OPTIMIZING ADHERENCE TO HIGHLY ACTIVE ANTIRETROVIRAL THERAPY AMONG MARGINALIZED, HIV-POSTIVE WOMEN WITH COMORBID DEPRESSION: THE ROLE OF THE NURSE PRACTITIONER

by

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PROJECT SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN NURSING: FAMILY NURSE PRACTITIONER

UNIVERSITY OF NORTHERN BRITISH COLUMBIA

November 2013

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Abstract

Women represent a growing proportion of new positive HIV tests in Canada and are more likely to experience comorbid depression. This is concerning because comorbid depression is associated with suboptimal adherence to highly active antiretroviral therapy (HAART) and poor HIV disease outcomes. The purpose of this project is to answer the question, “What is the role of the nurse practitioner (NP) in optimizing adherence to HAART amongst marginalized, HIV-positive women with comorbid depression?” By evaluating current literature this project found that social factors such as poverty, homelessness, food insecurity, post-traumatic stress disorder, stigmatization, gender or racial discrimination and injection drug use are risk factors for both comorbid depression and HAART non-adherence. Effective treatments for depression include cognitive behavioral therapy and pharmacological intervention with antidepressants. The role of the NP was inferred by extrapolating the findings from this literature search with the competencies required of NP practice. NPs have the skills, education and legislated authority to provide collaborative care that addresses the underlying social factors that contribute to comorbid depression and HAART non-adherence. These findings are limited by the scarcity of research conducted with HIV-positive female participants, that investigates NP practice or interventions to address underlying social factors.
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Acknowledgement

I would like to express my heartfelt gratitude to my advisory committee members Lela Zimmer PhD, RN and Tracey Day MScN, NP-F for their patience, guidance and encouragement in helping me create and complete this paper.
Dedication

I dedicate this project to:

- My husband, Garth, whose steadfast support and encouragement propelled me through this program;
- My son, Spencer Nolan, whose buoyant and inquisitive personality never to fail to brighten my day;
- My parents, Aly and Lynn, whose work ethic and commitment to social justice inspired me to embark on a career in nursing;
- My in-laws, Wilfred and Judith, whose dedicated support of Garth and Spencer allowed me to focus on my education; and finally,
- My dear, dear friend, Nicole Bouchard, who was there to step in and feed my family and cheer me on at every step of this journey.
CHAPTER ONE

Introduction

Throughout the Master of Science in Nursing program, I have been exposed to critical social justice theory and primary health care (PHC) principles that have sparked my interest in working with marginalized populations. Marginalization refers to social conditions or processes that make or treat, certain individuals or groups, as insignificant, and ultimately results in “a disproportionate burden of ill health and social suffering” (Barber, Fitzgerald, Howell, & Pontisso, 2006; Browne, et al., 2012, p.2). Marginalization can prevent an individual or group from achieving the beneficial determinants of health.

The social determinants of health refer to social, political and economic conditions that shape the environment within which people live. These factors are negatively affected by the inequitable distribution of wealth, power or resources. Many health disparities, such as infant mortality rates, incidence of childhood obesity or life expectancy at birth, are attributable to the social determinants of health. Key social determinants of health include education, gender, income, race/ethnicity, food security, housing, early childhood development, social exclusion, and health services (Mikkonen & Raphael, 2010; WHO, 2013a). The social determinants of health draw attention to the idea that health and health status are influenced more so by the social conditions imposed on individuals or groups, than by individual lifestyle or personal choice.

Gender is recognized as a key determinant of women’s health status (WHO, 2013b). The same social, sexual, and cultural factors that define gender and its associated roles, responsibilities, status and power, also directly interact with the other
determinants of health. This results in a compounding of gender based inequities that decrease women’s ability to achieve optimal health and decrease resiliency to diseases such as human immunodeficiency virus (PHAC, 2012b). For example, a homeless, single-mother may feel forced to enter into an abusive relationship in order to obtain housing and food for her children. Because she is reliant on and fearful of her partner, she may not be able to negotiate safer sexual practices and she becomes infected with HIV.

In the three decades since the human immunodeficiency virus (HIV) was identified as the causative agent behind acquired immunodeficiency syndrome (AIDS), HIV has changed from a terminal diagnosis, to a manageable, long-term chronic trajectory. While there is no cure for HIV, scientific advancements, public policies and grassroots initiatives have lead to strategies to prevent disease transmission and to alter the natural progression of this disease in those already infected. There is increasing recognition that vulnerability to HIV infection, access and response to treatment, and disease progression are heavily influenced by the social determinants of health (Public Health Agency of Canada [PHAC], 2012b).

Globally, HIV/AIDS is the leading cause of death for women of reproductive age (UNAIDS, 2012). Women account for 50% percent of people of living with HIV, and rates of new infections are twice as high for young females (age 15–24 years) than for similarly aged males (UNAIDS, 2012). Within Canada, a steady increase in the proportion of positive HIV tests among women has also been observed (PHAC, 2012b). Groups who appear to have increased vulnerability to HIV infection include Aboriginal women, women from HIV endemic countries and women who use injection drugs. The most common exposure
category for Canadian women is heterosexual contact (53.9%), followed by injection drug use (37.3%) (PHAC, 2012b).

With the introduction of highly active antiretroviral therapy (HAART) in 1996, the life expectancy and quality of life of individuals diagnosed with HIV has continuously improved and is almost that of non-HIV positive individuals (Antiretroviral Therapy Cohort Collaboration, 2008). However, HAART must be taken continuously, for the rest of an individual’s life with a high level adherence to the medication regimen to achieve optimal outcomes. Additionally, like vulnerability to HIV, HAART adherence is affected by a variety of co-morbid conditions such as substance abuse, and mental illness, as well as by the social determinants of health (BC-CfE, 2011). Depression is a common comorbidity with HIV and it both directly and indirectly impacts HIV disease progression, by altering biochemical progresses, psychological functioning, and HAART adherence (Schuster, Bornovalova, & Hunt, 2012). The intent of this paper is to review current literature in order to determine the role of the nurse practitioner (NP), working in British Columbia, in optimizing adherence to HAART amongst marginalized, HIV-positive women with co-morbid depression.

**Background**

**Overview Of HIV/AIDS Disease Process**

There are two strains of HIV, HIV-1 and HIV-2. HIV-1 is more virulent and prevalent worldwide, whereas HIV-2 is less virulent and predominantly isolated to Africa (Rang, Dale, Ritter, Flower, & Henderson, 2012). This project focuses exclusively on individuals infected with the HIV-1 strain. HIV is a blood borne pathogen contained in blood, vaginal and rectal fluid, semen and breast milk. The virus is transmitted either directly
into the blood stream or indirectly through the highly vascular mucous membranes of the oral, genital or anal tract (Rote & Heuther, 2010). Any activity where blood or body fluid is exchanged, such as blood transfusions, unprotected oral, vaginal or anal sexual contact, injection drug use or accidental occupational exposure carries the potential for infection with HIV. Additionally, HIV can be transmitted from mother to child (vertical transmission) during pregnancy and delivery, as well as breastfeeding.

Activities that carry the highest risk for contracting HIV, from a known HIV positive source are injection drug use (0.67%), and receptive anal intercourse (0.5-3%) (BC-CfE, 2012). Risk of contracting HIV for females during penile-vaginal intercourse is 0.1%, and this is twice as high as the 0.05% risk for males contracting HIV from females during penile vaginal intercourse (BC-CfE, 2012). The significance of this is that females are more susceptible to HIV infection than males during unprotected intercourse. This is particularly important for women who are unable to negotiated safer sexual practices due to unequal power relationships such as sex workers, or women in abusive relationships.

Once in the bloodstream, HIV targets cells that express the CD4+ molecule on their surface, most commonly, T-lymphocytic, also referred to as helper T (Th) cells. Th cells play a critical role in the maturation and differentiation of both B lymphocytic cells, whose function is to produce antibodies, and T lymphocytic cells, whose role is to produce cytoxic cells (CD8+) responsible for directly killing antigen infected cells (Rote & Heuther, 2010). Other immune cells targeted by HIV include: dendritic cells, macrophages, CD8+, natural killer (NK) cells, and neural cells. Infected immune cells are spread throughout the body through the lymphatic system (Rote & Heuther, 2010).
Clinically, both the absolute and fractional CD4+ counts are used for the initial staging of HIV, predicting disease progression, deciding when to initiate HAART or opportunistic infection prophylaxis and monitoring response to therapy (BC Center for Excellence in HIV/AIDS [BC-CfE], 2011). The absolute CD4+ count has traditionally been considered to be the best marker to monitor disease progression and response to therapy. However, there can be substantial individual variation due to acute illness and normal diurnal variation in this measure. Therefore, clinicians should be aware that changes in the absolute CD4+ count without corresponding changes in the CD4+ percentage, might be clinically insignificant (Pagana & Pagana, 2010). More stable and accurate indicators of disease progression are the CD4+ percentage and the CD4/CD8 ratio (Pagana & Pagana, 2010).

Because the majority of studies that have been used to base clinical practice guidelines, use absolute CD4+ counts, this measure is still the most commonly used measure to guide therapy, monitor disease activity and assess adherence to HAART.

Once inside the cell, HIV activates a viral enzyme, called reverse transcriptase, to convert the single stranded viral RNA, into double stranded DNA (Rote & Heuther, 2010). A second viral enzyme, integrase, inserts the viral DNA segment into the infected cell’s DNA where it may be dormant for a period ranging from weeks to decades before becoming re-activated. Once corrupted by viral DNA, the infected immune cell is reprogrammed to translate viral genetic information. HIV virons, released during lysis, destroy the infected immune system cell resulting in fewer functioning immune system cells (Rote & Heuther, 2010). The plasma HIV viral load is another clinically important indicator of patient prognosis, disease progression and the need for antiretroviral therapy and response treatment (BC-CfE, 2011). The viral load is a quantitative measure of the number of virus copies per
milliliter serum. The goal of HAART is to achieve HIV viral suppression, which is considered to be less than 40 HIV-RNA copies/mL (BC-CfE, 2013). Viral rebound or viral failure is diagnosed after two consecutive HIV-RNA viral load measurements of greater than 200 copies/mL (BC-CfE, 2013). Treatment failure is diagnosed if after six months of HAART treatment HIV-RNA load remains greater than 40 copies/mL, or if after initially achieving viral suppression of less than 40 copies/mL the viral load rebounds to greater than 200 copies/mL (BC-CfE, 2013). A diagnosis of viral rebound/failure or treatment failure should prompt genotypic testing to detect HAART resistant HIV strains. Additionally, a full assessment should be completed that includes a physical exam to detect any opportunistic infections and a history that includes an assessment of medication side effects, drug-drug interactions, or recent vaccinations. As well, a thorough evaluation of psychosocial factors that may impact the client’s adherence to HAART should be completed (BC-CfE, 2013). Referral to an HIV specialist is recommended for the diagnosis and management of treatment failure (BC-CfE, 2013).

The replication of viral DNA is prone to errors and mutations, so the immune cells that were initially able to recognize and destroy HIV infected cells, fail to identify infected subsequently cells. Coupled with the progressive destruction of CD4+ cells, the immune system completely collapses (Rang et al., 2012). In addition to the destruction of the immune system, a chronic inflammatory state is caused by the presence of HIV, and viral replication. This state of chronic inflammation is associated with endothelial dysfunction and end organ damage that manifests as cardiovascular disease, renal disease or diabetes mellitus in the older (> 50 years) HIV-positive individuals (BC-CfE, 2011). These diseases are also associated with the long-term complications of HAART use. As a consequence, clinicians
must routinely screen and manage both HIV and non-HIV related conditions in the older HIV-positive client, who is taking HAART.

Clinical manifestations and progression is highly variable but a general pattern and correlation between viral load, CD4+ count and clinical signs and symptoms exists. The primary infection period generally lasts for 1 – 3 weeks after the initial infection; during this time HIV rapidly infects CD4+ cells and quickly reproduces viral DNA. During the primary infection period, between 50% and 90% of individuals report non-specific symptoms of fever, swollen and tender lymph nodes, malaise, myalgia, diarrhea and headaches (BC-CfE, 2011). On average, these symptoms appear between 2 to 4 weeks after exposure (BC-CfE, 2011). These flu-like symptoms spontaneously resolve and the viral load is temporarily reduced by the action of cytotoxic lymphocytes (Rang et al., 2012). The initial 12 weeks of infection are also referred to as the window period. The immune system has not yet produced HIV antibodies, so the HIV tests during this period may be negative even though the person is highly infectious. CD4+ cells have not yet been corrupted so the CD4+ count is within the normal range of 500 – 1500 cells / mm³, however, the viral load may be extremely high with as many as 10 X 10^6 viral copies/mL (Rang et al., 2012; New York State Department of Health AIDS Institute, 2010). An estimated 50% of new HIV transmissions occur during the primary infection period is because the high viral load and infectiousness, continued high risk HIV transmission behaviors because the individual is unaware of their HIV status, and non-specific primary HIV infection symptoms are misdiagnosed as a non-HIV condition (BC-CfE, 2011). For that reason, all primary care providers should routinely screen for HIV in all clients, and especially for those clients presenting with non-specific, flu-like illnesses.
Identification of primary HIV infection is extremely challenging for health care providers because the prevalence of primary HIV infection among symptomatic ambulatory clients is relatively rare, ranging between 0.13% and 0.66% (Chu & Selwyn, 2010). Health care providers need to maintain a high index of suspicion for HIV when treating patients with influenza, or mononucleosis like symptoms of fever, myalgia, fatigue, nausea or vomiting, pharyngitis, headache or lymphadenopathy, and offer HIV testing. An additional challenge when treating patients presenting with primary HIV infection symptoms is that HIV testing conducted within the window period may be non-reactive, or negative. Therefore knowledge of testing window periods is imperative for the proper identification and diagnosis of primary HIV infection. This is important because it is only after a diagnosis of HIV that an individual can begin treatment and begin to make lifestyle adjustments to reduce the risk of transmitting the virus to others.

**HIV Testing in British Columbia**

In British Columbia, the initial HIV screening test is the third generation enzyme immunoassay (EIA) test, it detects the presence of HIV antibodies as early as three to four weeks after exposure (BC Center for Disease Control [BCCDC], 2010a). The fourth generation EIA test is used as a supplemental test following a reactive third generation EIA. The fourth generation EIA has a slightly earlier window period of two to three weeks because in addition to testing for HIV antibodies it also tests for an HIV specific p24 antigen protein (BCCDC, 2010a). The BCCDC is planning to begin using the fourth generation EIA as an initial screening test, and some hospitals in BC are already use this test as an initial screening measure (BCCDC, 2010a). After a potential exposure to HIV, the exposed person
should be tested, using a third or fourth generation EIA test, at time of presentation, then at three weeks, six weeks, six months and nine months after exposure (BCCDC, 2010b).

Overall, more than 95% of HIV positive individuals will show detectable HIV antibodies by four to six weeks post infection, The gold standard confirmation of HIV infection seroconversion, is the Western Blot test. This test detects HIV antibodies and directly tests their reactivity against HIV specific proteins (BCCDC, 2010a). This can be detected as early as four to six weeks, with 99% of HIV positive individuals having a positive Western Blot within three months post-exposure (BCCDC, 2010a). The individual RNA nucleic acid amplification test (NAAT), can be used to detect the presence of HIV RNA as early as one to two weeks post-exposure, as well as to confirm an HIV infection in individuals with indeterminate EIA or Western Blot tests (BCCDC, 2010a).

Current HIV screening recommendations in BC are to offer and recommend a routine HIV test to all adults who have not been tested in the past year when other blood work is ordered, when a sexually transmitted infection test or diagnosis occurs or when an HIV test is requested. Additionally, HIV testing may be repeated as often as every three to six months in patients with an identified risk, such as injection drug users or sex workers, and as part of routine prenatal care (HIV Testing Initiative in Family Practice, nd). The intent of these screening recommendations is to cast the widest net possible to identify more people earlier in the disease process, when viral loads and infectiousness are higher, and to initiate interventions to prevention transmission and slow disease progression (Gustafson & Steinberg, 2011).

After the resolution of the symptoms associated with the primary HIV infection, the individual moves into the clinical latency period. On average, this asymptomatic period lasts
approximately 10 years. Unfortunately, during this asymptomatic period, the virus is constantly replicating and gradually destroying CD+ cells. Consequently the person is infectious, able to unknowingly transmit HIV to others, and suffering progressive damage to their immune system and ultimately developing AIDS. A diagnosis of AIDS requires a confirmed HIV infection and either a CD4+ count less than 200 cells/mm$^3$, or the presence of one or more, AIDS defining illnesses (BCCDC, 2013; Alberta Health Services, nd). Examples of AIDS defining illness include: bronchial, tracheal, pulmonary or esophageal candidiasis, Kaposi’s sarcoma, recurrent bacterial pneumonia or pneumocystis jiroveci pneumonia and chronic intestinal cryptosporidiosis (Alberta Health Services, nd). Early diagnosis and treatment of HIV can reduce transmission risk, substantially improve the quality of life of PLWHA, and prevent the progression to AIDS.

**Provincial HIV/AIDS Programming**

British Columbia’s HIV/AIDS programming is guided by the BC-CfE. The cornerstone of BC’s HIV/AIDS programing is Treatment as Prevention (TasP). Pioneered by BC-CfE physician and researcher Dr. Julio Montaner, TasP operates on the premise that the concentration of HIV DNA in blood and body fluids is directly correlated with the likelihood of transmitting HIV (BC-CfE, 2013). As will be more completely discussed in the next section, decreasing the viral load of HIV-positive individuals through the use HAART drugs, has the potential to curb the spread of HIV. In 2009, BC’s Ministry of Health launched a four year, $48-million pilot project called Seek and Treat for Optimal Prevention of HIV/AIDS (STOP HIV/AIDS) in Vancouver and Prince George. The goals of the pilot were to increase HIV screening and testing to identify HIV positive individuals, and to increase the number of HIV positive individuals being treated with HAART (STOP HIV/AIDS, nd). Due to the
success of the STOP HIV/AIDS pilot project the provincial government has renewed funding of $19.9 annually for the next four years and expanded the program to the entire province (BC-CfE, 2013, April). Additionally, HAART medications are provided free of cost to all HIV positive individuals who meet the treatment criteria in the BC-CfE Therapeutic Guidelines, and who are either a BC resident with Medical Services Plan (MSP) coverage, or have Interim Federal Health coverage (refugee status) or have active medical plan coverage from another Canadian Province, while awaiting active MSP coverage (BC-CfE, nd).

Within Prince George, BC, the Medication Adherence Support Program (MASP) provides “an intensive seven day-a-week medication adherence support program for people living with HIV, HCV and tuberculosis, who are struggling with adherence…” (Northern Health [NH], 2012, p. 5). HIV-nurse clinicians provide nursing services including blood collection, dressing changes, support and advocacy. Additionally, an on-site HIV-pharmacist is available for medication reconciliation and support. MASP also includes both a safe physical space where clients can come to use the shower or laundry facilities, as well as, mobile outreach services and text-based medication reminders and support (NH, 2012).

**Highly Active Antiretroviral Therapy (HAART)**

Today, the foundation of HIV treatment is HAART. Since HAART was first introduced in 1996, it has demonstrated the ability to inhibit viral replication and thus decrease plasma viral load to nearly undetectable levels. The caveat to HAART is that because HIV is never completely eradicated from the body, interruptions in therapy are associated viral load rebound, and increased risk of HAART resistance strains of HIV (BC-CfE, 2011). There are several benefits of decreased viral load, first, immune system function is improved thereby reducing the risk of opportunistic infections, improving the quality of
life and decreasing the mortality rates of individuals infected with HIV (Montaner et al., 2006). For example, prior to the availability of HAART, the average life span of a 20 year-old diagnosed with HIV was 56.1 years in developed countries. Since the advent of HAART an HIV-positive person can expect to live to at least age 69.4 years (Antiretroviral Therapy Cohort Collaboration, 2008). Unfortunately, this is still 12 years less than the average life span of non-HIV positive British Columbians (Province of British Columbia, 2013). The second benefit of decreased viral load is a reduction in systemic inflammation caused by uncontrolled immune system activation. Systemic inflammation is associated with end organ damage, and may play a role in the early development of cardiovascular disease, renal disease, cancer and neurocognitive decline in HIV-positive individuals (BC-CfE, 2013, February).

Finally, by reducing the plasma viral load to virtually undetectable levels, transmission of HIV from mothers to infants, shared needles, and between uninfected/infected (serodiscordant) couples is dramatically reduced. For example, the sexual transmission of HIV in serodiscordant, heterosexual couples is reduced by 96% when HAART is used (BC-CfE, 2013). Ultimately, this has the potential to slow the spread of HIV within entire populations, not just at the individual level (Montaner et al., 2006). For example, BC witnessed at 52% reduction in HIV transmission, between 1996 and 2009, that is largely attributed to expanded access to HAART, as well as other harm reduction initiatives, such as safe injection sites, and needle exchange programs (Montaner et al., 2010). As of May 2013, in BC, there were a total of 6,374 individuals receiving HAART, of these 1,035 are female (BC-CfE, 2013, May). As of January 2013, within the Northern
Health Authority there are a total of 229 PLWHA, and 185 (80.8%) are receiving HAART (Hamour, 2013).

**Antiretroviral medications.** Individuals who have previously been treated with HAART, who have experienced treatment failure, or other serious HAART related complications are too complex for primary management by a nurse practitioner and should be referred for care by an HIV specialist physician (BC-CfE, 2011). For individuals who have never received HAART, first line medications typically consists of a combination of three antiretroviral drugs, two nucleoside/nucleotide reverse transcriptase inhibitors (nRTIs), combined with either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI) (BC-CfE, 2013). In this section these three classes of drugs will be briefly discussed with an emphasis on the recommended first line choices for treatment naïve individuals.

**Nucleotide reverse transcriptase inhibitors.** Nucleotide reverse transcriptase inhibitors (nRTIs) form the backbone of HAART. They are transformed into an active molecule during intracellular phosphorylation. Once active, they become incorporated into the viral DNA chain and inhibit the binding of the enzyme transcriptase, resulting in termination of DNA chain synthesis and ultimately, decreased viral DNA production (Safrin, 2004). Resistance may develop because viral replication is rapid and prone to errors that allow nRTI resistant strains to spontaneously develop. Additionally, poor HAART adherence increases the likelihood that resistant nRTI strains are allowed to replicate, causing treatment failure and potentially to be transmitted to other individuals. As a class, the most serious adverse effect of nRTIs is mitochondrial toxicity. It arises from the incidental inhibition of the host’s mitochondrial DNA polymerase by the active phosphorylated nRTI compound
(Rang et al., 2012). Potentially life-threatening manifestations of mitochondria toxicity include myopathy, peripheral neuropathy, hepatic steatosis and lactic acidosis (Rang et al., 2012). Other common unwanted side-effects associated with nRTIs include nausea, vomiting, abdominal pain, anemia or neutropenia, insomnia, dizziness and headache (Rang et al., 2012). Emtricitabine is a frequently used nRTI that is used in first-line combination drugs Truvada and Atripla. It is important to note that females are particularly likely to report unwanted side effects such as rash and gastrointestinal disturbance (BC-CfE, 2013, February). Tenofovir disoproxil fumarate (TDF) is generally well tolerated but long-term use, and/or concurrent with PIs or other nephrotoxic medications such as non-steroidal anti-inflammatory drug, has been associated with renal injury and should be avoided in patients with renal disease (BC-CfE, 2013, February). Another nRTI is abacavir (ABC), prior to initiating this drug, screening for the HLA-B*5701 allele must be completed. This is because individuals who possess the HLA-B*5701 allele are at increased risk for developing a potentially life-threatening hypersensitivity reaction (BC-CfE, 2013, February). Additionally, ABC may be associated with an increased risk of myocardial infarction (MI), and as such should be avoided in patients with cardiovascular disease (BC-CfE, 2013, February). In BC, the recommended first line dual nRTI combination drug is Truvada, (tenofovir/emtricitabine), a non-nephrotoxic alternative is Kivexa (abacavir/lamivudine), if HLA-B*5701 negative (BC-CfE, 2013, February). Both regimens are taken as a once daily, fixed dose, without any food restrictions (BC-CfE, 2013, February).

**Non-nucleoside reverse transcriptase inhibitors.** NNRTIs bind at a site close to, but distinct from nRTIs. They prevent the HIV-1 reverse transcriptase enzyme from adding nucleotides to the DNA strand, resulting in decreased viral replication (Rang et al., 2012).
The first line recommended NNRTI, for treatment naïve individuals is Efavirenz (BC-CfE, 2013, February). Common side effects include rash, fever, headache, insomnia, nightmares, anxiety, liver damage, lipodystrophy and pancreatitis. When considering the use of these drugs with co-morbid depression, it is important to note that approximately 50% of patients treated with Efavirenz experience psychiatric side effects such as increased anxiety, depression and suicidal ideation (Watkins, Pieper & Treisman, 2011). These psychiatric side effects are usually temporary lasting for the first four to six weeks of drug therapy. Efavirenz is also not recommended for use during the first trimester of pregnancy and women of childbearing age, who do not use reliable contraception because it is teratogenic (BC-CfE, 2013, February). The care of HIV-positive women who are pregnant or who are planning on becoming pregnant should be conducted with expert guidance such as that available through the Oak Tree Clinic at BC Women’s Hospital (BC-CfE, 2013, February). Additionally, NNRTIs are most commonly associated with drug resistance due to poor adherence and transmission of drug resistant strains of HIV (BC-CfE, 2013, February). Efavirenz is a once daily medication best taken on an empty stomach at bedtime. There are several multi-drug combination products that allow for more convenient once daily, single tablet dosing. For example, Atripla is the recommended first-line dual nRTI (tenofovir/emtricitabine) and NNRTI (efavirenz) combination drug (BC-CfE, 2013, February).

**Protease inhibitors (PIs).** PIs prevent the binding of the protease, an enzyme responsible for cleaving HIV-1 or HIV-2 precursors into active proteins. This results in the creation of immature, non-infectious viral particles (Safrin, 2004). Recommended dual PIs are atazanavir/ritonavir, and is taken as a once daily dose, preferable with food (BC-CfE, 2013, February). Common unwanted side effects associated with PIs include nausea,
vomiting, abdominal pain, anemia or neutropenia, hyperglycemia, non-pathologic jaundice, elevated transaminase, impaired renal function, kidney stones (Rang et al., 2012; BC-CfE, 2013, February).

Two additional classes of drugs that may be used as part of HAART therapy include integrase strand transfer inhibitors, and entry inhibitors. They will not be discussed as part of this paper because drugs from these classes should be reserved only for those clients who are unable to tolerate, or who have experienced treatment failure on the preferred first-line regimens (BC-CfE, 2013, February). As well, these more complex individuals should be followed and managed by an HIV specialist physician, with additional collaboration or consultation with an HIV specialist pharmacist.

**Highly Active Antiretroviral Therapy Adherence**

In order for HAART to achieve the ultimate goal of sustained, suppressed viral load, an extremely high level (> 95%) of medication adherence is required (BC-CfE, 2011). Clinically, optimal HAART adherence is reflected as a plasma viral load of less than 40 copies/mL, when measured using polymerase chain reaction assay, or less than 75 copies/mL, when branched DNA test is used (Harris, Montessori, & Montaner, 2011). Suboptimal adherence (80-95%) is associated with an increased likelihood of viral resistance to HAART, increased morbidity and mortality, and the transmission of drug-resistance HIV strains (O'Neil et al., 2012). Failure of viral suppression is represented by the inability to maintain HIV RNA levels below 200 copies/mL (BC-CfE, 2013, February; Harris et al., 2011).

While it is difficult to determine actual adherence rates of HAART, it is generally accepted that adherence is approximately 50% (Duggan, Lochear, Fink, Okonta, & Chakraborty, 2009). This is significantly less than the optimal 95% adherence rates required for optimal
clinical outcomes. As well, the public health concern is that HAART resistant HIV strains may become more prevalent, thus limiting the HAART treatment options to regimens that contain drugs with poorer safety and tolerability profiles.

Even though pharmaceutical advancements have dramatically decreased the daily number of pills and the side effects associated with HAART, these medications are not without significant side effects, and they must be taken everyday, without interruption, for the rest of the individual’s life. Factors such as patient readiness, pill burden, depression, drug and alcohol abuse, and medication side effects strongly affect HAART adherence (Duggan, Lochear, Fink, Okonta, & Chakraborty, 2009). Additional social and environmental factors that influence HAART adherence include gender, stable housing, income, participation in the sex trade, incarceration, family dynamics, access to health care and medication, and continuity of relationship with a health care provider (Werb et al., 2012). In much the same way that research has revealed that vulnerability to HIV infection is influenced more heavily by social and environmental factors than by individual choice, so too is vulnerability to HAART non-adherence (Krusi, Wood, Montaner, & Kerr, 2010).

Unfortunately, the incredible complexity, and interaction of the factors affecting adherence has made it difficult for researchers to make specific recommendations to improve HAART adherence in women. In BC, it is recommended that depression, substance abuse and other mental health conditions receive high priority as part of the care plan for individuals receiving HAART (BC-CfE, 2011).

**Depression and HIV/AIDS**
The intent of this paper is to examine depression in the context of HIV infection and HAART treatment and adherence. Depression affects between 37.6 – 48.6% of people living with HIV, making it one of the most common comorbidities associated with HIV infection (O’Neil et al., 2012). Depression not only negatively impacts an individual’s quality of life, it also predicts a three-fold increase in the likelihood of HAART non-adherence and poorer clinical outcomes, as measured by CD4+ and viral load (Gonzalez, Batchelder, Psaros, & Safren, 2011; Schuster et al., 2012). Additionally, there is evidence to suggest that depressed HIV-positive individuals are more likely to initiate HAART at a later stage with lower CD4+ counts and higher viral loads, two factors associated with poorer treatment outcomes (Tegger et al., 2008). Many of the symptoms of depression, outlined below, are also associated with HIV disease progression, and HAART medication side effects (Schuster, Bornovalova, & Hunt, 2012; Carrico et al., 2011). This is of importance to primary care providers because, as will be discussed in later sections, the identification and subsequent treatment of comorbid depression improves overall quality of life, and may increase HAART adherence and HIV treatment outcomes.

A diagnosis of depression, is made, if over the same two-week period, at least five of the follow symptoms are present on most or nearly every day:

- Depressed mood nearly every day
- Markedly decreased interest or pleasure in activities
- Greater than 5% unintentional change in body weight
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
Feelings of worthlessness or excessive or inappropriate guilt

- Diminished ability to think or concentrate, indecisiveness
- Recurrent thoughts of death, recurrent suicidal ideation with or without a specific plan, or suicide attempt (American Psychological Association [APA], 2013)

Additionally, for a diagnosis of depression, these symptoms must cause significant distress or impairment in social, occupational or other areas of functioning (APA, 2013). In the context of HIV, depression negatively impacts an individual’s ability to cope with the challenges associated with being HIV positive such as stigmatization and medication adherence (Bianco et al., 2011). For NPs working with HIV-positive clients in primary care settings, identification and treatment of comorbid depression is an important intervention to optimize HAART adherence and improve the quality of life. In BC, NPs are able to independently diagnose, treat and manage depression (CRNBC, 2012).

Nurse Practitioners

In BC, physicians are the main primary care providers who initiate and monitor HAART. However, nurse practitioners (NPs), competent in HIV/AIDS care, and in collaboration with an experienced physician can diagnose HIV/AIDS and renew existing HAART prescriptions (BC-CfE, nd; CRNBC, 2011). NPs are included under the umbrella term, advanced practice nurses, and have been practicing in BC since 2005. They are registered nurses, who have, most commonly, completed a graduate degree in nursing and have demonstrated proficiency during both practical and written examinations. There are three classifications, or streams, of practice for NPs in BC: family, adult and pediatric. An NP is able to independently diagnose and treat certain diseases and conditions as specified by CRNBC’s document Scope of Practice for Nurse Practitioners: Standards, Limits and
Conditions (2012). NPs collaborate with physicians, and other health care professionals when they are treating patients with diseases or conditions that fall outside of their scope of practice, or when they require support or guidance for diseases with which they are unfamiliar. The intent of the NP role is to increase access to primary care services for all British Columbians.

The foundation of practice and core competencies of NPs is the World Health Organization’s (WHO) five principles of primary health care (PHC): accessibility, public participation, health promotion, appropriate technology and intersectoral collaboration (Canadian Nurses Association [CNA], 2009; CRNBC, 2011, January). PHC is both a philosophy and model for health care delivery. PHC attempts to answer the question, “Why treat people, without changing what is making them sick (WHO, 2012)?” It recognizes that health and well-being are affected by factors lying both inside and outside the health care sector. These factors that are outside of the health care sector are referred to as the social determinants of health. In Canada, the social determinants of health include gender, income, race, Aboriginal status, food insecurity, job security, early childhood development, housing, social exclusion and social safety networks (Mikkonen & Raphael, 2010).

The four categories of CRNBC’s NP competency framework are: 1) professional role, responsibility, and accountability, 2) health assessment, 3) therapeutic management, and 4) health promotion and prevention of injury (CRNBC, 2011, January). This research project will be approached from a PHC stance and the discussion will be organized according to CRNBC’s NP competency framework. Structuring this research project within a PHC framework will help to ensure that this project will treat the problem of low HAART adherence amongst HIV-positive women with comorbid depression, in a holistic and
complete manner. Organizing the findings according to the competency framework will ensure that the role of the NP will be comprehensively explored.
CHAPTER TWO

Literature Search Strategy

The overarching question for this project is, what is the role of the nurse practitioner, working in British Columbia, in optimizing adherence to HAART amongst marginalized, HIV-positive women with co-morbid depression? In order to address this question, the following sub-questions were explored:

- How can depression be identified, treated and evaluated by NPs working with HIV positive women?
- How can the treatment of depression by NPs be incorporated into strategies to improve HAART adherence that are currently being utilized in British Columbia?

Background information was researched guided by another set of sub-questions:

- What is the prevalence of HIV in Canada?
- What is the prevalence of comorbid depression among HIV-positive individuals?
- What is the effect of comorbid depression on HAART adherence among HIV-positive individuals?
- What are the effects of comorbid depression on HIV-positive women?
- What are the major risk factors for comorbid depression among HIV-positive women?

The literature search was initiated with a hand search of articles already collected during the completion of other assignments that were part of this program. Next, relevant websites, such as, the BC Center for Excellence in HIV/AIDS, Public Health Agency of Canada, World Health Organization, The Body Pro, CATIE and
Canadian HIV/AIDS Pharmacists Network, were reviewed in an effort to obtain grey literature sources, and to familiarize myself with current research priorities and recommendations. The literature search was conducted using University of Northern British Columbia and Northern Health Authority libraries. Online computerized databases CINAHL, MEDLINE, Cochrane Reviews, and PubMed were searched using various combinations of the following search terms: HIV, AIDS, women, female, marginalization, Canada, British Columbia, highly active antiretroviral therapy, medication compliance, medication adherence, nurse practitioner, depression, mental health, and chronic disease.

Ancestry searching of the most recent and relevant articles was used to locate additional articles. Finally, key search terms, the names of frequently cited authors and study names, for example, ‘LISA’, were searched in Google, to obtain additional grey literature materials. Once saturation had been achieved, articles were then scanned and included or excluded according to the criteria summarized in Table 1. Because HIV care and HAART are rapidly evolving, the decision was made to limit articles to those published in the last five years in an effort to capture the most current snapshot of HAART adherence research. Similarly, studies were included only if the data set was from after 1996, when antiretroviral drugs entered the arena of HIV care.
Table 1

_Literature Search Inclusion and Exclusion Criteria_

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published after 2008</td>
<td>Published before 2008</td>
</tr>
<tr>
<td>Published in English</td>
<td>Published in language other than English</td>
</tr>
<tr>
<td>Research studies of any type</td>
<td>Non-research articles</td>
</tr>
<tr>
<td>Research conducted in Canada or USA</td>
<td>Non-Canadian or American research</td>
</tr>
<tr>
<td>Data used in study was from after 1996</td>
<td>Data used in study was from prior to 1996</td>
</tr>
<tr>
<td>Study population included females</td>
<td>Study population included only males</td>
</tr>
<tr>
<td>Topic of research was relevant to primary</td>
<td>Topic of research was not relevant to</td>
</tr>
<tr>
<td>care and/or nurse practitioner practice</td>
<td>primary care and/or nurse practitioner practice</td>
</tr>
</tbody>
</table>

Summary of Articles Retrieved

Once the articles were collected and included or excluded according to the criteria specified in Table 1, they were read and categorized according to themes. The dominant research themes that emerged were: incidence and prevalence of HIV in Canada, incidence of comorbid depression with HIV, effect of depression on HIV disease progression and adherence, factors correlated with comorbid depression and HIV, and management of HIV and comorbid depression. Table 2 summarizes the number of articles retrieved and analyzed according to each theme, with some articles fitting into more than one theme.
Table 2

*Articles Retrieved Categorized According to Themes*

<table>
<thead>
<tr>
<th>Major Theme</th>
<th>Number of Articles Retrieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence and prevalence of HIV in Canada</td>
<td>6</td>
</tr>
<tr>
<td>Incidence of depression in people with HIV/AIDS</td>
<td>18</td>
</tr>
<tr>
<td>Effect of comorbid depression on HIV disease progression and adherence</td>
<td>13</td>
</tr>
<tr>
<td>Factors correlated with depression in people living with HIV/AIDS</td>
<td>20</td>
</tr>
<tr>
<td>Management HIV and comorbid depression</td>
<td>25</td>
</tr>
<tr>
<td>Total articles retrieved</td>
<td>82</td>
</tr>
</tbody>
</table>
CHAPTER THREE

Literature Search Findings

Incidence and Prevalence of HIV/AIDS in Canada

As of 2011, the estimated prevalence of people living with HIV/AIDS (PLWHA) in Canada is 71,300, this represents an 11.7% increase since 2008 (PHAC, 2012a). There are approximately 16,600 Canadian women living with HIV (PHAC, 2012b). Heterosexual contact and injection drug use are the two most common exposure categories for Canadian women (PHAC, 2012b). Within BC, there are an estimated 11,700 PLWHA (BC Center for Disease Control [BCCDC], 2012). The incidence of new HIV infections in Canada has remained relatively stable with an estimated 3,175 new infections in 2011, compared with 3,335 new infections in 2008 (PHAC, 2012a). The literature has suggested that advances in HIV treatment have reduced the mortality of HIV, thus allowing an increase in the prevalence without a corresponding increase in transmission rates (PHAC, 2012a). In 2011, BC reported 289 new positive HIV tests, of these 24 (female = 10) were from Northern Health Authority (NHA); this represents the lowest incidence in the last three decades of this epidemic (BCCDC, 2012). Currently, in NHA there are approximately 220 PLWHA (Hamour, 2013). Consistent with overall exposure categories for the province, injection drug use is the predominant exposure category within NHA. The dramatic decrease in the incidence of HIV in BC is largely attributable to a reduction in HIV transmission amongst people who use injection drugs (BCCDC, 2012). The proportion of new HIV diagnoses due to injection drug use (IDU) has decreased from 30%, in 2008, to 12.1% in 2011 (BCCDC, 2012).
It is also important to discuss HIV/AIDS among Aboriginal people in Canada. Over the last decade, it has been observed that Aboriginal people are over-represented in the number of new diagnoses of HIV. HIV infection risk is estimated to be 3.6 times higher for Aboriginal people compared to non-Aboriginal people (PHAC, 2010). In 2008 there was an estimated 4,300 – 6,100 HIV-positive Aboriginal people, which represents a 24% increase in from 2005 estimates. Of these 1,691 lived in British Columbia (Hogg, Strathdee, Kerr, Wood, & Remis, 2005; PHAC, 2010). Among Aboriginal people, injection drug use was the predominant HIV transmission category and accounted for 66% of new diagnoses (PHAC, 2010). When examining a population of injection drug users in Vancouver, BC, Wood et al. (2008) found that the prevalence of HIV among Aboriginal people was significantly higher than among non-Aboriginal people (16.0% versus 25.1%; P< 0.001). Aboriginal women are disproportionately represented in the number of positive HIV tests. Women represented 48.1% of positive HIV tests within the Aboriginal population by comparison; in non-Aboriginal Canadian populations women represent only 20.7% of new diagnoses (PHAC, 2010).

**Incidence of Depression in People Living with HIV/AIDS**

A challenge that emerged in interpreting the research findings for this project relates to the fact that a wide variety of depression rating scales were utilized. As well, depression scores may be inflated because of the similarity between the cognitive and somatic symptoms of HIV disease progression, medication side effects and depression (Lima et al., 2007). However, both somatic and cognitive symptoms improve with depression treatment (Ferrando & Freyberg, 2008). The most frequently utilized scale was the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D was originally designed as a
research tool for use in non-psychiatric community samples and it commonly over estimates the prevalence of clinical depression in a population (Lima et al., 2007). Crane et al. (2010) validated the use of the Patient Health Questionnaire (PHQ-9) for use in clinical settings PLWHA but cautioned that differences were observed between African and Caucasian Americans, and results were not stratified by gender. Additionally, there are cultural differences in how depression is manifested in the clinical setting. Cain et al. (2011) found that Aboriginal people rarely used the term ‘sadness’ to describe their depression and that they associated social isolation and disconnection with depression more often than psychological feelings or mood. Additionally, Logie, James, Tharao, and Loutfy (2013) suggest that African, Caribbean and Black women may conceptualize depression differently, and that conventional depression screening tools may not accurately assess depression in these populations.

In addition to dissimilar depression rating scales, there is a wide variation in the estimates of depression among PLWHA due to varied population characteristics and time since diagnosis with HIV. Despite this variation, there was consistency in the findings that depression is significantly more prevalent among PLWHA, that women tend to experience depression more frequently than men, and that depression is associated with decreased adherence to HAART. In a longitudinal cohort study of 1,774 HIV-positive males and females, Teggar et al. (2008) found that 57% had a diagnosis of either depression or other mood disorder. Tedaldi et al. (2012) found that depression was significantly more prevalent among women (21.9%) compared to men (11.8%, p=0.005). Likewise, Applebaum, Richardson, Brady, Brief and Keane (2009) found that 77% of women, compared with 44% (P = 0.11; P< 0.05) of men were depressed, in a study of 67 HIV-positive outpatients. In a
longitudinal study, using data from the Women's Interagency HIV Study (WIHS), Kapadia et al. (2008) found that 47% (p < 0.001) of women enrolled in a drug abuse treatment program were classified as having significant depressive symptoms. Bhatia et al. (2011) found that in the 180 days immediately following diagnosis with HIV, 67% of people screened positive for depression and that women were more likely to be depressed than men ($\chi^2 = 4.2, P=0.04$). In the longitudinal observational study, Kacanek et al. (2010) found that 22% of PLWHA, without a history of depression, developed depression during the yearlong study period. Additionally, they found that women (37%) were significantly more likely to develop depression than men (18%; P=0.005) (Kacanek et al., 2010).

A study conducted by Logie et al. (2013) with a population of 173 HIV-positive, African, Caribbean and Black women in Ontario, found that 65% of study participants met the criteria for depression. In a study conducted in BC, 50% of HIV-positive individuals, enrolled in a drug treatment program, had significant depressive symptoms (Zhang et al., 2012). Results of another British Columbian study found that longitudinally tracked depression amongst participants ranged between 37.6% and 48.6% (O'Neil et al., 2012). Unfortunately the results were not stratified by gender, but the overall prevalence of depression in this population is similar to that of other studies conducted with PLWHA enrolled in substance abuse treatment programs.

A large gap in the literature is in research examining HIV, depression and HAART adherence among Aboriginal people. Depression and suicide among Aboriginal people is a serious concern because many Aboriginal communities experience rates significantly higher than the general Canadian population. For example, 21% of low-income Aboriginal people experienced depression, compared with 13% of low-income non-Aboriginal people (Reading
& Wien, 2009). Because poorly treated depression is a risk factor for suicide, it is important to note that suicide rates among First Nations youth are five to six times higher than non-Aboriginal people (Health Canada, 2013). Cain et al. (2011) found that half of the 72 HIV-positive Aboriginal people with comorbid depression, had either attempted or had recurring thoughts of suicide. By comparison, in an American study of 514 non-Aboriginal PLWHA, 15% reported having suicidal thoughts in the two weeks prior to the study period (Shacham, Nurutdinova, Satyanarayana, Stamm & Overton, 2009).

There is a large and rapidly evolving body of research examining the relationships between social determinants of health, colonization, the residential schooling legacy and Aboriginal health and wellness (Pearce et al., 2008). However, it is well beyond the scope of this project to thoroughly examine this fascinating body of knowledge. My intent is to draw attention to the idea that given the high prevalence of depression and suicide among non-HIV positive Aboriginal people, it is conceivable that depression among HIV-positive Aboriginals may be significantly higher as well. However, this literature search did not result in resources that supported this supposition.

This literature search found that HIV-positive individuals are two to four times more likely to suffer from depression than the general population, that depression rates are highest in the period after diagnosis with HIV, and that women are more likely to experience depression (Bhatia et al., 2011; Kacanek et al., 2010). There is evidence to indicate that the prevalence of depression among HIV-positive women ranges between 37% and 65% (Kacanek et al., 2010; Logie et al., 2013). However, there is a gap in the literature examining depression among HIV-positive women, and research that examines depression among HIV-positive Aboriginal people is essentially absent.
Effects of Co-morbid Depression on HIV Disease Progression and HAART Adherence

In the literature, evidence of adherence was measured either directly or indirectly. Direct measures of adherence include pill counts, electronic pill cap monitoring and self-reported adherence. A caution when interpreting the results of studies that used these direct measures of adherence is that, because the subjects knew they were being evaluated, their behavior may have changed. Additionally, these strategies were only employed for a limited amount of time, so researchers may have missed changes in adherence over time. Indirect measure of adherence entailed analyzing biochemical markers of HIV disease, such as CD4+ count and viral load. Unfortunately, because these biochemical markers of HIV represented the cumulative effect of all factors in an individual’s life, including adherence, a direct causal link with adherence could only be implied. However, from a clinical perspective, a clinician may find it useful to use both direct and indirect measures to assess HAART adherence.

Barriers associated with the clinical use of direct measures include the associated costs of administering electronic pill cap monitoring systems or clients forget to bring in their medications for pill-counts. Fortunately, in BC, all HAART medications are dispensed from a central pharmacy operated by the BC-CfE, this means that HIV clinicians can readily assess whether or not a client has at least obtained their medications according to schedule.

Biochemical effects of depression on HIV/AIDS. Review of the retrieved studies revealed that depression directly affects HIV disease progression by altering the physiological functioning of the immune system. In their systematic literature review, Gore-Felton and Koopman (2008) concluded that after controlling for adherence and substance
abuse, depression was directly correlated to biochemical markers of HIV disease progression. Schuster, Bornovalova and Hunt (2012) frame the discussion of the biochemical response to depression around dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. Physical and emotion stresses, such as depression, trigger the hypothalamus to release corticotrophin releasing hormone, which in turn stimulates the pituitary to release adrenocorticotropic hormone (ACTH). ACTH stimulates the adrenal cortex to secrete cortisol. Elevated cortisol impairs immune function by releasing inflammatory cytokines, triggering immune cell death, impairing T-cell production by the thymus, and inhibiting release of interleukins and interferon, which impairs lymphocytic response by natural killer (NK) cells to antigens (Schuster, Bornovalova, & Hunt, 2012). The net result of HPA axis mediated immune dysfunction is increased HIV replication leading to further destruction of CD4+, NK and other immune system cells and ultimately progression to AIDS. This relationship is partially illustrated by Carrico et al. (2011) who found that depressive symptoms predicted a 50% increase, from baseline, in mean HIV viral load, after controlling for CD4+ count at baseline. Tedaldi et al. (2012), found that depression was significantly associated with CD4+ count < 200 cell/mm³; however, they did not find a statistically significant correlation between depression and viral load. In a study of 127 IDUs, Springer, Chen and Altice (2009) found the improvements in depressive symptoms were significantly correlated with improvements in CD4+ counts and adherence. Conversely they found that worsening depressive symptoms were significantly associated with decreased CD4+, increased viral load, homelessness, female gender, poor self-efficacy, and use of illegal drugs (Springer, Chen & Altice, 2009). Psychological stress, such as depression, triggers HPA axis
dysfunction, which in turn causes impaired immunologic response to HIV infection and is associated with increased viral loads and poorer clinical outcomes.

Psychological Effects of Comorbid Depression

Five studies were retrieved that specifically examined the relationship between depression, behavior, psychosocial factors and HAART adherence. Wagner et al. (2011), sought to determine whether somatic or cognitive symptoms of depression differentially predicted non-adherence. The authors concluded that adherence, measured directly via electronic pill cap monitoring, negatively correlated with depression ($r = -0.08; p<0.01$) in a population of HIV-positive males and females. With further analysis they found that HAART non-adherence was significantly correlated with the following cognitive symptoms; depressed mood, loss of interest, hopelessness, guilt, poor concentration and a sense of worthlessness. The only somatic symptom of depression to significantly correlate with non-adherence was fatigue. Additionally, the authors found that their model fit when tested in a cross-sectional multivariate analysis against a number of different variables including race, sexual preference and gender (Wagner et al., 2011).

DiLorio et al. (2009), found that depression and poor self-efficacy, significantly predicted non-adherence, measured through a self-report questionnaire, in a mixed gender sample of PLWHA. They further added that poor social support strongly predicted increased levels of depression. Social support was described as, “having someone to share activities with, to work out a plan with, who lets me be myself, and who loves and cares (DiLorio et al., 2009, p. 16)”. They also found that stigma and satisfaction with medical care were directly related with self-efficacy, and self-efficacy was inversely correlated with depression.
Likewise, Cha, Erlen, Kim, Sereika, and Caruthers (2008), found that depressive symptoms did not directly influence self-reported HAART adherence, rather depression negatively impacted self-efficacy beliefs, which in turn determined whether or not an individual would be adherent to HAART. They also found that poor social support strongly predicted increased likelihood of depression in this sample of HIV-positive males and females (Cha et al., 2008).

Wendorf and Mosack (2013) found that the effect of depression on HAART adherence was mediated by coping strategies. Depression, along with HIV-related cues, and health and self-care belief, determined an individual’s coping style. HIV-related cues were referred to as any illness cues related to HIV disease progression or treatment such as intrusive side effects, stigma, medication reminders, or disappointing clinical results (Wendorf & Mosack, 2013). Higher levels of depression were associated with negative, or avoidance, coping strategies. Avoidance oriented coping strategies were directly correlated with HAART non-adherence (Wendorf & Mosack, 2013). They described depression as decreasing an individual’s ability to respond to the challenges associated with living HIV.

Similarly, Bianco, Heckman, Sutton, Watakasol and Lovejoy (2011), found that avoidance coping strategies, and poor social support significantly predicted depression among older (> 50 years) HIV-positive males and females.

In the only study retrieved that did not find any correlation between depression and adherence in male or female subjects, Applebaum et al. (2009), found that unwanted medication side-effects and alcohol use more strongly predicted non-adherence amongst HIV-positive women. While they found that depression affected 77% of females, compared to 44% of males, they did not find any significant differences between genders with respect
to adherence. The authors suggest that this finding may be due to characteristics of the sample population such as participation in a comprehensive HIV program that emphasized mental health and positive health practices (Applebaum et al., 2009).

Interestingly, despite the similarities in the findings on the relationship between psychosocial factors and depression in these five studies, they diverged when assessing whether depression predicted HAART non-adherence. Whereas Wendorf and Mosack (2013), DiLorio et al. (2009), and Cha et al. (2008), found that depression correlated with HAART adherence among males and females, Bianco et al. (2011) did not find a significant correlation between depression and adherence amongst older HIV-positive women, but they did find a correlation amongst HIV-positive men. It is possible that the contrasting findings from these studies are due to the influence of the male gender in the studies by Wendorf and Mosak (2013), and DiLorio et al. (2009) or yet unknown characteristics of HIV positive females. The contrasting findings from these studies illustrates the importance of research that stratifies findings according to gender, as well as research specifically examining co-morbid depression in HIV-positive women.

Depression impacts the progression of HIV in two ways. First it directly precipitates dysregulation of the HPA axis, which causes subsequent immunologic dysfunction. Second, it indirectly causes shifts in cognitive, emotional and behavior functioning that predispose an individual to become non-adherent with HAART. Non-adherence to HAART is associated with unchecked viral replication and hastened decompensation of the immune system. Depression is associated with decreased CD4+ counts and elevated viral loads, both indicators of HIV disease progression. The next section will discuss factors that are associated with comorbid depression.
Factors Correlated with Comorbid Depression

Much of the evidence found that depression was a risk factor associated with numerous biological and psychosocial factors related to HAART non-adherence. Analysis of the research revealed that many of the same risk factors related to increased susceptibility to contracting HIV, are also linked to increased risk of depression and HAART non-adherence. The biggest challenge that emerged in analyzing the research was interpreting the results to determine whether depression was an exposure risk or an outcome. This is because the majority of the studies were observational retrospective cohort studies, where significant depression was an incidental finding not necessarily the focus of the study.

Tedaldi et al. (2012) extensively examined depression in the context of HIV, and found that women were significantly more likely to experience depression than men, and they also correlated increased risk of depression with having no marital/sexual partner, being heterosexual, using injection drugs, being co-infected with Hepatitis C, and personal or family history of depression. In another study that specifically examined factors correlated with depression, Bhatia et al. (2011) found that in addition to being associated with female gender, depression directly correlated with income < $25 000, recent substance abuse, poor access to medical care, and low self-efficacy. As the risk factors for depression were not stratified by gender, caution should be used when interpreting these findings because readers are unable determine if any of these factors affect women differently than men.

There were a number of studies conducted using data from the Longitudinal Investigations into Supportive and Ancillary Health Services (LISA) cohort. The LISA cohort is particularly relevant to this paper because it is largely representative of the people receiving HAART in BC since 1996, including marginalized people such as women and
those who self-identify as Aboriginal (Palmer et al., 2011). Palmer et al. (2011) found that 47% of study participants had negative body image. Within the population of people with negative body image they also found that 49.76% (p<0.001) also reported high levels of stigma and depression. Unfortunately, the authors analyzed stigma and depression as a single variable, so it is difficult to determine the impact depression alone had on body image, or if stigma affected depression and vice versa. Blashill, Gordon and Safren (2012), studied a mixed gender sample of 89 PLWHA with opioid-dependence, and found that concerns about physical appearance were associated with increased depression and anxiety. Unfortunately, neither of these studies stratified the results by gender, however, they were included in this project because of the consistency in the relationship between body image and depression. Additionally, lipodystrophy, a redistribution of fat away from the face and deposition on the abdomen and trunk, is associated with both HIV disease progression as well as HAART side effects.

In another study with the LISA cohort, Parashar et al. (2011), found that among participants who had unstable housing, 70.3% also had depressive symptoms, compared to 50.8% of participants who had stable housing (P < 0.001). Additionally, they found that adherence among people who were unstably housed was 45.3%, compared to 62.7% (P <0.001) among stably housed HIV-positive individuals. This study did not find gender to be a significant predictor of homelessness or depression, nor did it reveal whether depression was a cause or effect of homelessness or unstable housing. Nonetheless this is an important study because it demonstrates the impact socioeconomic factors have on the mental and physical wellbeing of people living with HIV/AIDS. This study, as with the next study to be
discussed, highlights the importance of addressing the social and structural factors as well as factors within an individual’s control when addressing HAART adherence.

In the final study using data from the LISA cohort, Anema et al. (2011) found that 71% of participants experienced food insecurity. Among those who were food insecure, 66.7% also experienced depression, compared to 33.8% ($p<0.0001$) of those who had food security (Anema et al., 2011). Food insecurity is also closely associated with unstable housing, for example only 16% of unstably housed people were food secure compared to 50.8% ($P < 0.001$) of those who were stably housed (Parashar et al., 2011). By comparison, food insecurity among the general British Columbian population is estimated at 8.4% (Health Canada, 2012). Given that food insecurity is related to decreased adherence, lower body mass index, lower odds of viral suppression and increased risk of mortality, it is vitally important to assess food security among all HIV-positive individuals, but especially those who are unstably housed and depressed.

Nicotine dependence was found to significantly correlate with depressive symptoms in a study examining the relationship between nicotine dependence and HAART adherence by Webb, Vanable, Carey, and Blair (2009). Richardson et al. (2009) found a correlation between pain frequency and severity, depression, and longer duration of tobacco dependence. They found that depression significantly and directly correlated with the severity of pain. They also found that severe pain correlated with both a history of crack/heroin use, and with IDU as the mode of HIV transmission (Richardson et al., 2009). Findings by Tedaldi et al. (2012) supported this association between depression and nicotine dependence. While the mechanism linking depression with nicotine use is not clear, it is important to note that nicotine dependence is associated with increased rate of depression, pain severity and
frequency, and non-adherence to HAART (King et al., 2012). It is suggested that nicotine
dependence is an indicator of other socioeconomic factors such as poverty and low literacy
that influence depression risk and HAART non-adherence (King et al., 2012; Webb et al.,
2009).

Boarts, Buckley-Fischer, Armelie, Bogart and Delahanty (2009) examined depression
in a population of HIV-positive individuals who also had a diagnosis of post-traumatic
stress disorder (PTSD). In the sub-population of people with PTSD attributed to HIV
diagnosis, 69.2% met the criteria for depression, and in the sub-population with non-HIV
related PTSD 78.3% met the criteria for depression (Boarts et al., 2009). When examining
HAART adherence rates Boarts et al. (2008), found that adherence over time improved
among the sub-population with HIV-related PTSD, whereas adherence deteriorated over time
in the sub-population with PTSD related to other traumas. The importance of PTSD is
highlighted when examining the incidence of PTSD and depression among women IDU.

Amongst a population of HIV-positive Canadian African, Caribbean and Black
women, Logie et al. (2013) found that racial and gender discrimination had a significant
positive correlation with depression. They additionally found that the most significant
predictor of depression was HIV-related stigma, and was significantly correlated with racial
and gender discrimination. The influence of stigma on depression was also found among
HIV-positive Aboriginal people. Cain et al. (2013) found that stigmatization contributes to
the development of depression among Aboriginal PLWHA. Sources of stigmatization
include being Aboriginal in dominant non-Aboriginal Canadian society, as well as
stigmatization related to being HIV positive by their communities, family and friends (Cain
et al., 2013).
Interestingly, Cain et al. (2011), found that among HIV-positive Aboriginal people, the diagnosis of HIV was not the primary source of depression. Participants described racism, poverty, drug and alcohol use, childhood abuse, lack of housing and unemployment as key factors contributing to their depression, and that their depression was the underlying cause of behaviors that put them at risk for contracting HIV. This finding supports the idea that increased vulnerability to HIV among Aboriginal people is not based on individual choices or characteristics, rather it represents the cumulative effect of colonization, residential schooling legacy and social and economic marginalization (Pearce et al., 2008).

In a study by Eiboff, Somers and Moniruzzaman (2012), they found that among the 133 female participants, 72.7% of injection drug users met the criteria for depression, compared with 43.0% of non-injection drug users. Additionally, they found that PTSD occurred more frequently in female injection drug users (54.5%) than female non-injection drug users, and overall, the prevalence of depression and PTSD in females was higher than in males. Nolan et al. (2011) found that in the first year of antiretroviral treatment, only 30.3% of IDUs were ≥ 95% adherent to HAART. Of those who were adherent to HAART, 80.8% achieved HIV RNA suppression, whereas only 28.9% in the non-adherent group achieved viral suppression (Nolan et al., 2011). While the studies reviewed for this project did not reveal a causal link between depression and IDU, the high prevalence of depression and the low levels of adherence among IDUs make this an important population in the discussion of depression and HAART adherence. Furthermore, because injection drug use is one of the leading HIV exposure categories for both Aboriginal and non-Aboriginal women, HAART adherence is vitally important as part of the BC-CfE’s Treatment as Prevention program to
slow the spread of HIV by decreasing the prevalence of HIV at the population level (Montaner, 2010; O'Neil et al., 2011; PHAC, 2010).

There are numerous psychosocioeconomic factors associated with comorbid depression among HIV-positive individuals. The most obvious gap in the literature retrieved for this project is the limited number of studies that examined depression in females. Factors associated with comorbid depression among HIV-positive women include: injection drug use, discrimination, acute or chronic pain, PTSD, social support, and avoidance coping. Additional factors among both HIV-positive males and females include: poverty, relationship status, hepatitis C co-infection, personal or family history of depression, body image, unstable housing, food insecurity, nicotine dependence, self-efficacy and stigma. These psychosocial and economic factors are similar to the factors that increase vulnerability to HIV.

Depression has both a direct and indirect negative impact on HIV disease progression through its effect on immunological function, and cognitive, emotional or behavioral functioning that increase the likelihood of HAART non-adherence. Adherence to HAART is crucial at the individual level for decreasing HIV related morbidity and mortality, as well as at the population level to slow the spread of the virus. The next section will discuss strategies to treat depression among HIV-positive individuals in an effort to improve quality of life by decreasing depressive symptoms, as well as to increase adherence to HAART.

Management of HIV and Comorbid Depression in Primary Care

This literature search revealed a paucity of studies that investigated improving HAART adherence among HIV-positive women, with comorbid depression. Two clinical practice guidelines were retrieved that specifically addressed co-morbid depression among
people living with HIV/AIDS (PLWHA). Six interventional studies were retrieved, however, only three of these directly addressed depression among HIV-positive individuals, and none of these studies stratified the results by gender. My literature search findings are supported by a systematic review that examined interventions for the treatment of HIV and depression published in 2009 that found only 6.7% (n=97) of the studies exclusively used women, none of these studies met the inclusion criteria for this project (Sherr, Clucas, Harding, Sibley, & Catalan, 2011). In an opinion piece, Monforte et al. (2010), remark that women comprise less than 20% of participants in clinical trials, except for those trials evaluating vertical (mother to fetus) HIV transmission, and that this proportion is declining. The concern with the lack of studies involving HIV-positive women, is that females exhibit behavioral, cultural, and physiological differences from men that may result in different pharmacological effects and responses to HAART and antidepressant therapy (Montforte et al., 2010). However, due to the scarcity of research investigating HIV-positive women with comorbid depression, the studies discussed in this section reflect research conducted on predominantly male populations.

**Screening and identification of depression.** The New York State Department of Health AIDS Institute (2010), recommends that clinicians screen clients for depression, at least annually, and whenever depression symptoms are identified, with the following two-question screen:

- During the past month, have you often been bothered by feeling down, depressed or hopeless?
- During the past month have you been bother by little interest or pleasure in doing things?
If the client answers "yes" to either of these questions, then a more detailed evaluation using a validated depression rating scale is recommended. Commonly used depression rating scales include the CES-D, Beck Depression Inventory (BDI), Patient Health Questionnaire 9 (PHQ-9), and Hamilton Rating Scale for Depression (HAM-D/HDI). No specific recommendations were found indicating a superior depression rating scale, rather it was suggested that clinicians use a single rating scale best suited to their practice style and client characteristics (Relf, Eisbach, Okine & Ward, 2013). As discussed in an earlier section, an official diagnosis of depression is made using the diagnostic criteria specified in the DSM-V.

**Non-pharmacologic interventions.** Cognitive behavioral therapy (CBT) was the most commonly investigated non-pharmacological intervention for PLWHA with co-morbid depression. CBT is a short-term psychotherapy, which can be conducted in both individual and group settings. It focuses on the relationship between one's thoughts, feelings and actions. Through a series of 10–12 sessions participants are given strategies to change their patterns of behavior, thoughts or feelings that are contributing to and engraining their depression (Safren, Gonzalez & Soroudi, 2008). Safren et al. (2009) conducted a randomized controlled trial (RTC) that compared the effect of cognitive-behavioral therapy for HIV medication adherence and depression (CBT-AD) to the effect of a single session for adherence and letter to their physician documenting their diagnosis with depression. The authors did not stratify the results by gender. Regardless, they found that the CBT-AD group demonstrated improvements in HAART adherence, as well as decreases in both depressive symptoms and viral load. These improvements were maintained over 6 and 12-month follow-up. In a similar study conducted with HIV-positive injection drug users, Safren, O'Cleirigh,
Bullis, Stein, and Pollack (2012), found significant improvements in adherence and CD4+ counts, as well as decreases in depressive symptoms. However, in this study the authors found that these gains were not maintained beyond the 3, 6 or 12-month follow-ups. They recommend that amongst PLWHA who use injection drugs, CBT-AD, be continued beyond the usually 10-12 sessions (Safren et al., 2012). The efficacy of CBT is supported in the systematic review of the literature examining interventions for HIV and depression by Sherr et al. (2011), who found that psychological interventions, specifically CBT, was consistently the most effective.

Access to counseling services may be limited by availability, location or cost in many communities. Referral to an AIDS Service Organization (ASO) for additional support may be a strategy to access counseling services, as well as, receive peer and social support, HIV/AIDS education, and addictions counseling (BC-CfE, 2011; Positive Living North [PLN], nd). Additionally, ASOs may also participate in leadership, community HIV/AIDS advocacy and educational activities (PLN, nd). Another important community resource for any HIV-positive individuals struggling with HAART adherence are programs such as the Medication Support and Adherence Program, where clients can receive specialized HIV support as well as, access to a safe, clean environment.

Other non-pharmacologic interventions that may be of use with PLWHA with co-morbid depression include mindfulness-based stress reduction (MBSR) therapies such as yoga, meditation and breathing exercises (Relf, Eisbach, Okine & Ward, 2013). Hand, Lyerly, Jaggers, and Dudgeon (2009) conducted a systematic review of the literature investigating the effect of exercise on HIV-positive individuals, and found moderate-intensity aerobic exercise consistently decreases symptoms of depression and anxiety, but
had no effect on HAART adherence or CD4+ count or viral load. The authors suggest that physical inactivity and associated deconditioning may exacerbate HIV disease and treatment related symptoms such as fatigue and lipodystrophy factors associated with HAART non-adherence.

**Pharmacological interventions.** There was a significant amount of research examining the role and effectiveness of antidepressants in the care of HIV-positive individuals with comorbid depression. When discussing pharmacotherapy for depression, it is important to remember that psychotherapy combined with antidepressant therapy is the most effective regimen for most patients, and that for many clients with mild-moderate depression psychotherapy alone may be as effective as medications (New York State Department of Health AIDS Institute [NYHAI], 2010). An additional consideration is that the primary health care approach requires that clinicians also attend to the predisposing factors for depression such as poverty, unstable housing, substance abuse and food insecurity. Antidepressant therapy without concurrent strategies to improve an individual’s social determinants of health is unlikely to provide lasting and effective results.

As previously mentioned, enrollment of HIV-positive women in HIV related clinical trials is low. Females comprise less than 20% of participants in clinical trials, despite representing 50% of the worldwide HIV-positive population (Monforte, 2010). No studies were retrieved for this project that examined the effects of antidepressants among female participants. Again, due to the lack of existing evidence, findings for pharmacologic interventions will be extrapolated to females from studies conducted with predominantly gay/bisexual male participants. No evidence was found indicating that antidepressants were ineffective with HIV-positive individuals. In the studies retrieved treatment with
antidepressant medications were associated with decreases in depression symptoms, and some studies found improvements in CD4+ count and viral loads, and adherence to HAART medications. Selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) are the most commonly researched antidepressants for use with HIV-positive individuals.

Cruess et al. (2012), found that adherence was significantly higher among depressed PLWHA prescribed psychotropic medications, including antidepressants, compared with those who were not prescribed any psychotropic agents. Similarly, Tsai et al. (2010), found that antidepressant use was associated with a 25% increase in self-reported HAART adherence and 1.55 greater odds in achieving viral suppression among unstably housed or homeless participants. They suggested that the improvements in viral suppression were related to improved medication adherence and increased participation in HIV care services.

In a related study, Tsai et al. (2013) compared the effect of directly observed fluoxetine delayed release (once weekly) with the effect of referral to a community psychiatric program for unstably housed or homeless depressed HIV-positive individuals. Interestingly, the authors found that depression severity was significantly reduced with fluoxetine use, but there was no significant change in HIV RNA levels or HAART adherence. The authors attribute their small sample size with the statistically insignificant effect of Fluoxetine on HAART adherence in this study. Even though findings were not stratified by gender in any of these studies, these findings are relevant to this project because they address comorbid depression among HIV-positive people who are unstably housed or homeless, a risk factor for depression among women.
Horberg et al. (2008), specifically examined the effect of SSRIs on HAART adherence and found that individuals who were >80% adherent to SSRI regimen exhibited statistically similar HAART adherence and viral control as non-depressed HIV-positive individuals. The authors also found that people with comorbid depression, who were adherent to SSRIs, had greater improvements in CD4+ counts than untreated depressed HIV-positive people. This study also demonstrated that untreated depression significantly reduces the likelihood of achieving viral suppression. Kumar and Encinosa (2009) also found that treatment of depression, regardless of the treatment used, is associated with improved HAART adherence, comparable to the adherence rates of non-depressed HIV-positive people. They also found a direct correlation between the degree of depression and HAART non-adherence.

Safety and prescribing considerations for pharmacologic treatment of depression.
It is beyond the scope of this paper to conduct an in-depth discussion on the potential adverse interactions between HAART and antidepressants, or to review all the antidepressants available for use, but a brief overview is warranted for the purposes of this project and safe NP practice. The foundation of most drug-drug interactions involves cytochrome P450 (CYP450), a family of enzymes responsible for the metabolism of most medications. Medications can either induce or inhibit the CYP450 enzymes. If two or more drugs use the same CYP450 pathway, significant drug-drug reactions may occur because drug metabolism is altered and this may lead to toxic, or sub-therapeutic serum levels (Lynch & Price, 2007). In PLWHA the consequences may be drug discontinuation, viral load rebound or the development of resistant HIV strains (Tseng et al., 2012). Protease inhibitors, such as Ritonavir, are the most common HAART medication implicated in drug-drug interactions.
Ritonavir is a potent inhibitor of CYP450 enzymes, and most commonly results in increases in the serum levels of the concomitant drug, although serum levels of Ritonavir may also be increased to toxic levels with some drug combinations. For example, serum levels of SSRIs and TCAs metabolized via the CYP450 pathway are increased and this increases the risk of serotonin syndrome and TCA toxicity (NYHAI, 2010; HRSA, 2011). Other PIs and Efavirenz (NNRTI) may decrease the serum levels of other antidepressants such as paroxetine, sertraline and buproprion (HRHS, 2011). St. John’s Wort, a popular herbal medication used to treat depression, is contraindicated for those using PIs and NNRTIs because it can decrease the serum levels of these medications contributing to treatment failure and the development of HAART resistant HIV strains (HRSA, 2011).

Management of drug interactions may involve increasing or decreasing medication dosages, or completely avoiding certain combinations. There are several challenges to monitoring for potential drug interactions. First, PharmaNet, BC’s prescription monitoring system does not include HAART medications on client’s profiles (Kreutzwiser, 2013). The implication for both practitioners and clients is that if a client receives medical care outside of their HIV clinic, they may be unknowingly prescribed inappropriate medications. Primary care providers should counsel clients on this potential risk if they seek medical care outside of their regular primary care clinic. Due to concerns about inadvertent disclosure of HIV-positive status and HIV-related stigma, the inclusion of HAART medications on PharmaNet needs further consideration. The second challenge with HIV care is that the field of HIV-related medication interactions is rapidly evolving and much of the information in standard drug references is out of date by the time the reference becomes available. Collaboration and consultation with a specialized HIV pharmacist is recommended to decrease the risk of
clinically significant negative drug-drug interactions, decrease the risk of adverse drug reactions, and promote adherence to HAART (Health Resources and Services Administration HIV/AIDS Bureau [HRSA], 2011; Tseng et al., 2012; BC-CfE, 2013). The BC-CfE offers the Rapid Expert Advice and Consultation in HIV line, a 24-hour, toll-free hotline (1 800 665 7677) available for primary care providers to consult with HIV-specialist pharmacists or physicians. As well, it is recommended that practitioners use current resources to investigate potential drug interactions such as those available through British Columbia Center for Excellence in HIV (BC-CfE), Toronto General Hospital Immunodeficiency Clinic, or the AIDSinfo Drug Database (Tseng et al., 2012).

No direct comparison studies were retrieved comparing the efficacy of SSRIs, with TCA or serotonin-norepinephrine reuptake inhibitors (SNRIs). Selection of antidepressants should be guided by other properties of the drug such as sedation or activation qualities, weight gain or appetite suppression (Watkins, Pieper, & Treisman, 2011). SSRIs are the recommended first line medication for the treatment of depression due to safety considerations such as adverse effects and medication interactions (Freudenreich et al., 2010; NYHAI, 2010; Relf et al., 2013; Watkins et al., 2011). Specifically, Citalopram and Escitalopram may be reasonable first-line choices because enzymes of the CYP450 family do not metabolize them, so drug interactions with HAART medications are reduced (NYHAI, 2010).

Regardless of the antidepressant selected, the general principle for prescribing is to start at a low dosage and slowly titrate up until a therapeutic effect is achieved (Relf et al., 2013; Adams et al., 2013; HRSA, 2011). In the initial phase of treatment frequent appointments are recommended to monitor for adverse medication effects, drug-drug
interactions, tolerability, adherence and response to treatment (HRSA, 2011). Adams et al. (2012) developed an algorithm for antidepressant management by HIV clinicians. They recommend appointments to monitor for side effects every other week, and dosage adjustments, based on results of a validated depression rating scale, to occur every four to six weeks. Other guidelines recommend more frequent appointments, every one to two weeks, and more aggressive titration of medications to occur every two to four weeks if no adverse side effects are reported (GPAC, 2004; HRSA, 2011). Once the client has achieved resolution of depression symptoms, follow-up is recommended monthly to every other month for the duration of treatment. Generally, it is recommended that the duration of pharmacologic treatment for depression range between six to 12 months, with some individuals requiring life-long treatment (Freudenreich et al., 2010). Discontinuation of antidepressants due to remission of depression should be done as a gradual taper to avoid withdrawal or return of depressive symptoms (HRSA, 2011).

If after a four to six week therapeutic trial with antidepressants, the client has not experienced a significant reduction or complete resolution of depressive symptoms the clinician should consider a dosage increase or switching to a different antidepressant (HRSA, 2011; Freudenreich et al., 2010). For clients who do not experience any improvement in depressive symptoms, Freudenreich et al. (2010), suggest that acceptable second line treatments include switching to an SNRI (venlafaxine), a novel action antidepressant (bupropion), or a different SSRI, such as sertraline. When switching antidepressants clinicians should refer to clinical practice guidelines, such as the Guidelines and Protocols Advisory Committee (GPAC) Depression, for specific recommendations regarding washout periods. For clients who experience a partial resolution of symptoms, clinicians may consider
adding a second antidepressant from a different class (Freudenreich et al., 2010). Again, choice of a second line agent should be based on side-effect profile, potential drug interaction, and cost. Referral to psychiatry should be considered for all patients with severe depression, those with a high degree of suicidal ideation or intent, and those who do not exhibit a response to a therapeutic trial of antidepressant therapy. Additionally, referral to psychiatry should be made if there is uncertainty about the diagnosis or the presence of other mental illnesses, such as bipolar disorder or schizophrenia (NYHAI, 2010). Primary care providers should maintain contact and coordinate care with the psychiatrist or mental health clinician throughout the treatment course in an effort to maintain a relationship with that client and to attend to the client’s other medical needs (NYHAI, 2010).

**Models of HIV care delivery.** With the advent of HAART, the prevalence of comorbidities and mortality associated with HIV/AIDS has changed from predominantly opportunistic infections, to cardiac disease, diabetes, renal failure and non-HIV related cancers (Chu & Selwyn, 2011). The care of HIV positive people is shifting away from a HAART focused model with intense specialization and medicalization of HIV care, towards care that requires the management of multiple chronic diseases and other primary care needs. As HIV care becomes increasingly complex due to the presence of multiple chronic comorbidities, rapidly evolving HAART technology and the increased potential for adverse events related to polypharmacy, both specialized HIV clinicians, and generalist primary care providers struggle with the increasingly complex needs of HIV-positive clients (Chu & Selwyn, 2011). This section explores models of HIV care with potential to improve the outcomes of HIV-positive people with comorbid depression. There is a large body of literature examining HIV care models in the context of highly specialized American HIV
care clinics, but very few studies were found that examined models of care in primary care settings, with clients with comorbid depression or in Canadian settings.

A collaborative care model to manage depression within HIV specialty clinic was examined by Pyne et al. (2011). They compared depression severity, medication adherence and HIV symptoms severity in a RCT comparing collaborative care with usual care among a population of clients selected from a Veterans HIV clinic. Usual care involved screening, treatment and management of depression by the HIV-care specialist. The collaborative care model in this study involved a dedicated HIV depression care team consisting of a clinical pharmacist, a psychiatrist and a registered nurse case manager, who saw clients over a period of 12-months. This team communicated with the HIV-care specialist through an electronic medical record and weekly client care conferences. Clients who received care from the collaborative care team experienced improvements in their depression symptoms, but there was no statistical improvement in the severity of their HIV-related symptoms, or HAART adherence (Pyne et al., 2011).

Measurement-based care (MBC) is another model for depression treatment currently being evaluated for use within HIV specialty clinics as part of the SLAM DUNC study that will be completed in 2014 (Pence et al., 2012). The MBC approach has been shown to decrease depression severity, significantly improve CD4+ counts and decrease HIV viral load among a sample of 124 HIV positive clients (Coleman, Blashill, Gandhi, Safren, & Freudenreich, 2012). MBC is an evidence-based model of care that guides the pharmacologic management of depression in areas where access to specialized mental health clinicians is limited (Adams et al., 2012). Within the MBC model registered nurses, social workers or other trained team members use clinically validated tools to measure symptoms, assess
response to treatment and antidepressant tolerability. The non-psychiatric specialist prescriber uses this information to inform their clinical decisions. One of the promising features of MBC for depression is that it can be integrated into existing multi-disciplinary health clinics, without hiring new staff, or requiring clients to travel to a different location for services. The treatment algorithm recommended for use with HIV-adapted MBC is evidence-based and incorporates the choice of 6 antidepressants (citalopram, escitalopram, sertraline, mirtazapine, bupropion and venlafaxine) that are safest for use with HAART and have the most tolerable side effect profiles (Adams et al., 2012). The findings of the SLAM DUNC study are expected in late 2014 and may lead to the development of comprehensive clinical practice guidelines or recommendations for the treatment of comorbid depression.

The next two studies to be discussed did not meet the inclusion criteria because depression was not specifically addressed, but have been included in this study, because the research was conducted in Prince George, BC and the findings are of relevance to the larger picture of providing primary health care services to marginalized populations. Tu et al. (2013) explored the use of a Chronic Care Model (CCM) in an effort to improve HIV care among a predominantly Aboriginal population. CCM is flexible organizing framework based on six modifiable elements of healthcare delivery: organizational support, clinical information systems, healthcare delivery system design, decision support, client self-management support and community resources. The goal of CCM is “to promote uptake of evidence-based clinical recommendations, enhance clinical teamwork, and empower patients to better manage their own care” (Tu et al., 2013, p.652). They found that the use of CCM was associated with significant improvements in HAART uptake, and increases in viral load suppression rates among individuals on HAART. As well, the authors found significant
improvements in other measure such as rates of pneumococcal immunization, syphilis and tuberculosis screening (Tu et al., 2013). It is also important to note that the BC-CfE endorses the use of a CCM in the provision of holistic, interdisciplinary HIV care (BC-CfE, 2011). The relevance of these findings to this project is that because CCM encourages the adoption of clinical practice guidelines and encourages practitioners to identify patients in need of care, there is the potential that clinical practice guidelines for the screening and treatment of depression might successfully be integrated into the model.

The final study to be discussed takes an even broader look at health care delivery amongst marginalized populations in BC. Browne et al. (2012) examined how the delivery of primary health care services to marginalized populations could be improved through an equity-oriented primary health care model. Although this study does not specifically address HIV or depression it is relevant to this project because the findings suggest how primary health care systems can address the social and structural determinants of health among marginalized populations. Four key elements comprise the foundation of an equity-oriented PHC model. These key elements include: inequity responsive care, trauma and violence informed care, contextually tailored care and culturally competent care (Browne et al., 2012). The authors further suggest 10 strategies to directly address inequities in the social determinants of health and barriers to accessing PHC among marginalized individuals. These findings are important to consider in the context of HIV care because, as discussed earlier in this paper, vulnerability to HIV infection and disease outcomes are heavily influenced by the social determinants of health.

Summary of Literature Findings
The body of research evaluated for this project revealed a startling lack of studies conducted with female participants. As well as a conspicuous absence of studies involving NPs or NP practice. Evidence in the literature demonstrates that while overall HIV transmission rates are declining for the general Canadian population, transmission rates among marginalized groups such as Aboriginal people and women are increasing (PHAC, 2012b). HAART has improved the morbidity and mortality of HIV-positive people, however, it requires a high level adherence (≥95%) to be optimally effective. Overall, adherence to HAART is estimated to be approximately 50%. The concern with non-adherence is the risk for the development and transmission of HAART resistance HIV strains, and unsuppressed viral replication that ultimately could result in opportunistic infections and AIDS. A variety of socioeconomic factors including unstable housing, poverty drug and alcohol abuse, and depression are associated with increased risk of poor HAART adherence.

The incidence of depression is two to three times higher among HIV-positive people, and women were more likely to experience comorbid depression. This is concerning because depression is associated with worse disease outcomes, decreased adherence to HAART regimens and poorer quality of life. Factors associated with comorbid depression include: co-infection with hepatitis C virus, injection drug use, nicotine dependence, poverty, food insecurity, personal or family history of depression, PTSD, stigma, racial and gender discrimination, lipodystrophy, and unstable housing or homelessness.

HIV-positive people respond as well to conventional pharmacologic and non-pharmacologic treatments for depression as non-HIV positive people. Cognitive behavior therapy and treatment with antidepressants were shown to effectively treat depressive symptoms and improve HAART adherence. However, clinicians need to exercise caution in
the clinical application of research findings to female populations because the vast majority of studies were conducted with male participants. In an effort to improve the overall quality of life by reducing depressive symptoms and improving HAART adherence, clinicians should diligently screen and treat depression. Routine screening for depression, using a clinically validated tool, and monitoring for symptoms of depression should occur at least yearly and whenever symptoms suggestive of depression are present. CBT is the most commonly researched non-pharmacologic therapy for the treatment of depression. When considering pharmacological treatment for depression, health care providers need to be vigilant for potential drug interactions between HAART and antidepressants. Due to concerns of drug interactions and efficacy, recommended first-line treatments for depression are from the SSRI family, citalopram and escitalopram. Collaboration with an HIV specialist pharmacist is recommended to reduce the occurrence of drug-drug interactions and adverse side effects.

Studies investigating models of care designed to treated depression amongst HIV-positive individuals were scarce. Collaborative and measurement based care models were shown to be effective strategies to deliver depression treatment and management within HIV specialty care clinics. The chronic care model and an equity-oriented primary health care model were discussed. These studies did not meet the inclusion criteria but were included because the research was conducted locally within Prince George, BC and they approached the provision of care from a holistic stance and encouraged providers to address the social, structural and environmental determinants of health that influenced individual and community health status.
CHAPTER FOUR

Discussion: Role of the Nurse Practitioner

The aim of this project is to answer the question, “What is the role of the NP, working in BC, in optimizing adherence to HAART amongst marginalized, HIV-positive women with comorbid depression?” A literature search was conducted and it was found that treatment with cognitive behavioral therapy or antidepressants can both improve depressive symptoms and improve HAART adherence. This literature search found, that among HIV-positive women, injection drug use, racial or gender discrimination, chronic pain, post-traumatic stress disorder, poor social support and avoidance coping strategies were associated with increased risk of comorbid depression and HAART non-adherence (Bianco et al., 2011; Eiboff et al., 2012; Logie et al., 2013; Richardson et al., 2009; Tedaldi et al., 2012). In an effort to determine the role of the NP, these literature findings will be discussed in the context of the following four key competencies required of NP practice in BC (CRNBC, 2013):

- Establish and maintain professional role, responsibility, and accountability
- Assess and diagnoses client health/illness status
- Therapeutically manage health care
- Promote health and prevent illness/injury

When attempting to elucidate the role of the NP in caring for female, HIV-positive clients with comorbid depression, three challenges emerged. First, no studies were retrieved that directly addressed NP practice, second, little evidence was found to indicate effective strategies primary care providers can utilize when attempting to address the social determinants of health and finally, there was little evidence involving female, HIV-positive
participants. This is significant because not only do NPs have the legislated authority to provide collaborative care for HIV-positive clients, they also possess knowledge of health policy reform, community development and health program planning that provides them with the tools to directly address these social issues affecting the health of their clients. As well, the lack of research with female participants may mean that uniquely female factors that influence HIV-disease progression or HAART adherence are not identified and understood. Fundamental to NP practice is the expectation that the NP integrates awareness about the social determinants of health, cultural safety and diversity throughout all aspects of client care (CRNBC, 2010). Browne and Tarlier (2008) suggest that the key to NP role sustainability in Canada is the ability of NPs to transform awareness of the social determinants of health into action. This is particularly important when one considers that vulnerability to contracting HIV, as well as, adherence to HAART and overall disease outcomes, are strongly associated with the social determinants of health. Therefore, potential strategies, based on findings from this literature search, to address the social determinants of health that will allow NPs to attend to these social issues will be interwoven throughout this discussion in an effort to highlight the contributions NPs make in the care of HIV-positive women with comorbid depression.

**Professional Role, Responsibility and Accountability**

This competency addresses activities aimed at optimizing the delivery of primary care services to individuals and communities, as well as, guiding continuing competency and research projects (CRNBC, 2013). Three of the key activities associated with the professional role, responsibility and accountability competency are (a) practicing within
scope of practice, (b) collaboration, consultation and referral and to (c) engaging in relevant research activities (CRNBC, 2013).

**Practicing within scope of practice.** NPs have the legal authority and educational background to safely care for HIV-positive women with comorbid depression. In BC, the NP scope of practice stipulates that if a “nurse practitioner establishes or strongly suspects a diagnosis” of HIV, the NP should consult with a physician to confirm the diagnosis and/or develop a management plan (CRNBC, 2013, p.27). Additionally, NPs are able to independently diagnose and treat depression in adults (CRNBC, 2013). Part of the graduate level education for NPs includes the development of skills needed to research, critically appraise and apply literature relating to clinical practice issues such as HAART adherence. Staying abreast of current research is vitally important for NPs working with HIV-positive clients who are receiving HAART because of the rapidly changing research in the fields of HIV prevention and treatment. In addition to utilizing current clinical practice guidelines such as BC-CfE’s Primary Care Guidelines for the Management of HIV/AIDS in British Columbia (2011, March) and the Therapeutic Guidelines: Antiretroviral (ARV) Treatment of Adult HIV Infection (2013, February), the NP is expected to take additional training to attain and maintain competence in HIV/AIDS care. CRNBC and BC-CfE recommend that NPs who wish to practice in the field of HIV care or have at least five HIV-positive clients in their care, take a clinical course such as the John Ruedy Immunodeficiency Clinic Preceptorship Program for Nurse Practitioners (CRNBC, 2012; BCCfE, nd). HIV-positive clients cared for by competent NPs receive primary care services that are in accordance with the latest provincial or national guidelines and standard of care.

Cognitive behavioral therapy was identified as the most effective non-
pharmacological intervention for the treatment of depression in PLWHA, and was shown to improve HAART adherence (Safren et al., 2009; Safren et al., 2012; Sherr et al., 2011). In many communities access to trained counselors can be a barrier to implementing this intervention. NPs have the option to address this barrier by offering CBT to their clients. There is no restriction, in terms of scope of practice, placed on NPs who wish to offer CBT (CRNBC, 2013). In BC, the Cognitive Behavioral Interpersonal Skills (CBIS) manual and associated training sessions are a joint initiative between the BC Ministry of Health and the BC Medical Association and are available to primary care providers who wish to increase their competency in CBT techniques (CBIS Manual, 2009). As well, there are numerous other CBT training courses directed at primary care providers such as those offered by the Center for Addiction and Mental Health or CBT Canada. By offering in-office CBT to their clients, NPs have the opportunity to improve access to a highly effective non-pharmacologic treatment option for co-morbid depression.

Nicotine dependence is associated with both increased risk of depression and HAART non-adherence (Richardson et al., 2009; Tedaldi et al., 2012; Webb et al., 2009). Smoking cessation counseling is an important health promotion activity that all health care providers, including NPs, should provide to clients. This is particularly important for HIV-positive individuals because they are at increased risk for cardiovascular disease and smoking can compound the risk of developing heart disease by up to four times (BC-CfE, 2011; Health Canada, 2012b). Additionally, long-term HAART therapy is associated with increased risk of developing insulin resistance, diabetes mellitus, renal disease and osteoporosis, and these conditions may be exacerbated by nicotine use (Canadian Diabetes Association, 2013; Ejerblad et al., 2004; Papaioannou et al., 2010). NPs can use resources
such as BC Smoking Cessation Program or QuitNowCa for more information about funding for nicotine replacement therapy and specific tactics to use during smoking cessation counseling (Province of British Columbia, 2012; QuitNowCa, 2013).

The incredible complexity of many PLWHA and the need for comprehensive primary health care informed by an awareness of the social determinants of health is manifested in the discussion on substance abuse. Injection drug use is one of the most common HIV exposure categories for both Aboriginal and non-Aboriginal women (PHAC, 2012b). Injection drug use is identified as a risk factor for both HAART non-adherence and depression among HIV-positive individuals (Eiboff, Somers & Moniruzzman, 2012; Nolan et al., 2011; Richardson et al., 2012). As well, alcohol use was identified as a risk factor for depression among Aboriginal HIV-positive individuals (Cain et al., 2012). The root cause of substance abuse was not identified in this literature review; rather the intricate interactions between social conditions, individual actions, vulnerability to HIV, depression and HAART adherence were highlighted. For example, Cain et al., 2012, found that Aboriginal PLWHA identified drug or alcohol abuse, racism, stigmatization, childhood abuse, homelessness, poverty and unemployment as factors that contributed to the development of depression, and that depression was the driving force behind behaviors that caused them to contract HIV. This finding from Cain et al. (2012) demonstrates that interventions aimed at addressing a single issue, for example, prescribing an SSRI to treat depressive symptoms and improve HAART adherence, will not fully address underlying causes of this individual’s poor health status. Additionally, the range of factors that contribute to vulnerability to HIV, depression and HAART non-adherence, are too numerous and complex for a single, primary provider to address without collaboration with other healthcare providers and community stakeholders.
Collaboration, consultation and referral. NPs are relatively new primary care providers in the British Columbian health care sector. This newness may represent a tremendous opportunity for NPs to create a unique space within the health care system by promoting their expertise in providing collaborative primary care services, embedded in primary health care principles, that recognize and address the impact that the social determinants have on the health of their clients. HIV is a complex disease that requires both biomedical interventions such as pharmacological treatment, as well as, social interventions aimed at reversing the social inequities that predispose individuals to contracting this disease and experiencing poorer outcomes. A single care provider cannot provide the range of services required in the treatment and management of marginalized PLWHA, and attend to ameliorating the social determinants of health. Therefore, collaboration with other healthcare providers and community partners is required for comprehensive HIV prevention and care.

Collaborative practice is a process of “communications and decision making that enables the separate and shared knowledge and skills of care providers to synergistically influence the client/patient care provided (Canadian Nurse Practitioner Initiative [CNPI], 2006, p.21). Quinlan and Robertson (2013) suggest that NPs are skilled at sharing knowledge within collaborative teams because NP education spans the gap between medical, nursing and other allied health disciplines. This literature search found that comorbid depression and, in some instances, HAART adherence were improved with clients cared for within collaborative, multidisciplinary models of care (Adams et al., 2012; Coleman et al., 2012; Pyne et al., 2011). The applicability of these models to primary care practice is limited because these models were based on highly specialized mental health teams dedicated to the care of HIV-positive clients with comorbid depression. However, aspects of these
collaborative care models may have potential to be integrated into primary care collaborative practice. For example, Pence et al. (2012) recommend training clinic staff, such as, registered nurses, social workers, counselors or pharmacists to share the responsibility for the administration and scoring of depression-rating tools, and for screening for adverse side-effects related to antidepressant use.

The intent of collaborative practice is to increase the options available to clients for accessing primary care services. The unique feature of collaborative practice is that clients are able to directly access the type of services they need, when and where they need to (CNPI, 2006). For example, a client who is cared for within multidisciplinary, collaborative practice has the option to make an appointment directly with a mental health clinician because they have been having trouble since their recent HIV diagnosis. The mental health clinician may be able to use their knowledge and skills to manage this issue independently, or they may need to consult with another primary care provider, such as NP, to discuss the possibility of initiating medication to help manage this client’s issues.

As stipulated in CRNBC’s Scope of Practice for Nurse Practitioners: Standards, Limits and Conditions document, the NP must ensure at least yearly consultation with an HIV-specialist physician to review response to HAART (2013). Collaboration with an HIV specialist pharmacist is recommended to reduce the risk of adverse drug events. This relationship is particularly important when the NP considers initiating antidepressant therapy because of the potential for drug-drug interactions of medications that share the CYP450 pathways. Additionally, the NP may need to collaborate with physicians for clients who require prescriptions that fall outside the NP’s prescribing authority, such as methadone or opioids. For the management of comorbid depression, NPs may need to consult with a
psychiatrist for the diagnosis, treatment and management of clients with severe depression that are not responding to treatment, or other comorbid mental illnesses such as bipolar disorder or schizophrenia. A consideration specific to the care women, is childbearing potential. The risk of transmitting HIV from mother to child can be drastically reduced with appropriate HAART. However, due to concerns about teratogenicity of some HAART medications, the NP should refer all female clients, who are or considering becoming pregnant to an HIV specialist at a women’s health clinic, such as the Oak Tree Clinic in Vancouver, BC.

A collaborative practice approach is not confined for use with other healthcare professionals. An NP can use a collaborative approach with community partners such as ASOs, schools, cultural or special interest groups. Collaboration with community partners is important because it provides NPs with the opportunity to discover what and how services are being delivered, as well as, highlighting areas of service gaps or needs, that may direct future research or program development and avoid duplication of services. For example, in Prince George, it was identified that a potential barrier to women reporting sexual assaults was that the only way for the sexual assault examination to be completed was to present to the local emergency department for care. A partnership between the needle exchange program, other sister organizations and a specially trained NP was established to initiate a pilot project where the NP would be available to complete sexual assault examinations when and at whichever community partner that women presented to (T. Day, personal communication, October 8, 2013). In another example from Prince George, representatives from AIDS Services Organizations (ASOs), the needle exchange program and HIV clinicians meet on a monthly basis to discuss the clinical care of HIV positive clients who may be
Struggling with treatment issues. At these meetings strategies are devised and implemented with the input of team members to support that client to achieve optimal treatment outcomes (Tu et al., 2013).

**Engaging in relevant research activities.** The NP is expected to seek out opportunities to conduct or participate in research and to initiate the development and implementation of practice guidelines and standards of care (CRNBC, 2013). NP research should “be planned and patient-centric, and must demonstrate the contribution of the NP role to the team, defined by outcomes of care at the patient, organizational and healthcare system levels (Pogue, 2007, p.36)” NP participation in research will help to ensure that practice guidelines are relevant to NP practice, as well as to promote the NP perspective and contribution to health care. The NP is also expected to take a leadership role in adopting and disseminating new research findings or best practice guidelines (CRNBC, 2013).

**Considerations for future research.** A significant finding from this research project is the lack of research conducted with depressed female and/or Aboriginal participants, as well as research examining the role of the NP in the delivery of HIV care, despite NPs having the authority to collaboratively manage the care of PLWHA. The dearth of research with female participants is significant because HIV-positive women may posses uniquely female factors such as childbearing potential, family care-giving responsibilities, and metabolic differences that may be overlooked or devalued, leading to further marginalization. Likewise, cultural practices and the legacy of colonialism and residential school may create factors unique to Aboriginal people that impact HIV vulnerability and treatment outcomes in ways that are yet to be uncovered by researchers (Pearce et al., 2008).

This paper also identified several social determinants of health, such as, poverty, food
insecurity, homelessness and gender discrimination that are associated with both depression and HAART non-adherence; however, little evidence was found to recommend specific interventions to address these factors. Reutter and Kushner (2010) advocate for nursing participation in research that seeks to uncover the causal pathways between social inequity and poor health. This research will allow for the development of interventions to that will directly address the mechanisms by which social inequities threaten health status. They further suggest, that because many health inequities stem from public policy, nurses should engage in research that investigates the link between public policy and social inequity (Reutter & Kushner, 2010).

There is tremendous need for NPs who wish to initiate or address some of the gaps identified by this project. In an effort to increase the amount of research conducted with female participants, NPs can discuss, with their female or Aboriginal clients, the potential risks and benefits of participation in clinical trials or research projects. For example, the NP could provide information on the Canadian HIV Women’s Sexual and Reproductive Health Cohort Study that is currently enrolling female participants to examine factors that influence HIV-positive women’s access to health care services (Canadian HIV Women’s Sexual and Reproductive Health Cohort Study [CHIWOS], 2013).

As well, NPs can network with other NPs working with HIV-positive clients to discuss and learn about challenges and practice issues other NPs are struggling with and develop research proposals accordingly. In this way, research studies will reflect not only the issues affecting NPs, but will also be applicable to the clients and populations NPs are currently working with. These research findings can also guide the continued integration of
the NP role and to facilitate the transformation of healthcare delivery models that are inclusive of NP practice.

**Assess and Diagnose Client’s Health Status**

By utilizing the current, evidence-based practice guidelines and applying education and skills, the NP can provide care across the lifespan of HIV-positive women. By fostering an open and trusting relationship NPs can “work collaboratively with the clients to identify and mitigate health risks, promote understanding of health issues and support health behavior” (CRNBC, 2010, p. 12). The NP must be willing to take part in conversations about potentially sensitive topics; such as, sexual practices, drug or alcohol use, living arrangements or financial situation, so as to develop a complete, holistic picture of the client’s health status. Factors associated with HAART non-adherence and depression, such as coping style, stigmatization, annual income less than $15,000, or appearance concerns related to lipodystrophy may not be revealed by clients, without a respectful inquiry on behalf of the primary care provider (Bianco et al., 2011; Logie et al., 2013; O’Neil et al., 2011; Palmer et al., 2011). This highlights the value of NPs’ foundation in nursing, because nurses have a history of, and are comfortable and well versed in approaching health from a holistic perspective (CNPI, 2006; Quinlan & Robertson, 2013; Reutter & Kushner, 2010).

In my experience, both as a registered nurse and student NP, it can be challenging to balance the requirements of biomedical clinical practice guidelines while striving to identify and address the social factors that may be adversely affecting the health of my client. For example, my priorities for an appointment may be to review recent laboratory results, reassess severity of depression using the PHQ-9, and if necessary adjust the antidepressant dosage. However, the priority for the client may that they need a form completed so they
could obtain safer housing, or they may need assistance obtaining food, or simply need support because they are in emotional crisis. As an NP student it was overwhelming trying to address everything in each visit, however, from observing the practice of experienced NPs, it has become evident that NPs have the ability to simultaneously address the client’s current concerns, while diligently attending to the priorities of evidence-based care. NP education and practice are based on primary health care principles and an awareness of the social determinants of health. So, for example, as part of routine care, an NP is able to interpret the biological markers of HIV disease status, as well as, inquire about social issues such as unstable housing, food insecurity and poverty that contribute the client’s overall health status.

**Therapeutic Management of Client’s Health Care**

Two important findings from this project are that CBT and antidepressants were shown to both effectively treat depression and improve HAART adherence amongst depressed PLWHA, and that there were very few studies that specifically examined the treatment of depression and HAART adherence among female PLWHA. This not only highlights a potential area for research, it also calls for clinicians to be cautious when they apply existing research to clinical practice. In particular, the scarcity of pharmaceutical trials involving female participants may mean that clinicians are unaware of important pharmacokinetic or pharmacodynamic factors unique to female clients (Montforte et al., 2010). For example, the nRTI, emtricitabine, is more commonly associated with adverse gastrointestinal dermatological side effects in women (BC-CfE, 2013, February). Another example is when working with women of child-bearing age, it is important to be mindful of medications contraindicated during pregnancy, such as, the NNRTI, efavirenz, due to
concerns of teratogenicity (BC-CfE, 2013, February).

NPs are skilled at counseling clients on the risks and benefits of both non-pharmacologic and pharmacologic treatment options. The NP ensures that the information presented to the client is current, evidence informed, and is at a level appropriate to the client’s level of literacy and understanding. For example, while the NP does not initiate HAART medications, the role of the NP is to counsel the client on the general risks and benefits of treatment versus no treatment, to outline what treatment may entail, to answer any questions that the client may have, and to offer support regardless of the client’s decision of whether or not to initiate HAART. When counseling clients, it is important for NPs to be mindful that for many marginalized women, HIV is “just one of many competing problems” (McCall, Browne, Reimer-Kirkham, 2009, p. 1776). This means that the decision of an HIV-positive woman to enter into HAART may not be the most important decision that she has to make at that time because she has several other more pressing issues to address. For example, she may be struggling in an abusive relationship, caring for children or battling substance abuse. A fear of being judged for their decisions and life circumstances is cited as a reason why some HIV-positive women avoid seeking medical treatment (McCall et al., 2009). As primary care providers, their clients may view NPs as being in a position of power, and there is potential for further marginalization if NPs do not demonstrate that they respect and value their client’s decisions regarding treatment and lifestyle.

Successful treatment and management of HIV-positive clients relies heavily on pharmacotherapy. In order to provide comprehensive HIV care, NPs must resist the temptation to focus solely on the biomedical aspects of HIV care and, as stated above, make a conscious effort to engage in activities to address the social determinants of health. Browne
et al. (2012) suggest that comprehensive primary health care requires that clinicians work “to address these [social determinants of health] issues as legitimate and routine aspects of care, often as the main priority” (p. 11). In practical terms, this means that in addition to inquiring about their client’s social circumstances, the NP must be willing to assist their clients in activities aimed at achieving improved social determinants of health, such as assisting applying for income assistance, accessing safe housing, enrolling in drug treatment programs or acquiring paid employment (Browne et al., 2012). A potential barrier to addressing the social determinants of health is that changing the social conditions in which people live is often a slow process that may take several years or generations to accomplish, and outcomes may be difficult to demonstrate or articulate to the people in charge of providing funding to HIV-care programs on a year-to-year basis. This highlights the importance of NP participation in research, policy development and health program planning that includes outcome measures that reflect the benefits of care and services that NPs provide. For example, modifiable social determinants of health such as obtaining stable housing or food security can be incorporated into models of care for PLWHAs as target outcomes that are as important to achieve as viral suppression and HAART adherence.

As the primary care provider, the NP is responsible for coordinating their client’s health care plan. This includes ensuring that all consultations with HIV or mental health specialists, diagnostic testing and referrals to other specialists or programs are completed within a timely manner. The NP also ensures that any recommendations made by specialists, or other health care team members, are incorporated into the client’s care plan. Another important aspect of the NP role in the care of HIV-positive women is to ensure that all the other age or population specific screening and interventions such as immunizations, and
screening for cervical cancer, renal or cardiovascular disease, diabetes mellitus or osteoporosis are up to date according to current guidelines (BC-CfE, 2011). This is important because HIV-positive women, who are optimally treated with HAART, are living longer and as a consequence of both increased longevity and some HAART side-effects are developing non-HIV related chronic conditions such as heart disease, diabetes, osteoporosis and cancer (BC-CfE, 2011). Finally, as the primary care provider, the NP is responsible for addressing any acute conditions, which fall within the NP scope of practice that may be unrelated to HIV care.

**Promoting Health and Preventing Illness/Injury**

The final competency to be discussed is promoting health and preventing injury. To fulfill this competency NPs are expected to utilize a primary health care approach, and their knowledge of the social determinants of health to advocate for clients and their health care needs (CRNBC, 2013). NPs are also expected to provide care beyond the individual level, and implement interventions focused on improving the health of families, communities and entire populations. While activities associated with a high risk of HIV transmission, such as unsafe injection drug use or unprotected sexual intercourse, occur at the individual level, social factors, such as poverty, lack of education, or gender, create conditions that facilitate high-risk behaviors (Krusi, Wood, Montaner & Kerr, 2010). In the absence of a definitive cure for HIV, the only strategy to stop the spread of this disease is to prevent transmission. As part of routine care NPs can offer HIV screening to all sexually active adults at least yearly, after a potential HIV exposure, upon client request, or as part of routine prenatal care. In addition, NPs can counsel individuals on strategies to reduce HIV transmission risk such as safer sex and drug use habits.
Diligent screening for cervical cancer is important because HIV-positive women are ten-times more likely to have an abnormal papanicolaou than non-HIV positive women (BC-CfE, 2011). This many require more frequent screening than what is currently recommended in the cervical cancer screening guidelines for women. As well, the incidence of HPV is higher among HIV-positive women, and particularly those with low CD4+ counts (BC-CfE, 2011). The recommendation for the use of the human papilloma virus vaccine in HIV-positive women is unclear because, currently there are very few studies that have evaluated with safety, efficacy and immunogenicity of this vaccine among HIV-positive women. Again, this highlights the need for research specifically addressing the care of HIV-positive women.

At the population level, NPs can collaborate with community stakeholders such as public health agencies, ASOs, schools, or cultural societies to develop HIV awareness campaigns, programs to increase HIV screening, or initiatives to increase safe housing or meal programs to increase access to secure food sources. As well, NPs are required to advocate on behalf of their clients. This may take the form of lobbying local, provincial or federal policy makers to support increasing minimum wages, the creation of programs to increase food security for families, or to expand the capacity of drug treatment programs.

Nurse practitioners possess the educational background and legislated scope of practice to care for marginalized, HIV-positive women, with comorbid depression. The role of the NP in the care of this population includes traditional biomedical activities such as ordering and interpreting tests, prescribing medications and completing physical assessments and history taking. NPs also engage in activities such as collaboration with other health care providers or community partners, or lobbying policy makers to address the social
determinants of health that may be adversely affecting the health of their clients. NPs have
the potential to play an important role in primary prevention strategies to prevent the
transmission of HIV, and secondary prevention strategies to increase HIV screening rates in
all sexually active individuals. The NP role calls for participation in research that furthers
knowledge development in the field of HIV care, as well as NP practice.

Limitations

The biggest challenge that emerged from this study is the lack of research involving
female participants and NPs. This meant that the recommendations for practice are based on
findings from research conducted with predominantly HIV-positive males. As such, some of
the nuances unique to the care of HIV-positive women with comorbid depression might have
been inadvertently overlooked by this literature review. Similarly, the scope of this study was
too broad. In hindsight a more manageable approach to this project would have been to focus
on a single aspect of marginalization, for example, homelessness or food insecurity. In the
next section, specific recommendations for NPs working with marginalized HIV positive
women with comorbid depression are outlined.
CHAPTER FIVE

Recommendations for Practice

In the preceding chapter, the role of the NP caring for marginalized HIV-positive women with comorbid depression was discussed in terms of the four key competencies required of NP practice in BC: (a) professional role, responsibility and accountability, (b) assess and diagnose client’s health status, (c) therapeutic management of client’s health care, and (d) promoting health and preventing illness/injury. Based on the research articles reviewed, specific recommendations for NPs wanting to optimize HAART adherence among marginalized, HIV-positive women will be outlined in this section. These recommendations will be organized according to the key competencies required in NP practice discussed in the preceding chapter and presented in Table 3.

Table 3

Competencies Required of and Practice Recommendations for British Columbian Nurse Practitioners Seeking to Optimize Adherence to Highly Active Antiretroviral Therapy Among Marginalized HIV-Positive Women with Comorbid Depression

<table>
<thead>
<tr>
<th>Competency Required of Nurse Practitioners in British Columbia</th>
<th>Practice Recommendation Specific to the Care of Marginalized HIV-Positive Women with Comorbid Depression</th>
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| Establish & maintain professional role, responsibility & accountability | • Attend a BC-CfE HIV preceptorship program such as the John Ruedy Immunodeficiency Clinic Preceptorship Program for Nurse Practitioners  
  • Utilize current clinical practice guidelines such as:  
    o Primary Care Guidelines for the Management of HIV/AIDS in British Columbia (BC-CfE, 2011)  
    o Therapeutic Guidelines: Antiretroviral (ARV) Treatment of Adult HIV Infection (BC-CfE, 2013, February)  
    o Depression and Mania in Patients with HIV/AIDS (NY State Department of Health AIDS Institute [NYHAI], 2010)  
    o Evidence-based Clinical Practice Guidelines for |
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<th>Action Area</th>
<th>Details</th>
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| Assess and diagnose client’s health/illness status | Use the ‘Two Quick Questions’ or Patient Health Questionnaire 2 (PHQ-2) to screen for depression at least annually or when depressive symptoms are present (NYHAI, 2010)  
Use a clinically validated tool to diagnose and monitor response to depression treatment. Appropriate depression screening tools include:  
- Patient Health Questionnaire (PHQ-9)  
- Center for Epidemiologic Study Depression (CES-D) Rating Scale  
- Beck Depression Inventory (BDI)  
- Hamilton Rating Scale for Depression (HAM-D/HDI)  
Monitor for HAART adherence, adverse side effects, and potential medication interactions on each visit (BC-CfE, 2011)  
Ensure HIV related history and physical examination, including assessment of social determinants of health, are completed as per current guidelines (BC-CfE, 2011)  
Ensure all age appropriate and HIV/HAART related screening and blood work is completed according to current guidelines (BC-CfE, 2011) |
| Therapeutically manage client health care        | Foster a collaborative environment both with clients and other health care team members  
Engage in activities aimed at addressing social inequities as part of routine practice (Browne et al., 2012)  
Refer clients to AIDS Service Organizations &/or Medication Adherence Support Program |
Therapeutically manage client health care

- Provide information about the pharmacological and non-pharmacological options for the treatment of depression
  - Non-pharmacological:
    - First Line: Cognitive Behavioral Therapy (Safren et al., 2009)
    - Alternatives: Mindfulness-based stress reduction, yoga, meditation, breathing exercises and moderate intensity aerobic exercises (Reif et al., 2013; Lyerly et al., 2009)
  - Pharmacological:
    - First Line
      - Selective Serotonin Reuptake Inhibitors: Citalopram or Escitalopram
    - Second Line
      - Serotonin-Norepinephrine Reuptake Inhibitor: Venlafaxine
      - Novel Action Antidepressant: Bupropion (Freudenrich et al., 2010; NYHAI, 2010)
- Consultation and collaboration:
  - HIV-specialist physician upon diagnosis with HIV and at least yearly, or when diagnosed with opportunistic infections or evidence of treatment failure/intolerance (BC-CfE, 2011; CRNBC, 2013)
  - Oak Tree Clinic for care of women who are pregnant, considering pregnancy or inquiries regarding the care of HIV positive women and their family Telephone Line 1 888 711 3030
  - HIV-specialist pharmacist when initiating or adjusting medication regimens
  - Rapid Expert Advice and Consultation in HIV (REACH) Telephone Line 1 800 665 7677
  - Psychiatrist and/or mental health clinician in the diagnosis of depression that is not responding to treatment, or in the presence of other comorbid mental illnesses such as bipolar or schizophrenia (NYHAI, 2010)
  - Community partners to engage in advocacy, awareness or community development activities
| Promote health and prevent illness/injury | • Offer routine, annual HIV screening to all sexually active adults, or when a client reports a potential exposure or upon client request (HIV Testing Initiative in Family Practice, nd)  
• Offer HIV transmission, prevention and treatment counseling as part of routine care for all clients  
• Participate in the development of policies that promote and protect the social determinants of health for marginalized, HIV-positive women  
• Participate in community or health orientated activities aimed at raising HIV awareness |

**Conclusion**

HIV-positive women with comorbid depression are a concern for HIV clinicians because depression is associated with suboptimal adherence to HAART and poor disease outcomes such as inability to achieve viral suppression and a more rapid progression to AIDS. As well, suboptimal adherence is associated with increased risk of the development and transmission of HAART resistant strains of HIV. HIV-positive women are more likely to experience depression than men. Social factors such as poverty, homelessness, food insecurity, PTSD, stigma, gender or racial discrimination and injection drug use are associated both increased of HAART non-adherence and depression. This project found significant evidence that demonstrated HIV-positive individuals respond as well to depression treatment as non-HIV positive individuals, and that the treatment of depression is associated with both improved HAART adherence and improved quality of life and disease outcomes. Effective treatments for comorbid depression in HIV-positive people include cognitive behavioral therapy, and pharmacological intervention with SSRIs. However, several gaps were identified in the research reviewed for this project. First there was a scarcity of research conducted with female participants. This is of importance for HIV clinicians because females respond to some HAART medications and are affected by social
factors differently. The second gap in the research was that no studies evaluated strategies to address social inequities. The third gap was on the topic of NP practice with HIV-positive individuals.

The role of the NP caring for marginalized, HIV-positive women with comorbid depression was inferred by carefully extrapolating the findings of the literature search based on the competencies required of NP practicing in BC. NPs have the educational background, legislated scope of practice and competency framework that allows them to provide comprehensive and collaborative care. NPs possess the knowledge and skills to attend to the biomedical needs, such as renewing HAART prescriptions, completing comprehensive examinations, and ordering and interpreting diagnostic tests. NP education is steeped in an awareness of the social determinants of health, as well as theory on community development, program planning and social justice that allows NPs to put their awareness into action. A unique characteristic of the care that NPs can provide is their potential to foster collaborative relationships with healthcare team members, sister organizations and community stakeholders. This is important because care of HIV-positive individuals is tremendously complex and requires expertise from a wide range of both healthcare and non-healthcare related disciplines. As well, addressing the social inequities that are negatively impacting the health of PLWHA requires not only the efforts of NPs, but also participation from clients, community stakeholders and policy makers. NPs can take a leadership role in fostering collaborative environments in which to enact social change to better the living conditions of marginalized individuals.
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