obtaining medications, but may not be efficient in ensuring that medications are consumed on the proper schedule. This subtlety could not be captured by the current study.

A second, and more plausible explanation for the association between ART discontinuation and incarceration may concern HIV/AIDS-related discrimination experienced with prison systems. Many prisoners may avoid taking their ART medications in prison in an effort to conceal their HIV positive status. It is well known that disclosure of HIV positive status can result in significant negative consequences (e.g., intimidation, violence) for prisoners (deBruyn, 1998), and HIV-positive prisoners have been known to voluntarily enter protective custody to ensure their safety (Jurgens, 1996). The potential for HIV-related discrimination was highlighted by a study of provincial and federal prisons in Ontario that found that one third of prisoners reported avoiding or scaring off people with HIV/AIDS as a means of protecting themselves

from becoming infected with the virus (Calzavara et al., 1997; cited in de Bruyn, 1998). Unfortunately, keeping one's HIV status a secret in prison is difficult as the Expert Committee on AIDS and Prisons (1994) noted: "Little goes on in prisons that is not almost immediately known by almost all inmates and staff, and it has been said that when an HIV-positive person is in prison, her or his health status is usually circulated among both correctional officers and inmates" (p. 7).

Other substantive findings of the study are related to the second study hypothesis, and concern the associations between outcome expectancies, ART maintenance and adherence. Outcome expectations have been defined as judgements about the consequences produced by specific behaviours (O'Leary, 1985). The specific outcome expectation explored in this study focused on participants' beliefs that taking ART would make them sicker. The results indicate that participants with high negative outcome expectations are more likely to discontinue or fail to adhere to ART. This finding is consistent with the second study hypothesis, as well as the results of other studies examining similar beliefs. For example, Altice et al. (2001) found that mistrust in ART medication was an independent predictor of a failure to accept ART among prisoners. Mistrust in this case was measured by asking participants to rate the extent to which they "felt most friends who took HIV medication were made worse" (p.54). In another study of ART acceptance and adherence, Demas et al., (1998) found that the negative beliefs about ART side-effects were negatively associated with treatment duration. In this earlier study, the survey items specific to ART side-effects asked participants to rate to the extent to which they believed that ART made people sick with side-effects, and harmed one's blood and liver.

The concerns of participants noted in the present study regarding the adverse effects of ART may seem surprising in light of the observed efficacy of the drugs and the fatal consequences associated with HIV/AIDS. However, side-effects associated with ART are numerous, and often quite disabling (Rabkin & Chesney, 2000). Both qualitative and quantitative investigations have found side-effects to be associated with ART discontinuation and adherence (Gifford et al., 1999; Johnston-Roberts and Mann, 2000; Moatti et al., 2000). Outcome expectations are said to result from observed conditional relations between specific events and the outcomes given actions produce (Bandura, 1986). As Bandura (2001a) has noted, “in regulating their behavior by outcome expectations, people adopt courses of action that are likely to produce positive outcomes and generally discard those that bring unrewarding or punishing outcomes” (p.7). While the side-effects associated with ART are often experienced early in the therapy, the clinical benefits are rarely felt or observed in the short term unless the patient is symptomatic. When individuals taking ART experience side-effects in absence of observable clinical benefits, they may elect to discontinue ART. Participants in this study did in fact identify side-effects as one of the most common reasons for discontinuing ART. As well, when side-effects are experienced, individuals may maintain ART, but skip doses in an attempt to reduce toxicity (Heath et al., 2002). Alternatively, they may choose not to pick up their prescription refills until side-effects have subsided and HIV-related illness again becomes a pressing concern. Many participants in this study did in fact report that they missed doses of ART due to “being too sick with side-effects” and because they were attempting to “avoid side-effects.”

Other substantial findings are related to third study hypothesis, and concern the associations between efficacy expectations and ART maintenance and adherence. Participants with high adherence efficacy expectations were more likely to maintain and adhere to ART. Efficacy expectations in the present study related to specific behaviours required to maintain and adhere to ART. Participants were asked to rate their confidence in their ability to: remember to take medications at right time, remember how many pills to take, obtain food to be taken with medications, manage side-effects of medications, remember to pick up prescriptions, and arrange daily activities to take medications. These findings are consistent with all other known studies of ART maintenance and adherence that have included efficacy expectation variables (Gifford et al., 2000; Kalichman et al., 2001; Tuldra et al., 2001). However, the exact dimensions of adherence self-efficacy examined have varied considerably from study to study, with some studies assessing global adherence self-efficacy and others examining a subset of adherence behaviours.

It has been argued that no element of personal agency has more pervasive influence than beliefs concerning one's ability to exercise control over their own functioning (Bandura, 1997). In light of what is known about efficacy expectations, it is likely that efficacy expectations examined in the present study have similar effects on both ART maintenance and adherence. It has been pointed out previously (Bandura, 1997; O'Leary, 1985; Skinner, 1996), that efficacy expectations determine choice, effort, and persistence. In the case of ART maintenance and adherence, efficacy expectations likely mediate behaviour in several ways. First, because self-assessments of efficacy determine choices, decisions to initiate or continue taking a medication will

be mediated by self-efficacy. High efficacy expectations will also affect choice as it applies to other behaviours directly and indirectly related to adherence, such as the choice to refill prescriptions, action to manage side-effects, and obtaining required food. Second, efficacy expectations influence the amount of effort exerted in the face of challenges, and therefore will affect individual persistence in the face of medication side-effects and other challenges including incarceration, conflicting daily routines, concerns regarding privacy and discrimination.

Other substantive findings relate to the fourth study hypothesis, and concern the association between self-regulatory efficacy and ART maintenance and adherence. Self-regulatory efficacy was independently associated with ART maintenance but not ART adherence. Individuals with higher self-regulatory efficacy were more likely to maintain ART. The specific dimensions of self-regulatory efficacy examined were beliefs concerning one's ability to take ART as prescribed when using drugs, or when experiencing withdrawal from drugs (e.g., when "dopesick"). The ability to self-regulate has been previously associated with a variety of health promoting behaviours (Bandura, 2001a).

While self-regulatory efficacy was associated with ART adherence in the univariate analysis, it did not remain an independent predictor of adherence after adjusting for efficacy expectations and outcome expectations. This may be explained partially by confounding, as self-regulatory efficacy was found to be strongly correlated with efficacy expectations. However, it may simply be that the impact of self-regulatory efficacy, as it relates to drug use and withdrawal, may be greater for ART maintenance than adherence. It may be that some individuals make judgments about the

potential impact of their drug use on ART maintenance, as well as their inability to manage these impacts, and elect to discontinue ART. As Bandura (2001a) has pointed out, poor self-regulators often fail to expand their knowledge and cognitive competencies, and by consequence they may be depriving themselves of the opportunity to develop skills needed to maintain ART. Given the lack of an observed association between frequent drug use and ART maintenance and adherence in the present study, the perceived impact of drug use on ART maintenance and adherence may well be overestimated in these cases.

Other substantive findings relate to the fifth study hypothesis, and concern the relationships between social support, ART maintenance and adherence. The findings of this study suggest that social support was not associated with ART maintenance and adherence. Social support was assessed by asking participants to rate the extent to which various forms of support were available to them. These findings are inconsistent with previous findings that found social support to be associated with ART maintenance and adherence and a host of other positive health-related outcomes (Altice, 2001; Singh, 1999). Social support is believed to affect ART maintenance and adherence behaviours both directly (e.g., encouragement, systemic cues, positive reinforcements), and indirectly by buffering the adverse effects of negative events, emotional and cognitive states (Friedland, Renwick, & McColl, 1996; Singh et al., 1999). There are two possible explanations for the findings pertaining to social support. First, the effects of social support on adherence have been found to be mediated by depression. While both Gordillo et al. (1999) and Singh et al. (1996) were able to find univariate associations between adherence and social support, further multivariate

analyses revealed that social support was not an independent predictor of adherence after adjusting for depression. In the Gordillo et al. (1999) study, an interaction effect between depression was found and interpreted. The results indicated that social support was predictive of adherence only in the absence of depression. Given that high rates of psychopathology, including incidence of depression, have been observed previously in IDU populations, it is possible that the effect of social support on ART maintenance and adherence was confounded by the prevalence of depression (Rabkin et al., 1997).

The second explanation for the lack of association between social support and ART maintenance and adherence may also relate to the support networks of participants and the specific context of the Vancouver's Downtown Eastside (the location where most participants live). While much has been made about the positive effects of social networks, there is also evidence indicating that social networks can have negative effects, particularly within the context of HIV/AIDS (King, 1989, Igram et al, 1999). In fact, a recent study by Igram et al. (1999) found that negative social interactions accounted for a substantial portion of the variance in depression; a relevant finding given the aforementioned relationships between social support, depression, and adherence. Previous research has also indicated that IDU tend to rely primarily on other IDU for social support (Stowe et al, 1993). While it has been also been found that IDU do exercise concern for the health of others (McKeganey, Friedman & Mesquita, 1998), it is possible that the people providing support to participants in this study are also the people with whom they inject drugs. Injection of illicit drugs has been shown to be highly socially contextualized, and many of the most risky of injecting practices (e.g., sharing syringes, assisted injection) have been found to be confined to relationships

characterized by close social ties (Neaigus et al., 1994). Therefore, beneficial effects of IDU social networks may well be reduced by the negative effects that these same networks produce. This “canceling effect” may be further amplified within the unique context of Vancouver’s Downtown Eastside. In addition to having one of North America’s largest open drug markets, the area also has one of the most densely populated IDU communities. It is estimated that approximately 5,000 IDU reside within a ten-block area in the Downtown Eastside (Wood et al., 2000).

Other significant findings of interest relate to sixth study hypothesis, and concern the relationship between frequent drug use and ART maintenance and adherence. According to the results of this study, frequent drug use did not have a direct effect on ART maintenance and adherence. In the univariate analyses, frequent heroin use was significantly associated with ART maintenance and marginally associated with ART adherence. In multivariate analyses, frequent heroin use was neither an independent predictor of ART maintenance or adherence. This finding is inconsistent with previous studies that have found illicit drug use to be associated with poorer rates of ART maintenance and adherence (Lucas et al., 2001; Moatti et al., 2000; Samet et al., 92; Singh et al., 1996). However, other studies have produced findings consistent those of the present study that suggest that illicit drug use is not associated with ART adherence (Singh et al., 1999; Ferrando et al., 1996). One study by Ferrando et al. (1996) found that the effects of illicit drug use on adherence, while initially associated with adherence, were no longer associated after adjustment for mental health status. In the present study, it was found that the association between illicit drug use and ART maintenance and adherence that was observed at the univariate level was no

longer significant when incarceration, efficacy-expectations, outcome expectation, and self-regulatory efficacy are adjusted for.

In addition, an interaction between efficacy expectations and frequent heroin use was found in the multivariate analyses of ART maintenance. The interpretation of this interaction suggested that frequent heroin use mediated the effect on efficacy expectations on ART maintenance when efficacy expectations were low, but not when efficacy expectations were high. These findings taken in sum appear to suggest that injection drug use is not a barrier to maintaining and adhering to ART when efficacy expectations and self-regulatory efficacy is high, and negative outcome expectations are low.

The lack of an association between frequent heroin use and ART maintenance and adherence may be explained in a couple of ways. First, the cut-off of one or more injections per day may not be sensitive enough to reveal an effect of intensity of drug use on ART maintenance and adherence. However, this cut-off has been used in several previous analyses involving the participants from the Vancouver Injection Drug Users Study and been found to be sensitive enough to predict high risk syringe sharing, and other markers of social instability such as sex trade work (Spittal et al., in press; Wood et al., 2001). Furthermore, this cut-off is also clinically relevant given that heroin addicts require an injection of heroin at least once per day to stave off withdrawal symptoms, and due to the long half-life of heroin, few users inject heroin more than 3 times per day (Tyndall, in press). An alternative explanation may be that there has been a growing presence of programs in Vancouver based on harm reduction models of care that aim to serve active IDU. Included are programs that provide ART adherence

support to active IDU through outreach. Many of the more “at-risk” are identified by these programs, and outreach workers who deliver medications are assigned to provide care to these individuals. Finally, it may be that frequent heroin use does not lead to levels of instability high enough to disrupt ART maintenance and adherence behaviours. Evidence from previous studies have indicated that regular heroin users are able to maintain jobs and other activities of daily living in contrast to the social instability caused by frequent cocaine injection (Drucker & Vlahove, 1999).

Other substantial findings relate to the seventh study hypothesis, and concern the cojoint effects of the variables studied. In this study, ART maintenance was predicted by a combination of psychological variables and one contextual variable (efficacy expectations, self-regulatory efficacy, outcome expectations, recent incarceration, and an interaction term involving recent incarceration and outcome expectations). However, ART adherence was predicted by psychological variables only. As discussed previously, frequent heroin use and social support did not contribute to the prediction of ART maintenance or adherence. This result is inconsistent with the seventh study hypothesis and could be explained by various factors that have been discussed earlier.

The finding that ART maintenance was predicted by a combination of psychological variables and one contextual variable is consistent, in part, with the seventh study hypothesis and social cognitive theory that explains human functioning as a product of reciprocal causation (Bandura, 1986). According to this theory, “internal personal factors in the form of cognitive events, affective, and biological events, behavioral patterns, and environmental influence all operate as interacting

determinants that influence one another bidirectionally” in determining human functioning (Bandura, 2001a, p. 15). Reciprocal causation is said to produce highly dynamic and complex relationships and effects that cannot always “be dichotomized neatly into remote and proximal influences” (Bandura, 2001a, p. 15). The findings related to ART maintenance are also consistent with modern theories of population health suggesting that determinants of health in societies at an advanced stage of development typically include a range of social, economic, cultural and structural factors (Evans, Barer, & Marmor, 1994).

Participants in this study were asked to provide reasons for discontinuing ART. The main reason given for discontinuing ART was having been in jail. This finding is consistent with the above findings that indicated an association between recent incarceration and ART discontinuation. The finding is also consistent with studies by Palepu et al. (2001b) and Altice et al. (2001) who found high rates of ART discontinuation among individuals who had been incarcerated. While both HIV positive serostatus and incarceration are common among IDU, the impact of incarceration on ART maintenance and adherence has received little attention in the scientific literature. As mentioned earlier, there are many possible explanations for this finding. First there are many structural barriers to maintaining ART (deBruyn, 1998). As well, there is considerable stigma associated with HIV/AIDS in prison, and therefore prisoners may avoid taking ART to conceal their serostatus and ensure their safety (Jurgens, 1996).

The second most commonly given reason for discontinuing ART was the experience of side-effects. Several studies have identified side-effects of ART to be associated with ART discontinuation (Ahdieh Grant et al, 2001; d'Arminio Monforte A,

et al., 2000; Gifford et al., 1999; Johnston-Roberts and Mann; 2000; Moatti et al., 2000). It has been established that patients are more likely to adhere to a medication regimen when it produces immediate clinical benefit and does not produce side-effects (Friedland & Williams, 1999; Meichenbaum & Turk, 1987; Rabkin & Chesney, 1999). However, the characteristics of antiretroviral therapy are quite different from this optimal scenario. As mentioned above, ART is more likely to produce immediate and severe side-effects, while clinical benefits are rarely felt in the short term and may not be clinically detectable for some time.

The third most commonly given reason for discontinuing ART was pregnancy. In the present study all participants who were taken off ART by the doctor were removed from the analysis. Therefore, the participants who reported pregnancy as a reason for discontinuing ART stopped treatment of their own accord. Standard practice is to maintain treatment until a pregnant patient has reached an undetectable viral load (Yeni et al., 2002). In some instances, the specific regimen may be changed, but this would not have been designated as discontinuation in the present study. It plausible that participants stopped ART out of fear that the medication would cause harm to their unborn child. This explanation cannot however be verified by the current data and should be the subject of further study, given that ART discontinuation could lead to avoidable infant HIV infections.

Participants in the present study were also asked to provide reasons for missing doses of ART. The most commonly given reason for missing doses was forgetting. This finding is consistent with previous studies of reasons for missing doses of ART (Gifford et al, 2000; Chesney et al., 2000; Walsh et al., 2001). Most previous

investigators have assumed that forgetting in this instance refers to forgetting when a pill should be taken. However, ART adherence consists of a series of cognitive and behavioural tasks that includes both prospective and retrospective memory components (Parks & Kidder, 1996; Einstein & McDaniel, 1996), since patients must not only remember when to perform the adherence behaviour (e.g., the time to take one's medications), but they also must remember what the behaviour consists of (e.g., which medications to take, how many medications to take). Most studies of adherence, including the present study, fail to distinguish between these two types of forgetting. However, the results of a qualitative investigation of barriers to adherence suggest that the problem is indeed most often one of prospective memory (Johnston-Roberts & Mann, 2000). This type of forgetting has also been described in the cognitive science literature as "absent-mindedness" (Schacter, 1999).

In the case of adherence, medication-taking behaviour can be either a time-based or event-based task. An event-based task is externally cued and involves remembering to do something when a particular event occurs. Therefore, forgetting is likely to occur when a cue is not recognized. Time-based tasks require that patients remember to do something at a particular time, and therefore forgetting occurs when patients fail to generate appropriate cues ahead of time and then fail to perform the task when the appropriate time occurs (Parks & Kidder, 1996). Both types of forgetting likely apply to missing doses of ART.

While concerns have also been raised about the impact of neuropsychiatric complications and mental disorders on adherence to HAART, little attention has been paid to these issues (Albert et al., 1999; Rabkin & Chesney, 1999). It is likely that these

conditions will also limit patients' ability to adhere to ART. The common features of cognitive impairment among HIV-positive individuals have been well articulated (American Academy of Neurology AIDS Task Force, 1991). As Albert et al. (1999) point out, HIV-associated cognitive impairment occurs in approximately 20% of patients who meet established criteria for an AIDS diagnosis. The most common areas of impairment include memory, executive function, and visual motor coordination, and those with more advanced illness have been found to have difficulty with activities of daily living (Rabkin & Chesney, 1999). These types of impairment may also explain the high rate of forgetting that was reported by participants in this study.

While it is easy to explain why participants may be likely to forget to take doses of ART, it is more difficult to explain how they would be able to report these episodes of forgetting with any accuracy. The results of recent cognitive science studies have indicated that while people generally remember memory successes in everyday life, memory for forgetting in everyday life is poor (Morris, 1984; Joslyn, Loftus, McNoughton & Powers, 2001; Swartz, 1999). It seems that successful remembering is more memorable because it involves a positive experience and an additional rehearsal of the content, which in turn strengthens memory (Joslyn et al., 2001). Joslyn et al. (2001) have described memory for memory as a complex cognitive activity referred to as "metamemory" (p. 789). Herrmann (1979) referred to another related problem he called the "Memory Introspection Paradox" (cited in Morris, 1984). In short, this paradox refers to the problem that people who are most likely to make memory errors are also those most likely to forget that such an error has taken place. It may well be

that forgetting to take medications is in fact more of a problem than has been reported in this study and others like it.

Another reason given for missing doses of ART was falling asleep or sleeping through dose times. While this has been found to be a common reason for missing doses of ART in other studies of adherence (Gifford et al., 2000; Chesney et al, 2000), it is rarely reported as frequently as it was in the present study. Many ART regimens require that doses be taken at odd intervals, and therefore it is understandable that doses may be missed for this reason. Given the chaotic lifestyles of many IDU it is also understandable that sleeping through doses may be more of a problem for this population than others. Many IDU, especially those who use cocaine are known to stay awake for several days at time, after which many will sleep for long periods of time. For the same reason, it not surprising that many participants also reported missing doses due to being “too busy,” having a schedule conflict, or being “away from home.” The latter reason may also be confounded by the incidence of incarceration. As in the case of sleeping through doses, these reasons have been reported by participants in previous analyses (Chesney et al., 2000; Gifford et al., 2000), but not with the same frequency as in the present study.

Many participants also reported missing doses due to side-effects. Two items on the measures used to assess reasons for missed doses related to side-effects. The first, and the more frequently reported reason, related to already being too sick from side-effects, while the second related to wanting to avoid side-effects. This finding is also consistent with previous studies (Chesney et al, 2000; Gifford et al., 2000), and was not reported with any more frequency by IDU included in the present study.

Two other reasons for missing doses of ART given with equal frequency included being “too high” and feeling depressed. Intoxication as a reason for missing doses is consistent with previous studies reporting active drug use as determinant of non-adherence (Lucas et al., 2001; Moatti et al., 2000; Samet et al., 92; Singh et al., 1996); however, a review of the literature yielded no other studies of IDU populations reporting reasons for missing doses. Frequent drug use was marginally associated with ART adherence in the present study at the univariate level, but this association was not significant in the multivariate analysis. However, as stated previously, the measure of adherence used only assessed prescription refill adherence and therefore non-adherence resulting from missed doses could not be measured. The finding that depression was reported as a reason for missing doses is consistent with previous studies (Gordillo et al., 1999; Singh et al, 1999). Feeling depressed was reported in two previous studies examining self-reported reasons missed doses of ART (Chesney et al., 2000; Gifford et al, 2000). However, in the study that involved a greater number of IDU (17% versus 4%), depression was given as a reason for missing doses with greater frequency (27% versus 18%). Previous studies have found the incidence of depression to be high among HIV-positive IDU populations. For example, a study of psychopathology among HIV-positive and HIV-negative injection drug users, Rabkin et al. (1997) found that rates of major depression and dysthymia ranged from 15% (among HIV-negative men) to 33% (among HIV-positive men and HIV-negative women).

One other finding of interest pertaining to reasons given for missing doses was that very few participants (1%) reported that they missed doses because they “did not understand the instructions.” Despite high rates of drug use and psychiatric problems,

participants did not report difficulty understanding the instructions that accompany complex ART regimens. This could partially be explained by existing adherence supports in the local community, as well as widespread free distribution of medication storage boxes that help simplify regimens.

### ***Limitations of the Present Study***

While there is much to be gained from the present study, several limitations should also be noted. Among the most obvious are concerns regarding internal validity. The study relied on a nonexperimental design, and therefore the results do not demonstrate causal relationships between independent and dependent variables. This is particularly important when considering the relationship between self-efficacy variables (efficacy expectations, self-regulatory efficacy, and outcome expectations) and ART maintenance and adherence, since it is difficult to establish whether self-efficacy beliefs are causes or consequences of the behaviours under study. A similar concern relates to the observed relationship between incarceration and ART discontinuation. In this case, it is highly possible that third-variable causation accounts for both ART discontinuation and recent incarceration. However, one of the most likely confounders, frequent illicit drug use, was controlled for in this analysis. In addition, as mentioned previously, the lack of association between social support and the dependent variables may be explained by confounding that was not measured. For instance, depression, a known confounder of the effect of social support on adherence, was not measured in this study. Previous studies have indicated high rates of depression among HIV-positive injection drug users (Rabkin et al., 1998). Another potential confounder that was not measured was the negative impacts of social networks.

Another limitation of this study concerns external validity. It is possible that the VIDUS cohort may not be representative of IDU in other cities, which raises concerns regarding the generalizability of the study findings. Specifically, the dense concentration of IDUs in the Downtown Eastside and the prevalence of cocaine injection make this community unique (Tyndall et al., 2001a). As well, a growing number of harm reduction services have been implemented in recent years, including interventions that support active IDU in maintaining and adhering to ART. Many cities, particularly those in the United States do not provide the same level of support to HIV-infected IDU. Some of the limitations associated with using clinic-based samples were, however, not present in this study, as the VIDUS cohort is a community-based sample, and therefore does suffer from the same problems of generalizability.

There are also limitations related to measurement issues. Adherence in this study was measured using pharmacy-refill records. This method provides only limited information about adherence behaviour, and other important information concerning of adherence behaviour, such as medication-quantity, medication-interval, and medication-diet adherence, was not measured in this study. It is possible that some participants deemed highly adherent in this study picked up their prescriptions but did not consume all their medications. However, as mentioned previously, pharmacy-based adherence measures have been found to be highly predictive of virologic outcome and survival (Low-Beer, 2000; Wood et al., in press). A further problem concerns the cut-off used to determine whether participants were highly adherent or not. In this study, the continuous adherence variable was dichotomized at 95% adherence. There were however two reasons using this cut-off. First, this level of adherence has been found to

be required for viral suppression (Low-Beer et al., 2000), which is among the most critical measures of clinical efficacy. As well, because the distribution of adherence scores was so skewed, the variable could not be used in multivariate analyses where normality of the dependent variable is required (Tabachnick & Fidell, 1996).

Another limitation concerns the fact that many measures were obtained by self-report. This could lead to several problems, including problems with accuracy of reporting and socially-desirable responding. The latter issue may have been of particular concern when participants were asked to report ratings of efficacy expectations. Given the pressure placed on patients to adhere to ART, participants may have been inclined to exaggerate their confidence in their ability to adhere to ART.

Another issue related to measurement concerns the six-month follow-up period. For many questions, a six-month time frame was used. For example, participants are asked to indicate how often they injected specific drugs in the previous six months. This method does not capture variations in behaviours over the time period, and participants may have trouble accurately recalling events over such a long period of time. As well, because participants were asked to indicate if they have been incarcerated in the previous six months, it is not known when exactly the incarceration took place, and consequently it is not known if they discontinued ART prior to, during, or following their incarceration.

A further limitation concerns the question regarding reasons for missing doses of ART. In this study, participants were asked to select from a list all the reasons that applied to their situation. Therefore, the measure provides no information concerning

the relative importance of the reasons given (i.e., which reason accounted for the greatest number of missed doses).

Other limitations concern statistical challenges encountered with this study. The study involved two small samples, and therefore the associations between certain variables may have been underestimated or not detected. For example, only seven individuals in the ART Adherence Sample had been incarcerated in the previous six months, and therefore, there may not have been adequate statistical power required to detect an association between adherence and incarceration. A further problem concerned the skewed distributions of adherence and efficacy expectations scores. As mentioned previously, this led to the adherence variable being dichotomized, and may have resulted in deflated correlations between adherence, efficacy expectations and other variables of interest.

### ***The Implications for Future Research***

The findings presented also suggest several implications for future research. First there is an obvious need for more accurate and sophisticated methods of adherence measurement. As mentioned previously, the measure used in this study provides only limited information about adherence behaviour. Although the measurement of ART adherence is of critical importance, there has been a lack of rigorous study and validation of adherence measurement techniques (Liu et al., 2001; Steiner & Prochazka, 1997). Much future research is needed to develop more accurate methods for measuring adherence to these complex regimens. Emphasis should be placed on validating the measures currently in use, including tests involving the use of the best available objective measures of adherence and clinical outcome as a means to

establish concurrent validity. There is also need for increasing use of standardized measures among treatment-naïve populations, to ensure consistency across studies and a reduction in host factors that confound outcomes (e.g., resistance, pre-treatment viral load). Research that assesses the impact of neuropsychiatric complications and mental disorders on adherence measurement is also a priority. Finally, future studies of adherence should control for confounding that results from the uptake of adherence supports (e.g., ART-specific outreach services).

The study findings also indicate a need for further research on adherence self-efficacy. First, there is a need for longitudinal studies that examine the reciprocal relationship between self-efficacy and adherence. This would involve measuring adherence self-efficacy among larger samples of treatment-naïve patients, and then again after these patients have begun treatment. Simultaneous measures of adherence would then provide information about the causal relationship between adherence and self-efficacy. These measures of adherence should also ideally be validated by measures of clinical outcome. There is also a need for further study of the dimensions of adherence self-efficacy that were examined in this study. In particular, future studies should examine the relative strength, magnitude, and generality of these dimensions (Bandura, 1977). Future studies should also explore the impact of other outcome expectations and dimensions of self-regulatory efficacy on ART maintenance and adherence.

The results presented also suggest that future research should examine the impact of social support on ART adherence and maintenance using several measures of social support. It is possible that the measure used in the present study was

insufficiently sensitive to detect an association between adherence and social support. These studies should also control for the influence of depression on adherence, and the negative impact of social networks.

Further study of the impact of incarceration on ART maintenance and adherence is also needed. First, accurate recordings of when exactly incarcerations and ART discontinuations occur will permit a more meaningful analysis of the relationship between these variables. Also needed are studies that examine whether ART medications are actually consumed in prison. The present study only provided an assessment of whether prescriptions had been filled by individuals in prison. As well, complimentary qualitative investigation may help to explain the relationship between incarceration, ART maintenance and adherence.

Future research should also include studies of adherence interventions. The need for this type of research has been well established (Kelly et al., 1998). In particular, there is a need for research that systemically examines the influence of interventions on adherence self-efficacy, ART maintenance and adherence. Ideally, these interventions would include techniques previously found to increase adherence self-efficacy. This type of research should be based on randomized control designs that involve adjustment for all known confounders. Measures of clinical outcome should also be used to validate the efficacy of adherence interventions. These types of studies would also be well supported by qualitative investigations that provide in-depth analyses of how change occurs within the context of adherence interventions.

### *Implications for Theory*

The findings reported here have several implications for theory of adherence behaviour. At present, explanations of adherence behaviour have been informed by a vast array of research results that identify various determinants, some complementary, and some contradictory. With the exception of Broadhead et al.'s (1995) peer-driven intervention model and the accompanying theory of group-mediated social control (Heckathorn, 1990), and Kalichman et al.'s (2001) Information-Motivation-Behavioral Skills Model, there is a currently a lack of theory within the ART adherence literature. The findings of this study, and others examining ART adherence, suggest that social cognitive theory has much to offer theories of ART adherence. While concepts such as self-efficacy have been applied in HIV/AIDS prevention work (Fishbein, 2000), social cognitive theory has not been widely applied in the literature addressing HIV/AIDS treatment.

Many determinants of ART adherence behaviour have been identified by researchers, however, few constructs have been found to be so consistently and strongly associated with ART adherence as self-efficacy. The findings of this study suggest that core features of social cognitive theory such as self-efficacy, self-regulatory efficacy, and outcome expectations are germane to the understanding and explanation of adherence behaviour. The concept of adherence self-efficacy can help understanding and explanation of choice, effort, coping, and persistence as it relates to ART and related adherence behaviour. Efficacy expectations can also serve as indices of the conviction that one can successfully adhere to ART. The findings of this study suggest that certain specific efficacy expectations, when taken in sum, are particularly relevant

to ART adherence, including expectations pertaining to one's ability to remember to take medications at right time, to remember how many pills to take, to obtain food to be taken with medications, to manage side-effects of medications, to remember to pick up prescriptions, and to arrange daily activities in order to take medications as prescribed. The concept of self-regulatory efficacy may be particularly helpful in understanding and explaining how individuals cope with adherence in the face of challenging circumstances. The findings presented here are, however, limited to circumstances of illicit drug use and withdrawal. Given that self-regulatory efficacy has been associated with other health promoting behaviours (Bandura, 2001a), further investigation of this construct may prove usefully for theory building. The concept of outcome expectations may be helpful in understanding and describing beliefs about conditional relationships between ART and health, and the impact of these beliefs on ART adherence. The findings of this study suggest that outcome expectations related to negative impacts of ART (e.g., side-effects) are relevant to the understanding of ART adherence. Further support for this implication came from self-reports of reasons for discontinuing ART and missing doses of ART. In the present study many participants reported that side-effects were a reason for discontinuing ART or missing doses of ART. Given that people construct outcome expectations from observed conditional relationships, it seems that outcome expectations pertaining to side-effects of ART are most relevant to theories of adherence. Other implications for theory can be found in the study findings indicating support for the concepts of reciprocal causation. As discussed previously, social cognitive theorists have asserted that health is determined by dynamic reciprocal influences between physiological states, behaviours, cognitions, and the environment

(Bandura; 1986; O'Leary, 1985). This suggestion is supported by the present study which found that, structural (e.g., incarceration), psychological (e.g., outcome expectations, efficacy expectations), and physiological determinants (e.g., heroin use) interacted to produce complex associations with ART maintenance and adherence.

The observed association between incarceration and ART maintenance also suggests that theories should also account for the direct effects of structural or environmental determinants on adherence. This would be consistent with theories of population health that assert that the determinants of health in societies at an advanced stage of development are social, economic, cultural and structural factors at both the individual and population level, not the availability and utilization of hospital-based medical services (Evans, Barer and Marmor, 1994). Also, consistent with findings of this study that indicate that IDU have higher rates of ART discontinuation than other HIV-infected populations, population health theory asserts that individuals in lower socio-economic groups continue to have significantly poorer health outcomes than those in higher socio-economic groups (Evans, Barer and Marmor, 1994).

The findings of the present study also suggest that concepts derived from cognitive science are relevant to theories of adherence behaviour. In light of the finding that most participants missed doses of ART due to forgetting, more elaborate and specific concepts such as absent-mindedness, prospective memory, time and event-based tasks may serve to improve current theory of adherence. At present, there is a complete absence of theory in the adherence literature that can explain instances of forgetting.

Finally, the study findings pertaining to the lack of association between frequent drug use and ART adherence suggest that current harm reduction concepts may be germane to theories of adherence. Although harm reduction has been described in many different ways, the approaches derived from it generally aim to decrease the adverse health, social, and economic consequences of drug use without requiring abstinence from drug use (Canadian Centre on Substance Abuse, 2000). While harm reduction theorists do not preclude abstinence from illicit drug use as a worthwhile goal, they question the long established notion that abstinence is the only worthwhile objective of treatment, and an absolute prerequisite to medical treatment. The findings of the present study suggest that theories of ART adherence might adopt a similar stance in relation to illicit drug use, given that drug use did not significantly predict ART maintenance or adherence.

### ***Implications for Practice***

The need for evidenced-based ART adherence interventions has been well established (Kelly et al., 1998). The results of the present study suggest many implications for practice. In this study, negative outcome expectations were associated with ART maintenance and adherence. It has been previously suggested that fears resulting from negative beliefs about ART must be explored (Altice, 2001). However, it is also likely that psychoeducational methods focused on providing accurate information about HIV disease progression, drug resistance, and the clinical effects of ART may help to alter existing beliefs about conditional relationships between ART and health. Several variations on this type of approach have already been developed (Sorensen et al., 2000; Williams, 1999). As well, testimonials from others who have

experienced the benefits of ART may also serve as effective sources of verbal persuasion and vicarious experience. These testimonials will likely have a better chance of success if the accounts include experiences of side-effects and steps taken to overcome these challenges. However, the limitations of persuasory communication have been noted (Bandura, 1977), and therefore this approach should not be used in isolation.

Another method of countering the impacts of negative outcome expectations on ART maintenance and adherence would involve cognitive restructuring techniques to address negative assumptions about ART (Farber & McDaniel, 1999). Patients who think that ART may make them sicker could be trained to identify and interrupt these thoughts, and replace them with more adaptive cognitions that focus on the well-known benefits of ART. In a similar vein, cognitive reframing exercises could be employed to prompt patients to interpret side-effects as evidence of ART “doing its job” (i.e., reducing viral load and boosting immune functioning).

The observed associations between adherence self-efficacy, ART maintenance and adherence suggest many implications for practice. Several studies have demonstrated positive impacts on health of interventions based on concepts of self-efficacy theory (O’Leary, 1985). Because the sources of efficacy information are understood, many related interventions have been well articulated (Bandura, 1977). The findings of this study suggest that ART adherence interventions will likely be effective if they are focused on developing confidence in the ability to: remember to take medications at the right time, remember how many pills to take, remember to pick up prescriptions, obtain food to be taken with medications, manage side-effects of

medications, and arrange daily activities in order to adhere to ART. However, all findings of this study considered, it seems that interventions should focus first on the ability to remember to take medications, refill prescriptions, and the abilities to manage side-effects and arrange daily activities in order to adhere to ART. Methods focused on these dimensions of adherence self-efficacy will likely be most effective if they involve skill development and self-observation of performance accomplishments (Bandura, 1977). Interventions based on performance accomplishments should initially involve modelling, followed by guided practice, and later independent practice (Bandura, 1977). For example, patients could be given opportunity to observe another HIV-positive IDU working with a simple schedule in arranging his or her daily activities so that medications could be taken at correct times. Practice could include developing plans to deal with unexpected circumstances, including what to do when using drugs. Patients could then develop their schedules and coping plans with the assistance of a model, and then later on their own.

Adherence interventions should also involve setting proximal goals and the provision of feedback based on patient performance. One simple method of providing feedback would be to measure changes in adherence self-efficacy over time. However, feedback demonstrating the relationship between adherence behaviour and changes in viral load may help to further motivate patients. Previous studies have suggested that this method of providing feedback can increase adherence behaviour (Haubrich et al., 1999). Observed changes in viral load and CD4 cell count resulting from ART maintenance and adherence may also help to counter negative outcome expectations based on faulty assumptions concerning conditional relationships between ART and

health. It is likely that implementing adherence interventions at the start of therapy will not be sufficient, and therefore, in order to maintain adherence self-efficacy, additional “booster” sessions should be employed.

Several interventions could also be employed to enhance ability to remember when to take medications and pick up prescriptions. For example, one approach used in memory rehabilitation involves switching time-based prospective tasks to events-based tasks (Parks & Kidder, 1996). Previous studies have shown memory for event-based tasks to be more stable than memory for time-based events (Parks & Kidder, 1996). Most ART prescriptions come with time-based instructions. In order to improve prospective memory and reduce problems associated with forgetting, interventions should focus on assisting patients to link doses with regular daily events rather than specific times of day. As well, patients could be encouraged to develop an array of environmental cues that prompt them to take doses at specific times. These cues could also be supported with any of the specific memory aids (e.g., alarms) that are currently in use (Williams, 1999).

In order to further reduce problems associated with forgetting, interventions could include covert modeling techniques that reinforce encoding of adherence behaviour. In the case of adherence, this approach would involve having patients visualize scenes in which a model similar to the patient goes through the process of remembering to take their ART doses. The visualizations should ideally involve a coping model rather a mastery model, and therefore the model should experience, but eventually overcome challenges associated with completing the task (Bandura, 1971). Following this, the intervention could then switch to a “self-as-a-model” visualization

(Cormier & Cormier, 1991), in which the client visualizes him- or herself remembering to take their medication with all competing activities and salient contextual features included in the visualized scene.

The findings of this study also suggest that counsellors working with HIV-positive IDU should be familiar with harm reduction theory and interventions. Many participants in this study were able to maintain and adhere to ART despite ongoing illicit drug use. Therefore, rather than insist on abstinence from illicit drug use, counsellors should accept that people will often continue to engage in high-risk behaviours. Counselling interventions should instead focus on reducing harm associated with ongoing drug use, including the specific impacts on ART maintenance and adherence. As well, some harm reduction approaches, unlike 12-step approaches that focus on the powerlessness of the patient, are consistent with self-efficacy theory in emphasizing patient choice, skill development, and confidence in reducing the harmful effects of continued drug use (Denning, 2000). Harm reduction also often involves accepting, that for many people who use illicit drugs, treatment involves addressing needs beyond drug use. In the case of injection drug users, this often means securing appropriate housing, financial support, and access to other basic living needs.

Adherence to antiretroviral therapy among injection drug users continues to be a significant public health issue. Patients who take these medications intermittently or at reduced doses often experience sub-optimal drug levels thus increasing the chance of drug resistance and failure of therapy. The transmission of resistant virus by unsafe sexual and drug using practices may confer limitations in treatment options for those newly infected. Research that identifies determinants of ART maintenance and

adherence is critical at this time, and is essential in informing interventions that may potentially address these complex and significant public health issues. The results of this study suggest that psychological constructs such as self-efficacy are central to the understanding of adherence behaviour and the interventions that can change it.

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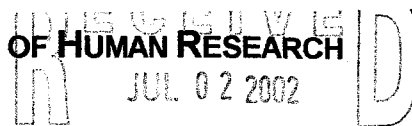
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**APPLICATION FOR WAIVER OF ETHICAL REVIEW OF HUMAN RESEARCH**  
**UNIVERSITY OF VICTORIA**



OFFICE OF VICE-PRESIDENT

Submit **one original and three (3) copies** to the Office of the Vice-President, Research. Handwritten applications will be returned immediately.

*Use of the accompanying Ethics Application Guidelines is strongly encouraged in completing this form.*

**OFFICE USE ONLY:**

VPR File No.:	207-02	Received:		To Chair:	
Sent Rev1:		Sent Rev2:		Notice:	
Return Rev1:		Return Rev2:		Annual Review:	JUL. 4, 2003

Special Review Information:

Reference Information for funding source

Committee Chair Approval Signature: \_\_\_\_\_

Date: July 5/02

**A. APPLICANT INFORMATION**

Principal Investigator:	Thomas Kerr
Department:	Educational Psychology and Leadership Studies
Mailing address:	2665 Carolina Street, Vancouver, B.C. V5T 3S9
E-mail address:	tkerr@intergate.bc.ca
Phone number(s):	604-708-3441

Are you:  Faculty  Staff  Graduate Student  Undergraduate Student

Thesis Supervisor (if applicable)

Name of Supervisor:	Dr. Anne Marshall	Department:	Educational Psychology
E-mail address:	amarshal@uvic.ca	Phone:	721-7815

**B. PROJECT INFORMATION**

Title of the Project:	<b>Psychosocial determinants of access and adherence to highly active antiretroviral therapies among injection drug users</b>
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Have you applied for funding for this project?  No  Yes (if "Yes" complete the following):

Source(s) of funding:	Exact title of grant(s):

Other Investigators on this project:

	Name(s)	Affiliation(s)	E-mail address(es)
1	Dr. Anita Palepu	Co-investigator, Assistant Professor, Faculty of Medicine, University of British Columbia	anita@hivnet.ubc.ca
2	Dr. Mark Tyndall	Co-investigator, Assistant Professor, Dept. of Health Care and Epidemiology, Program Director, Epidemiology, B.C. Centre for Excellence in HIV/AIDS	tyndallm@hivnet.ubc.ca

3	Dr. Martin Schechter	Professor and Head Department of Healthcare and Epidemiology/ University of British Columbia Director of Epidemiology/BC Centre for Excellence in HIV/AIDS Principle Investigator: Vancouver Injecting Drug Users Study	martin.schechter@ubc.ca
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Note: Investigators are NOT employees (research assistants etc.)  
If investigators change, provide this information to the Chair of the Human Research Ethics Committee.

Proposed Start Date:	(N.B.: allow 4-6 weeks required for review) August 1, 2002
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### C. SIGNATURES

Your signature indicates that you agree to abide by all policies, procedures, regulations and laws governing the ethical conduct of research involving humans,

Principal Investigator: \_\_\_\_\_ Date: \_\_\_\_\_

The signature of the supervisor below indicates that the supervisory committee has approved the student's proposal and that the supervisor has assisted the student in the preparation of this application.

Student's Supervisor: \_\_\_\_\_

The signature of the administrator indicates that adequate research infrastructure is available to conduct this research

Chair/Director or Dean: \_\_\_\_\_

If you downloaded this file, you can complete it on your computer. You will only have to print off your final version and manually complete the "tick-boxes".

### D. REQUEST FOR WAIVER

It is important to note that waiver of the requirement for ethical review is only permitted in very limited circumstances and such a waiver does not release researchers from any other applicable legal obligations such as violating a person's right to protect privacy, fulfilling copyright requirements etc.. If your study does not meet one of the following requirements, you will be required to apply for ethical approval.

Which of the following best represents the reason you believe this research qualifies for a waiver from ethical review:

- This research is limited to the use of materials that are in the public domain and for which all applicable copyright, patent, or other legal requirements and approvals have been either fulfilled or received. Databases must be supplied to the researcher in a completely anonymous form (attach a description of the materials you will use, all required approvals or permissions to use these materials and describe your methods).
- This research involves a living individual in the public arena, or is about an artist, based exclusively on publicly available information, documents, records, works, performances, or archival materials (attach a brief description of this research, including the name of the individual who will be the object of the research, your methods, and the types of materials you will be using in the course of the research).
- This is a quality assurance study, performance review or testing within normal educational requirements (attach a description of who will participate in the study, the context of the study, your methods, and copies of materials such as questionnaires etc.).
- This study involves observation of participants who are seeking public visibility such as speakers at public political demonstrations, public meeting etc.(attach a description of the types of people involved, the context in which the research will be conducted and your methods).

Provide details of your project on a separate page