Fatigue, Quality of Life, Physical Function and Participation in Social, Recreational, and Daily Living Activities in Women Living with HIV: a Descriptive Study

by

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Abstract

Objective(s): The purpose of this study was to describe the impact of fatigue on quality of life (QOL), physical function, and participation in social, recreational, and daily living activities (ADLs) in women living with HIV.

Methods: HIV-infected women (n=15; age 44±8 years) were recruited from the Clinical Immunological Outpatient Clinic (CIOC) and the HIV/AIDS Regional Services (HARS) in Kingston. Four questionnaires were completed to obtain information on demographics, fatigue (HIV-Related Fatigue Scale, HRFS), QOL (Medical Outcomes Survey HIV Healthy Survey (MOS-HIV), and valued social, recreational and daily living activities. Participants then performed the 6-minute walk test (6MWT) to assess their physical function. Assessments were conducted in the CIOC or in a gymnasium at another location.

Results: Mean length of HIV infection was 12±5 years and 14 of the 15 women were on anti-retroviral therapy. Seven of the 15 women did not have significant issues with fatigue on the HRFS. The other 8 reported that fatigue severely interfered with ADLs, socialization and mental functioning. QOL scores were significantly lower in the fatigued group compared with the non-fatigued group in 8 of 11 sub-scales of the MOS-HIV; the values being approximately 50% of those in the non-fatigued group. Socializing with friends, walking, grocery shopping and cleaning were listed as activities in which participants experienced limitations. No significant differences were found between the fatigued and non-fatigued groups for the distance walked in the 6MWT or for the percent of predicted distance walked.

Conclusions: Half of the women with HIV in this study reported that fatigue interfered with daily functioning and participation in day to day activities, impacting their QOL. These findings suggest that fatigue can be a major issue impacting QOL in this population; therefore, fatigue reduction should be one of the priorities of HIV-related medical management.
Co-Authorship

I acknowledge that I have collected and analyzed all of the data presented here and am responsible for writing this thesis with editorial revisions provided by my co-supervisors, Dr. Cheryl King-VanVlack and Dr. Wendy Wobeser.

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# Table of Contents

Abstract ............................................................................................................................................ ii

Co-Authorship ................................................................................................................................... iii

Acknowledgements ........................................................................................................................ iv

List of Figures .................................................................................................................................... vi

List of Tables ..................................................................................................................................... vii

Chapter 1 Introduction ..................................................................................................................... 1

Chapter 2 Literature Review .......................................................................................................... 6

Chapter 3 Methodology .................................................................................................................. 33

Chapter 4 Results .......................................................................................................................... 43

Chapter 5 Discussion ...................................................................................................................... 62

Chapter 6 Bibliography .................................................................................................................. 73

Chapter 7 Appendices ..................................................................................................................... 91
List of Figures

Figure 1: The number of 'fatigued' participants indicating a severe impact of fatigue on activities of daily living (ADLs) .......................................................................................................................... 47
Figure 2: The number of 'fatigued' participants indicating a severe impact of fatigue on socialization ........................................................................................................................................... 47
Figure 3: The number of 'fatigued' participants indicating a severe impact of fatigue on mental functioning ....................................................................................................................................... 48
Figure 4: The number of 'fatigued' participants identifying specific triggers of fatigue ............. 49
Figure 5: The number of 'fatigued' participants identifying specific alleviators of fatigue .......... 49
Figure 6: The number of 'fatigued' participants reporting specific descriptors of fatigue ............. 50
Figure 7: Scores from 6 of the 11 sub-scales of the MOS-HIV quality of life outcome measure using parametric statistics ........................................................................................................................................ 54
Figure 8: Box plot of Role Function sub-scale scores for the 'fatigued' and 'non-fatigued' groups ......................................................................................................................................................... 55
Figure 9: Box plot of Social Function sub-scale scores for the 'fatigued' and 'non-fatigued' groups ................................................................................................................................................. 55
Figure 10: Box plot of Health Distress sub-scale scores for the 'fatigued' and 'non-fatigued' groups ..................................................................................................................................................... 56
Figure 11: Box plot of Quality of Life sub-scale scores for the 'fatigued' and 'non-fatigued' groups ..................................................................................................................................................... 56
Figure 12: Box plot of Health Transition sub-scale scores for the 'fatigued' and 'non-fatigued' groups ..................................................................................................................................................... 57
Figure 13: The actual distance walked in metres (m) for the 6MWT and the age- and gender- predicted distance walked in the 'fatigued' and 'non-fatigued' groups ........................................................................................................... 58
Figure 14: The percentage of actual/predicted distance walked (%) for the 'non-fatigued' and 'fatigued' groups ................................................................................................................................................. 59
Figure 15: Relationship between the Physical Function sub-scale score on the MOS-HIV and distance walked on the 6-minute walk test ........................................................................................................................................ 61
List of Tables

Table 1: Demographic Information of Participants ................................................................. 44
Table 2: The Most Valued Social Activities Indicated by the Participants: ......................... 52
Table 3: The Most Valued Recreational/Leisure Activities Reported by Participants .......... 52
Table 4: The Most Valued Daily Living Activities Reported by Participants ...................... 53
Table 5: Physical and Mental Health Summary Scores from the MOS-HIV Quality of Life Questionnaire ................................................................................................................................. 58
Table 6: Cardiovascular Outcome Measures for the 6MWT for the 'Fatigued' and 'Non- Fatigued' Groups................................................................................................................................. 60
Chapter 1

Introduction

Approximately 71,000 people are living with human immunodeficiency virus (HIV) infection in Canada (Public Health Agency of Canada, 2012). Although relatively small compared to populations with cancer (~839,000 in 2009) (Canadian Cancer Society, 2013) and cardiovascular problems (1.3 million) (Public Health Agency of Canada, 2009), there is growing concern for this group due to the complex and debilitating nature of this condition. Over the past decades, HIV has been closely associated with the acquired immune deficiency syndrome (AIDS), a collection of pathological diseases resulting from opportunistic infections and HIV itself (McReynolds & Garske, 2001). Over time, the immune system is suppressed by HIV and the body becomes weakened to pathogens that enter the body. The presentation of HIV/AIDS varies from individual to individual, but there are some common physiological and psychological symptoms that appear in this population.

Headaches, diarrhea and fever are some of the common physical health issues that arise from HIV/AIDS (McReynolds & Garske, 2001). Nausea, fatigue and rash may also be present at the beginning stages of infection (Szadkowska & Chlabicz, 2008). With opportunistic infections, pathogens that invade the body weaken various systems that are responsible for daily functioning; for example, when the central nervous system (CNS) is attacked, neuropathies and gait problems may become present. This will negatively affect an individual’s ability to perform daily tasks and activities (McReynolds & Garske, 2001). In the later stages of AIDS, the brain, spinal cord and peripheral nerves may become severely damaged, resulting in poor physical function and cognitive abilities. Other symptoms include decreased appetite, weight loss and sleep problems. Although fatigue is noted to be a symptom of acute infection, it continues to play a major role in
limiting HIV-infected individuals from participating in many activities (Rusch et al., 2004). Chronic HIV infection is also associated with muscle weakness and wasting, which may lead to decreased functional work capacity (Bopp, Phillips, Fulk, & Hand, 2003). Although muscle wasting begins with HIV infection, it becomes aggravated by the lack of physical activity that occurs due to fatigue or the presence of other activity-limiting co-morbidities. With the recent development of highly active anti-retroviral therapy (HAART), AIDS has become a less common and severe phenomenon in developed countries; however, there are still many who suffer from it.

Although HIV/AIDS greatly affects the physical health of individuals, it is not limited only to this dimension. The mental well-being of infected individuals is often also compromised. Blashill, Perry and Safren (2011) suggest that depression is one of the greatest psychological symptoms associated with this condition; others include post-traumatic stress disorder, fear of social stigma and shame. The ignorance of the general population regarding HIV/AIDS, in combination with discriminatory attitudes, often leads to isolation and loneliness. Stigma from family, friends, and co-workers also adds to the psychological stress (McReynolds & Garske, 2001). With prolonged usage of HAART, many individuals experience morphological changes, such as fat accumulation in the abdominal area and lipoatrophy in the extremities (Sherer, 2003). Generally termed lipodystrophy, these negative effects of therapy present not only physical threats (i.e. greater risk of cardiovascular disease) but also psychological ones. HIV-infected individuals with these symptoms are likely to have negative views of their body image, which may lead to lower adherence rates to HAART (Blashill et al., 2011).

Chronic fatigue is one of the major symptoms of HIV infection and may lead to serious limitations in social activities and in the performance of activities of daily living (ADLs). Rusch et al. (2004) investigated the prevalence of physical impairments, activity limitations and
participation restrictions in HIV-infected individuals (n=762) living in British Columbia. In addition to depression, diarrhea, and problems with physical endurance, many of the people reported restrictions in activities such as doing laundry, household chores, and buying groceries. Further, when physical and role functioning were assessed in 2,836 adults living with HIV, greater limitations were found in complex role functioning, such as working on the job, attending school, and performing chores around the house, rather than specific physical tasks (Crystal, Fleishman, Hays, Shapiro, & Bozzette, 2000). More energy demanding tasks, such as climbing the stairs, were also challenging; these activity restrictions being more severe in those with more HIV symptoms.

Although HAART has been an effective treatment in prolonging the lifespan of infected individuals by reducing the speed of HIV replication in the body, many side effects have consistently appeared. Besides the morphological changes that have been already mentioned, metabolic profile changes (i.e., increased fasting levels of lipids and glucose) tend to occur (Lyon & Truban, 2000). Hyperlipidemia and hyperglycemia place this population at a higher risk for cardiovascular disease such as stroke or myocardial infarction (Friis-Moller et al., 2003).

As a result of the physical and psychological issues, HIV-infected individuals may participate in low levels of physical activity, potentially leading to reduced physical function. Consequently, many experience challenges in performing ADLs and participating in social and recreational activities. The majority of studies examining these aspects of health in HIV-infected individuals have used predominately male samples; this is not surprising, since almost 80% of the total HIV population in Canada are men (Public Health Agency of Canada, 2012). As a result, it is unclear whether many of the research findings are applicable to women with HIV. There is a
need for female-specific research which can identify the health issues of this population and develop tailored interventions to address these problems.
Purpose and Hypotheses

The purpose of this study is to assess the impact of fatigue on quality of life, social participation, physical function and performance of activities of daily living (ADLs) in women living with HIV. Using the HIV-Related Fatigue Scale, individuals will be classified as 'fatigued' or 'non-fatigued'. It is hypothesized that women who are fatigued will have lower quality of life and greater limitations in social participation and performing ADLs compared with those who are not classified as fatigued.

Associations between fatigue, quality of life and physical function will also be determined. It is hypothesized that negative associations will be found between functional physical capacity (as determined by the 6-minute walk test) and fatigue and quality of life.
Chapter 2

Literature Review

Fatigue

Fatigue is a common and often debilitating symptom of HIV infection, with various studies reporting fatigue prevalence ranging from 33 to 88% of the samples (Jong et al., 2010). Fatigue has been defined as a reduced capacity to work and is usually accompanied by a feeling of chronic tiredness (Williams & Stedman, 1990). Although the severity of fatigue differs from individual to individual, its impact on daily functioning and quality of life is significant. Some individuals have reported impairment in their physical function and ability to perform activities of daily living because of fatigue (O’Dell, Levinson, & Riggs, 1996; Simmonds, Novy, & Sandoval, 2005). Research studies have examined the predictors of and factors associated with fatigue in order to set the stage for the development of interventions aiming to eliminate or reduce fatigue in the HIV population. The relationships between fatigue and psychological factors such as depression (Barroso, Carlson, & Meynell, 2003; Barroso et al., 2010; Henderson, Safa, Easterbrook, & Hotopf, 2005) and anxiety (Barroso et al., 2003; Philips et al., 2004; Robbins, Phillips, Dudgeon, & Hand, 2004) have been well established, while the relationships between fatigue and physiological factors such as CD4 counts and viral load are not clear (Barroso et al., 2010). Currently, little is known about the prevalence of fatigue in the female HIV population because the majority of studies examining fatigue have used predominantly male samples. Furthermore, there is limited knowledge on how fatigue impacts HIV-infected women in social and recreational participation. A better understanding of the issue of fatigue in this population is needed in order to tailor appropriate interventions to this group.
Prevalence

Solano, Gomes, and Higginson (2006) compared symptom prevalence across various diseases and chronic conditions including AIDS. In the 9 studies examining symptoms in individuals diagnosed with AIDS from 1988-2003, depression (10-82%), fatigue (54-85%), and pain (63-80%) were listed as common symptoms experienced by individuals with AIDS.

Sullivan, Dworkin, and the Adult and Adolescent Spectrum of HIV Disease investigators (2003) examined the medical records of 13,768 HIV-infected individuals in the United States and found that 37% of these patients experienced fatigue. To be classified as fatigued, patients had to cite fatigue as a primary reason for the medical visit, that it was persistent, or that it interfered with work or recreation. Fatigue was more commonly reported by individuals who were diagnosed with AIDS, depression or had low hemoglobin concentrations. Wantland et al. (2011) assessed the frequency and intensity of HIV symptoms over 6 months in 240 individuals on ART (81 females) using the SSC-HIV. At baseline, 39% of participants reported experiencing fatigue, 42% had muscle aches, and 28% reported numbness in their feet and toes. At the end of 6 months, reports of fatigue and numbness decreased while muscle aches slightly increased. A significant relationship was found between numbness and fatigue throughout the 6 months (OR=2.70).

In a sample of 128 HIV-infected individuals, fatigue levels were assessed using the Fatigue Severity Scale over a period of 6 months (Schifitto et al., 2011). The tool is comprised of 9 items describing fatigue; participants were asked to rate each question on a scale of 1 (strongly disagree) to 7 (strongly agree). The sum of the scores was divided by 9 to obtain a final score. Participants with an overall score of 4 or more were classified as fatigued. The percentages of participants experiencing fatigue remained high over the course of the 6 months, despite dropouts (64% at baseline, 63% at 3 months, 55% at 6 months). Fatigue scores were higher in participants
who were younger, had more depression, and lower functioning compared with those who did not have these characteristics (5.44 vs. 2.78 respectively, p<0.001). In another study, 88% of the sample (n=372) experienced fatigue; 30% reported mild fatigue, 31% reported moderate fatigue, and 27% reported severe fatigue on a fatigue scale ranging from 0-12 in the SSC-HIV (Voss, 2005). Women (33%) reported significantly greater fatigue scores (6.1) than men (5.4).

Although the prevalence of fatigue in the HIV population ranges from study to study, the relatively high percentages of affected individuals indicates that interventions need to be focused on this symptom and on reducing the negative effects associated with fatigue.

**Predictors and Factors of Fatigue**

In a review of 42 studies regarding HIV-AIDS, Jong et al. (2010) found that the prevalence of fatigue ranged from 33-88% across investigations. The strongest associations were between fatigue and depression (r=0.43, p<0.01) (Millikin, Rourke, Halman, & Power, 2003; Voss, Portillo, Holzemer & Dodd, 2007), and fatigue and trait anxiety (r=0.53, p<0.01) (Barroso et al., 2003; Phillips et al., 2004; Robbins et al., 2004). Other predictors of fatigue included unemployment ($\beta$=1.15, p<0.01) and inadequate income ($\beta$=-0.56, p<0.01) (Harmon, Barroso, Pence, Leserman, & Salahuddin, 2008; Pence et al., 2009).

Henderson et al. (2005) evaluated the relationship between fatigue levels and demographic, physiological and psychological variables in 148 individuals with HIV (78% male). A strong correlation (r=0.71, p<0.001) was found between fatigue scores on the Chalder Fatigue Questionnaire and anxiety/depression scores on the General Health Questionnaire-12. All participants with higher fatigue levels scored lower on every dimension of health-related quality of life as determined by the MOS SF-36.
Barroso et al. (2003) examined the relationships between fatigue and physiological and psychological factors in 40 individuals with HIV-related fatigue. Participants completed the HIV-Related Fatigue Scale (HRFS), the State-Trait Anxiety Inventory and the Beck Depression Inventory II. Physiological markers included CD4 cell counts, viral load, anemia, thyroid function, and hepatic function. Significant correlations were found between fatigue severity and depression (r=0.40), fatigue and state anxiety (r=0.40) and fatigue and trait anxiety (r=0.46). No significant correlations were found between fatigue severity and CD4 count or viral load. A negative correlation (r=-0.36) was found between fatigue severity and thyroid-stimulating hormone (TSH), suggesting that thyroid dysfunction may potentially result in greater fatigue severity. In a later study Barroso et al. (2010) examined physiological and psychosocial factors in a larger sample of fatigued and non-fatigued HIV-infected individuals (n=128, 34% female) and found that depression (β=0.535), anxiety (β=0.568) and number of stressful life events (β=0.308) were significant predictors of fatigue. In addition, childhood trauma such as experiencing sexual or physical abuse, living with primary caregivers involved with substance abuse or being in foster care significantly but moderately predicted fatigue intensity (β=0.121, p=0.004). Social support was a predictor of fatigue-related impairment of functioning (β=-0.196, p=0.004), suggesting that social support may be important in reducing the impact of fatigue on daily functioning. Physiological factors such as hepatic, thyroid, and gonadal function did not appear to have any relationship with fatigue intensity or fatigue-related impairment of functioning. These findings indicate that interventions for alleviating fatigue should be focused on addressing psychosocial factors. Pence et al. (2009) examined fatigue intensity, its impact on functioning, and remission of fatigue in 84 HIV-infected individuals over the course of the 15-month study. They found that the
fatigue was persistent over time and unlikely to remit. Being employed at baseline was predictive of lower fatigue levels over time (OR=4.30).

The extent to which a person feels he or she is in control of forces significantly affecting his or her life (Pearlin, Lieberman, Menaghan, & Mullan, 1981) may also help to reduce the impact of fatigue on daily functioning, this trait being known as ‘mastery’. Rueda et al. (2013) examined whether mastery and social support moderated the negative effect of stigma on depression in HIV-infected individuals (n=825, 16% female). Mastery was assessed using Pearlin's Mastery Scale, a 7-item tool evaluating an individual's sense of personal control in life events, decision-making, and working through problems. Summary scores range from 7-28, with higher scores indicating higher levels of mastery. Individuals with low levels of mastery had greater symptoms of depression when they encountered higher levels of stigma associated with HIV, while those with high levels of mastery had relatively low levels of depression, regardless of the extent to which they were exposed to HIV-related stigma. These findings suggest that individuals who feel in control of their lives are able to cope with their problems more effectively, which may translate into lower depression, lower fatigue levels, and therefore, lower impairment of day to day functioning. This is supported by another study, which found that HIV-infected individuals (n=228, 44% female) with higher levels of mastery had little or no depression (Reis et al., 2011). Quality of life and depression were assessed using the HIV/AIDS Targeted Quality of Life (HATQoL) questionnaire and the Beck Depression Inventory (BDI), respectively. Sub-scale scores on the HATQoL ranged from 0-100, with higher numbers indicating better health. The HIV Mastery sub-scale scores of the HATQoL were highest among those with no depression (mean 71.8), followed by those with mild to moderate depression (mean 58.7). Individuals with severe depression had the lowest scores (mean 46.4). Interventions involving
mastery may be useful for reducing symptoms of depression, which in turn may lower fatigue and its impact on daily functioning.

Functional Physical Capacity

The high prevalence of fatigue in the HIV population may suggest that aerobic fitness is also reduced. Hand et al. (2008) reported that the baseline maximal oxygen consumption (VO₂\text{max}) of 30.5±1.8 ml/kg/min in 40 HIV-infected individuals (30 males, 10 females; majority on HAART) was lower than the age-predicted VO₂\text{max} value of 40.5±1.1 ml/kg/min; a 25% impairment in aerobic capacity. Dolan et al. (2006) also assessed cardiorespiratory fitness using cycle ergometry in 40 HIV-infected women (majority on HAART). Participants had much lower VO₂\text{max} values (mean 15.4 ml/kg/min) in comparison to those for healthy females (26-35 ml/kg/min). A limitation of this study, however, was that oxygen consumption was not directly measured but was calculated using a prediction equation that has not yet been validated in the HIV population. Scott, Oursler, Katzel, Ryan, and Russ (2007) found that the mean VO₂\text{max} of 27 HIV-infected men (22.6±5.0 ml/kg/min) was much lower compared with the age-predicted value in healthy individuals (36.1±2.9 ml/kg/min).

In contrast, Hetzler et al. (2009) used the Balke treadmill test to determine the VO₂\text{max} of 24 males and 2 females with HIV on HAART. Mean VO₂\text{max} was 37.73±6.95 ml/kg/min, indicating that the aerobic fitness of the participants was in the same range as that in non-infected individuals (Nieman, 1999). Similarly, another intervention study measured the VO₂\text{max} of 79 male and 20 female HIV-infected individuals (mean age 37 years, range 24-61) (Baigis et al., 2002). At baseline, the mean VO₂\text{max} value was 31.1±6.75 ml/kg/min, which was within the normative healthy range. Another study reported VO₂\text{max} values of 33±6 ml/kg/min in 30 HIV-
infected people with dyslipidemia and lipodystrophy, which are also within the normative healthy range (Terry et al., 2006). A pilot study examining the effect of a 16-week supervised exercise program in 9 sedentary HIV-infected individuals (1 female) reported a mean VO$_{2\text{max}}$ value of 31.1±5.9 ml/kg/min (Robinson, Quinn, and Rimmer, 2007). Stringer, Berezovskaya, O'Brien, Beck, and Casaburi (1998) reported that the VO$_{2\text{max}}$ value was 85% of the predicted value in 34 HIV-infected individuals (11% female), which was still considered to be in the normal range for healthy adults (Wasserman, Hansen, Sue, Whipp, & Casaburi, 1994). Mbada, Onayemi, Ogunmoyole, Johnson and Akosile (2013) reported significantly lower VO$_{2\text{max}}$ values in their sample of HIV-infected individuals (n=37, 60% female) compared with age and sex-matched healthy controls (n=37) (30±6 ml/kg/min vs. 37±6 ml/kg/min). However, the VO$_{2\text{max}}$ of the HIV-infected sample still appeared to be within the normative range. Overall, 5 studies have indicated that aerobic capacity in individuals with HIV is within the normal range for healthy individuals, and 3 have not. However, even those studies identifying HIV values within the normative range, suggest that these values are at the low end of the healthy spectrum for a given age range. It would appear that aerobic capacity may be impacted by HIV possibly due to being immunocompromised and/or anti-retroviral therapy.

The 6-minute walk test (6MWT) is another tool that can be used to assess aerobic capacity in healthy populations as well as in populations with chronic conditions (Enright, 2003). Simmonds et al. (2005) examined physical function in 100 patients with HIV (78 male, 22 female) using various tests such as the 50-foot fast walk and the 6MWT. Mean distance walked on the 6MWT (487±95 m) was 75% of the normative value for healthy adults of the same age range (180 m less), indicating reduced functional physical capacity in this population. Scott et al. (2007) also assessed physical function in 27 HIV-infected men using the 6MWT and found lower
distances walked compared to the predicted normative values (593±73 m vs. 666±52 m, respectively); nevertheless, the percentage of the predicted distance was still high (89%). Mbada et al. (2013) also reported significantly lower 6MWT distances in HIV-infected females (n=22) compared with healthy controls (n=22) (427±94 m vs. 526±65 m, respectively), with the HIV group achieving 81% of the distance walked by healthy controls. Dolan et al. (2006) used the 6MWT to measure physical function in 40 HIV-infected women. Although the distance walked at baseline was reported (482±17 m), the predicted normative values were not provided and could not be calculated (mean height and weight not provided). The findings from the functional tests of aerobic capacity by Simmonds et al. (2005), Scott et al. (2007) and Mbada et al. (2013) support a mild to moderate limitation in individuals with HIV.

Scott et al. (2007) examined the effect of central activation impairment on muscle force in HIV-infected men on HAART (n=27). Individuals with a low central activation ratio (CAR) (the maximum voluntary force produced divided by the force produced after the delivery of a supramaximal electrical stimulation; CAR<1) were compared with those with a normal central activation ratio (CAR=1). The force generated by ankle dorsiflexors and knee extensors was measured using the KinCom dynamometer. A significant relationship was found between the maximal voluntary contraction torque and the central activation ratio in the quadriceps muscle ($r^2=0.60$, p=0.005). Forty percent of subjects on HAART experienced weakness and decreased force during knee extension testing, indicating central activation deficits (CAR=0.72±0.12) in this muscle group. Individuals with a low CAR produced significantly lower quadriceps femoris MVC torque values compared with individuals who had a normal CAR (181±39 Nm vs. 233±53 Nm). There were no problems, however, with central activation of the dorsiflexor muscles.
In addition to muscle weakness, HIV-infected individuals may have impaired balance and locomotion. Rusch et al. (2004) reported that up to 30% of people with HIV surveyed in British Columbia (n=762) complained of issues related to locomotion and balance. Richert et al. (2011) used 6 functional tests to evaluate the physical performance of 324 HIV-infected individuals (80% male). The Berg Balance Scale, 1-leg-standing-with-eyes-closed test, and the timed-up-and-go (TUG) test were used to assess balance; the 6-minute walk test (6MWT) was used to assess walking ability; the functional reach test was used to assess forward reach ability and balance; and the 5-times sit-to-stand (5STS) test was used to assess lower limb muscular performance and balance. The results of these tests were compared with established norms in the general population. Poor outcomes were defined as a score of less than 46 on the Berg Balance Scale (Berg, Wood-Dauphinee, Williams, & Maki, 1992); a 6MWT value that was significantly lower than normative values (Enright and Sherrill, 1998); and scores that were greater than 2 standard deviations from the norms in the healthy population for the 5STS test and the remaining tests (Vereeck, Wuyts, Truijen, & Van de Heyning, 2008; Bohannon, Shove, Barreca, Masters, & Sigouin, 2007; Demura and Yamada, 2007). Fifty-three percent of the participants had poor performance on the 5STS test, 24% had poor performance on the 6MWT, 10% had poor performance on the TUG test, 11% had poor performance on the functional reach test, and only 2% had poor performance on the Berg Balance Scale. The high percentage of individuals struggling to perform the sit-to-stand test and the 6MWT suggests that there may be issues involving lower limb fatigue or central activation of these muscles.
Fillipas et al. (2008) used the International Physical Activity Questionnaire (IPAQ) to determine levels of self-reported physical activity in individuals with HIV (n=191) as well as in individuals with general infectious diseases (n=70) in Melbourne, Australia. In total, 226 males and 35 females participated in the study. The American College of Sports Medicine (ACSM) guidelines were used to assess whether participants met the physical activity recommendations (Pate et al., 1995). The IPAQ-short form was used to evaluate leisure activities, work-related activities, activity performed for transportation purposes, and domestic or gardening activities. Participants were asked about the type of activity (vigorous, moderate, walking), the frequency (in days), and the duration (in minutes) for each activity. Exercise that lasted for 10 minutes or more was recorded; time spent sitting was considered sedentary activity. Participants met the guidelines if they performed at least 30 minutes of moderate activity 5 times per week, or at least 20 minutes of vigorous activity 3 times per week. Approximately 74% of the HIV sample participated in moderate to high levels of activity, with walking being the most frequent activity reported. This left a substantial proportion of participants (26%) that did not meet the recommended guidelines. The high percentage of participants who met the criteria may be misleading because with self-reported physical activity questionnaires, people often overestimate their exercise levels (Ekelund, Tomkinson, & Armstrong, 2011). Further, social desirability bias may also have led the individuals to report healthier behaviours. Although a trend of HIV-positive individuals (mostly men) reporting greater participation in vigorous activities and for a longer duration than HIV-negative participants was noted, it is unclear how many individuals in the sample actually engaged in vigorous activity.
Another study also used the IPAQ to assess physical activity levels in 208 HIV-infected individuals (13% female) (Basta, Reece, & Wilson, 2008). Weekly energy expenditure that was less than 600 MET (metabolic equivalent) minutes was classified as low level; MET minutes ranging from 600-2,999 were considered moderate level; and expenditure greater than or equal to 3000 MET minutes was considered high level. The participants also completed the Stages of Change for Exercise (Short Form) to determine which stage of the Transtheoretical Model (TTM) they were in at the time of the study. The TTM consists of 5 possible stages that an individual may go through to make a behaviour change, including pre-contemplation (participant does not intend to exercise in the next 6 months); contemplation (participant intends to exercise in the next 6 months); preparation (participant intends to exercise in the next 30 days); action (participant exercises but for less than 6 months); and maintenance (participant exercises for more than 6 months) (Prochaska, Redding & Evers, 2002). A high proportion of participants (~60%) were physically active according to the Stages of Change for Exercise (Short Form), with 34% in the maintenance stage and 24% in the active stage. Sixteen percent were in the preparation stage, with the intention of engaging in physical activity in the next 30 days. According to the IPAQ, 48% of participants were engaged in high levels of physical activity, 34% performed moderate levels; only 11% were engaged in less than 600 MET minutes each week. Although almost 60% of participants classified themselves as active according to the Stages of Change for Exercise (Short Form), 82% reported engaging in high or moderate levels of physical activity in the IPAQ. This discrepancy suggests that some individuals may not consider certain forms of activity (e.g. walking) to be planned exercise. A possible explanation for the high levels of physical activity is that study participants were involved with 1 or more centres providing HIV care services, which may have helped to facilitate more engagement in health-promoting behaviours like exercise.
Clingerman (2003) surveyed 70 men and 8 women with HIV regarding their physical activity levels using the Physical Activity Questionnaire. Participants met the Healthy People 2010 guidelines for regular moderate physical activity if they participated in 30 minutes of moderate activity at least 5 times per week, or 20 minutes of vigorous activity at least 3 times per week (CDC & Center for Chronic Disease and Health Promotion, 2000). Walking was the most common physical activity cited by participants. Only 28% of participants met the recommendations for moderate activity levels and only 19% met the vigorous activity recommendation. Some participants met the recommendations for more than 1 activity (e.g. moderate as well as vigorous) and were therefore included in both. Approximately 40% of the participants did not meet any of the recommended exercise guidelines.

Caloric intake based on a 7-day food diary and physical activity levels using the Minnesota Leisure Time Physical Activity Questionnaire were assessed in 150 HIV patients on HAART (stavudine or zidovudine) (Domingo et al., 2003). Body composition, lipid profile, and other parameters of the metabolic profile were also determined. Participants were considered to be sedentary if they had a total activity metabolic index less than 143 kcal/day. Only 28% of individuals on stavudine and 25% of individuals on zidovudine were physically active. Of the 56 participants who did not have body fat redistribution, 43% were physically active while only 15% of the 20 individuals who did have body fat redistribution were physically active. These findings suggest that physical activity may be a protective factor against body fat redistribution in individuals on HAART or that individuals with these changes may be less likely to exercise.

A qualitative study by Hermann et al. (2013) examined the difficulties associated with living with HIV in 15 HIV-infected individuals, particularly in the areas of intimate relationships, stigma, and physical health. Some of the participants indicated that they experienced limitations
in physical activity for various reasons, such as having severe co-morbidities, pain, or fatigue. This often led to feelings of low motivation, resulting in low engagement in activities and social isolation. Others stopped participating in leisure physical activity (such as body contact sports) because of fear that HIV would be transmitted if their blood was spilled. Although the proportion of people experiencing physical limitations was unclear, these findings suggest that HIV infection can negatively affect some individuals' ability to engage in physical activity.

**Physical Function, Activities of Daily Living and Social Participation**

The fatigue experienced by HIV-infected individuals often limits performance of activities of daily living (ADLs) and can also affect mobility and communication (Ferrando et al., 1998; O'Dell et al., 1996). Smith and Rapkin (1995) interviewed 224 individuals (194 male, 30 female) living with HIV/AIDS to identify their unmet needs. Instrumental ADLs (IADLs) such as performing strenuous tasks and using transportation were reported to be the most challenging. Uwimana and Struthers (2008) explored the experiences of 250 HIV-infected people (71% female) with palliative health care service provision in Rwanda through questionnaires and focus-group discussions. Some participants reported challenges with performing some ADLs; those who had more HIV symptoms had greater difficulty with ADLs than those with fewer symptoms. A significant relationship was found between health status and performance of ADLs, however, the magnitude of the relationship was not reported. Crystal and Sambamoorthi (1996) examined the severity and time course of functional impairment in individuals with symptomatic HIV using longitudinal interview data from 246 participants. The ability to perform ADLs such as bathing, dressing, eating, and mobility and IADLs such as shopping, preparing meals, doing household chores and managing finances were assessed each month for up to 2 years. On average,
participants experienced issues with performing 3-4 out of the 16 tasks assessed. Using a multi-level model that addressed within-individual and between-individual variation, the researchers calculated that functional status slightly worsened over time (at a rate of 0.32 tasks per month). Participants did not experience a consistent decline each month, but rather had periods of improvement followed by marked exacerbations of impairment. Females demonstrated greater impairment (additional 1.88 tasks) than males. Shively, Gifford, Bormann, Timberlake, and Bozzette (1998) found that a greater HIV symptom frequency was significantly correlated with worsened health status ($r=0.63$), limitations in social activity ($r=-0.51$), and more days spent in bed ($r=0.46$) in 57 HIV-infected individuals.

The prevalence of impairments in 32 individuals with HIV was assessed using the Sign and Symptom Checklist for Persons with HIV Disease (SSC-HIV) and the impact of these impairments on participants' perceived competence was determined using the Occupational Self-Assessment (OSA) (Anandan, Braveman, Kielhofner, & Forsyth, 2006). The 5 most frequently identified impairments were fatigue (84% of the sample), fear and worry (78%), difficulty concentrating (75%), muscle aches (69%), and depression (66%). In terms of occupational competence, 68% of the participants reported difficulty with managing their finances and 36% experienced challenges with physically doing what they set out to do. Similarly, a study of HIV-infected individuals with and without HIV-associated neurocognitive impairment found that those with greater impairment had more difficulty managing finances (Ghandi et al. 2011). The San Diego Finances Test was an objective measure of participants' financial management; higher scores on the test indicated better performance. Participants were categorized as having no impairment at all, asymptomatic neurological impairment, mild neurocognitive disorder, or HIV-associated dementia. Higher scores were associated with decreased odds of cognitive impairment.
(OR=0.81, p<0.05). In addition, functional performance was assessed using the Karnofsky Performance Scale (scored from 0-100, where 100 indicates normal performance) and a questionnaire for IADLs assessing 14 common daily tasks (scored from 0-30, where 0 indicates no abnormality). Higher scores on the Karnofsky Performance Scale were associated with reduced cognitive impairment (OR=0.91, p<0.001) while greater scores on the IADL questionnaire were significantly correlated with increased impairment (OR=1.36). These findings suggest that performing some daily tasks such as working, driving, and managing finances can be challenging for some HIV-infected individuals with neurocognitive issues.

Gaidhane et al. (2008) examined the level of impairment in 194 individuals (82% male) at various stages of HIV/AIDS in India. Participants were interviewed and asked about their ability to perform ADLs such as bathing, eating, urinating and defecating. Approximately 65% of participants experienced 1 or more impairments categorized as mild, moderate, severe or complete problems. Approximately 11% of participants had issues with bathing their whole body, 15% had trouble eating, 25% had problems with drinking and urinating, and 45% had problems with defecating and maintaining personal health.

Little information is available with respect to social participation of HIV-infected individuals. Smith and Rapkin (1995) examined the unmet needs of 224 participants (87% male) involving IADLs, taking care of personal health, and social interaction. An inventory of activities was created based on literature reviews and focus groups in which the participations were asked to describe the level of difficulty and how much help they received in performing these activities. Twenty-two percent had an unmet need in starting an intimate relationship; 21% had an unmet need in relating to friends and family; 19% needed support in responding to others' reactions to
their AIDS diagnosis; and 14% needed help with socializing. These findings suggest that HIV/AIDS can have a significant impact on the social well-being of this population.

Anderson et al. (2008) explored the social experiences of 25 HIV-infected Caribbean people in the United Kingdom through semi-structured interviews. Some of the participants experienced discrimination at work, such as being fired or not being hired because of their HIV-positive status. Although stigma from family members was uncommon, those who did encounter this felt dirty (for example, objects in the house were constantly being cleansed) or in the extreme case, were not allowed to return home. Some participants reported reluctance or refusal to enter into intimate relationships because of fear that the partner would respond poorly. Those who were experiencing severe emotional distress limited their social activities out of shame, guilt, and fear that others would discover their status.

Quality of Life

Before the widespread use of HAART, health care workers focused on the survival of people with HIV/AIDS. However, the development of anti-retroviral therapies has increased the lifespan of this population and has shifted the focus of health care to improving quality of life (QoL) in individuals with HIV/AIDS. Health-related QoL has been defined as how a person feels about his/her life and how well he/she functions in daily activities (Lorenz, Shapiro, Asch, Bozette, & Hays, 2001). The Medical Outcomes Study Health Survey for individuals with HIV (MOS-HIV) is a validated and reliable tool that is commonly used to assess QoL in the HIV population (Wu, Revicki, Jacobson, & Malitz, 1997). Additional tools include the HIV Patients Assessed Report of Status and Experience (HIV-PARSE) and the HIV/AIDS Overview of Problem Situations Evaluation System (HOPES).
Quality of life (QoL) has been examined at various stages of HIV infection. Tsevat et al. (2009) evaluated perceptions of QoL before and after HIV diagnosis in 347 participants. Two interviews were conducted 12-18 months apart; participants were asked at the first interview how they rated their QoL before diagnosis and at the present time (after diagnosis). During the second interview, they were asked whether QoL had changed since the first interview. In the first interview, 31% of the participants indicated that life was better than before diagnosis. Twenty-eight percent indicated it was worse and the remainder reported that it was about the same or did not know. In the second interview, one-fifth of the participants reported improved QoL while one-sixth experienced a decline in QoL. Improvements between the first and second interview were positively correlated with religious coping (OR=1.07, p=0.008).

Friend-du Preez and Peltzer (2010) used the World Health Organization Quality of Life HIV Abbreviated questionnaire (WHOQOL-HIV BREF); a 31-item tool with six domains including physical, psychological, level of independence, social relationships, physical environment, and spirituality to assess QoL in a sample of 612 HIV-infected individuals (70% female) in South Africa. Physical health, independence and spiritual/religious beliefs were significant predictors of QoL (OR=1.41, 1.23, 1.22 respectively) in individuals without symptoms, while physical health, psychological health and independence were significant predictors of QoL (OR=1.44, 1.23, 1.54 respectively) in those with symptoms. Vosvick et al. (2003) examined physical functioning, energy and fatigue, social functioning and role functioning in a sample of 142 male and female participants with HIV/AIDS using the MOS-HIV. Low energy/fatigue scores were significantly and moderately associated with the use of self-distraction and behavioural disengagement (β=-0.17, -0.20 respectively). Social functioning scores were
significantly and moderately associated with behavioural disengagement and substance use ($\beta=-0.16$, -0.14 respectively).

Several studies have examined the relationship between QoL and CD4 counts or HAART use. Gill et al. (2002) used a short form of the HIV Patients Assessed Report of Status and Experience (HIV-PARSE) to assess physical function, role function, energy and health perceptions in a sample of 513 HIV-infected males and females. Other data collected included CD4 count, viral load and HAART use. Mean QoL scores for each sub-scale were lower with lower CD4 cell counts. For example, physical function scores were significantly lower (-6.7 points) in patients with CD4 counts between 200-500 cells/ml than patients with CD4 counts greater than 500 cells/ml. Although HAART appeared to have a negative initial impact on physical function (5.3 points less than non-HAART users, $p<0.05$), the authors suggest that good adherence to the treatment can result in other long-term benefits such as increased CD4 counts and suppressed viral load. Weinfurt, Willke, Glick, Freimuth, and Schulman (2000) found that improvements in QoL (MOS-HIV) were weakly correlated with increased CD4 counts ($r=0.23$, $p<0.05$) in 1,112 HIV-infected individuals. In a large study of 1,563 HIV-infected individuals, QoL was assessed using a tool adapted from the MOS-HIV (ACTG SF-21) (Safren et al., 2012). Scores for each of the QoL sub-scales significantly increased with increasing CD4 counts; for example, the General Health Perception mean scores increased from 48±26 (CD4<50) to 54±25 (CD4 50-99) to 62±23 (CD4 100-199) to 63±23 (CD4 200-249) and finally to 65±24 (250-299). Further, men (53%) reported greater impairments in the social functioning domain than women ($p<0.05$). Shor-Posner et al. (2000) used the Quality of Life Index to examine quality of life in five domains including activity, health, support, outlook and daily living in 75 HIV-infected drug users (24 females). Women were 6 times more likely to have low activity (working or household
management) scores than men (p=0.0038). Women with low activity scores also had less social support compared with those with high activity scores. Further, 63% of participants with CD4 counts below 200 also had low QoL scores in the activity domain. Magafu et al. (2009) assessed health-related QoL in 329 HIV-infected individuals (66% female) on HAART in Tanzania using the Short-Form 36 (SF-36); the tool upon which the MOS-HIV is based. In comparison with normative scores from the general population (Wyss et al., 1999), participants' mean scores were significantly lower in physical function, role physical, bodily pain, vitality, social function, and role emotional categories. For example, the Role Physical score in the HIV sample was 57±33 while the score in the general population was 84±31. Although CD4 count and adherence to HAART were not associated with QoL, a strong relationship between the mental health scores of the SF-36 and presence of additional chronic conditions (e.g. arthritis, low back pain, hypertension, and peptic ulcer disease) was found (OR=3.1, p=0.007). These findings suggest that other co-morbidities experienced by individuals with HIV negatively impact the mental health aspect of QoL. Similarly, Wang et al. (2009) compared QoL scores between HIV-infected individuals (n=113, 27% female) and normative values of the general population in Sichuan, China obtained from another study (n=2,249) (Li, Liu, Li, & Ren, 2001). The HIV group had significantly lower scores in all domains of the SF-36 compared with those of the general population. Within the sample, however, participants who consistently adhered to HAART had significantly higher physical function (F=9.72), general health perceptions (F=4.99), social functioning (F=7.78) and mental health (F=3.91) scores compared with those who did not adhere to their medications.

In a 12-month study of 1,397 HIV-infected individuals (21% female), low QoL scores were observed using the SF-12; a shortened version of the SF-36 (Mannheimer et al., 2008). At
baseline, the mean Physical Component Summary (PCS) score was 45±11 and the Mental Component Summary (MCS) score was 43±9. After 12 months, the scores had slightly increased to 48±10 and 44±9 respectively. Although the increase in PCS was statistically significant, the clinical significance of the change is controversial since even the baseline values were above the cut-off of 43, below which individuals perceive physical health to impede life functioning or are more likely to report psychological symptoms that might impede life functioning (Blanchard, Côté, & Feeny, 2004). Participants also reported the presence and severity of 13 symptoms (e.g. nausea, vomiting, diarrhea) using the Community Programs for Clinical Research on AIDS (CPCRA) Symptom Severity Form. Severity was ranked on a scale of 0-4, where 0 indicated no symptoms and 4 represented life-threatening symptoms. Changes in PCS and MCS scores over the course of the 12 months were significantly and inversely related with the number of symptoms experienced by participants. For example, participants who reported experiencing 0, 1, 2, 3, or >4 symptoms after 12 months had significant changes in mean PCS scores of 4.8, 2.9, 1.5, 1.3 and -0.6 respectively.

Although HAART plays an important role in improving immunological function in HIV-infected individuals, the side effects experienced by some individuals in this population have negatively impacted QoL. Blanch et al. (2004) assessed QoL in 84 participants with clinically diagnosed lipodystrophy and found that the fat redistribution had a strong, negative impact on psychosocial functioning and QoL. Specifically, 49% of participants felt ashamed of their body changes and 27% experienced disruptions in their sexual lives.

Very few studies have exclusively examined QoL in women with HIV. Sarna, van Servellen, Padilla, and Brecht (1999) used the HIV/AIDS Overview of Problem Situations Evaluation System (HOPES) to assess QoL (physical, psychological, social, sexual dimensions
and overall QoL) in 33 female participants (mean duration of HIV infection = 34±29 months). On a scale of 0-4, lower scores indicated less distress and higher QoL. Data were collected 3 times over a period of 4 months in order to determine whether QoL fluctuated in those living with HIV infection. The women experienced disruptions in QoL in most dimensions but over the course of the 4 months, physical summary scale scores (baseline: 1.45±0.66; 4 months: 1.18±0.66, p=0.004) and psycho-social summary scale scores (baseline: 1.79±0.80; 4 months: 1.50±0.76, p=0.003) decreased, indicating improved QoL. Potential reasons for this improvement included developing of positive coping strategies and having access to good treatment and support groups. More female-specific research on QoL and HIV/AIDS is needed in order to better understand the issues that women face and to develop interventions that can improve QoL in this population.

**Immune Function**

HIV infection affects the immune systems of individuals differently, with varying levels of severity. Although not very common, acute infection can lead to a rapid deterioration and depletion of CD4 cells and increase susceptibility to opportunistic infections (Vergis & Mellors, 2000). If HIV remains untreated, CD4 cell counts will continue to decline and viral replication will increase (Ho et al., 1995). Lyles et al. (2000) evaluated disease progression in 269 homosexual men with progressive HIV disease and reported a decline of 50-75 CD4 cells/year. Individuals with CD4 cell counts between 200-500 cells/µL are often physically asymptomatic or have mild symptoms (Vergis & Mellors, 2000). Patients with CD4 cell counts between 50-200 cells/µL tend to have more advanced immunosuppression and likely have manifestations of AIDS, with opportunistic infections such as *P. carinii* pneumonia (Lidman, Berglund, Tynell, & Lindback, 1992) or *Toxoplasma gondii* encephalitis (Porter and Sande, 1992). This was
demonstrated in a study which assessed clinical and immunological outcomes in 521 patients living with AIDS in China (Li, Xu, Nie, Xiang, & Wang, 2009). The mean CD4 count was 123 cells/µL, and a large proportion of the sample experienced severe symptoms (e.g. 72% had diarrhea 3-5 times each day for more than 3 months; over 50% experienced coughing and weakness; and 79% had irregular fever for more than 1 month). Individuals with less than 50 cells/µL have end-stage immunodeficiency, presenting with body wasting and CNS lymphoma (Vergis & Mellors, 2000).

Various studies have reported a range of CD4 counts and viral load values in HIV-infected individuals. Ena and Pasquau (2003) reviewed 8 studies of HIV-infected individuals who were beginning HAART. Mean CD4 counts at baseline ranged from 164-471 cells/µL, while mean viral loads ranged from 4.59-5.56 log_{10} copies/ml. Pant Pai, Lawrence, Reingold, and Tulsky (2011) reviewed 17 studies involving structured treatment interruptions for people with HIV. These individuals used HAART but the treatments were ineffective because of the drug-resistant viruses. Mean CD4 counts ranged from 28-383 cells/ µL, while viral load ranged from 7,943 to 540,000 copies/ml. Pichenot, Deuffic-Burban, Cuzin, and Yazdanpanah (2011) completed a systematic review and meta-analysis of 10 studies to determine the efficacy of new antiretroviral drugs for HIV-infected patients already on a form of HAART. The number of participants in each study ranged from 78-1,509 with a total of 6,401 individuals. The median CD4 counts at baseline ranged from 42-257 cells/µL and median viral load values ranged from 4.55-5.17 log_{10} copies/ml. The wide range of values in the immunological data emphasizes the unique, complex manifestation of HIV infection in different individuals.

In addition to depleted CD4 cell counts, natural killer T (NKT) cells are also destroyed with progressive HIV disease (Mureithi et al., 2011). NKT cells are important in the regulation of
the immune system and function to recruit and activate other cells in controlling and eliminating pathogens (Gumperz, Miyake, Yamamura, & Brenner, 2002). The levels of NKT cells and CD4 cells in 53 chronically infected patients in South Africa were assessed by Mureithi et al. (2011). A wide range of CD4 levels was observed; in 11 subjects treated with HAART; the mean CD4 count was 373 cells/µL (94-839 cells/µL) while 42 untreated subjects had a mean CD4 count of 373 cells/µL (86-948 cells/µL). A significant correlation was found between CD4 counts and absolute NKT cell numbers (r=0.50, p<0.001). With a reduction in NKT cells, the body is unable to respond efficiently and effectively to pathogens which in turn can lead to the onset of other diseases.

Antiretroviral therapy has allowed some HIV-infected individuals to maintain or regain higher levels of CD4 counts, slow the rate of viral replication, and reduce co-morbidities and mortality rates (Cameron et al., 1998; Palella et al., 1998; Valdez et al., 2001; Li et al., 2009). For example, the mean CD4 count increased from 123 cells/µL to 237 cells/µL 3 months after HAART initiation in 512 individuals with HIV (Li et al., 2009). Before treatment, there is a high expression of proinflammatory cytokines in lymph nodes (Andersson et al., 1998) which promotes expression of adhesion molecules and trapping of CD4 cells within the lymph nodes. The rapid increase of peripheral blood CD4 lymphocytes after HAART initiation can be attributed to the release of these cells trapped within lymphoid tissues (Bucy et al., 1999). Individuals who begin HAART earlier after diagnosis are more likely to reach normal CD4 counts than those who delay treatment initiation (Valdez, 2002). It is possible that during the period of untreated infection, viral replication occurs in the lymph nodes and renders CD4 cells dysfunctional.
In individuals with severe CD4 cell depletion, HAART may not be effective in fully restoring immune function. Lederman et al. (2003) examined immune function over 144 weeks in 199 HIV-infected subjects (87% male) who were initiating HAART. At baseline, the median CD4 count was 226 cells/mm³; by the 144th week, it had only risen to 358 cells/mm³ (increase of 132 cells over approximately 2.5 years). Additionally, 73% of participants lacked lymphocyte proliferation after receiving vaccinations for Hepatitis A and tetanus toxoid. These findings suggest that HAART can improve immune function to an extent in individuals starting with low CD4 counts, but cannot restore it completely. Further evidence was obtained in 438 HIV-infected individuals over approximately a 5-year period (Le Moing et al., 2007). Patients on HAART with CD4 levels over 200 cells/µL had an increase of 337 cells/µL (median value) while patients that started under 100 cells/µL were unable to increase levels above 200 cells/µL.

**Fatigue: Relationship with Quality of Life and Physical Function**

Functional disability (ADLs, IADLs and mobility) using the AIDS Time-Oriented Health Outcome Study disability measures and quality of life using the MOS-HIV were assessed in 546 HIV-infected individuals (18 females) (O'Dell et al., 1996). ADLs included dressing, hygiene, and eating; IADLs included running errands and shopping, doing household chores, and opening car doors; and Mobility included walking, climbing stairs, standing up from a chair and getting out of bed. A significant correlation was found between scores in the Energy/Fatigue Sub-scale of the MOS-HIV and total disability score in males \( r = -0.42 \) as well as in females \( r = -0.78 \). The stronger relationship in females suggests that women may experience greater fatigue and impairment in daily functioning compared with men and that fatigue may contribute to the experience of functional disability.
Baseline hemoglobin levels and quality of life using the MOS-HIV were assessed in 1,406 individuals with HIV, of which 34% were anemic (Semba, Martin, Kempen, Thorne, & Wu, 2005). Multivariate linear regression models were used to examine the associations between hemoglobin concentration and energy scores, and hemoglobin and physical function scores on the MOS-HIV. Energy and physical function scores were positively correlated with hemoglobin levels ( p<0.001) such that for every 1 g/dL change in hemoglobin, there were changes of 1.5-2.3 points in the energy score and changes of 2.6-2.7 in the physical function score. These findings indicate the need to increase hemoglobin levels in anemic individuals with HIV.

Pain, fatigue, physical performance and health status were assessed in 100 HIV-infected individuals (22 females) (Simmonds et al., 2005). Fatigue was measured using the Brief Fatigue Inventory, which consists of 9 scales, rated from 0 to 10 and quality of life was measured using the MOS-HIV. Ninety-eight percent of participants complained of fatigue (mean 5.4±2.3). Quality of life scores were higher (indicating better quality of life) in participants who had no pain and low fatigue levels and lowest in participants with high pain and high fatigue levels (Cognitive Function sub-scale: 73±26 vs. 38±28 respectively, Physical Function sub-scale: 60±26 vs. 37±22, Health Distress sub-scale: 65±26 vs. 34±26, Quality of Life sub-scale: 67±21 vs. 45±23). Performance of functional tasks such as the sit-to-stand task and the 6-minute walk test were impaired in the participants, potentially because of the pain and fatigue that many experienced. In the sit-to-stand task, participants were asked to sit in a standard chair, stand up, and sit down, repeating the process twice. In the 6-minute walk test, participants walked as far and as fast as they could in 6 minutes. Compared to the healthy normative values, participants took 4 times longer to complete the sit-to-stand task, and walked 75% of the distance of healthy individuals on the 6-minute walk test. These findings suggest that, although fatigue severity is
quite variable, fatigue is a common symptom of HIV infection and in combination with pain, can negatively impact quality of life and physical function.

Barroso, Harmon, Leserman, Madison, and Pence (2013) assessed the intensity and chronicity of fatigue as well as its impact on ADLs over a 3 year period in the same sample of 128 HIV-infected individuals as in another study (Barroso et al., 2010). The HRFS was used to determine the severe impact of fatigue on ADLs, socialization, and mental function, and to describe the triggers, alleviators and descriptors of fatigue in the population. Participants reported severe impairments in daily activities such as walking, shopping, carrying out day to day duties, planning activities ahead of time and working. Participants felt that fatigue interfered with work, family and social life, engaging in sexual activity, concentrating on tasks, and thinking quickly. Stress, depression, heat, work, and long periods of inactivity were cited as major triggers of fatigue while rest, sleeping and positive experiences were listed as alleviators of fatigue. Fatigue was described as causing low motivation, as being one of the top 3 disabling symptoms of HIV infection, as being different in quality and severity compared to before HIV infection, and that it made other symptoms worse.

In-depth personal interviews were conducted with 8 urban gay men with HIV in order to understand the daily life experiences of this population (Bedell, 2000). Although participants adapted to their health situation by developing strategies to conserve energy and simplify daily tasks, they reported experiencing physical and emotional fatigue that affected their ability to perform IADLs and work-related activities.
Summary

The research thus far indicates that fatigue can have a significant negative impact on the well-being of HIV-infected individuals. In conjunction with other health issues such as reduced functional physical capacity, pain and the presence of co-morbidities, fatigue may limit some individuals' ability to engage in day to day activities. The large proportion of males in most HIV studies has made it difficult to determine the prevalence and impact of fatigue in the daily lives of women with HIV. The current research study will address this question by examining fatigue and its impact on quality of life, physical function, social, recreational and daily living activities exclusively in the female HIV population.
Chapter 3

Methodology

Design

This was a cohort, non-experimental design study that sought to determine the relationships between physical function, quality of life and social, recreational and daily living activities in women with HIV who were either classified as 'fatigued' or 'non-fatigued'.

Recruitment and Participants

The first recruitment strategy was to distribute posters about the study to female clients at the HIV/AIDS Regional Services (HARS) in Kingston. Because of the low number of individuals recruited using this strategy (1 of the 15 participants in the study), another recruitment approach was required. After consultation with the research team, it was decided that the Clinical Immunological Outpatient Clinic (CIOC) in Hotel Dieu Hospital would be the site of recruitment because individuals could be approached when they arrived for their normally scheduled appointments. The majority of the participants in the study were recruited from the CIOC within the time frame from the end of November 2012 to the end of May 2013. During their scheduled clinic appointment visits, female patients were approached by the investigators to inform them of the study and to invite them to participate. To be included in the study, participants had to be HIV-infected women at least 18 years of age and able to communicate in English. Bus fare and a ten-dollar honorarium were provided to participants in recognition of their time and involvement in the study.
Estimates from the staff at HARS and the CIOC indicated that there were approximately 40 HIV-infected women living in Kingston and the surrounding areas. This study employed a sample of convenience with the intent to recruit as many women as possible from the Kingston area. Using 6-minute walk test (6MWT) data from a study by Mbada et al. (2013), the minimum sample size required to see statistically significant differences (with a power of 0.8) between HIV-infected women and healthy controls was 16 individuals per group. Henderson et al. (2005) examined differences in quality of life between fatigued and non-fatigued HIV-infected individuals and found that the minimum sample sizes required to see a statistically significant difference between groups in various sub-scale scores of the SF-36 ranged from 12-38 participants.

In total, 17 women were approached at the CIOC, 2 were referred to the study by one of the co-supervisors (an HIV physician), and one was recruited from HARS. Three women refused to participate because they did not want to be involved in the research or because of a lack of time. Two individuals were willing to participate but did not complete the study protocols because of a lack of time or because of health issues at the time.

All procedures in the study were reviewed and approved by the Health Sciences Research Ethics Board. Participants were provided with a letter of information and signed an informed consent form before participating in the study (Appendix A).

**Outcome Measures**

**Demographic Information**

Participants completed a demographics questionnaire (Appendix B) to determine age, height, weight, ethnicity, duration of HIV infection, medications, and co-morbidities. In addition,
socioeconomic data involving employment (e.g. full time or part time, on a disability plan, etc) and level of education (e.g. finished high school, college or university) were obtained. Patient charts were accessed in the CIOC to obtain immunological data (CD4 count and viral load).

Quality of Life

The Medical Outcomes Study HIV Health Survey (MOS-HIV) was used in this study to determine self-reported quality of life. The questionnaire consists of 35 questions with 11 sub-scales: general health perceptions, pain, physical functioning, role functioning, social functioning, mental health, energy/fatigue, cognitive function, health distress, quality of life and health transition (Appendix B). The evidence for reliability, validity, usefulness and responsiveness of the MOS-HIV have been widely reviewed (Wu et al., 1997). High internal consistency and reliability of the sub-scales have been reported in several studies (Scott-Lennox, McLaughlin-Miley, & Mauskopf, 1996; Burgess, Dayer, Catalan, Hawkins, & Gazzard, 1993; Revicki, Wu and Brown, 1995) in which Cronbach’s alpha coefficients were mostly found to be greater than 0.70. The construct validity of the scales has also been supported by multi-trait analyses (Wu et al., 1991; Revicki et al., 1995).

The questionnaire is responsive to clinically important changes; for example, patients with advanced HIV/AIDS who developed opportunistic infections during a pharmaceutical clinical trial had lower scores (indicating poorer health) after the trial compared to before (Safrin et al., 1996). Although many of the studies that have used this questionnaire were drug trials, some involved non-pharmaceutical interventions, such as exercise treatment (Roubenoff & Wilson, 2001; Wu, Clarke, Baigis & Chase, 1997). One of the limitations of this tool is that it has
not been used extensively in women, groups with lower socioeconomic status, and injection drug users (Wu, Revicki, Jacobson, & Malitz, 1997).

Participants answered questions by indicating their response on either a rating scale (e.g. from “not at all” to “extremely”) or to a yes/no prompt. Some of the questions required reversions; for example, a question valued at 6 in the questionnaire was reverted to a score of 1 for the final sum. The sums of each sub-scale were transformed into scores out of 100 using algorithms unique to each sub-scale (Wu, Revicki, Jacobson & Malitz, 1997). The maximum score for each sub-scale was 100, where higher values indicated better health and lower scores indicated poorer health. In addition, Physical Health Summary (PHS) and Mental Health Summary (MHS) scores were calculated using mean scores for each sub-scale. Means were transformed into z-scores and then entered into an algorithm to produce the PHS and MHS scores. Normative values for the PHS and MHS scores in the general population using the SF-36 (the tool which the MOS-HIV is based upon) are 50.5±9.0 and 51.7±9.1, respectively (Hopman et al., 2000). PHS scores lower than 43 suggest that individuals may perceive their physical health interferes with daily life functioning, while scores above 53 indicates that individuals are less likely to have physical problems which interfere with daily functioning. Similarly, participants with MHS scores below 39 are more likely to perceive that their psychological symptoms interfere with their lives than those with scores above 53 (Blanchard, Cote & Feeny, 2004).

Social, Recreational and Activities of Daily Living

Participants completed 3 lists of activities that they considered to be important for social activities, recreation and leisure, and activities of daily living (Appendix B). They were asked to provide a maximum of 5 activities in each list, and to rank them in order of importance (with #1
being the most important and #5 being the least important). Social activity was defined as involvement and interaction with other people (Human Resources and Skills Development Canada, 2012). Examples of social activities include volunteering, having dinner with relatives, going out for a movie with friends, and attending social group meetings (e.g. church, cultural groups). Recreation and leisure can be divided into 3 categories that involve social interaction, cognitive stimulation or physical exercise (Human Resources and Skills Development Canada, 2012). For the purposes of this study, the recreation and leisure category only included activities with cognitive stimulation or physical exercise such as playing sports and/or reading books.

Activities of daily living were defined as activities necessary for normal self-care, such as grocery shopping and climbing the stairs (Veterans Affairs Canada, 2012). Beside each activity, participants described how able or how limited they were in performing it (e.g. “cannot do it at all”, or “only once in a while”).

**Fatigue**

Fatigue plays a major role in limiting the social, role and physical functioning of HIV-infected individuals (Crystal et al., 2000; Rusch et al., 2004). The HIV-Related Fatigue Scale (HRFS) is a relatively new tool developed by Barroso and Lynn (2002) to assess the intensity of, circumstances surrounding, and consequences of fatigue experienced by this population (Appendix B). The HRFS is composed of sub-scales from 5 pre-existing tools; the Multidimensional Assessment of Fatigue (Belza, Henke, Yelin, Epstein, & Gilliss, 1993), the Fatigue Assessment Instrument (Schwartz, Jandorf, & Krupp, 1993), the General Fatigue Scale (Meek, Nail, & Jones, 1997), the Fatigue Impact Scale (Fisk, Pontefract, Ritvo, Archibald, & Murray, 1994) and the Sleep and Infection Questionnaire (Darko, McCutchan, Kripke, Gillin, &
Golshan, 1992). Additionally, 3 questions were developed by the authors in order to address concerns that were discussed by participants in a qualitative study on HIV-related fatigue (Barroso and Lynn, 2002). There are 56 items and 8 sub-scales in the HRFS; fatigue intensity, overall fatigue-related functioning, impact on activities of daily living, impact on socialization, impact on mental functioning, triggers of fatigue, alleviators of fatigue, and descriptive items. For each question, participants were asked to circle a number on a scale from 1-4, 1-7, or 1-10, where higher numbers indicate greater intensity, impact, importance of, or attribution to fatigue.

Because the HRFS is a newer tool, there is limited information on the psychometric properties of this scale. Overall, it has demonstrated high content validity and internal consistency (Pence, Barroso, Leserman, Harmon, & Salahuddin, 2008) but the test-retest correlation (performed 2 days apart) was only 0.43 indicating at best a moderate relationship (Barroso and Lynn, 2002). The latter finding may partially be due to the small sample of HIV-infected individuals (n=14) that completed the questionnaires at baseline and 2 days later. In addition, one of the developers of the HRFS indicated that fatigue was not necessarily expected to be stable from day to day (J. Barroso, personal communication, August 1, 2013). There was greater concern that the tool had strong internal consistency. In the current study, an excellent association (r=0.95, p<0.05) was found between the HRFS Total Fatigue Intensity Score and the MOS-HIV Energy/Fatigue sub-scale (which has demonstrated good validity and reliability). Therefore, we are confident that the HRFS scores are a valid reflection of fatigue experienced in the moment by the female participants of our study. To our knowledge no other indicators of test-retest reliability have been performed with the HRFS.

All participants completed Section I (the first 7 questions) of the HRFS. Those individuals who indicated ‘1’ or ‘2’ in response to all of these questions (n=7) were not required
to complete the remainder of the questionnaire and were categorized as ‘non-fatigued’ individuals. The remaining 8 individuals (who indicated ‘>2’ in response to each of the first 7 questions) were asked to complete the rest of the questionnaire which included sections on the impact of fatigue on activities of daily living, socialization, and mental function, on triggers and alleviators of fatigue, and on descriptors of fatigue and were categorized as ‘fatigued’ individuals. In reviewing the data, it was determined that for each category there were sub-populations of ‘high-scorers’ and ‘low scorers’. Accordingly, a decision was made to examine the fatigue responses with respect to the number of participants who indicated a severe impact of fatigue and strong triggers, alleviators and descriptors. Responses were labelled as severe or strong if participants ranked items as a 5, 6 or 7 on a scale of 1-7, or 7, 8, 9 or 10 on a scale of 1-10 (see example below). This method of reporting data is similar to that used by Barroso et al. (2013).

For example:

*In the past week, to what degree has fatigue interfered with your ability to do household chores?*

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>a great deal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*My motivation is lower when I am fatigued.*

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely disagree</td>
<td>Completely agree</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Aerobic Capacity**

The 6-minute walk test (6MWT) was used to assess the aerobic capacity of participants. The 6MWT has been used as a measure of aerobic capacity in many chronic disease/condition
populations such as stroke, COPD, fibromyalgia, heart disease and peripheral vascular disease (Finch, Brooks, Stratford, & Mayo, 2002) as well as in the HIV population (Dolan et al., 2006; Simmonds et al., 2005; Scott et al., 2007). The primary outcome of the test is the distance walked in metres by the participants. Each participant was asked to walk and cover as much distance as possible in the 6-minute time frame. Participants who completed the 6MWT in the hospital walked along a straight corridor which spanned 24 metres. Those who did the test at Bethel Church walked around the 45-metre perimeter of the gymnasium. Although the American Thoracic Society (2002) recommended using a 30 metre corridor for the test to reduce the number of times participants had to turn and reverse directions however, a multi-centre study found that there was no significant effect of the length of straight courses between 15-50 metres (Weiss et al., 2000).

Blood pressure, heart rate, O₂ saturation and Rating of Perceived Exertion (RPE) (Borg, 1982) were measured in order to monitor cardiorespiratory stress associated with the test (Appendix B). At rest, each participant sat in a chair and was asked to report her level of perceived exertion on the Borg scale of 6-20, where 6 indicates no exertion at all and 20 indicates maximal exertion. A Finger Pulse Oximeter (Vacumed©; http://www.vacumed.com) was placed on the right index finger to obtain oxygen saturation and heart rate. Simultaneously, blood pressure was obtained manually from the left arm using the auscultation method. Immediately after the 6MWT was completed, the participant sat down in a chair and the same measures were taken. This was repeated 6 minutes after the end of the test to ensure that cardiorespiratory parameters safely returned to near-baseline levels before participants left the facility.

Before participants started walking, standard instructions on how to perform the test were given. They were instructed to cover as much distance as possible within the 6-minute time
If they needed to stop and rest, they were able to, but the timer would continue to run. Standard encouragement (e.g. "keep up the good work!", "good job!", and "you can do it!") was given to all participants at the end of each lap in order to prevent attention bias that may lead to improved results (Enright, 2003). The amount of time remaining was stated to the participant after each minute, with 30 seconds left, and with 10 seconds remaining before the end of the test.

Test-retest reliability of the 6MWT was not performed in this study; however, other studies have demonstrated high intra-class correlation coefficient (ICC) values in other clinical populations. For example, ICC values ranging from 0.82 to 0.96 have been found in studies with participants with heart failure (O'Keeffe, Lye, Donnellan, & Carmichael, 1998; Roul, Germain, & Bareiss, 1998). An ICC value of 0.94 was found in a study with participants who had peripheral artery disease (Montgomery & Gardner, 1998). ICC values between 0.73 to 0.98 have been reported in studies involving participants with fibromyalgia (Pankoff, Overend, Lucy, & White, 2000; King et al., 1999). Criterion validity of the 6MWT has been established in a wide range of populations. VO$_{2\text{max}}$, which is the gold standard measure for aerobic capacity, has been correlated with 6MWT distance in individuals with pulmonary hypertension ($r=0.70$; Miyamoto et al., 2000) and individuals with end-stage lung disease ($r=0.73$; Cahalin, Pappagianopoulos, Prevost, Wain, & Ginns, 1995). Although 2 studies involving the HIV population included both the 6MWT distance and VO$_{2\text{max}}$ as outcome measures, the relationship between the 2 variables was not determined (Dolan et al., 2006; Scott et al., 2007).

**Protocol**

After reviewing the letter of informed consent and volunteering to participate, the women at the CIOC were asked to complete the demographics form, the MOS-HIV and the HRFS
questionnaire. Participants were then asked to list their top 5 most important activities with respect to social and recreational participation and ADLs. The questionnaires were completed while waiting for their clinic appointment. Two of the participants completed the questionnaires orally; one was better able to listen to and speak in English than read and write, and the other individual preferred the oral administration of the questionnaires. Once the participants finished all of their medical procedures, they completed the 6MWT in a long corridor within the hospital. The individuals who were recruited through HARS were asked to meet the investigators at the Bethel Church gymnasium located at 314 Johnson Street in Kingston. All forms and the 6MWT were completed at the gymnasium; the total time to complete data collection for each participant was approximately 45 minutes. All interviews were conducted and all measures were obtained by the same individual who was trained in the procedures.

Data Analysis

All data are reported as mean values ± standard deviations. Comparisons between ‘fatigued’ and ‘non-fatigued’ groups for quality of life and 6MWT were performed using t-tests or the non-parametric equivalent. Due to small participant numbers, normality and variance were first tested using Sigmasstat 3.5 (Systat©) to determine if parametric or non-parametric statistical analysis was required. A Spearman's correlation analysis was used to determine the relationships between performance on the 6MWT, scores on the MOS-HIV sub-scales, and total fatigue intensity score of the HRFS. Statistical significance was accepted at p<0.05. The lists of social, recreation and leisure activities and ADLs were analyzed thematically and the numbers of individuals indicating a similar type of activity that was valued were tallied under each of the categories of activity listed above.
Chapter 4

Results

Demographic Information

Fifteen women participated in the study (Table 1). On average, the duration of HIV infection was 12±5 years. All but one participant was on antiretroviral therapy. Individuals exhibited a large number of co-morbidities, with 10 participants having cardiorespiratory problems and 8 experiencing mental health issues. Medications were also numerous and varied, with 10 participants taking health supplements or vitamins, 7 individuals taking cardiorespiratory and 6 were taking psychogenic medications. This was not surprising given that these were the co-morbidities experienced by a large number of participants. Approximately half of the women completed secondary school and half completed or were in the process of completing post-secondary education. Half of the participants were on disability at the time of the study. As expected from the literature, there was a wide range of CD4 counts, although all participants had counts greater than 200 cells/µL. Viral load was undetectable in the majority of participants, indicating that the virus was under control in these individuals.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Participants</td>
<td>15</td>
</tr>
<tr>
<td>Age (years) (mean, SD, range)</td>
<td>44±8 (30, 56)</td>
</tr>
<tr>
<td>Weight (kg) (mean, SD, range)</td>
<td>77±24 (48, 127)</td>
</tr>
<tr>
<td>Height (cm) (mean, SD, range)</td>
<td>162±7 (152, 175)</td>
</tr>
<tr>
<td>Duration of HIV infection (years) (mean, SD, range)</td>
<td>12±5 (5, 23)</td>
</tr>
<tr>
<td><strong>ARV Therapy (# of participants)</strong></td>
<td></td>
</tr>
<tr>
<td>On ARVs</td>
<td>14</td>
</tr>
<tr>
<td>Ever interrupted for 3+ months</td>
<td>7</td>
</tr>
<tr>
<td>Duration of therapy use (years) (mean, SD, range)</td>
<td>9±3 (4, 15)</td>
</tr>
<tr>
<td><strong>Co-morbidities (# of participants)</strong></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal (e.g. osteoarthritis, fibromyalgia, knee pain)</td>
<td>5</td>
</tr>
<tr>
<td>Cardiorespiratory (e.g. hypertension, diabetes, anemia)</td>
<td>10</td>
</tr>
<tr>
<td>Mental health (e.g. drug and alcohol addictions, depression)</td>
<td>8</td>
</tr>
<tr>
<td>Neural (e.g. peripheral neuropathy, spina bifida)</td>
<td>3</td>
</tr>
<tr>
<td>Other (e.g. lipodystrophy, obesity, hepatitis C infection)</td>
<td>7</td>
</tr>
<tr>
<td><strong>Medications (# of participants)</strong></td>
<td></td>
</tr>
<tr>
<td>Vitamins and Supplements (e.g. Vitamin D, B12)</td>
<td>10</td>
</tr>
<tr>
<td>Psychogenic (e.g. Seroquel, Lorazepam)</td>
<td>6</td>
</tr>
<tr>
<td>Cardiorespiratory (e.g. Lipitor, Doxazosin)</td>
<td>7</td>
</tr>
<tr>
<td>Gastrointestinal (e.g. Pantaloc, Lomotil)</td>
<td>2</td>
</tr>
<tr>
<td>Anti-inflammatory (e.g. Naproxen)</td>
<td>2</td>
</tr>
<tr>
<td>Pain (e.g. Neurontin, Imipramine)</td>
<td>5</td>
</tr>
<tr>
<td>Other (e.g. Synthroid, Oxybutynin)</td>
<td>3</td>
</tr>
</tbody>
</table>
Table 1: Demographic Information (continued)

<table>
<thead>
<tr>
<th>Employment (## of participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working full-time</td>
</tr>
<tr>
<td>Working part-time</td>
</tr>
<tr>
<td>On Disability</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest Education Completed (## of participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elementary School</td>
</tr>
<tr>
<td>Secondary School</td>
</tr>
<tr>
<td>Post-secondary School</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immunological Data (median, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Recent CD4 Count (cells/mm³)</td>
</tr>
<tr>
<td>Nadir CD4 (cells/mm³)</td>
</tr>
<tr>
<td>Most Recent Viral Load (copies/ml) - undetectable</td>
</tr>
<tr>
<td>Most Recent Viral Load (copies/ml) - detectable (values)</td>
</tr>
</tbody>
</table>

Values as indicated in each section. ARVs: antiretroviral therapy; SD: standard deviation.

**HIV-Related Fatigue Scale (HRFS)**

Impact of Severe Fatigue on ADLs, Socialization, and Mental Function

Four of 8 ‘fatigued’ participants indicated that fatigue highly interfered with carry out duties and planning activities ahead while 3 indicated that walking was severely impacted by fatigue (Figure 1). Two of 8 ‘fatigued’ participants indicated a substantial impact of fatigue on their physical function, sustained physical function, exercise and shopping/errands.
Four of 8 'fatigued' participants indicated that fatigue highly interfered with their work, family, and social life while 3 indicated that fatigue severely impacted their ability to interact with people outside of their home (Figure 2). Only two individuals indicated that fatigue made it difficult to control their temper and one indicated a great impact of fatigue on visiting/socializing with family and friends.

Six of 8 'fatigued' participants indicated that fatigue significantly limited their ability to concentrate (Figure 3). Only one individual of the 8, indicated that fatigue severely limited her ability to either think quickly or think clearly.

These findings indicate that out of a total of 15 women surveyed with HIV-AIDS, 8 reported problems with fatigue. Further, of these 8 individuals, 6 reported that fatigue severely limited their ability to concentrate and 4 reported substantive limitations in two activities of daily living and with their work, family and social life.
Figure 1: The number of 'fatigued' participants (n=8) (x-axis) indicating a severe impact of fatigue on activities of daily living (ADLs) (y-axis). Phys func, physical function.

Figure 2: The number of 'fatigued' participants (n=8) (x-axis) indicating a severe impact of fatigue on socialization (y-axis). Rec, recreational.
Triggers, Alleviators and Descriptors of Fatigue

Six out of 8 ‘fatigued’ individuals reported that stress and depression were major triggers of fatigue (Figure 4). Five participants indicated that heat was a strong trigger, and 3 individuals felt that inactivity and performance of ADLs triggered fatigue. Only 2 reported that exercise and work were strong triggers, and only 1 indicated that HIV medications triggered fatigue.

Five out of 8 ‘fatigued’ individuals ranked positive experiences as a major alleviator of fatigue, while 4 ranked sleeping as an alleviator (Figure 5). Three participants indicated that resting and cool temperatures helped to alleviate fatigue.

Having low motivation most commonly characterized fatigue, with 6 of 8 participants reporting this as a strong descriptor (Figure 6). Five individuals felt that the fatigue that they now experienced was different in quality and severity than the fatigue they had before HIV infection. Four participants reported that fatigue made them feel drowsy, made them lose patience, was
worse in the afternoon, and was among the 3 most disabling symptoms of HIV infection. Three
participants indicated that fatigue was unpredictable, was the most disabling symptom, and that it
made other symptoms of HIV infection worse. Two reported that fatigue made them eat less, and
only 1 reported that fatigue was worse in the morning.

**Figure 4:** The number of 'fatigued' participants (n=8) (y-axis) identifying specific triggers of
fatigue (x-axis). HIV meds, HIV medications; ADLs, activities of daily living.

**Figure 5:** The number of 'fatigued' participants (n=8) (y-axis) identifying specific alleviators of
fatigue (x-axis).
**Figure 6:** The number of ‘fatigued’ participants (n=8) (y-axis) reporting specific descriptors of fatigue (x-axis). qual/sev, quality and severity.

**Social, Recreational/Leisure and Daily Living Activity Lists**

Items in each category were ranked in order of the most commonly valued activities. The number of ‘fatigued’ individuals who were able (third column) or limited (fourth column) in performing each activity is provided in brackets (F=). Categorization as ‘fatigued’ or ‘non-fatigued’ was based on the scores from the HRFS. Limitations in activity were attributed to physical, psychological or a combination of both restrictions.
Among the 10 participants who valued family-related activities, 3 individuals reported limitations in participation (Table 2). Three of 8 participants experienced limitations in socializing with friends. It is important to note that 8 of the 15 participants reported being socially isolated for various reasons, including avoidance of the psychological stress of not disclosing their HIV status; a lack of community from the same culture; lack of motivation; and poor lifestyle (i.e. drug addiction). One individual who listed socializing with friends as a valued activity reported social isolation because of the psychological stress and fatigue in not being able to disclose her HIV status to her friends. Among the 8 participants who were socially isolated, 5 of them were fatigued and had 'low motivation' as a strong descriptor of their fatigue.

Eleven participants reported that walking was a valued recreational activity, and 5 indicated experiencing limitations (Table 3). Only 2 of 10 participants felt limited in engaging in entertainment-related activities, such as going on the computer, watching television or doing puzzles. Only 1 out of 7 participants indicated limitations in performing physical activity such as playing sports or exercising.

Among the 12 participants ranking laundry as a valued activity, 4 reported limitations (Table 4). Six out of 10 individuals experienced limitations in grocery shopping, and 4 of 9 individuals reported limitations in cleaning, which included doing the dishes, dusting, and other forms of housework). Only 2 out of 7 participants felt limited in cooking, and 2 out 6 were limited in self-care activities such as showering. In all instances where individuals indicated they were too tired or felt limited in doing an activity, these were persons who were categorized as ‘fatigued’ as per the HRSF.
Table 2: The Most Valued Social Activities Indicated by the Participants

<table>
<thead>
<tr>
<th>Activity</th>
<th>Number of Participants</th>
<th>Able to do/not tired</th>
<th>Tired/limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family-related activities (e.g. spending time together, going to kids' events, helping kids with homework)</td>
<td>10</td>
<td>7 (F=2)</td>
<td>3 (F=3)</td>
</tr>
<tr>
<td>Visiting/spending time with friends</td>
<td>8</td>
<td>5 (F=1)</td>
<td>3 (F=3)</td>
</tr>
<tr>
<td>Going to church</td>
<td>3</td>
<td>2 (F=0)</td>
<td>1 (F=1)</td>
</tr>
<tr>
<td>Volunteering</td>
<td>2</td>
<td>2 (F=0)</td>
<td>0</td>
</tr>
</tbody>
</table>

F=, number of individuals classified as fatigued responding in this category.

Table 3: The Most Valued Recreational/Leisure Activities Reported by Participants

<table>
<thead>
<tr>
<th>Activity</th>
<th># of Participants</th>
<th>Able to do/not tired</th>
<th>Tired/limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Going for a walk</td>
<td>11</td>
<td>6 (F=2)</td>
<td>5 (F=5)</td>
</tr>
<tr>
<td>Entertainment (movies, TV, facebook, opera)</td>
<td>10</td>
<td>8 (F=6)</td>
<td>2 (F=2)</td>
</tr>
<tr>
<td>Exercising/sports (squash, aquatics, biking, going to the gym)</td>
<td>7</td>
<td>6 (F=2)</td>
<td>1 (F=1)</td>
</tr>
<tr>
<td>Mental activities (reading, puzzles)</td>
<td>5</td>
<td>4 (F=2)</td>
<td>1 (F=1)</td>
</tr>
<tr>
<td>Shopping</td>
<td>3</td>
<td>1 (F=1)</td>
<td>2 (F=2)</td>
</tr>
<tr>
<td>Playing with pet</td>
<td>1</td>
<td>0</td>
<td>1 (F=1)</td>
</tr>
</tbody>
</table>

F=, number of individuals classified as fatigued responding in this category
Table 4: The Most Valued Daily Living Activities Reported by Participants

<table>
<thead>
<tr>
<th>Activity</th>
<th># of Participants</th>
<th>Able to do/not tired</th>
<th>Tired/limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laundry</td>
<td>12</td>
<td>8 (F=4)</td>
<td>4 (F=4)</td>
</tr>
<tr>
<td>Grocery shopping</td>
<td>10</td>
<td>4 (F=0)</td>
<td>6 (F=6)</td>
</tr>
<tr>
<td>Cleaning (includes dishes, dusting, housework)</td>
<td>9</td>
<td>5 (F=1)</td>
<td>4 (F=4)</td>
</tr>
<tr>
<td>Cooking</td>
<td>7</td>
<td>5 (F=3)</td>
<td>2 (F=2)</td>
</tr>
<tr>
<td>Self-Care (includes showering)</td>
<td>6</td>
<td>4 (F=2)</td>
<td>2 (F=2)</td>
</tr>
<tr>
<td>Working</td>
<td>4</td>
<td>3 (F=1)</td>
<td>1 (F=1)</td>
</tr>
<tr>
<td>Picking up medications (daily)</td>
<td>1</td>
<td>1 (F=0)</td>
<td>0</td>
</tr>
<tr>
<td>Driving</td>
<td>1</td>
<td>1 (F=0)</td>
<td>0</td>
</tr>
<tr>
<td>Paying bills</td>
<td>1</td>
<td>1 (F=0)</td>
<td>0</td>
</tr>
<tr>
<td>Climbing stairs</td>
<td>1</td>
<td>1 (F=0)</td>
<td>0</td>
</tr>
<tr>
<td>Gardening</td>
<td>1</td>
<td>1 (F=0)</td>
<td>0</td>
</tr>
</tbody>
</table>

F=, number of individuals classified as fatigued responding in this category.

Quality of Life (MOS-HIV)

Participants were categorized as ‘fatigued’ (n=8) or ‘non-fatigued’ (n=7) based on the HRFS. The mean scores of each group for 6 of the 11 sub-scales (General Health Perceptions, Pain, Physical Function, Energy/Fatigue, Mental Health and Cognitive Function) which passed normality and variance tests were compared and are reported in the figure below. The other 5 sub-scales (Role Function, Social Function, Health Distress, Quality of Life and Health Transition) which did not pass the normality and variance tests are shown in subsequent box plots. Significant differences between groups are denoted by an asterisk (p≤0.05). Role Function, Cognitive Function and Health Transition were the only sub-scales in which no significant differences were found between groups. The largest differences between the ‘non-fatigued’ and
'fatigued' groups were found in the Health Distress and Energy/Fatigue sub-scales (96±7 vs. 36±30 and 78±13 vs. 31±13, respectively). When the values of the 3 sub-scales which were non-significant between groups were removed, the 'fatigued' group's overall mean score was 52% of the 'non-fatigued' group. The 'non-fatigued' group had mean scores ranging from 68±24 (Health Transition) to 96±7 (Health Distress), while the 'fatigued' group had scores ranging from 31±13 (Energy/Fatigue) to 58±25 (Cognitive Function).

Figure 7: Scores from 6 of the 11 sub-scales of the MOS-HIV Quality of Life outcome measure using parametric statistics. Values are means ± standard deviation. (*) represents significant difference between 'fatigued' (solid bars) and 'non-fatigued' (spotted bars) groups at p<0.05.
**Figure 8:** Box plot of Role Function sub-scale scores from the MOS-HIV for the 'fatigued' and 'non-fatigued' groups. The box plot indicates the median, scores in the 25th and 75th percentiles, minimum and maximum values. (*) represents significant difference between groups at p<0.05.

**Figure 9:** Box plot of Social Function sub-scale scores from the MOS-HIV for the 'fatigued' and 'non-fatigued' groups. The box plot indicates the median, scores in the 25th and 75th percentile, minimum and maximum values. (*) represents significant difference between groups at p<0.05.
Figure 10: Box plot of Health Distress sub-scale scores from the MOS-HIV for the 'fatigued' and 'non-fatigued' groups. The box plot indicates the median, scores in the 25th and 75th percentile, minimum and maximum values. (*) represents significant difference between groups at p<0.05.

Figure 11: Box plot of Quality of Life sub-scale scores from the MOS-HIV for the 'fatigued' and 'non-fatigued' groups. The box plot indicates the median, scores in the 25th and 75th percentile, minimum and maximum values. (*) represents significant difference between groups at p<0.05.
Figure 12: Box plot of Health Transition sub-scale scores from the MOS-HIV for the 'fatigued' and 'non-fatigued' groups. The box plot indicates the median, scores in the 25th and 75th percentile, minimum and maximum values. (*) represents significant difference between groups at p<0.05.

The mean values ± standard deviation for the Physical (PHS) and Mental Health Summary (MHS) scores for each group are listed in Table 5. The mean scores for both the PHS and MHS in the ‘non-fatigued’ group were greater than 53, indicating that participants in this group were less likely to report interference in daily functioning due to physical or psychological symptoms (Blanchard, Côté, and Feeny, 2004). In the ‘fatigued’ group, the PHS score was below 43 and the MHS score was below 39, suggesting that participants in this group were more likely to report that their physical and psychological symptoms interfered with their daily life functioning.
**Table 5:** Physical and Mental Health Summary Scores from the MOS-HIV Quality of Life Questionnaire

<table>
<thead>
<tr>
<th></th>
<th>Non-fatigued (n=7)</th>
<th>Fatigued (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Health Summary Score</td>
<td>54.8</td>
<td>38.0</td>
</tr>
<tr>
<td>Mental Health Summary Score</td>
<td>59.5</td>
<td>35.6</td>
</tr>
</tbody>
</table>

Values were calculated from the mean score of each sub-scale in the MOS-HIV.

**Six-Minute Walk Test (6MWT)**

The means and standard deviations of the actual distance walked, predicted distance, and percentage of actual/predicted distance in the 6MWT for the ‘fatigued’ and ‘non-fatigued’ groups are shown in Figures 8 and 9. One participant (P-10) did not complete the 6MWT because of physical exhaustion and other health limitations. There were no significant differences between groups for any of the variables.

![Graph](image)

**Figure 13:** The actual distance walked in metres (m) for the 6MWT and the age- and gender-predicted distance walked in the ‘fatigued’ (black bars) (n=8) and ‘non-fatigued’ (spotted bars) (n=7) groups. Values are means ± SD. 6MWT, 6-minute walk test.
Figure 14: The percentage of actual/predicted distance walked (%) for the 'non-fatigued' (n=7) and 'fatigued' (n=8) groups. Values are means ± SD.

The mean values ± standard deviation for blood pressure, oxygen saturation, heart rate, and rating of perceived exertion (RPE) at rest, immediately after the 6MWT and after 6 minutes of recovery from the 6MWT are listed in Table 6. The oxygen saturation data from 2 'non-fatigued' individuals could not be obtained due to poor readings on the Finger Pulse Oximeter. There were no significant differences between groups in any of the measures at each time point. In addition, group means for predicted HR_{max} and % HR_{max} were calculated and reported in Table 6. The HR_{max} of each participant was predicted using the female-specific equation $HR_{\text{max}} = 206 - 0.88(\text{age})$ (Gulati et al., 2010). The HR data from one 'non-fatigued' individual could not be obtained due to poor readings on the Finger Pulse Oximeter. There were no significant differences between groups for these measures.
### Table 6: Cardiovascular Outcome Measures for the 6MWT for the 'Fatigued' and 'Non-Fatigued' Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre</th>
<th>Post</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fatigued (n=7)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>119±6 (109, 126)</td>
<td>130±7 (122, 144)</td>
<td>117±11 (104, 128)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>77±9 (67, 94)</td>
<td>78±9 (70, 96)</td>
<td>79±8 (68, 90)</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>75±14 (59, 101)</td>
<td>85±15 (68, 115)</td>
<td>74±17 (58, 110)</td>
</tr>
<tr>
<td>O₂ saturation (%)</td>
<td>98±1.5 (95, 99)</td>
<td>97±2 (93, 99)</td>
<td>99±0.5 (98, 99)</td>
</tr>
<tr>
<td>RPE (6-20)</td>
<td>8±2 (6, 11)</td>
<td>11±3 (7, 15)</td>
<td>7±1 (6, 9)</td>
</tr>
<tr>
<td>Predicted HR&lt;sub&gt;max&lt;/sub&gt; (beats/min)</td>
<td>167±7 (156, 177)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Predicted HR&lt;sub&gt;max&lt;/sub&gt;</td>
<td></td>
<td>51±11 (40, 73)</td>
<td></td>
</tr>
<tr>
<td><strong>Non-Fatigued (n=7)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>116±3 (110, 120)</td>
<td>125±8 (116, 138)</td>
<td>116±7 (108, 128)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>74±4 (70, 79)</td>
<td>73±4 (70, 80)</td>
<td>73±5 (68, 80)</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>66±4 (60, 72)</td>
<td>84±13 (63, 100)</td>
<td>69±8 (57, 76)</td>
</tr>
<tr>
<td>O₂ saturation (%)</td>
<td>97±1 (95, 98)</td>
<td>95±6 (85, 98)</td>
<td>97±2 (95, 99)</td>
</tr>
<tr>
<td>RPE (6-20)</td>
<td>6±1 (6, 7)</td>
<td>9±2 (7, 11)</td>
<td>6±1 (6, 7)</td>
</tr>
<tr>
<td>Predicted HR&lt;sub&gt;max&lt;/sub&gt; (beats/min)</td>
<td>169±8 (159, 180)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Predicted HR&lt;sub&gt;max&lt;/sub&gt;</td>
<td></td>
<td>50±8 (38, 60)</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± standard deviation with the range of values reported in brackets for the cardiorespiratory and intensity measures during the 6MWT. Pre, measures taken before the test; Post, measures taken immediately upon completion of the test; Recovery, measures taken at 6 minutes following completion of the test. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RPE, rating of perceived exertion; HR<sub>max</sub>, maximum heart rate.
Relationships between Physical Function and Quality of Life

Spearman Rank Order Correlation tests were performed using Sigma Stat to determine if there were relationships between the distance walked on the 6-minute walk test, which is an objective measure of physical function and scores from the 11 sub-scales of the MOS-HIV, a self-reported measure. The only significant correlation identified was a strong, significant correlation between the distance walked on the 6MWT and the Physical Function sub-scale of the MOS-HIV (r=0.69, p=0.006) (Figure 10).

Figure 15: Relationship between the Physical Function sub-scale score on the MOS-HIV (y-axis) and distance walked on the 6-minute walk test (x-axis).
Chapter 5

Discussion

The primary findings of the current study were that half of the participants living with HIV experienced moderate to severe fatigue. For any given aspect of daily functioning (including performance of ADLs, socialization and mental health), at least half of the women reported that the fatigue severely interfered with their functioning. Fatigue mainly impacted socializing with friends, walking, grocery shopping, cleaning, being able to plan ahead of time, and concentrating on tasks. These individuals had significantly lower quality of life scores compared with participants who were not fatigued. There were no significant differences between the 'fatigued' and 'non-fatigued' groups in distance walked or in the percentage of predicted distance. The major triggers of fatigue were depression, stress and heat; the major alleviator of fatigue was having positive experiences.

The demographic characteristics of our participants (n=15) were similar to those in the Ontario HIV Treatment Network (OHTN) Cohort Study (n=337) (Benoit et al., 2013) in age (current study: mean 44±8 years; OHTN: median 43 years (range 35-50); duration of HIV infection (current study: mean 12±5 years; OHTN: median 11 years (range 6-16); employment (current study: 47% working part-time or full-time; OHTN 42% and current study: 47% on disability; OHTN: 50%); CD4 count (current study: 100% > 200 cells/µL; OHTN: 91%); and viral load (current study: 80% undetectable; OHTN: 74%). The women in our study had slightly higher education levels compared with those in the OCS study (47% had finished or were in the process of completing post-secondary education versus 38% in the OHTN study). Since the
demographics between the two groups were similar, the findings of the current study may be
generalizable to the female HIV population in Ontario.

Fatigue

Approximately half of the participants experienced fatigue which interfered with various
aspects of daily functioning. The mean fatigue intensity score for the 'fatigued' group was 5.4±2.3
(range 2.2 to 9.2), indicating moderate fatigue and is in agreement with that of other studies.
Barroso et al. (2003) reported a mean fatigue intensity score of 6.0±2.3 in 40 HIV-infected
individuals (27% female). Pence et al. (2009) reported a baseline mean fatigue intensity score of
5.9±2.2 in a sample of 126 individuals (34% female).

In our study, half of the fatigued participants felt that fatigue severely interfered with
planning activities ahead of time and carrying out their duties and responsibilities. Limitations in
these ADLs were not reported as common among participants by Barroso et al. (2003), but in
another study of 128 HIV-infected individuals, 32% experienced limitations in planning activities
and 60% had difficulty in carrying out their daily duties (Barroso et al., 2013). Furthermore,
Barroso et al. (2013) found that fatigue severely impacted work, family and social life for 61% of
participants, which is slightly higher than what was found in the current study (50%). Having
difficulty concentrating on tasks was also commonly reported by participants (68%), which is
consistent with our findings and that of others (Anandan et al., 2006; Barroso et al., 2003).

Participants listed stress (68%), depression (66%) and heat (61%) as major triggers of
fatigue, while rest (54%), sleeping (54%) and positive experiences (53%) were listed as major
alleviators of fatigue (Barroso et al., 2013). Sixty-three percent felt that the fatigue they now
experienced was different in quality and severity compared with before HIV infection, which is
consistent with the findings in the current study as well those of Barroso et al. (2003). Six out of
the 8 'fatigued' individuals in our study had low motivation which was also reported by Barroso et
al. (2003), although it is unclear how many participants in that study reported this feeling.
Barroso et al. (2013) also found that a large majority of the sample (73%) reported low
motivation. Five of the 8 women in our study who reported low motivation were also socially
isolated which may indicate that having social support may be important in increasing the
motivation of these fatigued individuals. The proportion of women reporting other descriptors of
fatigue in our study were similar to that of Barroso et al. (2013), who reported that fatigue was
among the 3 most disabling symptoms of HIV infection (66%), made participants feel drowsy
(65%), made participants lose patience (59%), made other symptoms worse (57%), was
unpredictable (55%), was the most disabling symptom of HIV and was worse in the afternoon
(49%), and that it started before other HIV symptoms (37%). To our knowledge, the current study
is only the third investigation to report the impact of fatigue on specific activities using the HRFS
and contributes to the understanding of how women are affected in the performance of day to day
tasks.

Approximately 50% of the participants in the current investigation had fatigue issues.
This percentage is slightly greater than that reported by Sullivan et al. (2003) and Wantland et al.
(2011), who found that 37% (n=13,768; 26% female) and 39% (n=240; 34% female) of the
participants reported fatigue. In contrast, others have reported higher proportions of fatigued
individuals. Henderson et al. (2005) found that 57% of the HIV-infected females reported having
fatigue while Schiffito et al. (2011) and Voss (2005) found that 64% (n=128; 13%) and 88%
(n=372; 33% female) of the participants reported fatigue. In the studies with both male and
female participants, the proportion of females that reported fatigue was not reported.

64
According to the lists of valued activities in our study, 5 fatigued individuals experienced limitations in walking, 4 fatigued individuals felt limited in doing the laundry and cleaning, and 6 fatigued individuals had issues with grocery shopping. These findings are similar to those of O’Dell et al. (1996) in which 56% of the women reported difficulty in walking, and 50% had issues with performing other daily activities such as shopping and doing household chores. A strong, significant correlation (r=-0.78) was found between fatigue (scores in the Fatigue/Energy Sub-scale in the MOS-HIV) and functional disability (perceived difficulty in performing various activities, as assessed by the HIV Health Assessment Questionnaire [HAQ]) in women (O’Dell et al., 1996), underscoring the relationship between fatigue and participation in day to day activities in our study. Some studies have reported that participants faced challenges in performing other ADLs or IADLs, such as bathing, eating, and managing finances (Anandan et al., 2006; Gaidhane et al., 2008; Ghandi et al., 2011). In the current study, fatigue did not appear to interfere with these activities. It is possible that early detection and appropriate treatment of HIV as well as the development of coping strategies enabled our participants to perform basic ADLs without issue.

Managing finances was not listed as a valued activity by the majority of participants, so it is unclear whether fatigue affected their ability to perform this task. To our knowledge, this is the first study which examined the impact of fatigue on social participation specifically in women with HIV. Out of the 4 ’fatigued’ individuals who listed socializing with friends as a valued activity, 3 of them felt limited (by physical or psychological fatigue). For these women, interventions targeting fatigue are recommended so that they can fully engage in the social activities which in turn will enhance their quality of life.

Indicators of good immune function (high CD4 count and low viral load) were evident among many of the fatigued individuals in the current study. Six of the 8 women had
undetectable viral loads and 6 had CD4 counts above 400 cells/µL, which is on the higher end of the range (200-500 cells/µL) for individuals who are asymptomatic or have mild symptoms (Vergis & Mellor, 2000). There was one individual in our study who had a non-progressive infection (with a CD4 count of 1,084 cells/µL at the time of the study) and did not take any HIV medications, yet she still experienced chronic fatigue. This suggests that there may be other physiological, psychological or external factors which lead to the onset of fatigue, regardless of immune function status. Others have also found no or weak, non-significant correlations between CD4 count and fatigue severity or viral load and fatigue severity (Barroso et al., 2003; Barroso et al., 2008).

Quality of Life

The ‘fatigued’ group had significantly lower scores in 8 of the 11 sub-scales of the MOS-HIV which were approximately 50% of those in the ‘non-fatigued’ group. Little research is available comparing quality of life between fatigued and non-fatigued HIV-infected individuals. Further, this is the first study to use the outcomes from the HRFS and MOS-HIV to describe quality of life in fatigued and non-fatigued women living with HIV. In a study of 148 HIV-infected fatigued and non-fatigued individuals (classified using the Chalder Fatigue Scale), Henderson et al. (2005) found that the non-fatigued group (13 females) had significantly higher scores on every sub-scale of the SF-36 compared with the fatigued group (17 females), with at least an approximate 20-point difference between groups in each sub-scale (e.g. 81±21 vs. 47±28, Social Functioning sub-scale). The Physical Role Function scores were vastly different between groups; the fatigued group had a median score of 0 (range 0-50) while the non-fatigued group had a median score of 100 (range 50-100). In the current study, no significant difference was found
between groups in Role Function, perhaps because a few of the women in the fatigued group were fully capable of performing the tasks described in the questions for Role Function (e.g. working at a job, doing work around the house, going to school). However, in reviewing individual data, 5 of the 8 fatigued women had scores of 50 or less, suggesting that role function may be negatively impacted by fatigue in more than half of HIV-infected women experiencing fatigue.

Simmonds et al. (2005) used the MOS-HIV to assess quality of life in 100 HIV-infected individuals (22% female). Ninety-eight percent of the participants were fatigued according to the Brief Fatigue Inventory. Participants with no pain and mild fatigue had significantly higher scores than participants with pain and moderate to severe fatigue in 4 sub-scales, namely, Cognitive Function (73±26 vs. 38±28), Pain (69±20 vs. 29±23), Energy/Fatigue (57±21 vs. 29±19) and Health Distress (65±26 vs. 34±26). These 4 sub-scale scores of the first group (no pain, mild fatigue) are lower than the scores of the 'non-fatigued' participants found in our study (Cognitive Function, 81±17; Pain,79±20; Energy/Fatigue, 78±13; Health Distress, 96±7). These findings suggest that even individuals with mild fatigue may experience significant negative impact on their quality of life.

In the current study, the 'non-fatigued' group had PHS and MHS scores (55 and 60, respectively) which were well above the normative values for the healthy population (50.5±9.0 and 51.7±9.1, respectively) (Hopman et al., 2000) and were greater than 53, indicating that these individuals were unlikely to perceive that their physical and mental health interfered with their daily functioning (Blanchard et al., 2004). In contrast, individuals in the 'fatigued' group had scores (38 and 36, respectively) well below the healthy population's normative values and less than 39, suggesting that they were likely to perceive that their physical and mental health
interfered with performing day to day activities (Blanchard et al., 2004). This stark differentiation in summary scores based on the presence of fatigue was not evident in the study by Mannheimer et al. (2008). At baseline the 1,397 HIV-infected participants (21% female) had a mean PCS score of 45±11 and a MCS score of 43±9 from the SF-36 and after 12 months, the scores had slightly increased to 48±10 and 44±9, respectively. Although fatigue was the most commonly reported symptom (according to the CPCRA Symptom Severity Form), with 75% of participants reporting having fatigue at least once over the course of the year; the extent of the fatigue in these participants was not clear. The scores at baseline and at 12 months were below the healthy normative values, but were still above the cut-off values (PHS, 43; MHS, 39). In another study by Stangl, Bunnell, Wamai, Masaba, and Mermin (2012), 947 HIV-infected individuals who were naive to HAART reported a mean PHS score of 39±10 and a MHS score of 40±11. The mean scores for women only (n=710) were also 39±10 and 40±11, respectively. Fatigue levels were not assessed in this study, so it is unknown whether fatigue impacted these summary scores; however, they are closer to the scores seen in the 'fatigued' group than in the 'non-fatigued' group. A few studies have reported summary scores which are close to that of the healthy population (Weinfurt et al., 2000; Hsiung et al., 2011), suggesting that fatigue may not have been an issue or was not as severe in the individuals in the 'fatigued' group in the current study.

Other studies which have used the MOS-HIV reported scores within the same range as this study. Vosvick et al. (2003) examined 4 sub-scales (Pain, Physical Function, Energy/Fatigue, Social Function and Role Function) in 142 HIV-infected individuals (43% women). The scores of each sub-scale were approximately halfway between those of the 'fatigued' and 'non-fatigued' groups in our study. For example, the mean score for the Pain sub-scale was 62±27, while in our
study the ‘non-fatigued’ group had a score of 79±20 and the ‘fatigued’ group had a score of 43±21. This was observed in studies by Hsiung et al. (2011), Ichikawa and Napratan (2004), Lau et al. (2006), and Safren et al. (2012).

In general, the sub-scale scores of the MOS-HIV reported in the current study are consistent with those in the literature. However, the differential analysis of sub-scale scores for the ‘fatigued’ and ‘non-fatigued’ individuals provides a better understanding of how quality of life can be impacted by fatigue in women living with HIV.

Physical Function

No significant differences were observed between groups in the 6MWT distances. Both ‘fatigued’ and ‘non-fatigued’ individuals completed approximately 80% of their predicted age, height, and weight-matched normative distance, suggesting that physical function may be slightly reduced in some women with HIV (regardless of fatigue status) compared with the healthy population. This percentage is similar to that of Simmonds et al. (2005), who found that participants (n=100; 22 females) walked 75% of their predicted distance, indicating some reduction in physical function. Dolan et al. (2006) did not report predicted distances for their sample of 40 HIV-infected women (mean age 42±2 years) but the mean 6MWT distance at baseline was 482±17 m, which is slightly higher than the mean distance of the women (fatigued and non-fatigued) in our study (448±69 m). The mean predicted distance could not be calculated because height and weight means were not provided; however, the mean ages of the participants in this study and ours are similar. Another study of 27 HIV-infected men reported that participants completed 89% of their predicted distance on the 6MWT (Scott et al., 2007), which is almost 10% higher than what we found for female participants in our study. Our findings appear
to be consistent with the literature, suggesting that, in the HAART era, physical function in the HIV population is not significantly impaired.

Although a difference between groups in 6MWT distance was not observed, the strong, significant correlation between Physical Function sub-scale scores in the MOS-HIV and the 6MWT distance ($r=0.69$, $p=0.006$) and the fact that these scores were significantly less in the 'fatigued' versus 'non-fatigued' group suggests that some limitation in physical function is associated with fatigue in women with HIV. To our knowledge, this is the first study to examine the relationship between self-reported and objectively measured physical function using the MOS-HIV and the 6MWT in the female HIV population.

**Limitations**

There were some limitations associated with the performance of the 6MWT. From the cardiorespiratory data, it was evident that the majority of participants were not exerting the expected level of effort to cover as much distance as possible in 6 minutes during the test. Although the standardized instructions indicated that participants were to cover as much distance as possible within the 6-minute time frame, they did not seem to have a sense of urgency during performance of the test and appeared to be walking at a leisurely pace. Further, the average Rating of Perceived Exertion (RPE) upon completion of the walk was $9\pm2$ in the 'non-fatigued' group and $11\pm3$ in the 'fatigued' group, which is only equivalent to very light or light work. Finally, at the end of the test participants in both groups had heart rates which were only approximately 50% of their HR$_{\text{max}}$. Another study assessed 6MWT distance in patients with COPD and reported increases in cardiorespiratory measures after the 6MWT, as would be expected (Turner, Eastwood, Cecins, Hillman, & Jenkins, 2004). Participants had heart rates that
were 82±11\% of their HR_{max}, and their RPE was similar to that observed at maximal aerobic capacity. Similarly, Pulz et al. (2008) found that the mean peak heart rate of chronic heart failure patients during the 6MWT was similar to the mean peak heart rate in the incremental shuttle walk test (a test where participants must incrementally increase speed over time). Additionally, a strong, significant relationship between 6MWT distance and VO_{2\max} (r=0.76) was found. These findings from other clinical populations suggest that our population of HIV-infected women may have misunderstood or misinterpreted the 6MWT instructions, resulting in less effort during the test. In future investigations, it may be necessary to alter the instructions or the standardized encouragement to facilitate greater effort in performing the test. Despite these concerns about insufficient effort, the values obtained from our participants for the 6MWT distance were similar to those reported by Dolan et al. (2006) (482±17 m) and Mbada et al. (2013) (427±94 m).

Another limitation of this study was the small sample size. With more participants, we may have seen statistically significant differences between groups in 6MWT distance and our findings may be more easily generalized to the female HIV population at large. We estimated that we would need between 12-38 participants in each group to see statistically significant differences; however, this was not feasible considering the small female HIV population in Kingston and the greater area.

Future Directions and Implications

Since the current study identified that fatigue significantly limits quality of life in approximately half of the female HIV population, there is a need to determine practical interventions for reducing fatigue and targeting the triggers such as depression and stress in order to optimize quality of life in women with HIV. The limitations in basic daily activities such as
grocery shopping, cleaning and doing laundry at this stage in the women's lives may worsen as the aging process continues, suggesting a need for early intervention. The current study did not explore the extent of social support (formal services as well as informal support from friends and family) available for our female participants. In light of the finding that over half of our fatigued women were socially isolated from friends and that social support is a predictor of fatigue-related functional impairment in HIV-infected individuals (Barroso et al., 2010), it is may be important to develop interventions which promote social support and community. Further, the data from our study are limited to the Kingston and surrounding areas and a multi-centre large scale study is indicated in order to broaden the scope of understanding daily life for women with HIV.

Presently, HARS and a local faith-based organization are in the process of discussing the implications of this study's research and the potential development of community-based health and wellness programs for individuals with HIV in Kingston. Through education and participation in exercise, nutrition and spiritual support programs, it is hoped that individuals with HIV will have greater social support, reduced fatigue, and increased quality of life.
Chapter 6

Bibliography


Chapter 6

Appendices
APPENDIX A

1. Original Ethics Approval (July 27, 2012)

2. Ethics Amendment Approval (Sept 12, 2012)

3. Ethics Amendment Approval (Oct 31, 2012)

4. Letter of Information and Informed Consent
Miss Abigail Hum  
School of Rehabilitation Therapy  
Louise D. Acton Building  
Room 033, 31 George Street  
Kingston, ON K7L 5P9

Dear Dr. Hum:

Study Title: REH-529-12 The effects of an 8-week moderate intensity aerobic and strength training exercise program on performance of activities of daily living and social participation in HIV-infected women File # 6007131

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol and consent form for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair's signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # 6007131 in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file 6007131 in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair's signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Chair, Research Ethics Board
July 27, 2012
QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD

The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards and operates in compliance with the Tri-Council Policy Statement; Part C Division 5 of the Food and Drug Regulations, OHRP, and U.S DHHS Code of Federal Regulations Title 45, Part 46 and carries out its functions in a manner consistent with Good Clinical Practices.

Federalwide Assurance Number: #FWA00004184, #IRB00001173

Current 2012 membership of the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board:

Dr. A.F. Clark, Emeritus Professor, Department of Biochemistry, Faculty of Health Sciences, Queen's University (Chair)

Dr. H. Abdollah, Professor, Department of Medicine, Queen's University

Dr. R. Brison, Professor, Department of Emergency Medicine, Queen's University

Dr. M. Evans, Community Member

Dr. S. Horgan, Manager, Program Evaluation & Health Services Development, Geriatric Psychiatry Service, Providence Care, Mental Health Services, Assistant Professor, Department of Psychiatry

Ms. J. Hudacin, Community Member

Dr. B. Kisilevsky, Professor, School of Nursing, Departments of Psychology and Obstetrics and Gynaecology, Queen's University

Mr. D. McNaughton, Community Member

Ms. P. Newman, Pharmacist, Clinical Care Specialist and Clinical Lead, Quality and Safety, Pharmacy Services, Kingston General Hospital

Ms. S. Rohland, Privacy Officer, ICES-Queen's Health Services Research Facility, Research Associate, Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute

Dr. B. Simchison, Assistant Professor, Department of Anesthesiology and Perioperative Medicine, Queen's University

Dr. A.N. Singh, WHO Professor in Psychosomatic Medicine and Psychopharmacology, Professor of Psychiatry and Pharmacology, Chair and Head, Division of Psychopharmacology, Queen's University
Amendment Acknowledgment/Approval Letter

September 12, 2012

Miss Abigail Hum
School of Rehabilitation Therapy
Queen's University

File #: 6007131 REH-529-12 The effects of an 8-week moderate intensity aerobic and strength training exercise program on performance of activities of daily living and social participation in HIV-infected women

Dear Miss Hum

I am writing to acknowledge receipt of the following:

- Request for approval of some amendments to the study:
  - The research coordinator, known to the patients, will call female patients to inform them of the study
  - Addition of one outcome measure – HIV-related Fatigue Scale (HRFS)
  - A copy of the revised proposal (September 4, 2012)

I have reviewed these materials and hereby give my approval. Receipt of these amendments will be reported to the Health Sciences Research Ethics Board.

Yours sincerely,

Albert Clark, Ph.D.
Chair
Research Ethics Board
Amendment Acknowledgment/Approval Letter

October 31, 2012

Miss Abigail Hum
School of Rehabilitation Therapy
Queen's University
Kingston ON K7L 3N6

Re: File #6007131 REH-529-12 The effects of an 8-week moderate intensity aerobic and strength training exercise program on performance of activities of daily living and social participation in HIV-infected women

Dear Miss Hum:

I am writing to acknowledge receipt of the following:

- Revised Letter of Information and Consent

I have reviewed these amendments and hereby give my approval. Receipt of these amendments will be reported to the Health Sciences Research Ethics Board.

Yours sincerely,

Albert Clark, Ph.D.
Chair
Research Ethics Board
Physical function, fatigue, performance of activities of daily living and social participation in women living with HIV: a descriptive study

Investigator: Abigail Hum, MSc Candidate  
Supervisor: Cheryl King-VanVlack, PhD

You are invited to participate in a research study that will investigate the impact of HIV on physical function, fatigue, performance of activities of daily living (ADLs) and social participation in women. Your participation in this study is entirely voluntary, and your decision to participate or not to participate will not affect any present or future medical treatment or health care. If you are a student or staff member at Queen’s University, your decision will not affect your present or future standing at school or work. The information in this form will be reviewed with you. It describes all of the procedures in the study and what is required of you if you agree to participate. After you review this information, you will be asked to sign the consent form and you will be given a copy of this form to take home for your records. Please do not hesitate to ask questions at any time. This study has been reviewed for ethical compliance by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.

Purpose of the study
The purpose of this study is to determine levels of physical function, fatigue, ability to perform ADLs and social participation in women living with HIV in the Kingston area. Social participation can refer to social gatherings or leisure and recreational activities.

Inclusion Criteria
To be included in the study, you must be at least 18 years old and diagnosed by a clinician as HIV-positive.

Exclusion Criteria
You cannot participate in this study if you cannot communicate in English.

Data Collection Procedures
You will be required to either come to the gymnasium in Bethel Church (314 Johnson Street) or Hotel Dieu Hospital to complete 4 questionnaires and a 6-minute walk test. The total time to complete these measures is approximately one hour. You will first be asked to complete a demographics questionnaire, the Medical Outcomes Study HIV Health Survey (MOS-HIV) and
the HIV-Related Fatigue Scale (HRFS). Also, your permission is requested for us to obtain medical information from the hard copy of your patient chart located in the clinic (CD4 count, viral load). The MOS-HIV is a tool which is used to assess different dimensions of health, such as physical and role functioning. The HRFS will be used to measure fatigue intensity and the impact of the fatigue on various aspects of your life (e.g. mental and social functioning, activities of daily living, etc). You will also be asked to complete 3 lists of activities under the following categories: Social Activities, Recreation/Leisure, and Activities of Daily Living. You can list up to 5 items under each category that you consider to be important, ranking #1 as the most important and #5 as the least important. Beside each activity, you will describe how limited you feel you are in performing the activity (e.g. “cannot do it at all”, or “only once in a while”). After you have finished the questionnaires, you will then perform a 6-minute walk test, which is used to assess physical endurance. You will be asked to walk around the perimeter of the gymnasium (or up and down a long corridor at HDH) trying to cover as much distance as possible within the 6 minute time frame. Prior to, immediately upon completion of the test and at 6 minutes of recovery, your blood pressure, heart rate, oxygen saturation and rating of perceived exertion will be measured. This is to determine that your body's responses to the exercise have been appropriate and have returned to resting levels prior to leaving the facility.

**Risks of Participation**
The risks of participating in this study are minimal. Exertion during the 6-minute walk test may cause short-term discomfort such as sore muscles the following day, especially if you are not normally active.

**Benefits of Participation**
By participating in this study, you will be able to contribute to the limited body of knowledge involving fatigue, physical function, performance of ADLs and social participation in women living with HIV.

**Compensation**
Upon completion of the testing session, you will receive $10 as a token of our appreciation for your participation in the study.

**Confidentiality**
Your confidentiality and your anonymity are important and will be protected as much as possible. You will be identified by a code number on all files that contain your data. Forms that identify you by name will be stored separately from the data and will be filed in a cabinet that remains in a secure location with restricted access. Your data will be kept for 5 years after the study is completed; at which time all electronic files will be deleted and any hard copies will be shredded. Only summary data and/or participant code numbers will be used during presentations or publication of the study results.

**Voluntary Nature of the Study**
Your involvement in this study is completely voluntary and you may withdraw at any time without any consequence.
**Liability**
If you experience any health problems during the 6-minute walk test, the investigators will help you to obtain the appropriate medical care. After signing the consent form, you will still retain your legal rights and the investigators will still be upheld to their legal and professional responsibilities.

**Offer to Answer Questions**
If you have any questions, please do not hesitate to contact Abigail Hum, MSc Candidate (information listed below) or Dr. Cheryl King-VanVlack, the Principal Investigator of the study.

If you have any concerns regarding the student’s authorization to perform this study you may contact Dr. Marcia Finlayson, the Director, School of Rehabilitation Therapy & Vice-Dean of the Faculty of Health Sciences at (613) 533-6103.

If you have any concerns regarding the rights of research participants, please contact Dr. Albert Clark, Chair of the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board at (613) 533-6081.
Participant Statement and Signature

As a participant in this study, I have read and understand the letter of information and consent form provided. The purpose and procedures have been explained to me, and I have been given sufficient time to consider the above information and to seek advice if I choose to do so. I have had the opportunity to ask questions which have been answered to my satisfaction. I understand that my participation is completely voluntary and that I can withdraw at any time. I am aware that all data collected will be secured by the investigators and that my data will be used for scientific purposes only. I am voluntarily signing this consent form and will receive a copy of the form to take home for future reference.

By signing this consent form, I am indicating that I agree to participate in this study.

_________________________________________  ____________________
Signature of Participant     Date

_________________________________________  ____________________
Person Obtaining Consent     Date

Investigators:

Abigail Hum            Cheryl King-VanVlack, PhD
MSc Candidate          Faculty Supervisor
School of Rehabilitation Therapy
Phone: 613-770-4635    Phone: 613-533-6341 (office)
Email: 11ah38@queensu.ca         Phone: 613-583-7042 (cell)
Email: kingce@queensu.ca
APPENDIX B

1. Demographics Form

2. MOS-HIV Quality of Life

3. Social, Recreational and Daily Living Activities Form

4. HIV-Related Fatigue Scale (HRFS)

5. Six-Minute Walk Test Data Collection Form
Demographics Questionnaire

Participant Code: _____________    Date:__________________

Year of Birth: __________________________  Age: ________
Ethnicity: _____________________________
Height (cm): ______________
Weight (kg): ________________

In what year were you diagnosed with HIV? __________

Have you ever been on HIV treatment (yes/no)? ___________

If yes:
What year did you start? __________  Medication: ______________
Have you ever interrupted treatment > 3 months (yes/no)? __________

Have you had any of the following medical conditions or issues?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
<th>Duration (years &amp; months)</th>
<th>Medication (if applicable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis C co-infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental health problems</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Addiction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections related to poor immune function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

102
Are you currently working?

If YES (check all that apply):
- full-time
- part-time
- casual
- for the government
- for a company
- self-employed
- other

If NO (check all that apply):
- on disability
- on welfare
- retired
- other: ________________________________________

What is the highest level of education that you graduated from?
- high school
- post-secondary - college
- post-secondary - university
- post-graduate studies (e.g. Master's, PhD, medical doctor, physical therapist, etc.)
- other

To be Completed by the Investigator

<table>
<thead>
<tr>
<th>Immunological Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable</strong></td>
</tr>
<tr>
<td>Most recent CD4</td>
</tr>
<tr>
<td>Nadir CD4</td>
</tr>
<tr>
<td>Most recent VL</td>
</tr>
</tbody>
</table>
MOS-HIV HEALTH SURVEY

INSTRUCTIONS TO THE STUDY COORDINATOR:

The following questionnaire asks the patient about many aspects of his/her health and health care. It should be given to the patient prior to the clinical exam and preferably in a quiet secluded area (e.g., exam room or other office).

It is important to be familiar with the content and format of the questionnaire before giving it to study participants. At the first visit, please begin by telling the participant:

"We would like you to answer some questions about how you are feeling and the kinds of things you are able to do. Your answers will help us understand the effects of the medication you are taking. We appreciate your filling out this questionnaire."

You should then briefly go over the format of the questions and how to complete them. Have the participant complete the questionnaire before vital signs, history and physical are completed.

The questionnaire is very brief and should take no more than 10 minutes to complete. Before giving the patient the questionnaire, please fill out the header(s) and DETACH THIS PAGE.

Each question is in the same general format. Note that the patient is always asked to check one box for each question. All questions refer to the PAST 4 WEEKS.

Collect the completed questionnaire before the clinical exam. Before going on, review the questionnaire for omissions. If the participant missed any of the questions, point this out and have him/her complete the omissions.

PLEASE COMPLETE THE FOLLOWING ITEMS AFTER PATIENT COMPLETES THE QUESTIONNAIRE OR AFTER YOU ASCERTAIN THAT THIS IS NOT POSSIBLE:

1. How was the questionnaire completed? ............. 1 □ Self administered by the study participant
   2 □ Face-to-face interview that you conducted
   3 □ Phone interview
   4 □ Not completed
   5 □ Other

   If Other, specify: ____________________________________________________________

2. If you answered 2 or 4, please indicate the reason(s) why:

   Patient refused initially: .................................................. 1 □ Yes  2 □ No
   Patient's reading level not adequate: .............................................. 1 □ Yes  2 □ No
   There was not enough time: ..................................................... 1 □ Yes  2 □ No
   Patient forgot reading glasses: ................................................... 1 □ Yes  2 □ No
   Other reason: ................................................................. 1 □ Yes  2 □ No

   If Other, specify: ____________________________________________________________
INSTRUCTIONS TO PATIENT: Please answer the following questions by placing a "\(\square\)" in the appropriate box.

1. In general, would you say your health is: (Check One)

   Excellent ................................................................. 1 \(\square\)
   Very Good .............................................................. 2 \(\square\)
   Good ..................................................................... 3 \(\square\)
   Fair ...................................................................... 4 \(\square\)
   Poor ...................................................................... 5 \(\square\)

2. How much bodily pain have you generally had during the past 4 weeks? (Check One)

   None ................................................................. 1 \(\square\)
   Very Mild ............................................................ 2 \(\square\)
   Mild ................................................................. 3 \(\square\)
   Moderate ........................................................... 4 \(\square\)
   Severe ............................................................... 5 \(\square\)
   Very Severe .......................................................... 6 \(\square\)

3. During the past 4 weeks, how much did pain interfere with your normal work (or your normal activities, including work outside the home and housework)? (Check One)

   Not at all ............................................................ 1 \(\square\)
   A little bit ........................................................... 2 \(\square\)
   Moderately ......................................................... 3 \(\square\)
   Quite a bit .......................................................... 4 \(\square\)
   Extremely ........................................................... 5 \(\square\)
4. The following questions are about activities you might do during a typical day. Does your health **now limit you** in these activities? If so, how much?

<table>
<thead>
<tr>
<th></th>
<th>YES, limited a lot</th>
<th>YES, limited a little</th>
<th>NO, not limited</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>The kinds or amounts of <strong>vigorous</strong> activities you can do, like lifting heavy objects, running or participating in strenuous sports.</td>
<td>1 □</td>
<td>2 □</td>
</tr>
<tr>
<td>b.</td>
<td>The kinds or amounts of <strong>moderate</strong> activities you can do, like moving a table, carrying groceries or bowling.</td>
<td>1 □</td>
<td>2 □</td>
</tr>
<tr>
<td>c.</td>
<td>Walking uphill or climbing (a few flights of stairs).</td>
<td>1 □</td>
<td>2 □</td>
</tr>
<tr>
<td>d.</td>
<td>Bending, lifting or stooping.</td>
<td>1 □</td>
<td>2 □</td>
</tr>
<tr>
<td>e.</td>
<td>Walking one block.</td>
<td>1 □</td>
<td>2 □</td>
</tr>
<tr>
<td>f.</td>
<td>Eating, dressing, bathing or using the toilet.</td>
<td>1 □</td>
<td>2 □</td>
</tr>
</tbody>
</table>

5. Does your health keep you from working at a job, doing work around the house or going to school?  
(Check One)

   1 □ Yes
   2 □ No

6. Have you been unable to do **certain kinds or amounts** of work, housework, or schoolwork because of your health?  
(Check One)

   1 □ Yes
   2 □ No
For each of the following questions, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

<table>
<thead>
<tr>
<th></th>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.</td>
<td>How much of the time, during the past 4 weeks, has your <strong>health limited your social activities</strong> (like visiting with friends or close relatives)?</td>
<td>1 ☐</td>
<td>2 ☐</td>
<td>3 ☐</td>
<td>4 ☐</td>
<td>5 ☐</td>
</tr>
<tr>
<td>8.</td>
<td>How much of the time, during the past 4 weeks:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a.</td>
<td>Have you been a <strong>very nervous person?</strong></td>
<td>1 ☐</td>
<td>2 ☐</td>
<td>3 ☐</td>
<td>4 ☐</td>
<td>5 ☐</td>
</tr>
<tr>
<td>b.</td>
<td>Have you felt <strong>calm and peaceful?</strong></td>
<td>1 ☐</td>
<td>2 ☐</td>
<td>3 ☐</td>
<td>4 ☐</td>
<td>5 ☐</td>
</tr>
<tr>
<td>c.</td>
<td>Have you felt <strong>downhearted and blue?</strong></td>
<td>1 ☐</td>
<td>2 ☐</td>
<td>3 ☐</td>
<td>4 ☐</td>
<td>5 ☐</td>
</tr>
<tr>
<td>d.</td>
<td>Have you been a <strong>happy person?</strong></td>
<td>1 ☐</td>
<td>2 ☐</td>
<td>3 ☐</td>
<td>4 ☐</td>
<td>5 ☐</td>
</tr>
<tr>
<td>e.</td>
<td>Have you felt so <strong>down in the dumps that nothing could cheer you up?</strong></td>
<td>1 ☐</td>
<td>2 ☐</td>
<td>3 ☐</td>
<td>4 ☐</td>
<td>5 ☐</td>
</tr>
</tbody>
</table>
For each of the following questions, please check the box for the one answer that comes closest to the way you have been feeling during the past 4 weeks.

<table>
<thead>
<tr>
<th></th>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.</td>
<td>How often during the past four weeks:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a.</td>
<td>Did you feel full of pep?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>b.</td>
<td>Did you feel worn out?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>c.</td>
<td>Did you feel tired?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>d.</td>
<td>Did you have enough energy to do the things you wanted to do?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>e.</td>
<td>Did you feel weighed down by your health problems?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>f.</td>
<td>Were you discouraged by your health problems?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>g.</td>
<td>Did you feel despair over your health problems?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>h.</td>
<td>Were you afraid because of your health?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
10. How much of the time, during the past 4 weeks:

<table>
<thead>
<tr>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Did you have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things?</td>
<td>1 □  2 □  3 □  4 □  5 □  6 □</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Did you forget things that happened recently, for example, where you put things and when you had appointments?</td>
<td>1 □  2 □  3 □  4 □  5 □  6 □</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Did you have trouble keeping your attention on any activity for long?</td>
<td>1 □  2 □  3 □  4 □  5 □  6 □</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Did you have difficulty doing activities involving concentration and thinking?</td>
<td>1 □  2 □  3 □  4 □  5 □  6 □</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

11. Please check the box that best describes whether each of the following statements is true or false for you. (Check one box on each line)

<table>
<thead>
<tr>
<th></th>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Not Sure</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. I am somewhat ill.</td>
<td>1 □</td>
<td>2 □</td>
<td>3 □</td>
<td>4 □</td>
<td>5 □</td>
</tr>
<tr>
<td>b. I am as healthy as anybody I know.</td>
<td>1 □</td>
<td>2 □</td>
<td>3 □</td>
<td>4 □</td>
<td>5 □</td>
</tr>
<tr>
<td>c. My health is excellent.</td>
<td>1 □</td>
<td>2 □</td>
<td>3 □</td>
<td>4 □</td>
<td>5 □</td>
</tr>
<tr>
<td>d. I have been feeling bad lately.</td>
<td>1 □</td>
<td>2 □</td>
<td>3 □</td>
<td>4 □</td>
<td>5 □</td>
</tr>
</tbody>
</table>
12. How has the quality of your life been during the past 4 weeks? That is, how have things been going for you? (Check One)

Very well; could hardly be better ................................................. 1 □
Pretty good .................................................................................. 2 □
Good and bad parts about equal .................................................... 3 □
Pretty bad .................................................................................... 4 □
Very bad; could hardly be worse ................................................... 5 □

13. How would you rate your physical health and emotional condition now compared to 4 weeks ago? (Check One)

Much better .................................................................................. 1 □
A little better ................................................................................ 2 □
About the same .......................................................................... 3 □
A little worse .............................................................................. 4 □
Much worse .............................................................................. 5 □

THANK YOU VERY MUCH
Social, Recreational, Leisure and Daily Living Activities

**SOCIAL - defined as involvement and interaction with other people**
Please list up to 5 social activities (e.g. having dinner with relatives, going to church) that you consider important. Rank them in order where #1 is the most important and #5 is the least important. Beside each activity, write a short description of how able you are to perform the activity (e.g. “cannot do it at all” or “once in awhile”).

<table>
<thead>
<tr>
<th>Activity</th>
<th>Describe how able you are to do this:</th>
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**RECREATION/LEISURE - defined as activities involving cognitive stimulation or physical exercise**
Please list up to 5 recreation/leisure activities (e.g. watching a movie or playing sports) that you consider important. Rank them in order where #1 is the most important and #5 is the least important. Beside each activity, write a short description of how able you are to perform the activity (e.g. “cannot do it at all” or “once in awhile”).

<table>
<thead>
<tr>
<th>Activity</th>
<th>Describe how able you are to do this:</th>
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</table>
**ACTIVITIES OF DAILY LIVING** - *defined as activities necessary for normal self-care*

Please list up to 5 activities of daily living (e.g. going grocery shopping, climbing the stairs, doing laundry) that you consider important. Rank them in order where #1 is the most important and #5 is the least important. Beside each activity, write a short description of how able you are to perform the activity (e.g. “cannot do it at all” or “once in awhile”).

<table>
<thead>
<tr>
<th>Activity</th>
<th>Describe how able you are to do this:</th>
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</table>
HIV-Related Fatigue Scale

These questions are about fatigue and its effects on your life. Please follow the directions for each section.

Please answer the following 2 questions.

1. My level of fatigue **today** is

   1 2 3 4 5 6 7 8 9 10

   No fatigue               Greatest possible fatigue

2. My level of fatigue **most days** is

   1 2 3 4 5 6 7 8 9 10

   No fatigue               Greatest possible fatigue

Now please complete the following items based on how you have been feeling, in general, during the past week.

3. To what degree have you experienced fatigue?

   1 2 3 4 5 6 7 8 9 10

   Not at all               A great deal

4. How severe is the fatigue which you have been experiencing?

   1 2 3 4 5 6 7 8 9 10

   Mild                   Severe

5. To what degree has fatigue caused you distress?

   1 2 3 4 5 6 7 8 9 10

   No distress               A great deal of distress

6. Over the past week, how often have you been fatigued? (**circle one**)

   4 3 2 1

   Every day              Most, but not all days       Occasionally, but not most days     Hardly any days

7. To what degree has your fatigue changed during the past week? (**circle one**)

   4 3 2 1

   Increased              Fatigue has gone up and down   Stayed the same                   Decreased

Participants who circled 1 or 2 to ALL of the above questions should stop HERE. Please return the form to the research assistant.

Participants who circled 3 or higher to ANY of the above questions should complete questions 8-56.

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Circle the number that most closely indicates to what degree fatigue has interfered, in general, with your ability to do the following activities during the past week.

In the past week, to what degree has fatigue interfered with your ability to:

8. Do household chores.

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<tr>
<th>1</th>
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<th>6</th>
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</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>A great deal</td>
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10. Bathe or wash.

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11. Dress.

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<td>Not at all</td>
<td>A great deal</td>
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12. Work.

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<td>Not at all</td>
<td>A great deal</td>
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</table>

13. Visit or socialize with friends or family.

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<td>Not at all</td>
<td>A great deal</td>
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</table>

15. Engage in leisure and recreational activities.

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<td>Not at all</td>
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</table>

16. Shop and do errands.

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<th>8</th>
<th>9</th>
<th>10</th>
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<tbody>
<tr>
<td>Not at all</td>
<td>A great deal</td>
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<tr>
<td>Question</td>
<td>Scale</td>
<td>Rating</td>
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<td>17. Walk.</td>
<td>1</td>
<td>A great deal</td>
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<tr>
<td>18. Exercise, other than walking.</td>
<td>1</td>
<td>A great deal</td>
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<td>19. Control your temper.</td>
<td>1</td>
<td>A great deal</td>
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<tr>
<td>20. Interact with people outside of your own home.</td>
<td>1</td>
<td>A great deal</td>
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<tr>
<td>21. Plan activities ahead of time because your fatigue may interfere</td>
<td>1</td>
<td>A great deal</td>
<td></td>
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<td>22. Think clearly.</td>
<td>1</td>
<td>A great deal</td>
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<td>23. Think quickly.</td>
<td>1</td>
<td>A great deal</td>
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<td>24. Learn new things.</td>
<td>1</td>
<td>A great deal</td>
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</table>
Below are a series of statements regarding your fatigue. Please read each statement and choose a number from 1 to 7, where "1" indicates that you completely disagree with the statement and "7" indicates that you completely agree. Please answer these questions as they apply to how you've been feeling generally during the last week.

<table>
<thead>
<tr>
<th>Statement</th>
<th>Completely Disagree</th>
<th>Completely Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>25. I feel that my HIV medicines cause me to be fatigued.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>26. My fatigue is unpredictable.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>27. My fatigue causes me to eat less than I normally would.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>28. I feel drowsy when I am fatigued.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>29. When I am fatigued, I lose my patience.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>30. My motivation is lower when I am fatigued.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>31. When I am fatigued, I have difficulty concentrating.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>32. Exercise brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>33. Heat brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>34. Long periods of inactivity bring on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>35. Stress brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
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<tr>
<td>36. Depression brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>37. Work brings on my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
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</tr>
<tr>
<td>38. My fatigue is worse in the afternoon.</td>
<td>1 2 3 4 5 6 7</td>
<td></td>
</tr>
<tr>
<td>39. My fatigue is worse in the morning.</td>
<td>1 2 3 4 5 6 7</td>
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<tr>
<td>40. Performance of routine daily activities increase my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
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<tr>
<td>41. Resting lessens my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
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<tr>
<td>42. Sleeping lessens my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
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<tr>
<td>43. Cool temperatures lessen my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
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<tr>
<td>44. Positive experiences lessen my fatigue.</td>
<td>1 2 3 4 5 6 7</td>
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<tr>
<td>Question</td>
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<td>2</td>
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<tr>
<td>45. I am easily fatigued.</td>
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<tr>
<td>46. Fatigue interferes with my physical functioning.</td>
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<td>47. Fatigue causes frequent problems for me.</td>
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<td>48. My fatigue prevents sustained physical functioning.</td>
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<tr>
<td>49. Fatigue interferes with carrying out certain duties and functioning.</td>
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<tr>
<td>50. Fatigue started before other symptoms of HIV.</td>
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<tr>
<td>51. Fatigue is my most disabling symptom.</td>
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<tr>
<td>52. Fatigue is among my 3 most disabling symptoms.</td>
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<tr>
<td>53. Fatigue interferes with my work, family, and social life.</td>
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<td>54. Fatigue makes other symptoms worse.</td>
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<tr>
<td>55. Fatigue that I now experience is different in quality and severity than the fatigue I experienced before I developed HIV.</td>
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<tr>
<td>56. I experience prolonged fatigue after exercise.</td>
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Please note:
Questions 1-2 adapted from Nail (1997); Questions 3-18 adapted from Belza (1990); Questions 19-21 adapted from Fisk, Pontefract, Ritvo, Archibald & Murray (1994); Questions 22-24 adapted from Darko, McCutchan, Kripke, Gillin, & Golshan (1992); Questions 25-27 developed by Barroso (1999); Questions 28-56 adapted from Schwartz, Jandorf, & Krupp (1993)

Rev. 9/9/99
SIX MINUTE WALK TEST

Participant Code: _________________ Date: _________________

DISTANCE WALKED:

1 lap = ______ metres

Distance Walked = ______ laps x ( ______ metres) + ______ metres = ______ metres

CARDIOVASCULAR & EFFORT VARIABLES

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>REST</th>
<th>END 6MWT</th>
<th>RECOVERY (6 min)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure (mmHg)</td>
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<tr>
<td>Heart Rate (bpm)</td>
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<tr>
<td>O₂ Saturation (%)</td>
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<tr>
<td>RPE (6-20)</td>
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