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An examination of health-related quality of life for individuals with HIV-infection.

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An Examination of Health Related Quality of Life

for Individuals with HIV-Infection

by

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ABSTRACT

With the improvements in morbidity and mortality as a result of new antiretroviral treatments, the examination of health related quality of life (HRQOL) has become an important consideration of client care. This study was a 15-month prospective examination of the underlying factor structure, test-retest reliability, and clinical utility of the widely used Medical Outcomes Study-HIV HRQOL instrument (MOS-HIV). Factor analysis of the MOS-HIV Physical Function, Role Function, Pain, Social Function, Overall Health, Fatigue, Cognitive Function, Health Distress, Quality of Life, and Mental Health dimensions resulted in mental health (MHS) and physical health (PHS) summary factors. Analysis of the individual MOS-HIV items generally revealed Physical Function, Overall Health, Cognitive Function, Health Distress, Mental Health, and Functional Status factors. MOS-HIV dimensions and factors typically had moderate to good test-retest reliability. Poor reliability coefficients generally occurred for dimensions that were only composed of 1 or 2 items. Multiple regression analyses were conducted to determine the impact of demographic, medical, depression, and neuropsychological variables on various HRQOL domains. Depression and medical symptom scores were the strongest predictors of HRQOL, with depression more highly related to mental health domains and medical symptoms more highly related to physical health domains. Neuropsychological variables, specifically psychomotor efficiency, were more likely to be related to physical function. Demographic and HIV status variables had less of an impact on HRQOL than depression and medical symptoms. The results of this analysis support the use of MHS and PHS scores and MOS-HIV item factors to convey HRQOL information. In addition, the results indicate that treatment of depressive and medical symptoms could result in a significant improvement in HRQOL.

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LIST OF ABBREVIATIONS

AANATF	= American Academy of Neurology AIDS Task Force
AIDS	= Acquired Immunodeficiency Syndrome
BDI	= Beck Depression Inventory
BDI-Affective	= Beck Depression Inventory - Affective component (items 1-13)
BDI-Somatic	= Beck Depression Inventory - Somatic component (items 14-21)
CD4	= Lymphocyte cells involved in orchestrating the immune response
CVLT	= California Verbal Learning Test
MHS	= MOS-HIV Mental Health Summary Factor
HIV	= Human Immunodeficiency Virus
HRQOL	= Health related quality of life
MOS	= Medical Outcomes Study HRQOL Instrument
MOS-HIV	= Medical Outcomes Study - HIV HRQOL Instrument
MRI	= Magnetic Resonance Imaging
PHS	= MOS-HIV Physical Health Summary Factor
RNA	= Ribonucleic acid, a nucleic acid important for protein synthesis
QOL	= Quality of Life

INTRODUCTION

It is estimated that approximately 34 million adults worldwide are living with Human Immunodeficiency Virus (HIV) infection, and these numbers continue to increase (Victor & Ropper, 2000). HIV is a retrovirus that produces a failure in immune functioning. As a result, a wide range of opportunistic infections and unusual neoplasms may develop in individuals that can affect virtually all body systems, including the central nervous system. HIV is associated with varying degrees of neurological, psychological, and systemic complications, which alone or in combination can lead to significant decrements in health-related quality of life and everyday functional limitations. With new developments in antiretroviral therapies, there has been a dramatic reduction in the incidence of systemic complications and mortality (Bouwman, Skolasky, Hes, Selnes, Glass, Nance-Sproson, Royal, et al., 1998). These changes in morbidity and mortality have led to a paradigm shift in the clinical management of HIV-infection from that of a terminal disease to a chronic and generally tolerable illness. As such, the enhancement of health-related quality of life (HRQOL) for those with HIV-infection has become an important consideration (Freidland, Renwick, & McColl, 1996).

This paper will address determinants of HRQOL of individuals with HIV-infection. First, a brief introduction to the pathophysiology of HIV will be outlined. This will be followed by a description of clinical features of HIV, including medical symptoms, neurocognitive deficits, and depression, and the relationships of these factors to each other and HRQOL. Next, issues related to HRQOL measurement will be presented. Finally, commonly used HIV HRQOL measures will be described in terms of their research findings. For the purposes of this paper, the term HIV-infection will be used to describe individuals with asymptomatic HIV, symptomatic HIV, and Acquired Immunodeficiency Syndrome (AIDS).

PATHOPHYSIOLOGY OF HIV-INFECTION

HIV is characterized by a gradual decline of the immune system, primarily through damage of the CD4 lymphocyte cells (Bellenir, 1999; Libman, 1992; Wiley, 1994). These are immune system cells that protect the body from viral, fungal, and protozoal infections. After exposure, the HIV virus replicates and spreads rapidly through the body, reducing CD4 cells by 20 to 40 percent. During the second to fourth week post-infection, the majority of infected individuals will experience flu-like symptoms, including fatigue, malaise, fever, aches and pains, and occasionally headaches, photophobia, and stiff neck. Production of CD4 cells is accelerated, increasing cell counts to 80 to 90 percent of original levels. During this asymptomatic stage, which lasts five to eight years, individuals rarely experience symptoms. However, CD4 levels gradually decline, and once they fall below 200/cubic milliliters (1/4 to 1/6 original levels), opportunistic infections, cancers, and/or neurological illnesses may develop. The symptomatic stage is comprised of relatively benign systemic manifestations (e.g., diarrhea, malaise, weight loss). With disease progression, individuals may develop opportunistic infections or AIDS-defining conditions, such as cryptoccocus, cytomegalovirus, Kaposi's sarcoma, lymphoma, HIV-related dementia, toxoplasmosis, and progressive multifocal leukoencephalopathy (Victor & Ropper, 2000).

In adults, the rate of progression from initial infection with HIV to AIDS is estimated to be an average of 10 years (Janssen, 1997; Ward & Drotman, 1998). It is widely believed that disease progression is associated with numerous factors, including age at infection, genetic variables, virulence and strain of virus, and co-infections (Bellenir, 1999; Janssen, 1997). Progression of HIV is also affected by the use of new potent antiretroviral therapies, which significantly reduce viral replication both within and outside of the central nervous system (Swindalls, Zheng, & Gendelman, 1999).

HIV does not appear to directly infect neurons (Epstein, Gendelman, & Lipton, 1997). Instead, HIV in the brain tends to be localized in mononuclear, glial,

and endothelial cells (Grant, 1990). The mechanism of brain damage by HIV remains obscure. It is believed that HIV-infection results in the chronic activation of mononuclear phagocytes (macrophages and microglia) and the production of excitotoxins, which damage neurons and supporting cells (Bouwman, et al., 1998; Epstein et al., 1997; Libman, 1992; Swindells et al., 1999).

HIV produces brain atrophy, white matter and basal ganglia lesions, and abnormal metabolism, which can be observed with neuroimaging (Ammassari, Cingolani, Pezzotti, Bouwman et al., 1998; Chang, Ernst, Leonido-Yee, Walot, & Singer, 1999; De Luca, Murri, et al., 2000; Hinkin, van Gorp, Mandelkern, Gee, Satz, Holston, et al., 1995; Navia & Price, 1998; Paul, Cohen, Navia, & Tashima, 2002; Swindells et al., 1999; van Gorp, Mandelkern, Gee, Hinkin, Stern, Paz, et al., 1992). White matter volume loss can even been observed in asymptomatic HIV-positive individuals (Jernigan, Archibald, Hesselink, Atkinson, Velin, McCutchan, et al., 1993). HIV predominantly occurs in the subcortical regions of the brain, although the neocortical regions may also be affected (Weis, Haug, & Budka, 1993; Wiley, 1994). In one study, metabolic abnormalities indicating increased glial proliferation were observed to occur in the frontal white matter region in early stages of symptomatic HIV-infection, suggesting this brain area may be affected by HIV-infection first (Chang et al., 1999). With the development of AIDS dementia, neuronal loss and greater abnormalities in glial activity are observed in the frontal white matter, basal ganglia, and to a lesser extent, frontal gray matter. Increased permeability of the blood brain barrier has also been noted in HIV-infection (Berger, Nath, Greenberg, Anderson, Greene, Bognar, et al., 2000; Sotrel & LaGuardia, 1998). Overall, neuroimaging abnormalities are observed in approximately 50 percent of individuals with symptomatic HIV (but not AIDS) and 75 percent of those with AIDS (Grant, Atkinson, Hesselink, Kennedy, Richman, Spector, et al., 1987, 1988; Wiley, 1994).

Neuropathological changes that occur with HIV-infection include myelin pallor, microglial nodules, necrotic foci, foci of demyelination, and collections of

multinucleated giant cells (Glass, Wesselingh, Selnes, & McArthur, 1993; Grant, 1990; Navia & Price, 1998; Sharer, Saito, & Blumberg, 1997; Swindells et al., 1999). Dendritic and synaptic damage may also occur (Wiley, Masliah, Morey, Lemere, DeTeresa, Grafe, et al., 1991), even for those with mild HIV-related cognitive disorders (Everall, Heaton, Marcotte, Ellis, McCutchan, Atkinson, et al., 1999). Although some relationships between pathology and clinical presentation have been noted (e.g., between neuropathological changes and severity of dementia, Glass et al., 1993; or between neuronal loss and the extent of neurological deficits, McConnell, Swindells, Ong, Gmeiner, Chu, Brown, et al., 1994), associations do not always occur (Bouwman et al., 1998; Dooneief, Bello, Todak, Mun, Marder, Malouf, et al., 1992).

Cerebral spinal fluid may have nonspecific abnormalities, with slight elevations in protein or a mild pleocytosis (Ellis, Hsia, Spector, Nelson, Heaton, Wallace, et al., 1997a; Sotrel & LaGuardia, 1998; Swindells et al., 1999; Victor & Ropper, 2000). Levels of immunosuppression (i.e., CD4 counts) were not related to CSF RNA levels (Ellis et al., 1997a). Higher cerebral spinal fluid, but not plasma, levels of HIV RNA were associated with a greater severity of dementia (McArthur, McClernon, Cronin, Nance-Sproson, Saah, St Clair, et al., 1997). However, in another study, the relationship between cerebral spinal fluid RNA and neurocognitive functioning only held for individuals with CD4 counts less than 200 (Ellis et al., 1997a). For those with CD4 counts above 200, there were no associations with cognition function.

CLINICAL PRESENTATION OF HIV-INFECTION

With the progression of HIV-infection, medical symptomology, mood disturbances, and neurocognitive impairments become more common, especially during the latter stages of the illness (Grant & Atkinson, 1990). Neurobehavioural complications occur in 30-50 percent of those with HIV-infection, ranging from subtle deficits with little impact on daily life to a severe and debilitating dementia

(Heaton, Grant, Butters, White, Kirson, Atkinson, et al., 1995; Marcotte, Grant, Atkinson, & Heaton, 2001). The clinical presentation of individuals with HIV-infection may reflect brain dysfunction or attempts to cope with the infection of a fatal disease and its resulting complications (Grant & Atkinson, 1990).

Neurological and Medical Symptoms

The average number of symptoms is approximately 10 for individuals with asymptomatic HIV and 17 for individuals with symptomatic HIV and AIDS (Revicki, Wu, & Murray, 1995). Neurological signs and symptoms increase with disease progression (Marder, Liu, Stern, Dooneief, Bell, Schofield, et al., 1995) and are more common when CD4 counts are low (Marder et al., 1995). The most commonly occurring symptoms were fever, adenopathy, pharyngitis, rash, and myalgia or arthralgia (Brew & Tindall, 1997). Symptoms are strong predictors of physical functioning (Wilson & Cleary, 1996), overall quality of life (Justice, Rabeneck, Hays, Wu, & Bozzette, 1999; Revicki, Sorensen, Wu, 1998; Revicki, et al., 1995; Wachtel, Piette, Mor, Stein, Fleishman, & Carpenter, 1992), and non-adherence of medication (Holzemer, Corless, Nokes, Turner, Brown, Powell-Cope et al., 1999). Individuals with symptomatic HIV were less likely to be employed (employment rate was 74 percent for asymptomatic HIV versus 26 percent for AIDS) and more likely to have lower income levels (Ganz, Schag, Kahn, Petersen, & Hirji, 1993), no health insurance, and greater financial concerns than those with asymptomatic HIV (Kass, Munoz, Chen, Zucconi, Bing, Hennessy, et al., 1994). In addition, individuals with AIDS-defining symptoms have poorer HRQOL (Lenderking, Testa, Katzenstein, & Hammer, 1997), a higher dependance on others for activities of daily living, and a greater risk of mortality (Stanton, Wu, Moore, Rucker, Piazza, Abrams, et al., 1994). HRQOL variables are associated with specific HIV/AIDS-related symptoms. Wasting, the involuntary loss of 10 percent or more of premorbid body weight, is related to mortality, morbidity, impaired HRQOL, and decreased ability to perform activities of daily living (Roubenoff, 2000; Testa & Lenderking, 1999). Pain is linked

to depressive symptomology and poorer HRQOL (Rosenfeld, Breitbart, McDonald, Passik, Thaler, & Portenoy, 1996).

Mood Disturbances

Affective disturbances are more common among adults with HIV-infection than in the general population (Atkinson & Grant, 1997; Ciesla & Roberts, 2001; Dew, Becker, Sanchez, Caldararo, Lopez, Wess, et al., 1997; Perkins, Stern, Golden, Murphy, Naftolowitz, & Evans, 1994). A recent meta-analysis revealed that prevalence rates for a diagnosis of major depression were 9.4 percent for individuals with HIV infection and 5.2 percent for those without HIV-infection (Ciesla & Roberts, 2001). As such, individuals with HIV-infection were approximately twice as likely to have depression than HIV-negative individuals. Similar rates of major depression have been found in other chronic medical illnesses (e.g., stroke, Multiple Sclerosis, Huntington's Disease; Atkinson & Grant, 1997; Marcotte et al., 2001). The presence of a dysthymic disorder was also approximately twice as high for individuals with HIV-infection than those without HIV-infection (4.2 percent and 2.0 percent, respectively), although statistical analysis of this difference produced mixed results (i.e., significant differences using one methodology but non-significant differences using two other methodologies; Ciesla & Roberts, 2001).

Mood disorders may result from the direct or indirect involvement of the central nervous system, a breakdown in coping capacities due to an HIV-related experience, and/or premorbid tendencies that emerge during HIV-infection but are not necessarily associated with HIV either directly or indirectly (Fishman, Lyketsos, Schwartz, & Treisman, 1998). Although more frequent episodes can occur, most individuals with HIV-infection experience widely spaced, mild to moderate episodes of depression. Remission typically occurs spontaneously or with treatment (Marcotte et al., 2001).

It appears that the risk of depression is generally equivalent across HIV-infection stages (Ciesla & Roberts, 2001; Rabkin, Goetz, Remien, Williams, Todak,

& Gorman, 1997); however, some researchers have found an increase in depressive symptoms with the development of AIDS (i.e., up to 18 months prior to AIDS diagnosis; Lyketsos, Hoover, Guccione, Senterfitt, Dew, Wesch, et al., 1993). There are mixed results concerning the relationship of depression to the progression to AIDS (Burack, Barrett, Stall, Chesney, Ekstrand, & Coates, 1993; Leserman, Jackson, Petito, Golden, Silva, Perkins, et al., 1999) or death (Burack et al., 1993; Lyketsos, et al., 1993; Ickovics, Hamburger, Vlahov, Schoenbaum, Schuman, Boland, et al., 2001; Rabkin et al., 1997). Depressive symptoms are associated with medical symptoms (Drebing, van Gorp, Hinkin, Miller, Satz, Kim, Holston, & D'Elia, 1994; Rabkin, Ferrando, Jacobsberg, & Fishman, 1997), physical limitations (Griffen, Rabkin, Remien, & Williams, 1998), perceived (but not actual) neurocognitive deficits (Moore, van Gorp, Hinkin, Stern, Swales, & Satz, 1997; Rourke, Halman, Bassel, 1999a; 1999b), poorer quality of life (Griffen et al., 1998; Kaplan, Anderson, Patterson, McCutchan, Weinrich, Heaton, et al., 1995; Kemppainen, 2001; Osowiecki, Cohen, Morrow, Paul, Carpenter, Flanigan, et al., 2000), nonadherence to medication (i.e., not following provider advice and missing appointments; Holzemer et al., 1999), and unemployment (Lyketsos, Hoover, Guccione, Dew, Wesch, Bing, et al., 1996). Level of stress (Folkman, Chesney, Pollack, & Coates, 1993; Patterson, Semple, Temoshok, Atkinson, McCutchan, Straits-Troster, et al., 1993), ineffectual coping strategies (Fleishman & Fogel, 1994; Patterson et al., 1993), lack of satisfaction with social support (Hays, Turner, & Coates, 1992), limited social support (Gielen, McDonnell, Wu, O'Campo, & Faden, 2001; Kelly, Murphy, Bahr, Koob, Morgan, Kalichman, et al., 1993; Lyketsos et al., 1996), and an external locus of control (Kelly et al., 1993) are also related to depression. Depression is not typically correlated with CD4 lymphocyte counts (Marcotte et al., 2001).

Neuropsychological Impairment

The risk of neuropsychological impairment generally increases with each

successive stage of HIV-infection (Center for Disease Control, 1992; Heaton et al., 1995; Slenes, Galai, McArthur, Cohn, Royal, Esposito, et al., 1997). Recent reviews of the literature suggest that 35 percent of asymptomatic, 44 percent of mildly symptomatic, and 55 percent of adults with AIDS exhibit neurocognitive impairments, particularly in the areas of complex attention, speed of information processing, learning efficiency, and psychomotor skills (Heaton et al., 1995; White, Heaton, Monsch, & HNRC Group, 1995). Frequently, neuropsychological impairments are mild and may not be observed through routine examination (Velin, Heaton, Grant, & HNRC Group, 1994). Therefore, extensive neuropsychological testing is required for detection of these deficits (Butters, Grant, Haxby, Judd, Martin, McClelland, et al., 1990; Grant, 1990; Marcotte et al., 2001; Heaton et al., 1995; White et al., 1995). Based on the severity of their neuropsychological impairment, individuals can be classified as having HIV-associated minor cognitive/motor disorder or HIV-associated dementia.

The majority of HIV-infected individuals who develop HIV-related neuropsychological impairments exhibit a mild neurocognitive disorder termed HIV-associated minor cognitive/motor disorder (Marcotte et al., 2001; American Academy of Neurology AIDS Task Force or AANATF, 1991). Diagnosis of minor cognitive/motor disorder requires deficits in two or more domains of function which produce at least a mild disruption in more demanding everyday tasks and activities. Typically, impairments in concentration and attention, psychomotor speed, and learning and recall are observed, although deficits in problem solving, abstract reasoning, and/or verbal fluency may also occur (Marcotte et al., 2001). Neuropsychological profiles are generally consistent with a subcortical pathology (Heaton et al., 1995; Law & Mapou, 1997). Approximately 5 percent of individuals with asymptomatic HIV-infection meet the minor cognitive/motor disorder criteria, which increases to 25 percent for individuals with symptomatic HIV (with or without AIDS-defining conditions; McArther & Grant, 1998). Imaging scans for individuals with minor cognitive/motor disorder are typically normal (AANATF, 1991).

HIV-associated cognitive/motor complex or HIV-associated dementia (AANATF, 1991) is defined by more significant cognitive impairments which markedly disrupt functional ability. Neuropsychological evaluation typically reveals moderate to severe deficits in learning and recall, psychomotor speed, fluency, and executive functioning (Back, Miller, & Cummings, 1998; Fishman et al., 1998; Grant, 1990; Marcotte et al., 2001). Affective lability, irritability, withdrawal, apathy, or inappropriate behaviours may also occur. With disease progression, ataxia, weakness, and incoordination may become prominent (Grant, 1990). HIV-associated dementia occurs primarily in those with advanced HIV-infection, affecting approximately 0.8 percent of individuals with asymptomatic HIV, 2.6 percent of individuals with mildly symptomatic HIV, and 7.0 percent of individuals with AIDS (McArther & Grant, 1998). Neuroimaging of individuals with HIV-associated dementia frequently reveals cerebral atrophy and nonspecific white matter changes (AANATF, 1991; Sharer et al., 1997). Physiological indicators of HIV-infection (CD4 counts, viral load) are predictive of HIV-associated dementia (Childs, Lyles, Selnes, Chen, Miller, Cohen, et al., 1999).

HIV-associated neuropsychological deficits are associated with increased rates of unemployment (Benedict, Mezhir, Walsh, & Hewitt, 2000; Heaton, Marcotte, White, Ross, Meredith, Taylor, et al., 1996; Heaton, Velin, McCutchan, Gulevich, Atkinson, Wallace, et al., 1994; Van Gorp, Baerwald, Ferrando, McElhiney, & Rabkin, 1999; Velin et al., 1994), and for those that are employed, reductions in their ability to fulfill job demands (Albert, Marder, Dooneief, Bell, Sano, Todak, et al., 1995; Heaton et al., 1994; Heaton et al., 1996; Velin et al., 1994). Neuropsychological impairments are also associated with poorer social planning and medical management (Benedict et al., 2000), impaired performance on driving simulations (Marcotte, Heaton, Wolfson, Taylor, Alhassoon, Arfaa, et al., 1999), poorer physical functioning (Dana Consortium on Therapy for HIV Dementia and Related Cognitive Disorders, 1996; Schifitto, Kieburtz, McDermott, McArthur, Marder, Sacktor, et al., 2001), decreases in HRQOL (Kaplan et al., 1995; Trepanier,

Krzyzanowski, Bayoumi, & Rourke, 2001) particularly physical functioning (Osowiecki et al., 2000; Rourke, Trepanier, & Bayoumi, 2001), and an increased risk of mortality (Ellis, Deutsch, Heaton, Marcotte, McCutchan, Nelson, et al., 1997b; Sacktor, Bacellar, Hoover, Nance-Spronson, Selnes, Miller, et al., 1996; Mayeux, Stern, Tang, Todak, Marder, Sano, et al., 1993).

MEASUREMENT OF HEALTH-RELATED QUALITY OF LIFE

Traditionally, the medical perspective has viewed cure and survival as primarily goals of treatment. However, the use of morbidity or physiological indicators as outcome measures may not adequately reflect the effectiveness of treatments that prolong life without providing a cure (Murdaugh, 1998). Medications or other medical interventions that prolong life may negatively impact HRQOL, through side-effects, frequent or lengthy hospitalizations, and/or intrusive and painful procedures. These negative aspects of treatment are unlikely to be detected by biomedical indices. The use of a standardized, psychometrically sound HRQOL instrument provides a more sensitive outcome measure. As a result, clinicians are able to better understand the impact of HIV-infection and its treatments on health status and daily functioning.

Definition of HRQOL

Quality of life (QOL) is a vague, multidimensional concept that is difficult to define, despite general agreement of its basic components (Shumaker, Ellis, & Naughton, 1997). Definitions of QOL vary in comprehensiveness, specificity, and theoretical relevance (McSweeny & Creer, 1995), and are often based on the goals of the investigator and the instruments selected for use. The perspective through which QOL is described can include individuals with HIV, caregivers, health care providers, and society at large. These groups are likely have different opinions of what constitutes a "good" versus "harmful" outcome, how desired goals should be reached, and how outcomes should be measured, further complicating QOL

research (McSweeny, 1990; McSweeny & Creer, 1995). In spite of the variations in definition and perspective, it is generally accepted that QOL is a "multidimensional construct with physical, psychological, and social core dimensions" (p. 603; Berzon, Leplege, Lohr, Lenderking, & Wu, 1997).

Health is an important contributing factor to overall QOL, and medical research typically views QOL in terms of health-related QOL (HRQOL; Berzon et al., 1997). HRQOL can be defined as "people's subjective evaluations of the influences of their current health status, health care, and health promoting activities on their ability to achieve and maintain a level of overall functioning that allows them to pursue valued life goals and that is reflected in their general well-being" (p. 476; Shumaker et al., 1997). Social, physical, emotional, and cognitive function, mobility, and self care are all believed to be important domains of HRQOL.

Issues in HRQOL Measurement

HRQOL measurement is used in various types of research. As such, different measurement tools are preferred for different types of research questions (e.g., clinical intervention trials, cost-analyses, descriptive analyses). Selection of HRQOL instruments is dependant on the nature of the research, objectives of study, and needs of the audience (Berzon et al., 1997). Some of the major differences in HRQOL measurement will be briefly discussed below.

Measurement of HRQOL in HIV can be conducted using either generic or HIV-specific instruments (Berzon et al., 1997; Franchi & Wenzel, 1998; McSweeny & Creer, 1995). The generic approach provides a comprehensive and general overview of HRQOL. It can be used to compare a variety of populations, including those with different diagnoses. Examples of these measures include the Sickness Impact Profile, Quality of Well Being Scale, and Medical Outcome Study instruments. The second approach to measurement involves measures that examine HRQOL for a specific disease or condition, in this case, HIV-infection. Specific measures are more sensitive than generic measures for detecting clinically

significant changes or responsiveness to interventions. Examples of HIV-targeted HRQOL measures include the Fanning Quality of Life Scales, HIV-Overview of Problem Situations Evaluation System, and MOS-HIV. These measures will be discussed in greater detail later.

The scope of HRQOL instruments range from a global assessment of functioning to a focus on only one aspect, such as mortality (Palombi, Mancinelli, Liotta, Narciso, & Marazzi, 1997), employment (Albert et al., 1995; Heaton et al., 1994; Heaton et al., 1996; Kaplan et al., 1995; Kaplan, Patterson, Kerner, Atkinson, Heaton, et al., 1997), driving behaviour (Marcotte et al., 1999), medication adherence (Holzemer et al., 1999), or social support (Friedland et al., 1996; Koopman, Gore-Felton, Marouf, Butler, Field, Gill, et al., 2000). In general, HRQOL measurement in HIV includes both universal dimensions of HRQOL as well as aspects of HRQOL that are specific to HIV-infection (Shumaker et al., 1997). As such, most HRQOL instruments used in HIV research include physical, psychological, and social function, and perceived health dimensions. In addition, test items usually examine general and HIV-specific symptoms, and/or possible side effects of medications for drug trials (Berzon et al., 1997). Other important domains of HRQOL functioning that may be assessed include sexual function and sexual satisfaction, mastery or control over life and illness, concerns related to disclosure and possible discrimination, financial issues, general health perception, cognitive function, energy/vitality, and ability to perform instrumental activities of daily living.

HRQOL instruments may summarize information into multiple dimensions that reflect the complexity of functioning for each individual or a single summary score (McSweeney, 1990). For instruments that provide multiple dimension scores, data can be further reduced in one of two ways. The first method uses factor and profile analysis to reduce variables into a smaller number of domains of functioning (Kaplan et al., 1997). Alternately, information may be compiled into a single composite score, such as a "well-year"or quality adjusted life year (Kaplan & Bush, 1982). Quality adjusted life years are equivalent to the number of years free of

health-related problems, which adjusts for an individual's current illness-related degree of impairment and the duration of time spent in that impaired state. Through use of quality adjusted life years, health care providers can determine the cost-effectiveness of treatments and/or degree of disease progression (e.g., Holtgrave & Pinkerton, 1997).

Information obtained from HRQOL assessments can be used in various ways (Tsevat, Weeks, Guadagnoli, Tosteson, Mangione, Pliskin, et al., 1994). In a clinical setting, treatments with similar effects on survival may need to be balanced against potential changes in HRQOL. Clinicians can use patient's health values to choose the best treatment options for each individual patient. For example, some patients may tolerate weight loss but not fatigue or visa versa. HRQOL assessment also enables the evaluation of clinical trials, by allowing comparison of the costs and benefits of different treatments or interventions. Information obtained from HRQOL assessments can be used for resource allocation decisions, by determining the relative cost-utility of different clinical interventions and health care programs (Hays, Sterwart, Sherbourne, & Marshall, 1993; Holtgrave & Pinkerton, 1997; Hornberger, Redelmeier, & Petersen, 1992; Testa & Lenderking, 1992). This would provide some basis for the development of policies and the selection of programs for funding when limited resources are available. Finally, HRQOL research can aid social and medical service planning for individuals with HIV-infection by identifying and directing attention towards specific areas of quality of life that are in need of intervention (Wu & Rubin, 1992).

Requirements of Good HRQOL Measures: Psychometric Properties

In order to produce meaningful information, HRQOL instruments must have sound psychometric properties, namely reliability and validity (Franchi & Wenzel, 1998). Reliability is the ability of a measure to report consistent and accurate information (de Boer, van Dam, & Sprangers, 1995; Franchi & Wenzel, 1998; McSweeny & Creer, 1995). It can be obtained by measuring the stability of test

scores over time (test-retest reliability), determining whether instrument items measure the same dimension/construct (internal consistency), examining if two or more judges would obtain similar results (interrater reliability), and comparing the similarity of two alternate forms of the instrument, if applicable (alternate form reliability). Validity scores indicate whether the instrument measures what it is purported to measure. Instruments should appear to be sound and cover the intended aspects of HRQOL (face validity), adequately sample desired domains of functioning (content validity), measure behaviours that consumers of information deem important (social validity), fit within a theoretical structure comprised of other psychological constructs (construct validity), have a strong relationship with similar measures (convergent validity) and a weaker or lack of relationship with dissimilar measures (divergent validity), and be sensitive to changes including treatment effects (responsiveness) which can be related to significant changes in health status (interpretability).

HRQOL instruments must also have norms based on a large, representative sample, specific diagnostic groups, or both (McSweeny & Creer, 1995). Norms that are broken down by age, sex, education, stage of HIV-infection, or other categories of interest may be useful. HRQOL instruments should produce a considerable range of scores, to prevent ceiling effects in early infection and floor effects during the latter stages of infection (Berzon et al., 1997; Shumaker et al., 1997). Finally, HRQOL measures must be applicable to diverse populations both within and across national boundaries (Shumaker et al., 1997).

Interpretation of HRQOL Research Findings

Care must be taken in the interpretation of HRQOL research, due to variations in HRQOL definitions, instrument selection, subject inclusion/exclusion criteria, use of control groups, sample sizes, and demographic characteristics of samples (Heaton et al., 1996). HIV-infection occurs in a sociodemographically diverse group (O'Keefe & Wood, 1996); however, most research has focused on

primarily Caucasian, highly educated, gay and bisexual, early to middle aged adult males. Research findings from this select group may not generalize to other HIV groups such as children, women, minorities, and intravenous drug users. For example, HIV-infected women have significantly poorer positive well-being than their male counterparts, even with less advanced disease (Cederfjall, Langius-Eklof, Lidman, & Wredling, 2001). Generalizability of HRQOL research is also limited as HRQOL instruments were primarily developed for English-speaking Western populations (O'Keefe & Wood, 1996). The use of these measures in other areas of the world may be confounded by cultural variations in concepts of health and inaccuracies of translation. Therefore, the research findings presented in this paper may not be applicable to all groups of individuals with HIV-infection.

GENERIC HRQOL MEASURES

Several instruments have been designed to measure HRQOL in individuals with various medical conditions. A brief review of the most common measures will follow. These measures are also compared in Table 1.

Karnofsky Performance Status Index

The Karnofsky Performance Status measure (Karnofsky & Borchenal, 1949) is a widely used physician-rated functional scale (Schag, Ganz, Kahn, & Petersen, 1992). Individuals are ranked on a scale from 0 (death) to 100 (no impairment) at 10 point intervals based on their clinical presentation and an interview (O'Dell, Lubeck, O'Driscoll, & Matsuno, 1995). The Karnofsky Performance Status measure was able to differentiate between HIV-infected and uninfected groups (Wenzel, Pindur, Morsdorf, & Giacchi, 1998) and stage of disease severity (O'Dell et al., 1995). Karnofsky Performance Status scores are related to CD4 counts (Kaplan et al., 1995; Murri, Scoppettuolo, Damiano, Ammassari, Fantoni, & Antinori, 1996), number of symptoms (Murri et al., 1996; O'Dell et al., 1995; Vogl, Rosenfeld, Breitbart, Thaler, Passik, McDonald, et al., 1999), symptom distress (Vogl et al.,

Table 1. Comparison of Generic HRQOL Measures

HRQOL Measure	Description of Measures	Psychometric Properties	Sensitivity to HIV Stage	Relationship with Clinical Variables	Relationship with HRQOL Measures
Karnofsky Performance Scale [a]	-single score of physical function	-ceiling effects -lack of interrater reliability information	-sensitive to HIV stage -mixed evidence for treatment sensitivity	-related to CD4 counts, medical symptoms, symptom distress, mood, & work variables	-stronger relationship with physical than psychosocial aspects of HRQOL
Quality of Well-Being Scale [b]	-10-20 minutes long -mobility, social, physical, symptom scales -combines morbidity, mortality data, & duration of impaired state to get quality adjusted life years	-adequate test-retest reliability and discriminant and convergent validity	-differentiates between HIV stages	-related to CD4 count, mood symptoms, neurological & NP dysfunction, MRI abnormalities, & work status -predicts mortality	-stronger associations with physical than psychological functioning
Sickness Impact Profile [c]	-15-20 minutes long -has 12 content areas emphasizing physical dysfunction -total score & physical & psychosocial summary scores also available	-adequate test-retest reliability & internal consistency -scores have non-normal distributions -items negatively worded & may cause response bias	-unable to differentiate between AIDS-related complex and AIDS -lack of research on the stability and sensitivity to clinical changes	-related to ratings of dysfunction, sickness, & ability to perform activities of daily living	-correlated with other comprehensive HRQOL measures -poorly correlated with time trade-off, standard gamble, & categorical scaling rank
Medical Outcomes Study Measures [d]	-time dependant on version -dimensions typically include: general health, pain, fatigue, & emotional, social, physical, cognitive & role function -physical and mental health summary factors -in 30+ languages	-internal consistency, good, lower reliability of single item scales -discriminant & convergent validity of dimensions -ceiling and/or floor effects for physical, role, emotional, & social function, & pain	-sensitive to HIV stage, disease progression, and treatment effects	-related to demographic, work, iv drug use, mood, medical symptoms, & social support variables -physical health related to in-patient admissions & visits to emergency -mixed findings for relationship with CD4 counts	-significant associations with other measures of HRQOL

HRQOL=health-related quality of life; iv=intravenous

[a] Franchi & Wenzel, 1998; Ganz et al., 1993; Kaplan et al., 1995; Murri et al., 1996; Neto & Siciliano, 2000;O'Dell et al., 1995; Schag, et al., 1992; Vanhems et al., 1996; Vogl et al., 1999 Wenzel et al., 1998; Wu et al., 1990; Wu & Rubin, 1992; Zinkernagel et al., 1999

[b] Kaplan et al., 1994; 1995; 1997;McSweeny, 1990; Revicki & Kaplan, 1993; Vanhems et al., 1996

[c] Bergner et al., 1976b; 1981;1992; Pollard et al., 1976; Ragsdale & Morrow, 1990; Tsasis, 2000;

[d] Arpinelli et al., 1996; Bastardo & Kimberlin, 2000; Bing et al., 2000; Bozzette et al., 1995a; Burgoyne & Saunders, 2001;Call et al., 2000; Cunningham et al., 1998; Delate & Coons, 2000; Fleishman et al., 1994; Hays et al., 2000; Holmes et al., 1996; Huba et al., 2000; Low-Beer et al., 2000; Piette et al., 1995; Sherbourne et al., 2000; Smith et al., 1996; Sousa et al., 1999; Stewart et al., 1989; Tsevat et al., 1996; Wachtel et al., 1992; Wu et al., 1997a

1999), mood (Kaplan et al., 1995), and employment parameters (e.g., days missed from work; O'Dell et al., 1995). Relationships between the Karnofsky Performance Status scores and more comprehensive measures of HRQOL reveal stronger correlations with physical than psychosocial scales (Ganz et al., 1993; Kaplan et al., 1995; Murri et al., 1996; O'Dell et al., 1995; Schag, et al., 1992). There is mixed evidence for the sensitivity of the Karnofsky Performance Status measure; treatment effects have been detected by Karnofsky Performance Status measure in some studies (e.g., Franchi & Wenzel, 1998; Neto & Siciliano, 2000) but not others, even though improvements were noted by another HRQOL measure (e.g., Wu, Mathews, Brysk, Atkinson, Grant, Abranson, et al., 1990; Zinkernagel, Ledergerber, Battegay, Cone, Vernazza, Hirschel, et al., 1999).

Although the Karnofsky Performance Status measure is brief and easy to use, ceiling effects occur (Murri et al., 1996), ratings may be insensitive to clinical change (O'Dell et al., 1995), and there is a lack of information about interrater reliability (Franchi & Wenzel, 1998). Karnofsky Performance Status scores may also be inaccurate measures of HRQOL, because ratings are based on physical dysfunction, which does not reflect impairment in other areas, such as cognitive and emotional function (Vanhems, Toma, & Pineault, 1996; Wu & Rubin, 1992). As such, more comprehensive instruments than the Karnofsky measure are required for adequate assessment of HRQOL.

Quality of Well Being Scale

The Quality of Well Being Scale is a preference-weighted decision-theory based measure of symptoms and functioning that is expressed on a continuum from 0 (death) to 1.0 (optimum functioning; Franchi & Wenzel, 1998). The Quality of Well Being Scale takes 10-20 minutes to complete and requires a trained interviewer. A self-administered form is also available, but it is difficult to use and can result in numerous errors (Kaplan et al., 1997). The Quality of Well Being Scale is composed of mobility, physical activity, and social activity functional domains as

well as a symptom measure (Kaplan et al., 1997; Vanhems et al., 1996). All of the Quality of Well Being Scale items have associated weighted coefficients derived from a general population sample that are used to calculate overall well being (Wu & Rubin, 1992). The Quality of Well Being Scale is able to combine morbidity and mortality data with the duration of stay in the impaired state (Kaplan, McCutchan, Navarro, & Anderson, 1994). Information derived from the Quality of Well Being Scale can be used to calculate quality adjusted life years in order to quantify the effectiveness of interventions for different individuals with HIV-infection.

Test-retest reliability and discriminant and convergent validity of the Quality of Well Being Scale have been established (McSweeny, 1990). It has been used as a treatment outcome measure for a variety of populations, including AIDS, back pain, chronic obstructive pulmonary disease (COPD), cystic fibrosis, osteoarthritis, peripheral vascular disease, rheumatoid arthritis, severe burns, pneumoccocal vaccine recipients, and elderly persons (McSweeny, 1990; McSweeny & Creer, 1995). In HIV-infected males, Quality of Well Being Scale scores are significantly related to CD4 count, with poorer HRQOL for those with CD4 counts less than 500 (Kaplan et al., 1994; 1995; 1997). At one and two year follow-up, significant differences in Quality of Well Being Scale scores occur between HIV-infection severity stages, with differences becoming more pronounced when deaths are included into the analysis (Kaplan et al., 1994, 1995). The mean difference between AIDS and asymptomatic HIV-infected groups was .14 units of well-being, which was equivalent to a one year loss of life for each seven HIV-infected individuals. The Quality of Well Being Scale is also sensitive to treatment effects (Wu et al., 1990).

In general, the Quality of Well Being Scale is more strongly associated with physical than psychological functioning (Revicki & Kaplan, 1993). It is correlated with Karnofsky Performance Status scores, measures of mood dysfunction, clinician ratings of neuropsychological impairment, neurologist ratings of neurological dysfunction, and the presence parenchymal abnormalities on MRI. After controlling for antiretroviral therapy use and socioeconomic status, Quality of Well Being Scale

scores were predicted by depressive symptoms, CD4 counts, neurologist ratings, and neuropsychological ratings (total predicted variance = 28 percent). Significant differences on the Quality of Well Being Scale were found between working and work-disabled groups (Kaplan et al., 1995). In a smaller sample, Quality of Well Being Scale scores at one year follow-up for individuals who lost their jobs was better than baseline or overall cohort scores, suggesting that a reduction in work demands may have health benefits (Kaplan et al., 1997). Quality of Well Being Scale scores were significant predictors of mortality over a median follow-up time of 30 months (Kaplan et al., 1995).

Overall, the Quality of Well Being Scale is viewed as an appropriate general health outcome measure for use in observational and clinical studies (Kaplan et al., 1997). The advantages of the Quality of Well Being Scale is that it provides one overall index of health status which takes both morbidity and mortality into consideration. Quality of Well Being Scale scores can be used to determine health care costs (McSweeny, 1990; McSweeny & Creer, 1995), which is useful for the evaluation and selection of health programs (Copfer, Ampel, Hughes, Gregor, Dols, Coons, et al., 1996). In addition, the Quality of Well Being Scale is unlikely to have ceiling or floor effects (Kaplan et al., 1997). The Quality of Well Being Scale has been criticized because it requires a trained interviewer and may not be useful for individual clinical assessment. It also requires some knowledge of decision theory and utility analysis in order to fully appreciate its advantages (McSweeny, 1990; McSweeny & Creer, 1995). Another disadvantage of the Quality of Well Being Scale is that it lacks the discriminative ability of instruments that have multiple scales (Copfer et al., 1996). Also, the use of preference weights is controversial because they are subjective and derived from the general population, rather than an HIV-specific group. However, individuals with HIV-infection were found to assign similar values to preference weights (Hughes, Coons, Kaplan, & Draugalis, 1994).

Sickness Impact Profile

The Sickness Impact Profile (Bergner, Bobbitt, Kressel, Pollard, Gilson, Morris, 1976a) is a 15-20 minute, self- or interviewer-administered questionnaire that assesses illness-related behaviour dysfunction (Tsasis, 2000). It is comprised of 136 questions that are grouped into 12 content areas: sleep and rest, emotionality, body care and movement, home management, mobility, social interaction, ambulation, alertness, communication skills, work, recreational pastimes, and eating. Scores are obtained using preset weights and are expressed as percent impairment. Results can be reduced to physical and psychosocial composites or a total summary score.

Twenty-four hour test-retest reliability ($r=.88$ to $.92$ for overall score, $r>.60$ for content areas) and internal consistency (Cronbach's alpha coefficient $>.90$) are adequate (Bergner, Bobbit, Carter, & Gilson, 1981; Pollard, Bobbit, Bergner, Martin, & Gilson, 1976). The Sickness Impact Profile also has good convergent and discriminant validity (i.e., with ratings of dysfunction, sickness, and ability to perform activities of daily living; Bergner et al., 1981; Bergner, Bobbitt, Pollard, Martin, & Gilson, 1976b). Norms based upon a stratified random sample from a Western American state are available for comparison (Bergner et al., 1981). The Sickness Impact Profile has been used with various populations, including back injury, head injury, chronic obstructive pulmonary disease, cancer, and myocardial infarction.

Within individuals with HIV-infection, Sickness Impact Profile scores reflected impairment within the psychosocial domains. However, the Sickness Impact Profile was unable to differentiate between individuals with AIDS-related complex and AIDS (Ragsdale & Morrow, 1990). For a small sample of individuals with HIV recruited from a dialysis clinic, the Sickness Impact Profile scores was moderately correlated with two indexes of well being, and poorly correlated with time trade-off (willingness to trade life years for perfect health versus staying in current health state), standard gamble (risk immediate painless death for perfect health versus staying in current health state), and categorical scaling rank (HRQOL

rated on scale from 0-100; Hornberger et al., 1992) measures.

The Sickness Impact Profile has a wide breadth of coverage and good reliability and validity. However, it emphasizes physical dysfunction, with little examination of psychosocial and emotional function. In addition, all items are worded in a negative fashion and could result in response bias. Another disadvantage of the Sickness Impact Profile is that scores have leptokurtic, positively skewed distributions, especially for unimpaired and mildly impaired populations (McSweeny, 1990). There is also a lack of research on the stability and sensitivity to clinical changes for this measure.

Medical Outcomes Study Measures

The Medical Outcomes Study (MOS) was a four-year observational study of health-care delivery systems that analyzed effects of provider characteristics, patient variables, and structural characteristics of health care on patient outcomes (McSweeny & Creer, 1995). A major goal of the study was to develop practical tools that can monitor patient outcomes in medical practice (Wu, Hays, Kelly, Malitz, & Bozzette, 1997a). The MOS scales appear to capture important components of HRQOL and are widely accepted within the medical establishment (Piette, Wachtel, Mor, & Mayer, 1995). As such, they are the most frequently used measures of HRQOL (De Boer et al., 1995).

One hundred forty-nine functioning and well-being items were administered to a wide variety of populations, including hypertension, congestive heart failure, myocardial infarction, diabetes, depression, and healthy groups (McSweeny & Creer, 1995). However, most MOS instruments are composed of a subset of these items, forming shorter HRQOL questionnaires that vary in the number of domains that are included and the number of questions addressing each domain (Wu et al., 1997a). Typically, physical function, role function, pain, social function, emotional well-being, cognitive function, general health perception, and energy/fatigue are assessed, usually with a reference period of the previous four weeks. These

domains fall under the two overarching dimensions of physical and mental health, which have been supported by factor analysis (Bing, Hays, Jacobson, Chen, Gange, Kass, et al., 2000). Among the numerous versions available (see Wu et al., 1997a), the most frequently used are the 20-item and 36-item instruments.

The 20-item version (Stewart, Greenfield, Hays, Wells, Rogers, Berry, McGlynn, & Ware, 1989) takes only 4 or 5 minutes to administer and has good internal consistency within various populations with HIV-infection (Cronbach's alpha range = .73 to .89; Holmes, Bix, & Shea, 1996; Smith, Feldman, Kelly, DeHovitz, Chirgwin, & Minkoff, 1996; Wachtel et al., 1992). Items were highly correlated to overall scores of other items within the same dimension (r= .60 to .80; Wachtel et al., 1992). Dimensions were interrelated (r=.26 to .62), with higher correlations between related dimensions. Ceiling and/or floor effects were noted for pain and physical, role, emotional, and social function (Bastardo & Kimberlin, 2000; Smith et al., 1996; Wachtel et al., 1992). The 36-item MOS instrument builds on the 20-item version by adding an energy/fatigue dimension as well as a measure for perceived changes in health status (Wu et al., 1997a). It requires 5-10 minutes to complete and is available in greater than 30 languages. Internal consistency reliabilities of 36-item instrument dimensions were high (Cronbach's alpha range = .74 to .91; Bing et al., 2000; Hays, Cunningham, Sherbourne, Wilson, Wu et al., 2000).

Construct validity of the MOS-derived tests has been demonstrated by studies that have found significant associations with other measures of HRQOL (e.g., rankings of physical performance, Quality of Well Being Scale, HRQOL ratings, time trade off, mental health inventories; Arpinelli, Visona, Bruno, DeCarli, & Apolone, 2000; Smith et al., 1996; Tsevat, Solzan, Kuntz, Ragland, Currier, Sell, et al., 1996). The MOS was sensitive to HIV stage (Bastardo & Kimberlin, 2000; Tsevat et al., 1996), disease progression (Smith et al., 1996; Tsevat et al., 1996), and treatment effects (Bozzette, Kanouse, Berry, & Duan, 1995a; Low-Beer, Chan, Wood, Yip, Montaner, O'Shaughnessy, et al., 2000).

Older age, female gender, non-Caucasian race, a less than high school education, intravenous drug use, and numerous medical symptoms were associated with lower MOS scores (Hays et al., 2000; Piette et al., 1995; Smith et al., 1996; Wachtel et al., 1992). Together, these clinical and sociodemographic characteristics explained between 26-40 percent of the variance of the MOS dimensions (20-item version; Wachtel et al., 1992). The strongest determinant of well being was total number of symptoms (Bastardo & Kimberlin, 2000; Burgoyne & Saunders, 2001; Cunningham, Shapiro, Hays, Dixon, Visscher, George, et al., 1998; Hays et al., 2000; Sousa, Holzemer, Henry, & Slaughter, 1999; Wachtel et al., 1992). MOS scores were also related to the availability of social support (Bastardo & Kimberlin, 2000), depressive symptomology (Sherbourne, Hays, Fleishman, Vitiello, Magruder et al., 2000), and employment factors (Hays et al., 2000; Huba, Melchior, Cherin, Steinberg, Smereck, Richardson-Nassif, et al., 2000; Smith et al., 1996). After controlling for stage of disease, lower physical function scores were associated with greater numbers of emergency room visits and in-patient admissions (Fleishman, Hsia, & Hellinger, 1994). However, there were mixed findings about the ability of the MOS to differentiate between different levels of CD4 counts, because relationships have been detected by some researchers (Bing et al., 2000; Call, Klapow, Stewart, Westfall, Mallinger, DeMasi, et al., 2000; Delate & Coons, 2000; Piette et al., 1995), but not others (Arpinelli et al., 2000; Burgoyne & Saunders, 2001).

HIV-infection has been compared to other chronic medical illness groups using MOS Physical and Mental Health factors. Physical functioning of individuals with asymptomatic HIV was similar to the general population and better than other chronic disease groups (Hays et al., 2000; Wachtel et al., 1992). However, with progression of HIV-infection, Physical Health was impaired relative to other chronic conditions, such as epilepsy, gastroesophageal reflux disease, prostate cancer, clinical depression, and diabetes. Mental Health was significantly lower for those with HIV-infection than the general population and other chronically ill groups, with

the exception of clinical depression.

Overall, advantages of the MOS scales include brevity, reliability, and validity. The availability of norms for the general population and different medical groups is also beneficial, because it allows for comparisons across groups (Wu et al., 1997a). The MOS measures are also available in numerous languages. Disadvantages include floor and ceiling effects, and the lower levels of reliability for the single item scales (e.g., social function, pain). Since subjects are asked about functioning over the previous month or more extended time intervals, MOS scales may not be sensitive to brief changes in health status (Piette et al., 1995).

HIV-SPECIFIC HRQOL MEASURES

The HIV-specific HRQOL measures were developed in order to focus on HRQOL issues that are most relevant to HIV-infection. The most commonly used measures will now be examined. These are displayed in Table 2.

HIV Overview of Problems-Evaluation System

The HIV Overview of Problems-Evaluation System (Schag et al., 1992) was developed from a well-validated HRQOL instrument used in cancer research. It is a self-administered questionnaire that takes an average of 15 minutes to complete. The HIV Overview of Problems-Evaluation System was designed to obtain detailed information about the daily impact of HIV-infection. It consists of a minimum of 106 items, including some screening questions that may lead to additional items (maximum=163). Thirty-five subscales represent discrete aspects of daily functioning, such as ambulation, pain, weight loss, difficulty working, psychological distress, and sexual interest. Factor analysis of the subscales resulted in the following five domains: physical, psychosocial, medical interactions, marital/partner, and sexual function. In addition to these five summary scores, a global score can be calculated (Schag et al., 1992).

Table 2. Comparison of HIV-Specific HRQOL Measures

HRQOL Measure	Description of Measures	Psychometric Properties	Sensitivity to HIV Stage	Relationship with Clinical Variables	Relationship with HRQOL Measures
HIV Overview of Problems-Evaluation System [a]	-about 15 minutes long -contains 35 subscales of daily function -five factors: physical, medical interactions, marital/partner, sexual, & psychosocial function -global summary score	-internal consistency of subscales is adequate -scales typically have moderate intercorrelations -all items are negatively worded, which may cause response bias	-differentiated between HIV stages -sensitive to disease progression	-lower scores for those with CD4 counts <200 -related to age, mood, ratings of adjustment to chronic illness, work status and income, physical activity ratings, use of pain medications	-good convergent validity with other HRQOL measures
Fanning HRQOL Scale [b] **(Fanning & Emmott, 1993)**	-35 items tapping various domains (e.g., physical, psychological, social, & financial function, daily activities, relationships with caregivers, & search for personal identity) -composed of 2 factors: intimacy/relationships & physical/psychological integrity	-adequate split-half & test-retest reliability	-mixed evidence for sensitivity to HIV stage	-associated with mood, time since AIDS diagnosis, emotional & (lack of) tangible support, & perception-oriented coping -unrelated to time since HIV diagnosis, number of hospitalizations, & severity of symptoms	-unknown
MOS-HIV [c] **(Wu et al., 1997a)**	-about 5 minutes long -contains 10 dimensions that are composed of 34 items -additional item to indicate if change in health status has occurred -available in 14 different languages	-multi-item dimensions have high internal consistency -convergent and divergent validity of dimensions -2-week test-retest reliability was generally moderate (Spanish sample) -ceiling &/or floor effects for half of the dimensions	-differentiated between HIV stages -sensitive to clinical changes & treatment effects	-related to demographic variables, iv drug use, mood, medical symptoms, HIV-related hospitalization or disability, history of AIDS illness, time HIV+, & mortality -mixed evidence of relationship with CD4 counts	-convergent and divergent validity with other HRQOL measures

HRQOL=health-related quality of life; iv=intravenous

[a] de Boer et al., 1996; Ganz et al., 1993; 1994; O'Leary et al., 1998; Schag et al., 1992

[b] Fanning & Emmott, 1993; Renwick & Freidland, 1996

[c] Badia et al., 1999; 2000; Burgess et al., 1993; Cohen et al., 1998; Copfer et al., 1996; Delate & Coons, 2001; Holmes & Shea, 1999; Hughes et al., 1997; Kaplan et al., 1997; McDonnell et al., 2000; Nieuwkerk et al., 2000; O'Leary et al., 1998; Revicki et al., 1995; 1999; Schag et al., 1992; Scott-Lennox et al., 1998; Wu et al., 1991; 1997a; 1997c

Internal consistencies of HIV Overview of Problems-Evaluation System subscales were generally high (Cronbach's alpha coefficients are typically greater than .70; Ganz, Schag, Kahn, & Petersen, 1994; Schag et al., 1992; de Boer, Sprangers, Aaronson, Lange, & Van Dam, 1996). Scale intercorrelations were generally moderate, although sexual and medical interaction scales were only weakly correlated. All summary scores were correlated with the global score.

Comparison of the HIV Overview of Problems-Evaluation System to measures of HRQOL or related constructs (e.g., MOS-HIV, Karnofsky Performance Status scores, linear analogue assessment of HRQOL, physical activity self-rating, rating of adjustment to chronic illness, mood) indicated good convergent validity (Ganz et al., 1993, 1994; O'Leary, Ganz, Wu, Coscarelli, & Petersen, 1998; Schag et al., 1992). HIV Overview of Problems-Evaluation System scores were also related to CD4 counts, with greater impairment in HRQOL for those with less than 200 CD4 counts. However, for those with CD4 counts over 200, HRQOL was highly variable and poorly predicted by CD4 counts (Ganz et al., 1993). Therefore, CD4 counts were only useful for identifying individuals with severe impairments in HRQOL. HIV Overview of Problems-Evaluation System scores differentiated between asymptomatic HIV, symptomatic HIV, and AIDS groups (Ganz et al., 1993; Schag et al., 1992), and was sensitive to disease progression (de Boer et al., 1996). Together, HIV status, Karnofsky Performance Status scores, age, CD4 count, current work status, use of pain medication, and income predicted 35 percent of the variance of HIV Overview of Problems-Evaluation System scores, with the majority of the variance (32 percent) predicted by both Karnofsky Performance Status scores and HIV status.

Overall, the HIV Overview of Problems-Evaluation System is a psychometrically sound, problem-oriented scale. The HIV Overview of Problems-Evaluation System examines difficulties and other negative aspects of HIV-infection, and neglects positive changes (e.g., forming better relationships with family members) that may also influence HRQOL. In addition, all items are phrased

in a negative direction, which may result in response bias.

Fanning HRQOL Scale

The Fanning HRQOL Scale (Fanning & Emmott, 1993) is a 35-item, self-administered HRQOL instrument. It addresses various aspects of HRQOL, such as physical and psychological health, activities of daily living, financial and social function, relationships with health care professionals, and the search for personal identity and meaning. The Fanning HRQOL Scale has adequate split-half reliability and test-retest stability. However, it's sensitivity to stage of HIV infection is not well established. Fanning and Emmott (1993) found significant differences between AIDS and HIV-infection groups for overall score and several individual items (i.e., physical health, occupational function, sexual desire, recreational activities, exercise, and sense of physical attractiveness). However, no significant differences were found between asymptomatic HIV, symptomatic HIV, and AIDS groups in another study (Renwick & Freidland, 1996).

Fanning HRQOL Scale scores was associated with depressive symptoms (Fanning & Emmott, 1993) and time since receiving a diagnosis of AIDS, but was unrelated to time since HIV diagnosis, number of hospitalizations, and symptom severity scores (Renwick & Freidland, 1996). Emotional support and perception-oriented coping (e.g., positive reappraisal of one's situation) were positively related to Fanning HRQOL Scale. However, tangible social support was negatively related to Fanning HRQOL Scale scores, possibly because subjects perceived tangible support as an indication of greater disability and poorer HRQOL. Future occupation, creation of new intimate friendships, physical strength and stamina, optimism for the future, psychological and emotional well-being, sexual desire, physical health, and control over one's own life were most negatively affected by HIV-infection. However, HIV-infection was positively related to commitment to present lover, openness as a gay individual, sense of affirmation within the gay community, satisfaction with time spent alone, spiritual beliefs, and

interest in life. Factor analysis produced two major factors which represented intimacy/relationships and physical/psychological integrity (Fanning & Emmott, 1993). Overall, the Fanning HRQOL Scale has adequate reliability and enables users to report the positive, as well as negative, aspects of HIV-infection. However, it may lack sensitivity for the progression of HIV illness.

MOS-Derived Measures

MOS questionnaires have been modified to produce HIV-specific HRQOL measures, including the HIV Patient Reported Status and Experience Survey, AIDS Health Assessment Questionnaire, and widely used MOS-HIV (Wu et al., 1997a).

The HIV Patient Reported Status and Experience Survey is a 38-item measure that was developed for clinical trials. It includes demographic, life circumstance, health status, health service utilization, disability, and symptom impact items and has good internal consistency and test-retest stability (Bozzette, Hays, Berry, & Kanouse, 1994). HIV Patient Reported Status and Experience Survey scores were related to CD4 count, the number and impact of medical symptoms, disability days, and health care utilization (Bozzette, Hays, Berry, Knouse & Wu, 1995b). Despite its strong psychometric properties, the use of this test has been limited due to concern with its length (Wu et al., 1997a).

The AIDS Health Assessment Questionnaire is composed of a symptom checklist in addition to 27 items reflecting disability, energy, global health perception, pain, cognitive function, mental health, social function, and health distress dimensions. AIDS-HAQ dimensions have high internal consistencies and convergent and divergent validity (Lubeck & Fries, 1997). The AIDS Health Assessment Questionnaire was able to differentiate between asymptomatic HIV, symptomatic HIV, and AIDS groups, and was sensitive to disease progression (Lubeck & Fries, 1992; 1997) and CD4 count declines of greater than 20 percent over time (Lubeck & Fries, 1997).

The MOS-HIV is the most frequently used HIV-specific HRQOL measure

(Wu, Rubin, Mathews, Ware, Brysk, Hardy, et al., 1991). It was developed from the 20-item MOS instrument. The 10 dimensions of MOS-HIV are composed of 34 items (the number of items within each dimension is provided in parentheses): Overall Health perception (5 items), Pain (2 items), Physical Function (6 items), Role Function (2 items), Social Function (1 item), Fatigue (4 items), Mental Health (5 items), Health Distress (4 items), Cognitive Function (4 items), and Quality of Life (1 item). An additional dimension, Health Transition (1 item), records changes in health status. Factor analysis-based physical health and mental health summary scores have also been generated (Wu et al., 1997a). The MOS-HIV takes only five minutes to complete and is available in 14 languages. In a small, advanced HIV sample, there were minimal differences in responding when using self, interviewer, or telephone administration (Wu, Jacobson, Berzon, Revicki, van der Horst, Fichtenbaum, et al., 1997b). However, when surrogate respondents were asked to rate the functioning of others with HIV-infection, ratings of mental health, health distress, pain, and energy/fatigue were significantly lower than the self-ratings of the individuals with HIV-infection.

Internal consistency of the multi-item dimensions were high (Cronbach's alpha typically exceeds .75; Badia, Podzamczer, Garcia, Lopez-Lavid, Consiglio, & Spanish MOS-HIV and MQOL-HIV Validation Group, 1999; Burgess, Dayer, Catalan, Hawkins, & Gazzard, 1993; Copfer et al., 1996; Holmes & Shea, 1999; Kaplan et al., 1997; Wu, Revicki, Jacobson, & Malitz, 1997c). Items generally had higher correlations with items from the same dimension then items from other dimensions (Holmes & Shea, 1999; Wu et al., 1997c). Dimensions were intercorrelated, and showed convergent and divergent validity (Holmes & Shea, 1999; McDonnell, Gielen, Wu, O'Campo, & Faden, 2000). In a small Spanish sample, test-retest reliability over two-weeks was moderate for those reporting no change in condition, with lowest reliability for the Social Function dimension (intraclass correlation range .24 to .85; Badia et al., 1999). Ceiling effects have been demonstrated for Physical, Role, Social, and Cognitive Function, Pain, and

Health Transition while floor effects occurred for Role Function (Badia, Podzamczer, Casado, Lopez-Lavid, Garcia, & the Spanish MOS-HIV and MQOL-HIV Validation Group, 2000; Delate & Coons, 2001; Holmes & Shea, 1999; McDonnell et al., 2000).

MOS-HIV scores were related to age (Hughes, Kaplan, Coons, Draugalis, Johnson, & Patterson, 1997; McDonnell et al., 2000) and other sociodemographic variables (sexual orientation, race, education, income, injection drug use; Holmes & Shea, 1999). Discriminant and convergent validity of the MOS-HIV with other HRQOL measures has also been demonstrated, including the Karnofsky Performance Status measure (Copfer et al., 1996), HIV Overview of Problems-Evaluation System (O'Leary et al., 1998; Schag et al., 1992), Quality of Well Being Scale (Copfer et al., 1996; Hughes et al., 1997), and others (Badia et al., 1999; Burgess et al., 1993; Delate & Coons, 2001). Although CD4 count was unrelated to mental health dimensions, relationships have occurred with physical health-related MOS-HIV dimensions (e.g., Overall Health, Physical Function, Role Function, Social Function, Pain, Fatigue; Burgess et al., 1993; Hughes et al., 1997; McDonnell et al., 2000). However, these associations were not always found (Badia et al., 1999; Copfer et al., 1996).

MOS-HIV scores differentiated between asymptomatic HIV from symptomatic HIV and AIDS groups (Badia et al., 1999; Burgess et al., 1993; Copfer et al., 1996; Kaplan et al., 1997; Revicki et al., 1995; Schag et al., 1992; Wu et al., 1991), and were sensitive to clinical changes (Badia et al., 1999; Badia et al., 2000; Holmes & Shea, 1999) and treatment effects (Cohen, Revicki, Nabulsi, Sarocco, Jiang, & the Advanced HIV Disease Ritonavir Study Group, 1998; Nieuwkerk, Gisolf, Colebunders, Wu, Danner, & Sprangers, 2000; Revicki, Moyle, Stellbrink, & Barker, 1999; Scott-Lennox, Mills, & Burt, 1998; Wu et al., 1997c). The degree of HIV-related impairment (e.g., presence or history of an AIDS illness, HIV-related hospitalization, or HIV-related disability; Holmes & Shea, 1999), number of HIV-related complications, time since first positive HIV test (Burgess et al., 1993),

number (Badia et al., 1999; Wu et al., 1991) and development of clinical symptoms (Badia et al., 2000; Revicki et al., 1995), and mortality (Kaplan et al., 1997) were also associated with MOS-HIV scores.

Individuals with asymptomatic HIV-infection reported better health status for most MOS-HIV dimensions (not Mental Health, Health Distress, or Health Transition) than patients with diabetes, recent myocardial infarction, hypertension, and depression (Wu et al., 1991). HRQOL for those with symptomatic HIV-infection was better than those with a recent myocardial infarction or depression, worse than those with diabetes, and similar to those with hypertension.

Factors of MOS-Derived HRQOL Measures. Factor analysis of the MOS-HIV dimensions produced two moderately correlated (r=.56) summary factors, Physical and Mental Health (Gielen et al., 2001; Revicki et al., 1998; Rourke et al., 2001; Trepanier et al., 2001). These factors were similar to those obtained with the 36-item MOS instrument (Bing et al., 2000). Physical Function, Pain, Role Function, and Social Function had higher loadings on the Physical Health summary factor, while Health Distress, Quality of Life, and Cognitive Function had greater associations with the Mental Health summary factor (Revicki et al., 1998). Fatigue and Overall Health dimensions tended to load on both factors. The dimension-based summary factors had high internal consistencies and moderate to high 4-month test-retest reliabilities (Pearson correlation coefficients: Physical Health =.72, Mental Health =.60; intraclass correlation coefficients: Physical Health =.72; Mental Health =.53). Lower Physical and Mental Health summary factor scores occurred for those with advanced HIV disease, depression and/or anxiety, a higher number of HIV-related symptoms, lower clinician ratings of functional status (Karnofsky Performance Status scores), worse self-ratings of current health, perceived declines in health status (Revicki et al., 1998), and poorer social support (Gielen et al., 2001). CD4 counts were associated with Physical Health, but not Mental Health, summary factor scores (Delate & Coons, 2001; Tsevat et al., 1996). This indicates

that disease stage is more strongly associated with physical than mental health, and provides evidence for discriminate validity.

In a preliminary cross-sectional study, the Physical and Mental Health summary factor scores were differentially related to depression, neuropsychological performance, medical symptoms, and stage of HIV-infection (Rourke et al., 2001). The Mental Health summary factor was only predicted by depression scores. However, neuropsychological impairments, medical symptoms, and stage of HIV-infection were all independent predictors of the Physical Health summary factor. Examination of the two MOS-HIV factors using neuropsychology and depression scores as independent variables revealed a main effect for depression and the Mental Health factor, and a depression-neuropsychological impairment interaction for both of the Physical and Mental Health factors (Trepanier et al., 2001). These findings need to be verified using larger samples.

Factor analysis of the individual items of the MOS-HIV has also been conducted. In one study, five factors were produced that were represented by the following dimensions: physical function, general health perception, mental health/health distress/cognitive function, mental health/energy/QOL, and pain/role function/social function (Holmes & Shea, 1999). The health transition item did not significantly load on any of the factors. Preliminary results by Rourke and his colleagues (2001) revealed a six factor solution comprised of overall health, pain and fatigue, physical and social function, role function, mental health, and cognitive symptoms. These factors were differentially affected by neurobehavioural complications (neuropsychological impairment and depression), medical symptoms, and HIV stage of infection. Physical, social, and role function domains were associated with neuropsychological impairments. Mental health, overall health, and cognitive symptoms were related to depression. Pain, fatigue, physical function, and social function were linked to medical symptoms. Finally, overall health and role function were associated with stage of HIV-infection. The use of item-based factors may provide more refined and discriminative HRQOL constructs than the 10 MOS-

HIV Dimensions. However, additional research is necessary for confirmation of these factors and to examine their stability over time.

Overall, the MOS-HIV is a brief, easily administered, and widely-used HRQOL measure with good psychometric properties. It is responsive to clinical changes and treatment group differences in a broad range of individuals with HIV-infection, has a growing bank of reference scores, and is available in many different languages (Wu et al., 1997a). HRQOL dimensions that are shared with generic MOS measures can be used for comparisons to other disease groups and healthy controls (Holmes & Shea, 1999). The use of profile and factor scores allows clinicians to obtain detailed information about the functioning of individuals with HIV that can be examined for changes over time and/or with treatment (Copfer et al., 1996; Hughes et al., 1997). Disadvantages of the MOS-HIV include ceiling and floor effects for some dimensions and the use of single item scales that provide less precise estimates of functioning (Wu et al., 1997a). The MOS-HIV has also been criticized for lacking indices of somatic symptoms, sleeping and eating disturbances, and sexual dysfunction, which are associated with HIV-infection (Wu et al., 1997c).

SUMMARY

HIV-infection produces deficits in immune functioning which result in the development of an array of opportunistic infections and neoplasms. As a result, neurological, psychological, and systemic complications occur which are significantly related to HRQOL and other aspects of functional status, such as the ability to maintain employment. HRQOL research is complicated by a lack of a precise, universal definition of HRQOL, variations in the selection of HRQOL instruments, and cultural and demographic compositions of subjects. Research is primarily conducted with English-speaking, highly educated, 30 to 45 year old, gay or bisexual, Caucasian males from the United States of America and Canada. As such, research findings can not be generalized to other populations with HIV-

infection, including non-North Americans, minority cultural groups, females, intravenous drug users, or children.

Various HIV HRQOL measures have been developed which differ in comprehensiveness, specificity (i.e., generic versus HIV-specific), and outcome variables. These include the Quality of Well Being Scale, Sickness Impact Profile, HIV Overview of Problems-Evaluation System, Fanning HRQOL Scale, and the most frequently used MOS-derived measures. Most HRQOL measures include physical, psychological, cognitive, and social core components of HRQOL and have acceptable construct validity and internal consistency. However, few studies have examined the stability and sensitivity of HRQOL instruments over time. Systematic evaluation of the reliability, validity, stability, and clinical utility of HRQOL instruments is necessary, in order to ensure meaningful results can be obtained.

PURPOSE OF THIS STUDY

The purpose of this study was to evaluate the (I) factor structure and the (II) test-retest reliability of MOS-HIV HRQOL instrument. In addition, the (III) clinical utility of the MOS-HIV instrument will be evaluated by determining the impact of demographic, medical, and neurobehavioural variables on various aspects of HRQOL.

PART I. FACTOR STRUCTURE OF THE MOS-HIV

The factor structures of the 34 items and 10 dimensions of the MOS-HIV were determined for subjects at baseline and at 1 year follow-up. Based upon the findings of Revicki (Revicki et al., 1998) and others (e.g., Burgess et al., 1993; Gielen et al., 2001), the following hypotheses were made:

(a) Factor analysis of the 10 MOS-HIV dimensions would produce Mental

and Physical Health Summary Factors (MHS and PHS, respectively). Physical Function, Role Function, Pain, and Social Function were expected to have higher loadings on PHS than MHS, while Mental Health, Health Distress, Quality of Life, and Cognitive Function were expected to have higher loadings on MHS than PHS. Fatigue and Overall Health dimensions were predicted to load highly on both factors.

(b) Factor structure of the 10 MOS-HIV dimensions will be consistent using baseline and follow-up data, indicating factor stability.

(c) Factor analysis of the 34 MOS-HIV items would result in 6 factors, based on preliminary findings by Rourke and colleagues (2001) using a subset of the baseline sample. Four of these factors would be composed of the Overall Health, Role Function, Mental Health, and Cognitive Function dimensions, while the other two factors would be composed of pairs of dimensions: Pain/Fatigue and Physical/Social Function.

(d) Factor structure of the 34 MOS-HIV items obtained at baseline and follow-up will be consistent, indicating factor stability.

PART II. TEST-RETEST RELIABILITY OF THE MOS-HIV

Intraclass and Pearson correlation coefficients were calculated as measures of test-retest reliability. Three-, 6-, 9-, and 16-month test-retest reliabilities of the MOS-HIV dimensions and summary factors were determined using two separate samples, which are described in greater detail in the method section. For both samples, reliability coefficient calculations were obtained for all available subjects as well as for those with a stable clinical course (e.g., similar depression scores for both assessments). The following predictions were made:

(a) Test-retest reliabilities of all of the MOS-HIV dimensions and summary factors were predicted to be moderate to high (approximately .5 or

higher) based on previous findings (Badia et al., 1999; Revicki et al., 1998)

(b) Test-retest reliability coefficients obtained from mood stable subjects were expected to be higher than those obtained from the overall (all-inclusive) sample.

PART III. CLINICAL UTILITY OF THE MOS-HIV

The clinical utility of the MOS-HIV was determined by examining the impact of demographic (i.e., age, education, gender, and race), medical (i.e., history of AIDS-defining conditions, recent CD4 count, and current medical symptoms) and neurobehavioural (i.e., depressive symptoms and neurocognitive status) variables on MOS-HIV dimensions and factor scores. Multiple regression analyses were conducted using baseline, follow-up, and change scores (i.e., the difference in score between time 1 and 2) to determine the relative contribution of these clinical variables for predicting each HRQOL domain. Predictions were as follows:

(a) Medical and neurobehavioural status would be associated with MOS-HIV dimensions and factor scores, and predictors of MOS-HIV dimensions and factors were expected to be consistent at baseline and follow-up.

(b) Changes in MOS-HIV scores between baseline and follow-up were expected to be associated with changes in medical and neurobehavioural functioning.

(c) Medical variables and neuropsychological performance was expected to have greater associations with physical health-related dimensions (e.g., Pain and Physical, Role, and Social Function)

(d) Depressive symptoms were predicted to have stronger relationships with mental health-related dimensions (e.g., Mental Health, Health Distress, Quality of Life, and Cognitive Function).

METHOD

SUBJECTS

Two different samples of adults with HIV-infection were used for this study. For both samples, HIV-infected participants were recruited from a variety of sources (research pool, primary care HIV medical clinic, and psychiatric service) between January 1997 to May 2002. Demographic information of the samples is provided in Table 3.

Primary Sample

As part of an ongoing study of neurobehavioural complications in HIV and their impact on everyday functioning (Rourke et al., 1999a), 293 participants with HIV-infection were evaluated on various medical, mood, and neurocognitive variables (see Table 3). Of this sample, 231 adults (94% male; 89% Caucasian; 63% with an AIDS diagnosis as defined by a history of AIDS-defining conditions or a CD4 count < 200), completed the MOS-HIV HRQOL instrument. After an average time period of 15 months, participants were re-contacted or referred for a second evaluation. One hundred thirty-six participants (97% male; 90% Caucasian; 55% with an AIDS diagnosis as defined by a history of AIDS-defining conditions or a CD4 count < 200) completed follow-up testing, including medical, mood, and neurocognitive measures and the MOS-HIV. The 231 participants at baseline and 136 participants at follow-up who completed the MOS-HIV were used for to determine the factor structure of the MOS-HIV.

The average age at baseline was 41.4 (SD=8.4) years. Test-retest intervals were an average of 15.4 (SD=9.9) months. The sample had an average of 14 years of education (SD=3.0) and their mean estimated IQ, as determined by a measure of reading skill (Adult North American Reading Test; Spreen & Strauss, 1991), was 115.8 (SD=7.6) or high average. At the time of entry into the study, the mean CD4 count was 358 (SD=249) and 49 percent of the sample had an undetectable plasma

Table 3. Demographic Data of the Primary and Supplementary Samples

	Primary Sample: Baseline (n=231)		**Primary Sample: Follow-up** (n=136)		**Supplementary Sample: Baseline** (n=98)	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age (years)	41.4	8.4	43.9	8.2	40.8	7.0
Education (years)	14.0	3.0	14.4	2.7	13.2	2.4
Estimated IQ (ANART)	115.8	7.6	n/a	n/a	n/a	n/a
Test-Retest Interval (Days) [a]	468.8	301.7	n/a	n/a	162.6	76.7
BDI - Total Score [a]	19.1	10.9	14.3	10.8	9.8	9.5
Medical Symptoms [a]	3.0	2.1	2.5	2.0	2.1	1.8
CD4 Lymphocyte Count [a]	358.7	249.2	386.7	251.1	416.7	238.0
	%		**%**		**%**	
Gender (%Male)	94.1		97.1		78.9	
Race (%Caucasian)	89.2		90.4		81.5	
Undetectable Viral Load (≤500) [a]	49.0		64.0		60.9	
AIDS Status [a]	63.3		54.8		53.2	

BDI = Beck Depression Inventory

[a] Significant differences between Baseline for Primary and Supplementary Samples

viral load (i.e., counts less than 500). At follow-up, the sample had a mean CD4 count of 387 (SD=251) and 64 percent had an undetectable viral load.

Of the 136 participants who completed follow-up testing, only 100 individuals were given the MOS-HIV at both baseline and follow-up because the MOS-HIV was introduced into the testing battery after the first 36 participants were tested. The 100 participants with baseline and follow-up MOS-HIV scores were used for the test-retest reliability and clinical utility (multiple regression) analyses. Comparison of the 100 individuals with the MOS-HIV at baseline and follow-up to those with the MOS-HIV at only baseline (n=131) indicated that the groups did not differ on demographic, depression, medical status, neurocognitive performance variables (see Table 4). Given the similarity of these groups and the larger sample size at baseline, the factor coefficient values obtained with the baseline sample (n=231) were used in the calculation of baseline and follow-up factor scores for use in the reliability and clinical utility analyses. In terms of HRQOL, the group with MOS-HIV scores at baseline and follow-up had significantly higher MOS-HIV Physical Function dimension scores than those with only baseline MOS-HIV scores.

For the 100 participants with MOS-HIV scores at baseline and follow-up, significant differences were found between baseline and follow-up data for mood, medical, neurocognitive, and HRQOL variables (see Table 5). Participants at follow-up were less likely to have a detectable plasma viral load, and had fewer depressive symptoms (for all indices of the BDI) and lower verbal learning and memory performance (i.e., CVLT-Total recall). In addition, significantly higher scores than baseline for the MOS-HIV mental health summary factor, and MOS-HIV Social Function, Cognitive Function, Quality of Life, and Mental Health dimensions occurred at follow-up. Differences between these HRQOL domains at baseline and follow-up remained after controlling for changes in depressive symptoms. However, after covarying for CVLT-Total recall scores, no group differences were found. This suggests that the decline in learning and memory performance was associated with changes in mental health related aspects of HRQOL.

Table 4. Comparison of Subjects with only Baseline MOS-HIV Scores to Those with MOS-HIV Scores at Baseline and Follow-Up (Primary Sample)

	MOS-HIV at Baseline Only (n=131)		MOS-HIV at Both Times (n=100)		Group Differences ($p < .01$)
Demographic Variables	**Mean**	**(SD)**	**Mean**	**(SD)**	**t/Z value**
Age (years)	41.1	8.7	42.1	8.1	ns
Education (years)	13.8	3.2	14.2	2.7	ns
Gender (%Male)	92.9 %		96.0 %		ns
Race (%Caucasian)	89.0 %		89.0 %		ns
Depressive Symptomology	**Mean**	**(SD)**	**Mean**	**(SD)**	**t value**
BDI-Total Score	18.8	11.2	19.6	11.1	ns
BDI-Affective Score	10.8	7.8	11.5	7.7	ns
BDI-Somatic Score	8.0	4.3	8.0	4.3	ns
Medical Status	**Mean**	**(SD)**	**Mean**	**(SD)**	**t/Z value**
Medical Symptoms	3.2	2.3	2.8	1.9	ns
CD4 Lymphocyte Count	326.1	242.0	371.5	239.6	ns
Undetectable Viral Load($\leq$500)	49.0 %		57.4 %		ns
AIDS Status	62.7 %		60.7 %		ns
Neuropsychological Variables	**Mean**	**(SD)**	**Mean**	**(SD)**	**t value**
Estimated IQ	104.3	34.3	109.7	28.5	ns
Digit Symbol Scaled Score	8.1	3.2	8.2	3.7	ns
Digit Span Scaled Score	9.8	2.7	10.3	2.6	ns
CVLT-Total Recall	46.9	10.7	48.2	9.8	ns
Grooved Pegboard-Average	78.7	21.9	78.0	22.5	ns
MOS-HIV HRQOL Domains	**Mean**	**(SD)**	**Mean**	**(SD)**	**t value**
Physical Function	61.2	26.9	70.3	24.6	**-2.6**
Role Function	32.3	41.1	32.0	43.5	ns
Pain	58.8	27.1	61.2	26.6	ns
Social Function	58.4	29.3	59.8	31.2	ns
Overall Health	35.1	23.9	36.7	26.4	ns
Fatigue	38.1	21.7	38.5	22.6	ns
Cognitive Function	53.1	24.0	50.2	25.2	ns
Health Distress	55.9	26.6	59.5	31.0	ns
Quality of Life	51.0	24.9	48.0	25.3	ns
Mental Health	53.8	22.6	50.6	25.5	ns
Physical Health Factor	57.5	25.8	61.3	27.0	ns
Mental Health Factor	58.4	22.6	56.9	25.8	ns

BDI=Beck Depression Inventory; CVLT-Total Recall=California Verbal Learning Test-Total Recall of List A, Trials 1-5; HRQOL=health-related quality of life; MOS-HIV=Medical Outcomes Study HIV HRQOL Instrument; ns=non-significant

Table 5. Comparison of Baseline and Follow-Up Variables for Subjects with MOS-HIV Scores at Both Times (Primary Sample, n=100)

	Baseline		Follow-up		Differences ($p < .01$)
Depressive Symptomology	**Mean**	**SD**	**Mean**	**SD**	**t value**
BDI-Total Score	19.6	11.1	14.7	10.5	**4.4**
BDI-Affective Score	11.3	7.6	8.0	6.4	**4.3**
BDI-Somatic Score	8.0	4.3	6.3	4.2	**4.1**
Medical Status	**Mean**	**SD**	**Mean**	**SD**	**t/Z value**
Medical Symptoms	2.7	1.9	2.5	2.0	ns
CD4 Lymphocyte Count	393.8	250.2	389.7	225.9	ns
Undetectable Viral Load (≤500)	49.0 %		65.2 %		**-3.6**
AIDS Status	45.0 %		49.0 %		ns
Neuropsychological Variables	**Mean**	**SD**	**Mean**	**SD**	**t value**
Digit Symbol Scaled Score	8.7	2.7	9.3	3.4	ns
Digit Span Scaled Score	10.1	2.7	10.3	2.7	ns
CVLT-Total Recall	47.4	10.3	44.2	11.4	**3.4**
Grooved Pegboard - Average	77.4	17.9	75.1	16.3	ns
MOS-HIV HRQOL Domains	**Mean**	**SD**	**Mean**	**SD**	**t value**
Physical Function	70.3	24.6	69.1	25.7	ns
Role Function	32.0	43.5	37.5	45.2	ns
Pain	61.2	26.6	59.6	28.3	ns
Social Function	59.8	31.2	68.0	29.0	**-2.9**
Overall Health	36.7	26.4	40.3	26.3	ns
Fatigue	38.5	22.6	44.0	22.9	ns
Cognitive Function	50.2	25.2	60.7	23.9	**-4.3**
Health Distress	59.5	31.0	67.2	27.2	ns
Quality of Life	48.0	25.3	57.5	23.2	**-3.2**
Mental Health	50.6	25.5	59.2	24.3	**-3.3**
Physical Function	2.73	.62	2.70	.65	ns
Functional Status	1.00	1.04	1.12	1.03	ns
Overall Health	-3.14	1.15	-3.05	1.15	ns
Cognitive Function	4.01	1.35	4.58	1.28	**-4.4**
Health Distress	4.82	1.63	5.30	1.38	**-3.0**
Mental Health	-1.00	1.43	-.56	1.35	**-3.0**
Physical Health Factor	61.3	27.0	65.2	26.9	ns
Mental Health Factor	56.9	25.8	65.9	23.9	**-3.6**

BDI=Beck Depression Inventory; CVLT-Total Recall=California Verbal Learning Test-Total Recall of List A, Trials 1-5; HRQOL=health-related quality of life; MOS-HIV=Medical Outcomes Study HIV HRQOL Instrument; ns=non-significant

Supplementary Sample

A supplementary sample was used in the reliability analyses in order to determine the 3-, 6-, and 9-month test-retest reliability of MOS-HIV dimensions and factors. This sample was obtained from an ongoing study examining factors related to medication adherence that was being conducted within the same HIV-research laboratory as this project. Twelve of the subjects in the supplementary sample were also participants in the primary sample. Ninety-eight adults (79% male; 82% Caucasian; 53% had an AIDS diagnosis as defined by a history of an AIDS-defining condition or CD4 counts < 200) were retested approximately every 3 months for a maximum of 4 testing sessions (see Table 3). Subjects had an average age and education of 40.8 (SD=7.0) and 13.2 (SD=2.4) years, respectively. At baseline, mean CD4 count was 417 (SD=238) and 61 percent of the sample had an undetectable plasma viral load.

Comparison of the Primary and Supplementary Samples

The supplementary sample was significantly different from the primary sample at baseline (see Table 3). In addition to the expected differences in test-retest interval (t=9.9, p<.001), subjects from the supplementary sample were less likely to have an AIDS diagnosis (Z=-2.6, p<.05), and more likely to have an undetectable viral load (Z=-2.7, p<.01) and higher CD4 count (t=-2.3, p<.05) than the primary sample. In addition, the supplementary sample had lower scores on a depression inventory (i.e., Beck Depression Inventory; t=8.5, p<.001) and fewer HIV-related medical symptoms (t=3.6, p<.001) than the primary sample. Overall, these differences indicated slightly better overall health functioning at baseline for the supplementary sample as compared to the primary sample. No significant differences in age, education, gender, and race were found between the supplementary and primary sample groups (for all analyses, p>.05). These differences between the primary and supplementary samples may result in discrepancies in test-retest reliability coefficients between these groups, particularly

if clinical status is not stable over the test-retest interval.

STUDY INSTRUMENTS

Health-Related Quality of Life (HRQOL)

As described previously, the MOS-HIV (Wu et al., 1991) is a self-report HRQOL questionnaire developed for adults with HIV-infection. It is composed of 34 items that assess ten domains of HRQOL: Overall Health, Pain, Physical Function, Role Function, Social Function, Fatigue, Mental Health, Health Distress, Cognitive Function, Quality of Life, and Health Transition. The MOS-HIV has good internal consistency, is responsive to clinical changes, and has demonstrated construct, concurrent, and discriminative validity (Badia et al., 1999; Burgess et al., 1993; Copfer et al., 1996; Holmes & Shea, 1999; Kaplan et al., 1997; Wu et al., 1997c).

Neuropsychological Impairment

HIV-infection is most commonly associated with impairments in complex attention, speed of information processing, psychomotor skills, and learning efficiency (Heaton et al., 1995; White et al., 1995). As such, neuropsychological tests that assess these areas of functioning were chosen as predictor variables for the multiple regression analyses of this study. The following four test scores were selected because they are generally believed to assess the neuropsychological domains of interest and were consistently given to the subjects during baseline and follow-up testing sessions:

(1) ***Wechsler Adult Intelligence Scale-Revised Digit Span Subtest - Scaled Score*** (Wechsler, 1981). Subjects were asked to recite orally presented numeric sequences either in the same order (repetition) as presented or the reverse order. Scores are based upon the number of numeric sequences correctly recalled for both the forward and backward portions of the test.

(2) ***Wechsler Adult Intelligence Scale-Revised Digit Symbol Subtest - Raw Score*** (Wechsler, 1981). Subjects were given a series of symbols that are each associated with a number from 1 to 9. For 90 seconds, they were asked to write the correct symbols in as many number-associated blanks as possible based upon the provided symbol-number pairings. A score was obtained based on the number of correctly filled blanks.

(3) ***Grooved Pegboard Test - Dominant Hand score*** (Reitan & Wolfson, 1985). Subjects were asked to put a key-shaped peg into each of 25 lock-shaped holes as quickly as possible using only their dominant hand. The obtained score is the amount of time (in seconds) required to complete the task.

(4) ***California Verbal Learning Test - Total Recall of List A, Trials 1-5*** (CVLT-Total Recall; Delis, Kramer, Kaplan, & Ober, 1987). Subjects were given five learning trials in which they were read a list of 16 semantically-related words (i.e., 4 words for each of 4 semantic clusters, such as fruit or clothing). They were then asked to recall as many of the words from the list as possible. Total recall was the total number of words correctly recalled over all five trials.

Depression

The Beck Depression Inventory (BDI; Beck & Steer, 1993) is a self-report scale composed of 21 items tapping affective (items 1-13; e.g., pessimism, guilt, sadness) and somatic (items 14-21; e.g., work inhibition, sleep disturbance, loss of appetite) symptoms. All items are graded on a scale from 0 to 3 to reflect increasing symptomology. Affective and somatic items are added to produce a total score (range 0 to 63). Internal consistency reliabilities (coefficient alphas) of the BDI range from .73 to .95 for various psychiatric and non-psychiatric samples, while test-retest correlation coefficients are typically greater than .60. The BDI has adequate concurrent, discriminative, and construct validity (for a review, see Beck,

Steer, & Garbin, 1988). The BDI-Affective score was primarily used in these analyses, because the somatic portion of the measure contains symptoms that commonly occur with HIV (e.g., fatigue and weight loss) which may artificially inflate the severity of depressive symptomology.

Medical Symptoms

Medical symptoms were assessed using a checklist of 12 common HIV-related symptoms, based on the measure derived by Rabkin and colleagues (1991). Participants were asked if they had experienced any of the following symptoms during the previous week: persistent fatigue, oral candida or thrush, night sweats, diarrhea, persistent fever over 100°C, persistent or unusual headaches, unintentional weight loss, new skin rash, new or unusual cough, persistent sore throat or mouth, unusual bump, bruise, or skin discolouration, and persistent shortness of breath. The number of currently experienced medical symptoms was added to produce a total score ranging from 0 to 12.

CD4 Counts

Recent CD4 lymphocyte counts, a measure of immune status, were obtained at both baseline and follow-up. These values were self-reported. CD4 counts are considered to be the best indicator for the development of opportunistic infections (Bellenir, 1999).

AIDS Status (History of AIDS-Defining Conditions)

Diagnosis of AIDS was based on the Center for Disease Control classification system for HIV-infection (Center for Disease Control, 1992). Subjects were categorized according to membership in HIV-positive without AIDS (i.e., asymptomatic or mildly symptomatic) and AIDS groups. AIDS diagnosis was based on a history of AIDS-defining conditions alone. Nadir CD4 counts were not included in the determination of AIDS status because CD4 counts were also selected as a

predictor of HRQOL.

PROCEDURE

All participants were informed prior to study participation that they would be asked to provide information about their developmental, neuromedical, and psychiatric history, current mood status, and HRQOL, in addition to completing neuropsychological testing. Participants were required to provide written consent if they were willing to take part in this research study. The BDI, MOS-HIV, Symptom Questionnaire, CVLT, WAIS-R, and Grooved Pegboard test was administered by a trained psychometrist as part of a larger battery. Standard administration procedures described in test manuals was employed for all tests. Overall, testing sessions took approximately 3-4 hours to complete, including a short break. Participants recruited for this research project were paid $30 for participation in this study; however, participants that were clinical referrals (i.e., referred from primary care doctors, infection disease specialists, or psychiatrists for neurocognitive testing) did not receive monetary compensation. All participants were given the opportunity to receive feedback of their neurocognitive performance and have a summary report sent to their primary physician, infectious disease specialist, psychiatrist, and/or other professionals involved in their care.

Participants were re-contacted for participation in the follow-up portion of this study after a time interval of approximately one year. The procedure for the follow-up visit was identical to that described for the baseline session. Recruitment and testing of participants for this study was approved by University of Windsor and St. Michael's Hospital Research Ethics Boards.

STATISTICAL ANALYSIS

Data Screening

All data analyses were carried out using SPSS for Windows, Version 10.0. Data were screened for normality and (univariate and multivariate) outliers using

techniques described by Tabachnick and Fidell (1996). Univariate outliers were defined as variables with Z-scores less than - 3.0 or greater than + 3.0. Multivariate outliers were identified through Mahalanobis distance calculations with $p<.001$. For the remainder of the analyses, statistical significance was be defined as $p<.05$. Missing data were replaced with median scores in the multiple regression analyses to prevent subject loss.

PART I. Factor Structure of the MOS-HIV

Factor analysis (namely Principle Factors Extraction) was performed on both the 34 MOS-HIV items and the 10 MOS-HIV dimensions, in order to determine underlying factor structures. An eigenvalue of at least 1.0 was the criterion for the retention of factors. Since MOS-HIV items and dimensions are intercorrelated, it was expected that MOS-HIV factor scores would also be related. As such, Promax (oblique) rotation of the factors was selected because it allows for the intercorrelation of obtained factors. Pearson Intercorrelations of the factors were obtained, in order to verify the use of oblique rotation. Factor Analyses were conducted separately for the MOS-HIV items and dimensions both at baseline (n=231) and at follow-up (n=136). The factor structures of MOS-HIV baseline and follow-up data were compared, in order to determine factor stability.

Calculation of Factor Scores. During factor analysis, factor coefficients were obtained based on the loadings of MOS-HIV items or dimensions on summary factors. These factor coefficients can be used in regression equation formulas in order to calculate MOS-HIV factor score values for each subject. For the purposes of this study, factor scores were derived by using the same factor coefficients to derive the dimension-based and item-based factors. The consistent use of the same factor score equations allowed factor scores to be more readily comparable than factor scores derived from different regression equations. The factor coefficients from the largest sample were selected for use in the factor regression equations.

Therefore, the baseline coefficients for the primary sample were selected to determine the factor scores of all primary and supplementary, baseline and follow-up sample groups. These factor scores were then used in both the MOS-HIV summary factor test-retest reliability and clinical utility (multiple regression) analyses.

PART II. Test-Retest Reliability of the MOS-HIV

Two-way mixed effect intraclass (see McGraw & Wong, 1996; Shrout & Fleiss, 1979), and Pearson correlation coefficients were used to determine the test-retest reliability of the MOS-HIV dimensions and dimension-based factor scores. Both of these reliability coefficients indicate the degree of similarity between scores obtained at baseline and follow-up for each subject. Coefficients can range from 0.0 (completely unrelated) to +/-1.0 (perfect agreement). Intraclass correlation coefficients are the ratio of between-person variability to total score variability (Deyo, Diehr, & Patrick, 1991). They are sensitive to linear relationships between test-retest scores as well as systemic changes in score values. Pearson correlation coefficients are based on a linear relationship between baseline and follow-up scores, and they are not sensitive to systemic changes in mean responding (e.g., practice effects; Hays, Anderson, & Revicki, 1993).

Test-retest reliability of the MOS-HIV dimensions and factor scores was conducted for both the primary and supplementary samples. Three-, 6-, and 9-month test-retest reliabilities were calculated for the supplementary sample while 1.3 year reliability coefficients were obtained from the primary sample. Given the relatively large test-retest intervals, significant changes in overall health may have occurred between the two time points which could negatively affect reliability coefficients. In an attempt to control for changes in health functioning between baseline and follow-up, additional test-retest analyses were conducted using only participants with stable clinical status.

BDI Total scores were used to determine clinical stability because they reflect

both affective and somatic symptomology. As such, changes in BDI-Total scores likely reflect changes in clinical status. Two definitions of mood stability were used for this study. The more restrictive mood sample was based on BDI-Total score differences of less than 4 points between baseline and follow-up. A larger sample size was obtained using a more lenient definition of clinical stability, namely BDI-Total score differences of less than 6 points. These cutoff scores were arbitrarily chosen with the intention of maximizing sample sizes while minimizing the difference between baseline and follow-up depression scores.

Reliability coefficients of the mood stable samples were calculated for test-retest intervals of 3-months (supplementary sample) and 1.3 years (primary sample). Similar analyses with 6- and 9- month test-retest intervals (supplementary sample) were not conducted because of the smaller initial sample size. Correlation coefficients obtained with the mood stable and overall subjects were compared using $\underline{z}$-tests (α_1=.05; see p. 307, Glass & Hopkins, 1984) in order to determine if significant improvements in reliability occurred when controlling for mood status.

PART III. Clinical Utility of the MOS-HIV

Univariate regressions were performed for each of the MOS-HIV dimensions and factors using demographic information (age, gender, years of education, Caucasian vs. non-Caucasian race), HIV status variables (asymptomatic and symptomatic subjects vs. those with a history of AIDS defining-conditions, CD4 count), medical and depressive (BDI-Affective score) symptoms, and neurocognitive performance (Grooved Pegboard, Digit Span, Digit Symbol, and CVLT-Total score). Variables that significantly predicted each of the MOS-HIV scores were then entered together in a multiple regression analysis, in order to determine which of the variables were the strongest unique predictors. The backwards variable entry/removal technique was chosen because it allowed for all variables to be initially evaluated together. Variables that did not contribute any significant unique variance were then excluded from the final regression equation.

RESULTS

There were three major objectives of this research study: **PART I.** Factor analysis of the MOS-HIV items and dimensions were performed using data collected at baseline and approximately 1 year later, in order to determine the factor structure and factor stability of the MOS-HIV items and dimensions. **PART II.** The test-retest reliability of MOS-HIV dimensions and factor scores was calculated in order to better understand the psychometric properties of this HRQOL instrument. **PART III.** The clinical utility of the MOS-HIV was determined by examining the extent to which demographic (age, education, race, and gender), medical (medical symptoms, CD4 counts, and AIDS-defining conditions), and neurobehavioural (depression and neuropsychological performance) variables impact upon various domains of HRQOL. The results of each of these analyses are discussed below.

PART I. FACTOR STRUCTURE OF THE MOS-HIV

Prior to conducting the factor analyses, the MOS-HIV dimensions and item scores were screened. These measures had adequate normality, with no significant skewness or kurtosis. There were no univariate outliers. One multivariate outlier was identified using the Mahalanobis Distance technique (Tabachnick & Fidell, 1996) at both baseline and follow-up for the 10 MOS-HIV dimensions. Examination of the 34 MOS-HIV items revealed 11 multivariate outliers at baseline and 3 outliers at follow-up. No significant differences occurred between factor analyses conducted with samples including and excluding outliers for the MOS-HIV dimensions at baseline and follow-up, and the MOS-HIV items at baseline. However, the factor solution for the MOS-HIV items at follow-up differed when outlier subjects were included in the analyses (i.e., splitting of the Mental Health/Fatigue factor into two separate Mental Health and Fatigue factors). To be consistent, the factor analysis results obtained from samples excluding the outlier variables will be presented below.

The factor analysis results described in this study were obtained using

principle axis factoring with promax rotation. It should be noted that as a result of using an oblique rotation technique, factor loadings that exceeded 1.000 were obtained. Higher factor loadings represent stronger associations of MOS-HIV dimensions or items with obtained factors. As such, factor loadings greater than .700 indicate stronger associations while loadings less than .300 indicate weaker associations. The results obtained with various factor analysis extraction methods (i.e., principle components analysis, maximum likelihood, principle axis factoring) and rotation techniques (i.e., varimax, promax, oblimin) were generally comparable, with the exception of the maximum likelihood factor extraction technique in the factor analysis of baseline MOS-HIV items.

A. Factor Structure of the 10 MOS-HIV Dimensions

A1. Factor Structure at Baseline. The 10 dimensions of the MOS-HIV were reduced to two factors, Mental and Physical Health Summary Scores (MHS and PHS, respectively). Together, these factors accounted for 61 percent of the total variance of the MOS-HIV dimensions (see Table 6). PHS had an eigenvalue of 4.66 and accounted for 53 percent of the variance. Physical Functioning, Role Functioning, Pain, Social Functioning, Overall Health, and Fatigue loaded more strongly on PHS than MHS. With an eigenvalue of 4.59, MHS accounted for 8 percent of the variance. It was strongly and independently influenced by Mental Health, Quality of Life, Health Distress, and Cognitive Function dimensions. Fatigue and Overall Health loaded on both PHS and MHS, although associations were stronger for PHS.

A2. Factor Structure at Follow-Up. MHS and PHS factors were also produced from factor analysis of the MOS-HIV dimensions at follow-up (see Table 7). MHS had an eigenvalue of 5.01 and accounted for 57 percent of the variance. It was most strongly influenced by Mental Health, Quality of Life, Health Distress, Overall Health, Cognitive Function, and Fatigue dimensions. Physical Function,

Table 6. Rotated FA Factor Matrix of the 10 MOS-HIV Dimensions at Baseline

MOS-HIV Dimensions	Summary Factors		Communality[a]
	Physical Health (PHS)	Mental Health (MHS)	
Physical Function	**.894**	-.125	.660
Role Function	**.793**	-.143	.492
Pain	**.659**	.089	.524
Social Function	**.609**	.211	.593
Overall Health	**.506**	**.331**	.597
Fatigue	**.515**	**.402**	.714
Cognitive Function	.288	**.401**	.404
Health Distress	.145	**.676**	.613
Quality of Life	-.052	**.841**	.649
Mental Health	-.183	**1.038**	.848
Eigenvalue	4.66	4.59	
Percent Variance	53.27	7.69	60.95

[a] the variance of each dimension which is accounted for by MHS and PHS

Table 7. Rotated FA Factor Matrix of the 10 MOS-HIV Dimensions at Follow-Up

MOS-HIV Dimensions	Summary Factors		Communality[a]
	Mental Health (MHS)	Physical Health (PHS)	
Mental Health	**1.002**	-.144	.818
Quality of Life	**.899**	-.096	.694
Health Distress	**.666**	.162	.624
Overall Health	**.537**	**.347**	.676
Cognitive Function	**.416**	**.368**	.528
Fatigue	**.391**	**.502**	.686
Role Function	.091	**.568**	.405
Social Function	.209	**.654**	.668
Pain	.031	**.760**	.613
Physical Function	-.222	**.974**	.688
Eigenvalue	5.01	4.95	
Percent Variance	56.89	7.10	63.99

[a] the variance of each dimension which is accounted for by MHS and PHS

Pain, Social Function, Role Function, Fatigue, Cognitive Function, and Overall Health loaded highly on PHS. PHS had an eigenvalue of 4.95 and accounted for 7 percent of the variance. Overall Health, Fatigue, and Cognitive Function were associated with both factors. Together, MHS and PHS accounted for 64 percent of the total variance of the MOS-HIV dimensions.

A3. Comparison of Baseline and Follow-Up Factor Structure Results. Both baseline and follow-up factor analysis results indicated the presence of two factors, MHS and PHS, which accounted for over 60 percent of the total variance of the MOS-HIV dimensions. These factors were generally consistent for the baseline and follow-up analyses. Mental Health, Quality of Life, and Health Distress loaded on MHS while Physical Function, Pain, Social Function, and Role Function loaded on PHS. Overall Health and Fatigue consistently loaded on both factors. Cognitive Function loaded on MHS at baseline and on both factors (although more strongly on MHS) at follow-up.

B. Factor Structure of the 34 MOS-HIV Items

B1. Factor Structure at Baseline. Factor analysis of the 34 MOS-HIV items at baseline produced 6 factors. These factors accounted for 65 percent of the total item variance (see Table 8).

(i) Mental Health Factor. Mental Health accounted for 43 percent of the variance and had an eigenvalue of 11.2. Mental Health and Quality of Life had the highest loadings on this factor, along with the "feeling full of pep" item from the Fatigue dimension and the "feeling bad lately" item from the Overall Health dimension.

(ii) Functional Status Factor. Pain and Role Function dimension items, as well as most of the Fatigue dimension items (i.e., "lacking the energy to do what is wanted", "feeling worn out", and "feeling tired") loaded most strongly on the second factor. Social Function also weakly loaded on this factor (loading=.315).

Table 8. Rotated FA Factor Matrix of the 34 MOS-HIV Items at Baseline

MOS-HIV Items	Factors						
	Mental Health	Function-al Status	Health Distress	Cognitive Function	Overall Health	Physical Function	Commu-nality[a]
8d (MH)	**-.969**	.131	.078	.087	-.147	-.147	.754
8b (MH)	**-.900**	.203	.045	.019	-.180	.016	.706
8c (MH)	**.722**	.123	.177	.060	-.200	-.067	.721
8e (MH)	**.638**	.170	.283	.003	-.252	-.095	.666
12 (QL)	**-.634**	.008	-.260	.088	-.042	-.029	.645
9a (FT)	**-.573**	-.145	.236	-.013	**-.407**	.057	.668
8a (MH)	**.551**	-.163	.163	.240	-.093	.082	.538
11d (OH)	**.447**	.040	.262	.033	.160	.013	.636
2 (PN)	-.187	**-.874**	.113	.063	.212	-.028	.637
3 (PN)	-.132	**-.819**	.022	.088	.216	-.143	.664
6 (RF)	-.271	**.783**	.150	.011	.218	-.208	.562
5 (RF)	**-.421**	**.710**	.171	-.016	.253	-.119	.487
4a (PF)	.099	**.553**	-.191	-.063	.211	.148	.571
9b (FT)	.255	**.518**	.010	.127	.081	-.054	.670
9c (FT)	.151	**.488**	.056	.206	.055	-.063	.596
9d (FT)	-.237	**-.328**	.012	-.133	-.277	.074	.573
7 (SF)	.060	**.315**	.174	.087	.143	.168	.568
9g (HD)	.100	.022	**.877**	.007	-.024	-.026	.884
9f (HD)	.115	.027	**.800**	-.027	.052	.053	.859
9h (HD)	.013	-.133	**.759**	.074	.086	.088	.662
9e (HD)	.114	.141	**.678**	-.114	.089	.088	.763
10c (CF)	.033	-.172	-.041	**.998**	.044	-.005	.847
10d (CF)	-.001	-.094	-.003	**.948**	.061	.020	.853
10a (CF)	.122	.059	.098	**.701**	-.060	-.047	.694
10b (CF)	-.149	.255	-.037	**.676**	-.113	.045	.522
11b (OH)	-.048	.132	-.025	-.040	**-.826**	-.201	.645
11c (OH)	-.055	-.060	-.043	.058	**-.816**	.003	.777
11a (OH)	-.016	.048	.124	-.012	**.600**	-.007	.454
1 (OH)	-.175	-.244	-.012	.087	**-.361**	-.175	.561
4e (PF)	-.046	-.107	.098	-.014	-.054	**.882**	.656
4f (PF)	.012	-.173	.122	-.026	-.002	**.777**	.513
4d (PF)	-.154	.203	.019	.036	.073	**.602**	.571
4b (PF)	-.006	**.439**	-.089	.002	.010	**.474**	.635
4c (PF)	-.051	**.319**	-.136	.156	.085	**.464**	.599
Eigenvalue	11.18	11.66	9.13	8.75	8.38	7.59	
% Variance	43.22	8.13	5.07	3.93	2.52	2.31	65.17

CF=Cognitive Function; FT=Fatigue; HD=Health Distress; MH=Mental Health; OH=Overall Health; PF=Physical Function; PN=Pain; QL=Quality of Life; RF=Role Function; SF=Social Function

[a] the variance of each variable which is accounted for by all of the factors

The Functional Status factor had an eigenvalue of 11.7 and accounted for 8 percent of the item variance.

(iii) Health Distress Factor. The Health Distress factor accounted for 9 percent of the variance and had an eigenvalue of 9.1. It was composed of the four items from the Health Distress dimension which all loaded highly on this factor.

(iv) Cognitive Function Factor. The four Cognitive Function dimension items loaded highly on the Cognitive Function factor. Cognitive Function had an eigenvalue of 8.8 and accounted for 4 percent of the item variance.

(v) Overall Health Factor. Four of the five Overall Health dimension items loaded together on the Overall Health factor. Loadings were high (i.e., ≥.6), with the exception of the general health rating item (item number 1; loading=.361). Overall Health accounted for 3 percent of the variance and had an eigenvalue of 8.4.

(vi) Physical Function Factor. The Physical Function factor was composed of five Physical Function dimension items and accounted for 2 percent of the variance. It had an eigenvalue of 7.6. Loadings were higher for the less intensive activities (e.g., walking uphill or climbing stairs, bending or lifting, walking one block, and eating, dressing, or bathing) as compared to moderate and vigorous activities (e.g., lifting or moving heavy objects, participating in sports).

As mentioned previously, there were some inconsistences in the factor solution obtained with Maximum Likelihood as compared to the Principle Components Analysis and Principle Axis Factoring techniques. Mental Health/Quality of Life, Overall Health, Health Distress, and Cognitive Function factors remained consistent for all analyses. However, instead of the Functional Status and Physical Function factors described above, the Maximum Likelihood analysis resulted in a fifth factor composed of Pain and Role, Social, and Physical Function dimensions, and a sixth factor composed of two Fatigue dimension items (i.e., "feeling worn out" and "feeling tired" using Oblimin rotation and "feeling tired"

and "having enough energy to do what is wanted" using Promax rotation).

B2. Factor Structure at Follow-Up. Five factors were obtained from factor analysis of the MOS-HIV items at follow-up (see Table 9). These factors accounted for 65 percent of the total item variance.

(i) Mental Health/Fatigue. All of the Mental Health and Quality of Life dimension items, three of the four Fatigue dimension items, and the "feeling bad lately" item from the Overall Health dimension loaded on the Mental Health/Fatigue factor. This factor accounted for 46 percent of the variance and had an eigenvalue of 13.3.

(ii) Physical Function/Pain. All of the Physical Function and Pain dimension items loaded together on the Physical Function/Pain factor. This factor was also most highly associated with the Social Function and "having enough energy to do what is wanted" item from the Fatigue dimension; however, the loadings of these items was very weak (i.e., less than .300). The Physical Function/Pain factor accounted for 7.9 percent of the item variance and had an eigenvalue of 10.3.

(iii) Role Function/Overall Health. The Role Function/Overall Health factor was composed of the two Role Function and four of the five Overall Health dimension items. It had an eigenvalue of 11.5 and accounted for 5 percent of the item variance.

(iv) Cognitive Function Factor. The four Cognitive Function dimension items loaded strongly on the Cognitive Function factor. This factor accounted for 3 percent of the variance and had an eigenvalue of 9.6.

(v) Health Distress Factor. With an eigenvalue of 7.6, the Heath Distress factor accounted for 3 percent of the item variance. It was composed of the four Health Distress dimension items.

Table 9. Rotated PCA Factor Matrix of the 34 MOS-HIV Items at Follow-up

MOS-HIV Items		Factors					Commu-nality[a]
		Mental/ Fatigue	Physical/ Pain	Role/ Overall	Cognitive Function	Health Distress	
8d	(MH)	**-1.014**	.063	.127	.102	-.060	.778
8b	(MH)	**-.906**	.094	.092	-.033	-.032	.705
8c	(MH)	**.891**	-.132	-.242	.121	.200	.798
8e	(MH)	**.791**	-.003	-.254	.130	.116	.629
9a	(FT)	**-.711**	-.121	-.252	.133	.215	.658
12	(QL)	**-.644**	.164	-.142	-.101	-.121	.640
9b	(FT)	**.623**	.163	.153	.065	-.130	.677
11d	(OH)	**.594**	-.172	.209	.000	.271	.707
9c	(FT)	**.579**	.167	**.325**	-.055	-.201	.691
8a	(MH)	**.537**	.007	-.037	.218	.054	.494
4d	(PF)	.016	**1.070**	**-.300**	-.081	.064	.764
4e	(PF)	-.147	**.852**	-.181	-.034	.265	.561
4b	(PF)	-.100	**.773**	.086	.062	-.067	.638
4c	(PF)	-.204	**.752**	.109	.077	.106	.644
4a	(PF)	.032	**.533**	**.335**	-.067	-.071	.583
3	(PN)	-.163	**-.500**	-.105	-.141	.050	.580
2	(PN)	-.286	**-.487**	-.084	-.082	.159	.559
4f	(PF)	-.177	**.416**	.085	-.078	.218	.197
7	(SF)	.153	.293	.212	.224	.111	.635
9d	(FT)	-.289	-.290	-.183	-.180	.003	.619
6	(RF)	-.272	-.075	**.880**	.180	-.005	.574
5	(RF)	-.252	-.089	**.764**	.324	-.031	.528
11b	(OH)	-.202	.013	**-.742**	.265	-.072	.640
11c	(OH)	-.081	-.001	**-.699**	.107	-.157	.612
11a	(OH)	-.024	-.041	**.639**	-.034	.189	.455
1	(OH)	**-.333**	-.085	**-.422**	.060	-.128	.624
10d	(CF)	.006	.003	.045	**.837**	.010	.759
10c	(CF)	.117	.031	-.006	**.835**	-.098	.776
10a	(CF)	.154	-.134	.035	**.760**	.072	.718
10b	(CF)	.007	.123	.000	**.746**	.042	.712
9h	(HD)	.019	.149	.061	.003	**.719**	.676
9f	(HD)	.127	.071	.223	-.035	**.714**	.873
9g	(HD)	.290	.097	-.111	.035	**.697**	.803
9e	(HD)	.246	.054	.179	.033	**.575**	.809
Eigenvalue		13.25	10.30	11.47	9.59	7.59	
% Variance		46.25	7.91	4.59	3.44	2.86	65.04

CF=Cognitive Function; FT=Fatigue; HD=Health Distress; MH=Mental Health; OH=Overall Health; PF=Physical Function; PN=Pain; QL=Quality of Life; RF=Role Function; SF=Social Function

[a] the variance of each variable which is accounted for by all of the factors

B3. Comparison of Baseline and Follow-Up Factor Structure Results. Six factors were produced from the MOS-HIV items at baseline while five factors were produced at follow-up. Health Distress and Cognitive Function factors were consistently obtained at baseline and follow-up. The (4-item) Mental Health, (6-item) Overall Health, and (5-item) Physical Function factors were similar for both analyses although additional items were included with these factors at follow-up that were in the baseline Functional Status factor. Specifically, the 2 Fatigue items loaded with Mental Health, the 2 Role Function items loaded with Overall Health, and the 2 Pain items and 1 Physical Function item loaded together to form a Physical Function/Pain factor.

C. Intercorrelations of MOS-HIV Item- and Dimension-Based Factors

The use of an oblique (rather than orthogonal) rotation technique was supported by the intercorrelations of the factors, as shown in Table 10. For the Item based factors, Pearson correlations ranged from .38 for Overall Health and Cognitive Function to .83 for Functional Status and Physical Function. PHS and MHS were highly correlated (r=.73). Examination of the correlations between item- and dimension-based factors indicated the same pattern as dimension loadings on dimension factors, namely, stronger relationships for Physical Function and Functional Status factors with PHS and Mental Health and Health Distress with MHS. Overall Health and Cognitive Function items had similar association with both MHS and PHS.

D. Summary of the MOS-HIV Factor Structure Analyses

Factor analysis of the 10 MOS-HIV dimensions at baseline and follow-up resulted in Mental and Physical Health Summary factors (MHS and PHS, respectively). Examination of the factor structure of the 34 MOS-HIV items revealed Health Distress, Cognitive Function, Mental Health, Overall Health, and Physical Function factors. In addition, a Functional Status factor was obtained at baseline.

Table 10. Intercorrelations of MOS-HIV Item- and Dimension-Based Factors

	Item-Based Factors					Dimension-Based Factors	
Item-Based Factors	**Functional Status**	**Overall Health**	**Cognitive Function**	**Health Distress**	**Mental Health**	**Physical Health (PHS)**	**Mental Health (MHS)**
Physical Function	.83	.59	.52	.47	.48	.90	.56
Functional Status		.60	.64	.61	.69	.96	.75
Overall Health			.38	.50	.51	.68	.56
Cognitive Function				.54	.65	.64	.67
Health Distress					.75	.65	.85
Mental Health						.64	.97

Dimension-Based Factors	**Mental Health (MHS)**
Physical Health (PHS)	.73

Pearson correlations are all $p < .001$

Overall, the factor structure of the MOS-HIV items and dimensions was generally consistent at baseline and follow-up. MOS-HIV factors were moderately to highly intercorrelated.

It should be noted that the sample size of the baseline and follow-up samples were 231 and 136, respectively. Ideally, a sample size of 300 should be available for analysis (Tabachnick & Fidel, 1996). Although a larger sample was not available, factor analysis results of the MOS-HIV dimension and items produced very similar solutions at baseline and follow-up, indicating factor stability. Additional research using larger sample sizes is required to confirm the factor structure of the MOS-HIV items. The regression equations derived from the baseline factor scores were used to calculate the factor scores at follow-up because there was a larger sample size at baseline. By using the same factor score equations, factor scores could be more readily comparable than factor scores derived from different regression equations. These obtained factor scores were used in both the MOS-HIV summary factor test-retest reliability and clinical utility analyses.

PART II. TEST-RETEST RELIABILITY OF MOS-HIV DIMENSIONS

In previous research, examination of the psychometric properties of the MOS-HIV has typically excluded analysis of test-retest reliability. Therefore, this study was designed to determine the test-retest reliability of the MOS-HIV dimensions and factor scores. Test-retest coefficients were calculated for four test-retest intervals, specifically 3-, 6-, 9- month (supplementary sample) and 1.3 year (primary sample). Reliability values were obtained using intraclass and Pearson correlation coefficients (see Tables 11, 12, and 13). Spearman correlation coefficients were also calculated to determine if correlation values were influenced by any non-normality of the MOS-HIV dimension and factor score distributions, even though no significant skewness or kurtosis of the data was found. The results of the Pearson and Spearman correlation analyses were generally consistent. As such, it was decided that the results obtained using parametric analysis (i.e., Pearson

correlations) would be presented for the test-retest analyses.

For the purposes of this study, high reliability coefficients were defined as scores greater than or equal to .70. Moderate scores are those with values from .50 to .69. Finally, low reliability scores were defined as values less than .50.

A. Overall Samples

The test-retest reliability coefficients for the MOS-HIV dimensions and factor scores using the entire sample are presented in Table 11. Test-retest intervals ranged from 3-months to 1.3 years.

A1. MOS-HIV Dimensions. High reliability coefficients generally occurred for only the Overall Health dimension. Fatigue, Physical Function, Pain, Health Distress, Social Function, and Cognitive Function had moderate to high test-retest reliability scores. Poor to moderate reliability coefficients occurred for Mental Health, Role Function, and Quality of Life.

A2. MOS-HIV Item-Based Factors. Test-retest coefficients were also determined for the MOS-HIV item-based factors. Moderate to high test-retest reliability scores occurred for Functional Status, Overall Health factors, and Physical Function factors. Cognitive Function, Mental Health and Health Distress generally had poor to moderate test-retest reliability scores, with the lowest scores for the largest test-retest interval (i.e., 1.3-year delay primary sample).

A3. MOS-HIV Dimension-Based Factors. Test-retest reliabilities for MOS-HIV dimension-based factors were generally moderate to high for PHS and MHS.

B. Clinically Stable Samples

Test-retest reliability analyses were also conducted using clinically stable samples, as test-retest intervals were relatively long and changes in clinical function may have occurred that could impact upon HRQOL. As a result, MOS-HIV scores

Table 11. MOS-HIV Test-Retest Reliabilities for the Overall Primary and Supplementary Samples

MOS-HIV Dimensions	MOS-HIV Test-Retest Intervals							
	Supplementary Sample						Primary Sample	
	3.3 Months (SD=.9) **All Subjects** (n=65)		**6.0 Months** (SD=.9) **All Subjects** (n=59)		**9.1 Months** (SD=1.3) **All Subjects** (n=45)		**1.3 Years** (SD=.8) **All Subjects** (n=100)	
	ICC[a]	r[b]	ICC[a]	r[b]	ICC[a]	r[b]	ICC[a]	r[b]
Physical Function	.50**	.51**	.53**	.55**	.58**	.58**	**.70****	.69**
Role Function	.56**	.57**	.36*	.38*	.54**	.57**	.63**	.63**
Pain	.52**	.52**	.52**	.52**	.65**	.65**	.66**	.66**
Social Function	.59**	.61**	.50**	.51**	.48**	.49*	.54**	.56**
Overall Health	**.71****	**.72****	**.71****	**.71****	**.78****	**.78****	.67**	.67**
Fatigue	**.72****	**.72****	.53**	.53**	**.80****	**.80****	.51**	.53**
Cognitive Function	.68**	**.71****	.63**	.65**	.58**	.60**	.46**	.50**
Health Distress	.58**	.64**	.60**	.61**	.69**	**.70****	.49**	.50**
Quality of Life	.67**	**.70****	.43**	.43*	.48**	.48*	.24*	.26*
Mental Health	.65**	.66**	.41**	.43*	.65**	.67**	.43**	.45**
Item Factors								
Physical Function	.57**	.58**	.56**	.57**	.59**	.59**	**.71****	**.71****
Functional Status	**.73****	**.73****	.67**	.67**	**.83****	**.83****	.69**	.69**
Overall Health	**.71****	**.73****	.69**	.69**	**.81****	**.81****	**.70****	**.70****
Cognitive Function	.68**	**.71****	.64**	.65**	.59**	.60**	.47**	.51**
Health Distress	.50**	.57**	.51**	.52**	.65**	.67**	.44**	.46**
Mental Health	.67**	.68**	.53**	.54**	**.70****	**.72****	.43**	.45**
Dimension Factors								
Physical Health	**.74****	**.75****	.67**	.69**	**.77****	**.78****	**.72****	**.73****
Mental Health	**.73****	**.76****	.58**	.60**	**.72****	**.73****	.47**	.50**

* $p<.01$; ** $p<.001$; otherwise $p<.05$ for shown values

[a] Two-way mixed effect intraclass correlation coefficient (absolute agreement definition)

[b] Pearson correlation coefficient

could change over time, and because of these changes, the results of the correlational analyses may not accurately reflect the test-retest reliability of the MOS-HIV scales. Clinical stability was defined in two ways using the BDI-Total score changes between baseline and follow-up. The more restricted clinically-stable sample had BDI-Total score changes of less than four points while the more inclusive sample had score changes of less than six points. This analysis was conducted using the supplementary sample for 3-month test-retest interval and the primary sample for the 1-year test-retest interval. Analysis of the 6- and 9-month test-retest interval subjects was not conducted because of the smaller sample size. Reliability values for the complete and clinically stable samples are presented in Table 12 for the 3-month test-retest interval group and Table 13 for the 1-year test-retest interval group. Results of the mood stable test-retest analyses generally produced higher correlation coefficients for the 1-year test-retest interval sample, even though the test-retest interval was approximately five times longer than the 3-month test-retest interval sample.

In addition to calculating the reliabilities for the MOS dimensions and factors, the overall and mood stable samples were compared to determine if significant differences in reliability coefficients occurred (underlined values in Table 12 and 13). It is important to note that the determination of correlation coefficient differences was dependant on sample size. As such, it is likely that additional MOS-HIV dimensions and factors would have significantly higher scores for the mood stable subjects than overall group if sample sizes were larger.

B1. MOS-HIV Dimensions. Overall Health, Mental Health, Cognitive Function, and Fatigue had high reliability coefficients. Moderate test-retest scores generally occurred for Physical Function, Health Distress, Quality of Life, and Social Function. Role Function and Pain had poor 3-month correlation coefficients, even though scores were adequate for test-retest intervals greater than 1 year.

In the 3-month test-retest reliability sample, only the restrictive mood stable

Table 12. MOS-HIV Test-Retest Reliabilities for Supplementary Complete and Mood Stable Samples

MOS-HIV	MOS-HIV Test-Retest Intervals					
	3.3 Mths (SD=.9) **All Subjects** (n=65)		**3.3 Mths** (SD=.4) **BDI Total Δ<4** (n=28)		**3.4 Mths** (SD=.7) **BDI Total Δ<6** (n=40)	
Dimensions	ICC[a]	r[b]	ICC[a]	r[b]	ICC[a]	r[b]
Physical Function	.50**	.51**	.64**	.65**	.60**	.62**
Role Function	.56**	.57**	.40	.40	.40*	.40
Pain	.52**	.52**	ns	ns	ns	ns
Social Function	.59**	.61**	.54*	.53*	.61**	.61**
Overall Health	**.71****	**.72****	**.78****	**.78****	**.77****	**.77****
Fatigue	**.72****	**.72****	**.76****	**.75****	**.70****	.69**
Cognitive Function	.68**	**.71****	**.78****	**.78****	**.73****	**.75****
Health Distress	.58**	.64**	**.75****	**.79****	.62**	.65**
Quality of Life	.67**	**.70****	.62**	.61*	.62**	.61**
Mental Health	.65**	.66**	**.84****	**.84****	**.72****	**.72****
Item Factors						
Physical Function	.57**	.58**	.67**	.67**	.63**	.64**
Functional Status	**.73****	**.73****	.62**	.62**	.63**	.62**
Overall Health	**.71****	**.73****	**.81****	**.81****	**.75****	**.75****
Cognitive Function	.68**	**.71****	**.73****	**.73****	.65**	.65**
Health Distress	.50**	.57**	**.74****	**.79****	.54**	.57**
Mental Health	.67**	.68**	**.83****	**.82****	**.77****	**.77****
Dimension Factors						
Physical Health	**.74****	**.75****	**.74****	**.74****	**.73****	**.74****
Mental Health	**.73****	**.76****	**.86****	**.86****	**.81****	**.82****

BDI Total = Beck Depression Inventory-Total Score; Mths=Months; ns= not significant
Underlined correlation coefficient values are significantly higher for the mood stable sample than the complete sample (z-test, for $\alpha_1 = .05$)
* p<.01; ** p<.001; otherwise p<.05 for shown values
[a] Two-way mixed effect intraclass correlation coefficient (absolute agreement definition)
[b] Pearson correlation coefficient

Table 13. MOS-HIV Test-Retest Reliabilities for Primary Complete and Mood Stable Samples

MOS-HIV Dimensions	MOS-HIV Test-Retest Intervals: 1.3 Years (SD=.8) All Subjects (n=100) ICC[a]	1.3 Years r[b]	1.4 Years (SD=.7) BDI Total Δ<4 (n=36) ICC[a]	1.4 Years r[b]	1.6 Years (SD=.9) BDI Δ<6 (n=48) ICC[a]	1.6 Years r[b]
Physical Function	**.70****	.69**	**.73****	**.77****	**.72****	**.74****
Role Function	.63**	.63**	**.72****	**.72****	.63**	.63**
Pain	.66**	.66**	**.80****	**.83****	**.76****	**.79****
Social Function	.54**	.56**	**.77****	**.76****	.69**	.69**
Overall Health	.67**	.67**	**.85****	**.85****	**.81****	**.81****
Fatigue	.51**	.53**	**.80****	**.80****	**.70****	.69**
Cognitive Function	.46**	.50**	**.70****	**.72****	**.70****	**.71****
Health Distress	.49**	.50**	**.79****	**.79****	**.79****	**.79****
Quality of Life	.24*	.26*	.65**	.67**	.63**	.63**
Mental Health	.43**	.45**	**.83****	**.83****	**.82****	**.82****
Item Factors						
Physical Function	**.71****	**.71****	**.73****	**.77****	**.73****	**.75****
Functional Status	.69**	.69**	**.91****	**.92****	**.83****	**.84****
Overall Health	**.70****	**.70****	**.80****	**.80****	**.81****	**.81****
Cognitive Function	.47**	.51**	**.75****	**.77****	**.73****	**.74****
Health Distress	.44**	.46**	**.77****	**.77****	**.76****	**.76****
Mental Health	.43**	.45**	**.86****	**.87****	**.84****	**.84****
Dimension Factors						
Physical Health	**.72****	**.73****	**.91****	**.91****	**.85****	**.85****
Mental Health	.47**	.50**	**.88****	**.88****	**.86****	**.86****

BDI Total = Beck Depression Inventory-Total Score

Underlined correlation coefficient values are significantly higher for the mood stable sample than the complete sample (z-test, for $\alpha_1 = .05$)

* p<.01; ** p<.001; otherwise p<.05 for shown values

[a] Two-way mixed effect intraclass correlation coefficient (absolute agreement definition)

[b] Pearson correlation coefficient

(i.e., BDI-Total score change <4 points) supplementary sample had significantly higher correlation coefficient scores for Mental Health than the overall sample. In the primary sample, higher reliability coefficients generally occurred for both mood stable groups, as compared to the overall sample, for Overall Health, Cognitive Function, Health Distress, Quality of Life, Mental Health, and Fatigue. In addition, the more restrictive mood stable primary sample (i.e., BDI-Total score change <4 points) had significantly better reliability for Social Function (intraclass and Pearson correlation coefficients) and Pain (Pearson correlation coefficients only) than the overall primary sample.

B2. MOS-HIV Item-Based Factors. For all of the mood-stable samples, Mental Health and Overall Health had high test-retest reliabilities. Moderate to high test retest reliabilities occurred for Physical Function, Cognitive Function, Functional Status, and Health Distress.

In the restrictive mood stable (BDI-Total score change <4 points) supplementary sample, the Health Distress item-based factor had significantly higher 3-month test-retest reliability coefficients as compared to the overall sample. Functional Status, Cognitive Function, Health Distress, and Mental Health reliability coefficients were significantly higher in the mood stable primary sample groups than the overall group for 1-year test-retest reliability intervals.

B3. MOS-HIV Dimension-Based Factors. PHS and MHS correlation coefficients were high for all mood stable samples. Significantly higher reliability scores for MHS and PHS occurred in the mood stable primary sample than then overall sample for 1-year test-retest reliability intervals. There were no significant differences in reliability coefficients for the mood stable and overall samples for the 3-month test-retest interval supplementary sample.

C. Summary of Overall Test-Retest Reliability Analyses

Based on the results from the overall and mood stable samples, the following conclusions can be drawn. High test-retest reliability coefficients were obtained for Overall Health, Mental Health, Cognitive Function, and Fatigue dimensions. Health Distress, Quality of Life, Physical Function, and Social Function dimensions had moderate to high reliability, while Role Function and Pain dimensions had unacceptable test-retest reliability.

MOS-HIV factors generally had acceptable test-retest reliability. Overall Health and Mental Health item-based factors had high reliability coefficients, while Cognitive Function, Physical Function, Health Distress, and Functional Status item-based factors had moderate to high reliability values. The MOS-HIV dimension-based factors, MHS and PHS, both had high test-retest reliabilities.

PART III. CLINICAL UTILITY OF THE MOS-HIV

The clinical utility of the MOS-HIV dimensions and factor scores was examined by determining the impact of demographic, medical status, depression, and neuropsychological variables on HRQOL function. The relationship of these variables to MOS-HIV measures was identified using baseline and follow-up data. In addition, changes scores (i.e., subtracting baseline from follow-up scores) were obtained in order to identify medical and neurobehavioural predictor variables that had the greatest impact on changes in various MOS-HIV domains. Following data screening, significant predictor variables of MOS-HIV measures were identified using univariate regression analyses. Significant predictors for each MOS-HIV measure were then entered together in a multivariate regression analysis to determine the most important predictors for each aspect of HRQOL.

Preliminary screening of the variables revealed 30 univariate outliers (i.e., Z-scores >+/- 3.0: (A) Baseline: 3 CD4 count outliers, 1 medical symptom score outlier, 1 BDI-Affective outlier, 1 CVLT-Total score outlier, and 3 Physical Function dimension outliers; (B) Follow-Up: 3 CD4 outliers, 3 medical symptom outliers, 2

BDI-Affective outliers, and 3 Grooved Pegboard outliers; (C) Change Scores: 4 CD4 count outliers; 2 Functional Status item-based factor outliers; 1 Overall Health item-based factor outlier; 3 Physical Function item-based factor outliers). The outlier values were modified to become one measurement unit larger/smaller than the next most extreme score in the distribution, in order to reduce their impact (as suggested by Tabachnick & Fidell, 1996). There were no multivariate outliers obtained after modification of univariate outliers at baseline. However, one multivariate outlier occurred for the follow-up data and 3 multivariate outliers occurred for the change score data. These outliers were excluded from the multiple regression analyses. Outliers did not differ from the remainder of the sample on any demographic, medical status, or clinical variables.

A. Univariate Analyses

Univariate regressions were performed for each MOS-HIV dimension and factor to identify significant predictor variables that were then used in a multivariate analysis. Predictor variables included demographic information (age, gender, years of education, Caucasian vs. non-Caucasian race), medical status (history of AIDS-related condition vs. no history of AIDS-related condition, recent CD4 count, and number of HIV-related medical symptoms), depressive symptoms (BDI-Affective score), and neuropsychological performance (Grooved Pegboard-dominant hand performance, Digit Span scaled score, Digit Symbol raw score, CVLT-Total Recall score). It should be noted that recent rather than nadir CD4 count values were used in the analysis because recent values had stronger relationships with more MOS-HIV measures than nadir CD4 counts. The R^2 values of the significant predictors of MOS-HIV dimensions and factors for the baseline, follow-up, and change score univariate regression analyses are presented in Table 14, 15 and 16.

A1. MOS-HIV Dimensions.

(i) Physical Function Dimension. At baseline and follow-up, Physical

Table 14. Univariate Regression Results for MOS-HIV Scores at Baseline (N=100)

MOS-HIV	Demographic Variables				Medical Variables			Depres.	Neurocognitive Performance			
	Age	Gender	Edu-cation	Race	AIDS Status	CD4 Count	Medical Sx.	BDI-Affective	Grooved Pegs	Digit Span	Digit Symbol	CVLT-Total
Dimensions	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2
Physical Function					.07		.24	.14	.19	.04	.19	.13
Role Function					.06	.05	.11		.06		.08	.05
Pain							.26	.22	.05		.08	
Social Function					.06		.23	.18	.08		.15	.08
Overall Health					.05		.18	.33	.09		.12	
Fatigue							.21	.32	.04		.04	
Cognitive Function							.18	.34	.05		.08	
Health Distress							.16	.37			.07	
Quality of Life							.09	.42				
Mental Health							.17	.70				
Item Factors												
Physical Function					.09		.28	.14	.19	.05	.22	.14
Functional Status							.32	.29	.08		.11	.04
Overall Health					.06		.10	.15	.09		.12	
Cognitive Function							.17	.37	.04		.07	
Health Distress							.14	.37			.06	
Mental Health							.19	.69				
Dimension Factors												
Physical Health					.06		.30	.25	.12		.17	.07
Mental Health							.22	.64			.05	

Depr.Sx.=depressive symptoms; Race (Caucasian vs. Other); Medical Sx =number of medical symptoms; BDI-Affective=Beck Depression Inventory-Affective Subscale score; Grooved Pegs=Grooved Pegboard time, dominant hand; CVLT=California Verbal Learning Test-Total Recall
$p < .05$ for shown values

Table 15. Univariate Regression Results for MOS-HIV Scores at Follow-Up (N=100)

	Demographic Variables				Medical Variables			Depres.	Neurocognitive Performance			
MOS-HIV	Age	Gender	Edu-cation	Race	AIDS Status	CD4 Count	Medical Sx.	BDI-Affective	Grooved Pegs	Digit Span	Digit Symbol	CVLT-Total
Dimensions	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2
Physical Function							.32	.10	.09		.13	.06
Role Function							.20	.09			.04	.04
Pain			.04				.25	.14	.04		.10	.08
Social Function							.30	.24	.07		.09	
Overall Health							.23	.22	.08		.12	
Fatigue							.31	.24	.05			
Cognitive Function							.19	.32	.12		.11	
Health Distress					.06	.04	.20	.32				
Quality of Life							.27	.47				
Mental Health	.07						.21	.69				
Item Factors												
Physical Function			.04				.36	.12	.10		.16	.07
Functional Status							.40	.25	.07		.12	.04
Overall Health					.05		.15	.08	.06		.06	
Cognitive Function							.21	.34	.11		.11	
Health Distress					.06	.04	.19	.35			.04	
Mental Health	.04						.27	.66				
Dimension Factors												
Physical Health							.42	.23	.09		.13	.05
Mental Health							.33	.64				

Depr.Sx.=depressive symptoms; Race (Caucasian vs. Other); Medical Sx =number of medical symptoms; BDI-Affective=Beck Depression Inventory-Affective Subscale score; Grooved Pegs=Grooved Pegboard time, dominant hand; CVLT=California Verbal Learning Test-Total Recall
$p < .05$ for shown values

Table 16. Univariate Regression Results for MOS-HIV Change Scores (N=100)

	Demographic Variables				Medical Variables			Depr. Sx.	Neurocognitive Performance			
MOS-HIV	Δ Age	Gender	Edu-cation	Race	Δ AIDS Status	Δ CD4 Count	Δ Med. Sx.	Δ BDI-Affective	Δ Groov. Pegs	Δ Digit Span	Δ Digit Symbol	Δ CVLT Total
Dimensions	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2	R^2
Physical Function							.06	.06				
Role Function									.08		.05	.04
Pain	.07						.09	.13			.06	
Social Function	.07				.05		.14	.12	.04			
Overall Health	.05							.25	.05		.09	
Fatigue	.11						.07	.24				
Cognitive Function	.11						.11	.25	.05		.14	
Health Distress	.04						.07	.39			.05	
Quality of Life		.06					.06	.39				
Mental Health	.11						.05	.63	.04			
Item Factors												
Physical Function	.04						.08	.05				
Functional Status	.11						.14	.27	.04		.08	
Overall Health								.07			.04	
Cognitive Function	.15						.09	.28			.12	
Health Distress							.06	.38	.04		.05	
Mental Health	.12						.08	.64	.05			
Dimension Factors												
Physical Health	.11						.15	.23	.07		.07	
Mental Health	.11						.09	.63	.05			

Depr. Sx.=depressive symptoms; Race (Caucasian vs. Other); Med. Sx =number of medical symptoms; BDI-Affective=Beck Depression Inventory-Affective Subscale score; Groov. Pegs=Grooved Pegboard time, dominant hand; CVLT=California Verbal Learning Test-Total Recall
$p < .05$ for shown values

Function dimension scores were significantly predicted by medical and depressive symptoms, and indicators of psychomotor speed and learning efficiency (Grooved Pegboard, Digit Symbol, and CVLT-Total Recall). AIDS status (defined by a history of an AIDS-defining condition) and Digit Span also accounted for a portion of the variance of Physical Function dimension at baseline. Physical Function change scores were associated with changes between baseline and follow-up in medical and depressive symptoms.

(ii) Role Function Dimension. At baseline, Role Function was predicted by medical symptoms, AIDS status, CD4 count, psychomotor speed, and learning efficiency (Digit Symbol score, Grooved Pegboard performance, and CVLT-Total Recall). Medical symptoms, depression, Digit Symbol score, and learning efficiency (CVLT-Total Recall) predicted Role Function at follow-up. Only neuropsychological variables, specifically Grooved Pegboard, Digit Symbol, and CVLT-Total Recall performance, predicted Role Function dimension change scores.

(iii) Pain Dimension. At baseline, Pain was associated with medical symptoms, BDI affective scores, and psychomotor efficiency (Grooved Pegboard and Digit Symbol). These variables, in addition to years of education and CVLT-Total recall, predicted Pain scores at follow-up. Changes in age, depression, medical symptoms, and Digit Symbol performance between baseline and follow-up were associated with Pain dimension change scores.

(iv) Social Function. Medical symptoms, depression, Digit Symbol scores, and Grooved Pegboard performance predicted Social Function at baseline and follow-up. In addition, AIDS status and CVLT-Total recall accounted for a portion of the variance of Social Function at baseline. Social Function change scores were predicted by differences in age, AIDS status, medical symptoms, depression, and Grooved pegboard scores between baseline and follow-up.

(v) Overall Health Dimension. AIDS status, medical symptoms, depression, Digit Symbol scores, and Grooved Pegboard performance predicted Overall Health at baseline. With the exception of AIDS status, these variable also

predicted follow-up Overall Health. Overall Health dimension change scores were associated with differences in age, depressive symptoms, Grooved Pegboard performance, and Digit Symbol scores between baseline and follow-up.

(vi) Fatigue Dimension. Both baseline and follow-up analyses indicated that depression scores, medical symptoms, and Grooved Pegboard performance significantly predict MOS-HIV Fatigue scores. In addition, Digit Symbol scores were associated with Fatigue at baseline. Changes in age, depression, and medical symptoms predicted Fatigue dimension change scores.

(vii) Cognitive Function Dimension. The Cognitive Function dimension was consistently predicted by depression, medical symptoms, Digit Symbol scores, and Grooved Pegboard performance. Differences in age, depression, medical symptoms, Digit Symbol scores, and Grooved Pegboard performance between baseline and follow-up were associated with Cognitive Function score changes.

(viii) Health Distress Dimension. Health Distress was predicted by medical symptoms, depression, and Digit Symbol scores at baseline. At follow-up, medical symptoms, depression, AIDS status, and CD4 counts were associated with Health Distress dimension scores. Change in Health Distress was predicted by age, medical symptoms, depression, and Digit Symbol performance changes between baseline and follow-up.

(ix) Quality of Life Dimension. Quality of Life dimension scores were associated medical and depressive symptoms in all analyses. In addition, gender had an impact on quality of life change scores; males had reported greater declines in Quality of Life over time.

(x) Mental Health Dimension. Medical and depressive symptoms predicted baseline and follow-up Mental Health scores. In addition, older age was associated with better reported Mental Health at follow-up. Differences between baseline and follow-up for age, medical symptoms, depression, and Grooved Pegboard performance were predictive of Mental Health dimension change scores.

A2. *MOS-HIV Item-Based Factors.*

(i) Physical Function Factor. At baseline and follow-up, Physical Function item factor scores were significantly predicted by medical symptoms, BDI-Affective scores and Grooved Pegboard, Digit Symbol, and CVLT-Total Recall performance. AIDS status (defined by a history of an AIDS-defining condition) and Digit Span also predicted Physical Function at baseline while years of education predicted Physical Function at follow-up. Physical Function change scores were accounted for by changes in age and medical and depressive symptoms.

(ii) Functional Status Factor. Baseline and follow-up Functional Status factor scores were predicted by medical symptoms, depression, and performance on Digit Symbol, Grooved Pegboard, and CVLT-Total Recall tasks. Changes in age, depression, medical symptoms, and psychomotor efficiency (Digit Symbol and Grooved Pegboard) between baseline and follow-up predicted Functional Status factor change scores.

(iii) Overall Health Factor. AIDS status, medical symptoms, depression, Digit Symbol scores, and Grooved Pegboard performance were predictive of Overall Health factor scores at baseline and follow-up. However, Overall Health factor change scores were only predicted by depressive symptoms and Digit Symbol scores.

(iv) Cognitive Function Factor. Cognitive Function was predicted by depression, medical symptoms, and psychomotor efficiency (Digit Symbol and Grooved Pegboard) at baseline and follow-up. Variations in age, depression, medical symptoms, and Digit Symbol scores between the two time points were also associated with Cognitive Function score changes.

(v) Health Distress Factor. Medical symptoms, depression, and Digit Symbol performance predicted Health Distress factor scores at baseline. These variables, in addition to AIDS status and CD4 count, were associated with follow-up Health Distress. Change in Health distress scores was predicted by differences in baseline and follow-up medical and depressive symptoms, Grooved Pegboard

performance, and Digit Symbol scores.

(vi) Mental Health Factor. Medical and depressive symptoms predicted Mental Health factor baseline, follow-up, and change scores. In addition, follow-up Mental Health scores were associated with age while change in Mental Health scores were associated with changes in age and Grooved Pegboard performance.

A3. MOS-HIV Dimension-Based Factors.

(i) PHS. At baseline and follow-up, PHS was predicted by medical symptoms, BDI-Affective scores, Digit Symbol performance, Grooved Pegboard scores, and CVLT-Total Recall. Also, 6 percent of the variance of PHS at baseline was predicted by AIDS status. Change in PHS scores were associated with change in age, depression scores, medical symptoms, and psychomotor efficiency (Digit Symbol and Grooved Pegboard performance).

(ii) MHS. Baseline and follow-up MHS scores were predicted by BDI-Affective scores and medical symptoms at baseline and follow-up. In addition, Digit Symbol performance predicted 5 percent of the variance of MHS at baseline. Changes in age (i.e., test-retest interval), depression, medical symptoms, and Grooved Pegboard scores predicted differences in baseline and follow-up scores for MHS.

B. Multivariate Analyses

Multiple regressions (with backwards variable selection) were conducted with demographic, medical, depression, and neuropsychological variables that were significant univariate predictors for each MOS-HIV dimension and factor score. The results of these analyses using baseline, follow-up, and change scores are presented in Tables 17, 18, and 19, respectively. Each table lists the standardized regression coefficients or beta-weights (β), proportion of unique variance of HRQOL predicted by each variable ($\underline{sr^2}$), multiple correlation coefficients (R), proportion of variance of HRQOL variables predicted by all significant variables (R^2), adjusted R^2,

Table 17. Multivariate Regression Results for MOS-HIV Scores at Baseline (N=100)

MOS-HIV	Medical				Depression		Neurocognitive								
	CD4 Counts		Medical Symptoms		BDI-Affective		Grooved Pegboard		Digit Symbol		CVLT-Total				
Dimensions	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**	**R**	**R^2**	**Adj.R^2**	**F** [a]
Physical Function			-.32	.08	-.22	.04	-.20	.03	.21	.03	.18	.03	.69	.48	.45	17.4
Role Function	.24	.06	-.32	.10					.24	.05			.48	.23	.20	9.4
Pain			-.34	.09	-.32	.08			.22	.05			.62	.38	.36	19.9
Social Function			-.30	.07	-.29	.07			.28	.06	*.15*	*.02*	.65	.42	.39	16.9
Overall Health			-.17	.02	-.49	.20			.30	.09			.68	.46	.44	27.4
Fatigue			-.24	.05	-.46	.17			*.16*	*.02*			.63	.40	.38	21.5
Cognitive Function			*-.17*	*.02*	-.50	.20			.24	.06			.66	.43	.41	24.2
Health Distress					-.60	.36			.24	.06			.65	.43	.41	35.9
Quality of Life					-.65	.42							.65	.42	.41	70.4
Mental Health					-.84	.70							.84	.70	.70	229.1
Item Factors																
Physical Function			-.36	.10	-.21	.03	*-.17*	*.02*	.25	.04	.18	.02	.72	.52	.50	20.5
Functional Status			-.37	.11	-.37	.11			.27	.07			.71	.50	.48	31.6
Overall Health					-.37	.14			.33	.11			.51	.26	.24	16.8
Cognitive Function			*-.16*	*.02*	-.53	.23			.22	.05			.67	.44	.42	25.3
Health Distress					-.60	.36			.22	.05			.65	.42	.41	34.7
Mental Health					-.83	.69							.83	.69	.68	213.5
Dimension Factors																
Physical Health			-.36	.10	-.33	.09			.35	.12			.71	.51	.49	32.9
Mental Health			*-.12*	*.01*	-.74	.45			.18	.03			.83	.69	.68	71.2

BDI-Affective=Beck Depression Inventory-Affective Score; CVLT=California Verbal Learning Test-Total Score

p<.05 for all non-italicized predictors, italicized values are trends (p=.05 to .09)

[a] p < .001

Table 18. Multivariate Regression Results for MOS-HIV Scores at Follow-Up (N=99)

MOS-HIV Dimensions	Demogr	Medical			Depr.	Neurocognitive						
	Age	AIDS Status	CD4 Counts	Medical Sympt.	BDI-Affective	Grooved Pegs	Digit Symbol	CVLT-Total				
	β sr²	β sr²	β sr²	β sr²	β sr²	β sr²	β sr²	β sr²	R	R^2	Adj. R^2	F [a]
Physical Function				-.50 .25			.24 .06		.59	.34	.33	25.2
Role Function				-.37 .13	*-.17 .03*			*.16 .03*	.49	.24	.22	10.1
Pain				-.38 .13	-.22 .05			.21 .04	.55	.30	.28	13.8
Social Function				-.40 .15	-.32 .09		*.16 .02*		.63	.39	.37	20.4
Overall Health				-.35 .11	-.36 .12		.28 .07		.67	.45	.44	26.1
Fatigue				-.48 .21	-.38 .13				.69	.48	.47	44.5
Cognitive Function				-.25 .06	-.45 .18		.23 .05		.65	.42	.40	22.5
Health Distress		-.17 .03	.19 .04	-.31 .08	-.52 .25				.75	.56	.54	30.2
Quality of Life				-.33 .10	-.58 .31				.75	.56	.55	61.9
Mental Health	.13 .02			-.23 .05	-.76 .51				.88	.78	.77	111.8
Item Factors												
Physical Function				-.53 .27			.28 .08		.63	.40	.38	31.6
Functional Status				-.50 .22	-.31 .09		.21 .04		.72	.52	.50	33.8
Overall Health				-.37 .12	-.22 .04		.25 .06		.57	.33	.30	15.3
Cognitive Function				-.27 .07	-.47 .20		.23 .05		.68	.46	.44	26.5
Health Distress		-.17 .03	.19 .03	-.28 .07	-.55 .27				.75	.56	.54	30.1
Mental Health				-.31 .09	-.75 .51				.89	.79	.78	178.6
Dimension Factors												
Physical Health				-.52 .24	-.29 .07		.23 .05		.73	.54	.52	36.7
Mental Health				-.36 .12	-.71 .46				.89	.79	.78	178.9

Adj. R^2=Adjusted R^2; BDI-Affective=Beck Depression Inventory-Affective Score; CVLT=California Verbal Learning Test-Total Score; Demogr.=Demographic Variables; Depr.=Depression; Grooved Pegs=Grooved Pegboard time, dominant hand; Sympt.=Symptoms
$p<.05$ for all non-italicized predictors, italicized values are trends ($p=.05$ to .09); [a] $p < .001$

Table 19. Multivariate Regression Results for MOS-HIV Change Scores (N=97)

MOS-HIV	Demographic				Medical		Depr.		Neurocognitive							
	Δ Age		Δ AIDS Status		Δ Med. Symptoms		Δ BDI-Affective		Δ Groov. Pegboard		Δ Digit Symbol		Δ CVLT-Total			
Dimensions	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**	**β**	**sr^2**			**β**	**sr^2**	**R**	**R^2**	**Adj.R^2**	**F** [a]
Physical Function					-.21	.04	-.18	.03							.29	.09	.07	4.4
Role Function									-.24	.06					.24	.06	.05	5.9
Pain					-.23	.05	-.31	.09							.41	.17	.15	9.5
Social Function			-.23	.05	-.37	.13	-.24	.06							.53	.28	.25	11.8
Overall Health							-.47	.22							.47	.22	.21	27.0
Fatigue	-.22	.04					-.44	.17							.55	.30	.29	20.1
Cognitive Function					-.19	.03	-.42	.17			.22	.04			.57	.33	.31	15.2
Health Distress							-.58	.34							.58	.34	.33	48.3
Quality of Life							-.60	.36							.60	.36	.35	53.0
Mental Health	-.16	.02					-.75	.51							.81	.66	.65	91.5
Item Factors																		
Physical Function					-.26	.07									.26	.07	.06	7.0
Functional Status	*-.17*	*.02*			-.22	.04	-.42	.16							.58	.34	.32	16.1
Overall Health							-.22	.05							.22	.05	.04	5.0
Cognitive Function	-.21	.04					-.44	.18			.18	.03			.61	.38	.36	18.8
Health Distress							-.58	.34							.58	.34	.33	48.2
Mental Health	-.18	.03					-.74	.50							.82	.67	.66	94.2
Dimension Factors																		
Physical Health	-.19	.03			-.24	.05	-.36	.11							.57	.32	.30	14.6
Mental Health	-.17	.03					-.73	.48							.80	.64	.63	82.6

Adj. R^2=Adjusted R^2; AIDS Status (Asymptomatic/Symptomatic vs. AIDS-defining condition); BDI-Affective=Beck Depression Inventory-Affective Score; CVLT=California Verbal Learning Test-Total Score; Depr.=Depression; Med.=Medical; Groov. Pegboard=Grooved Pegboard
p<.05 for all non-italicized predictors, italicized values are trends (p=.05 to .09)
[a]p < .001 for all F-values except Physical & Role Function dimensions, & Physical Function & Overall Health Item Factors (p<.05)

F-value, and significance level of the F-value.

The proportion of MOS-HIV dimension and factor score variance predicted by medical, depressive, and neuropsychological variables for baseline, follow-up, and change analyses are presented in Figures 1 to 7. Overall, the amount of variance predicted by demographic, medical, and neurobehavioural variables was highest for the Mental Health dimension and factors (range=65 to 74 percent), and lowest for the Role Function dimension (range=7 to 22 percent). For PHS and the remaining MOS-HIV dimensions and factors, predictor variables accounted for between 26 to 56 percent of the variance at baseline and follow-up, and 5 to 38 percent of the variance for the change score analyses. In general, the amount of MOS-HIV score variance accounted for by predictor variables was lowest for the change score analyses.

B1. MOS-HIV Dimensions.

(i) Physical Function Dimension. At baseline, 48 percent of the variance of the Physical Function dimension was accounted for by medical symptoms, depression, psychomotor speed (Digit Symbol and Grooved Pegboard), and learning efficiency (CVLT-Total recall). More than half of the variance of baseline Physical Function was shared, with medical symptoms uniquely accounted for an additional 8 percent of the variance and the remainder of the predictor variables each uniquely accounting for 3 to 4 percent of the variance. At follow-up, medical symptoms uniquely accounted for 25 percent of the variance, Digit Symbol uniquely accounted for 6 percent of the variance, and both variables together accounted for an additional 9 percent of the variance of the Physical Function dimension (R^2=.40). In the change score analysis, only 9 percent of the variance of Physical Function change scores was accounted for. Medical symptoms and depression uniquely predicted 4 and 3 percent of the variance of Physical Function change scores, respectively, and together, contributed another 2 percent of shared variance.

(ii) Role Function Dimension. Approximately 23 percent of the variance of Role Function was accounted for by predictor variables at baseline and follow-up. Medical symptoms was the largest predictor and uniquely accounted for 10 percent of the variance at baseline and 13 percent of the variance at follow-up. CD4 counts and Digit Symbol scores each uniquely predicted an additional 5 or 6 percent of the variance at baseline while depression and CVLT-Total Recall both uniquely predicted 3 percent of the variance at follow-up. Role function change scores were solely predicted by Grooved Pegboard performance, which only accounted for 6 percent of the variance.

(iii) Pain Dimension. For the Pain dimension, 38 percent of the baseline variance, 30 percent of the follow-up variance, and only 17 percent of the change score variance was accounted for by predictor variables. Medical and depressive symptoms predicted Pain scores for all analyses, uniquely accounting for between 5 to 13 percent of the variance. In addition, Digit Symbol scores uniquely predicted an additional 5 percent of the variance at baseline while CVLT-Total Recall uniquely predicted an additional 4 percent of the variance at follow-up.

(iv) Social Function Dimension. Approximately 40 percent of the variance of baseline and follow-up Social Function was predicted by medical symptoms, depression, and neuropsychological variables. At baseline, each of these areas contributed about 7 percent of unique variance, with an additional 20 percent of shared variance. Fifteen percent of the variance of follow-up Social Function scores was uniquely predicted by medical symptoms. Depression uniquely accounted for an additional 9 percent and Digit Symbol uniquely accounting for an additional 2 percent of the variance of follow-up Social Function. Change in number of medical symptoms was the best predictor of Social Function change scores, as this variable uniquely accounted for approximately half of the 28 percent predicted variance. AIDS status and depression change scores each contributed another 5 to 6 percent unique variance.

(v) Overall Health Dimension. Approximately 45 percent of the variance

of the Overall Health dimension was predicted by depression, medical symptoms, and Digit Symbol scores. Depression was the strongest predictor at baseline and uniquely accounted for 20 percent of the variance. At follow-up, depression and medical symptoms each accounted for 11 to 12 percent of the variance and were the best predictors of Overall Health. Variations in depression scores between the two assessments accounted for 22 percent of the variance of Overall Health dimension change scores.

(vi) Fatigue Dimension. Forty percent of the variance of baseline Fatigue scores was predicted by depression, medical symptoms, and Digit Symbol scores, with the former variable uniquely accounting for 17 percent of the variance and the latter variables both uniquely accounting for less than 6 percent of the variance. Depressive and medical symptoms were also strong predictors of Fatigue at follow-up, uniquely accounting for 21 and 13 percent of the follow-up variance, respectively. Together, these variables contributed another 14 percent of shared variance. Thirty percent of the variance of Fatigue change scores was accounted for by changes in depression (uniquely predicting 17 percent of the variance) and age (uniquely predicting 4 percent of the variance) between baseline and follow-up.

(vii) Cognitive Function Dimension. Depression scores uniquely predicted approximately half of the total variance of Cognitive Function baseline (20 of the 43 percent explained variance), follow-up (18 of the 42 percent explained variance), and change scores (17 of the 33 percent explained variance). In addition, Digit Symbol and medical symptoms both uniquely accounted for between 2 to 6 percent of the variance for all analyses.

(viii) Health Distress Dimension. Depression scores uniquely predicted 36 percent of the variance of baseline Health Distress dimension scores. An additional 6 percent unique variance was predicted by Digit Symbol scores. Together, these variables accounted for 43 percent of the variance of baseline Health Distress. At follow-up, 56 percent of Health Distress dimension scores was predicted by depression (contributing 25 percent unique variance), medical

symptoms (contributing 8 percent unique variance), CD4 counts (contributing 4 percent unique variance), and AIDS status (contributing 3 percent unique variance). Alterations in depressive symptoms between baseline and follow-up predicted 34 percent of the variance of Health Status dimension change scores.

(ix) Quality of Life Dimension. Quality of Life baseline and change scores were solely predicted by depression, which accounted for 42 percent of the baseline variance and 36 percent of the change score variance. At follow-up, Quality of Life was predicted by depression (uniquely accounting for 31 percent of the variance) and medical symptoms (uniquely accounting for 10 percent of the variance). Together, these variables accounted for a total of 56 percent of the variance of follow-up Quality of Life dimension scores.

(x) Mental Health Dimension. Seventy percent of the variance of baseline Mental Health was accounted for by BDI-Affective scores. At follow-up, depression uniquely accounted for 51 percent of the Mental Health variance, with medical symptoms and age uniquely accounting for less than 6 percent of the variance. Together, these variable predicted 78 percent of the variance of follow-up Mental Health. Mental Health change scores were strongly predicted by depression scores (accounting for 51 percent unique variance), although change in age between baseline and follow-up contributed another 2 percent of unique variance. Overall, 66 percent of the variance of Mental Health was accounted for by these two predictor variables.

B2. MOS-HIV Item-Based Factors.

(i) Physical Function Factor. At baseline, 52 percent of the variance of the Physical Function factor was accounted for by medical symptoms, depression, psychomotor speed (Digit Symbol and Grooved Pegboard), and learning efficiency (CVLT-Total recall). Medical symptoms uniquely accounted for 10 percent of the variance of Physical Function, with the remainder of the predictor variables uniquely accounting for only 2 to 4 percent of the total variance. Forty percent of the

variance of follow-up Physical Function was predicted by medical symptoms (uniquely accounting for 27 percent of the variance) and Digit Symbol scores (uniquely accounting for 8 percent of the variance). Variations in medical symptoms between baseline and follow-up assessments were the sole predictor of Physical Function change scores, and accounted for 7 percent of the variance.

(ii) Functional Status Factor. An average of 51 percent of the variance of the Functional Status factor was predicted by medical symptoms, depression scores, and Digit Symbol performance at baseline and follow-up. Medical and depressive symptoms each uniquely predicted 11 percent of the variance at baseline, with 7 percent unique variance contributed by Digit Symbol. At follow-up, medical symptoms uniquely accounted for 22 percent, depression uniquely accounted for 9 percent and Digit Symbol uniquely accounted for 4 percent of the variance. Functional Status change scores were predicted by changes in depression (uniquely accounting for 16 percent of the variance), medical symptoms (uniquely accounting for 4 percent of the variance), and age (uniquely accounting for 2 percent of the variance) between the two testing sessions. Together, these three variables accounted for 34 percent of the variance of Functional Status factor change scores.

(iii) Overall Health Factor. Twenty-six percent of the variance of baseline Overall Health was predicted by depression and Digit Symbol scores, which each variable contributing 11 to 14 percent unique variance. These two predictors only uniquely accounted for between 4 to 6 percent of the variance of Overall Health at follow-up, with medical symptoms uniquely accounting for 12 percent of the variance. Overall, 33 percent of variance for the follow-up Overall Health factor was accounted for by these variables. Variations in depression scores between baseline and follow-up accounted for only 5 percent of the variance of Overall Health factor change scores.

(iv) Cognitive Function Factor. Depression scores uniquely predicted approximately half of the total variance of Cognitive Function baseline (R^2=.44),

follow-up (R^2=.46), and change (R^2=.38) scores. Digit Symbol performance and medical symptoms each contributed an additional 2 to 5 percent unique variance at baseline and 5 to 7 percent unique variance at follow-up. Differences in Digit Symbol scores and age between baseline and follow-up also accounted for 3 to 4 percent of the Cognitive Function change score variance.

(v) Health Distress Factor. Depression scores uniquely predicted 36 percent of the variance of baseline Health Distress factor scores. An additional 5 percent unique variance was predicted by Digit Symbol performance. Together, these variables accounted for 42 percent of baseline Health Distress. At follow-up, 56 percent of the Health Distress factor was predicted by depression (accounting for 27 percent unique variance), medical symptoms (accounting for 7 percent unique variance), CD4 counts, and AIDS status (both accounting for 3 percent unique variance). Variations in depressive symptoms between baseline and follow-up uniquely predicted 34 percent of the variance of Health Status factor change scores.

(vi) Mental Health Factor. Depression scores were the sole predictors of Mental Health at baseline, accounting for 69 percent of the variance. In addition, depression uniquely accounted for 51 percent of the variance at follow-up, with medical symptoms contributing an additional 9 percent unique variance. Together, these variables accounted for a total of 79 percent of the variance of follow-up Mental Health. Sixty-seven percent of the variance of Mental Health change scores was predicted by differences in depression scores (uniquely accounting for 50 percent of the variance) and age (uniquely accounting for 3 percent of the variance).

B3. MOS-HIV Dimension-Based Factors.

(i) PHS. Baseline and follow-up PHS scores were predicted by medical symptoms, depression scores and Digit Symbol performance. Together, these predictor variables accounted for 51 to 54 percent of the baseline and follow-up

PHS score variance. At baseline, each predictor uniquely accounted for approximately 10 percent of the variance while at follow-up, medical symptoms uniquely accounted for 24 percent of the variance and depression and Digit Symbol performance each predicted an average of 6 percent of additional variance. Thirty-two percent of the variance of PHS change scores was associated with differences in age, medical symptoms, and depression scores between baseline and follow-up. Depression uniquely accounted for 11 percent of the variance, medical symptoms uniquely accounted for 5 percent of the variance, and age uniquely accounted for 3 percent of the variance of PHS change scores.

(ii) MHS. Depression, Digit Symbol raw score, and medical symptoms accounted for 69 percent of the variance of baseline Mental Health. Forty-five percent of the variance was uniquely accounted for by depression scores, with the other predictors contributing 3 percent of less unique variance. At follow-up, 79 percent of the variance of Mental Health was predicted by depressive (46 percent unique variance) and medical symptoms (12 percent unique variance). Sixty-four percent of the variance of MHS change scores was accounted for by age and depressive symptom change scores. Of this, depression uniquely accounted for 48 percent of the variance.

Summary of the Clinical Utility Analyses

Examination of how demographic and clinical predictor variables impacted upon HRQOL domains indicated that many similarities occurred between analyses using MOS-HIV dimension or factor scores using baseline, follow-up, and change score data. These relationships are briefly summarized below and can be seen in Tables 17 to 19 and Figures 1 to 7.

Demographic Variables. Demographic variables were not strong predictors of MOS-HIV dimensions and factors at baseline and follow-up. Of the demographic information included in the analyses, age was the only significant predictor and it

Figure 1. Proportion of Variance of MOS-HIV Dimensions Predicted by Medical and Neurobehavioural Variables at Baseline

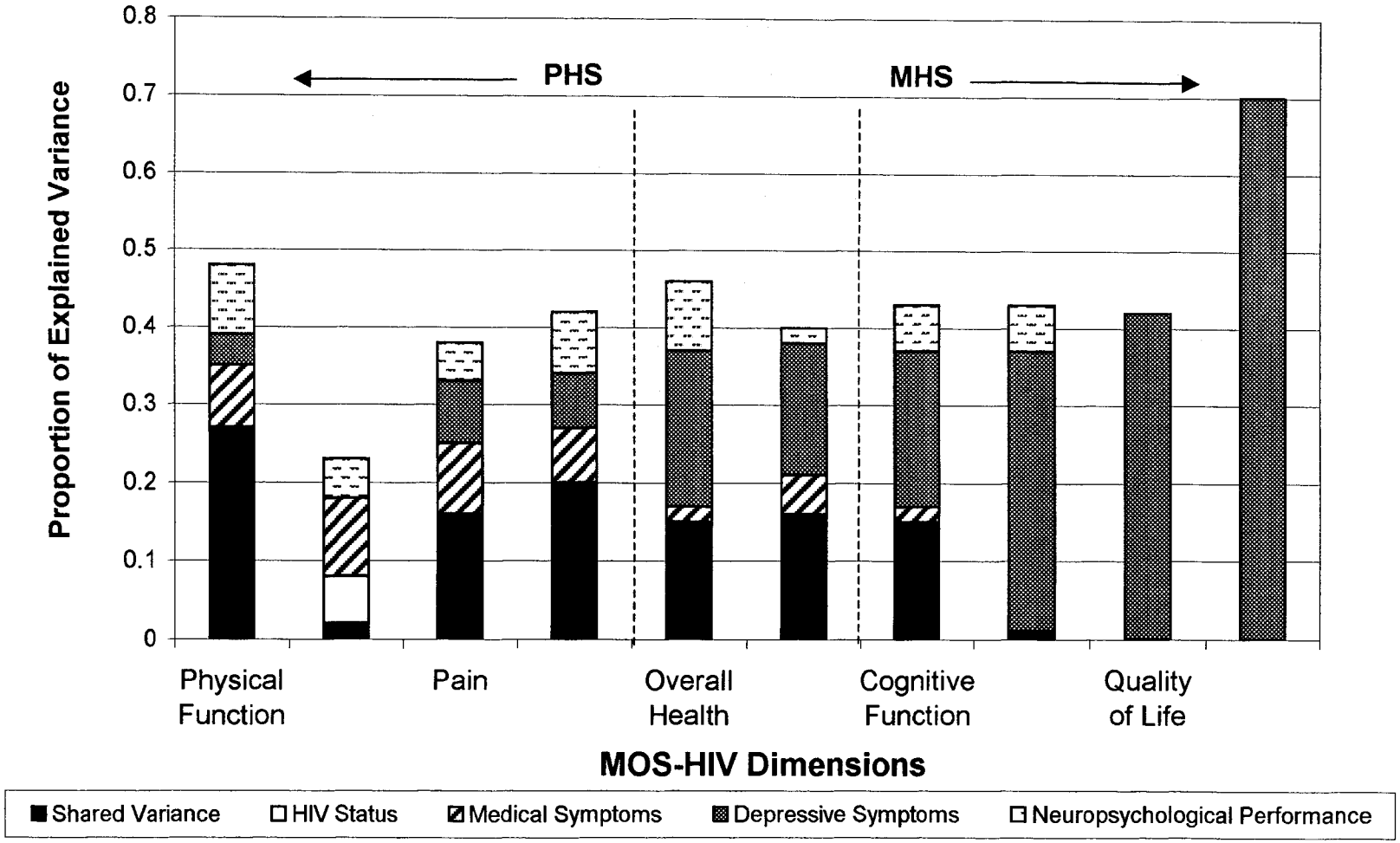


Figure 2. Proportion of Variance of MOS-HIV Dimensions Predicted by Age, Medical, and Neurobehavioural Variables at Follow-Up

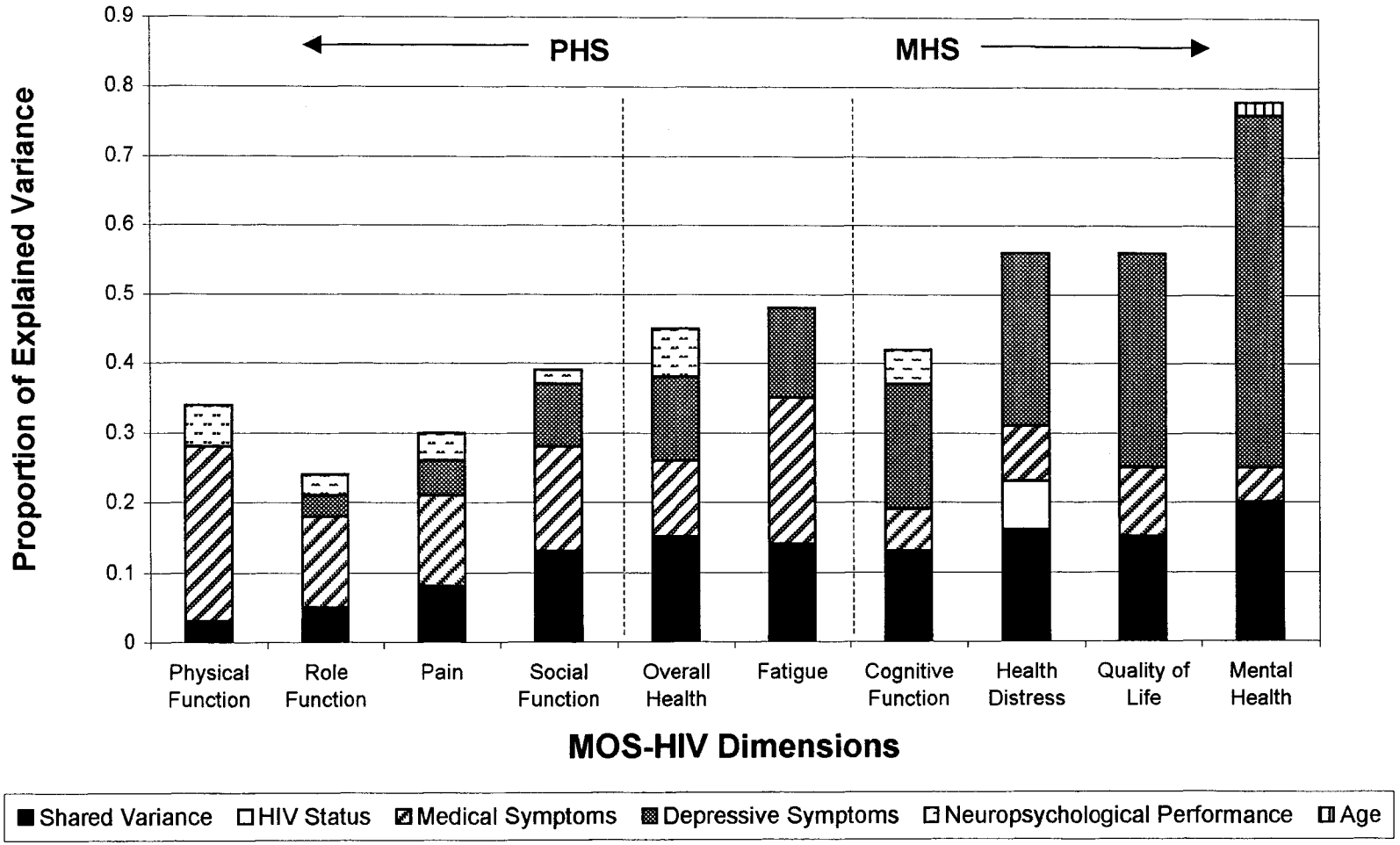


Figure 3. Proportion of Variance of MOS-HIV Dimension Change Scores Predicted by Age, Medical, and Neurobehavioural Variables

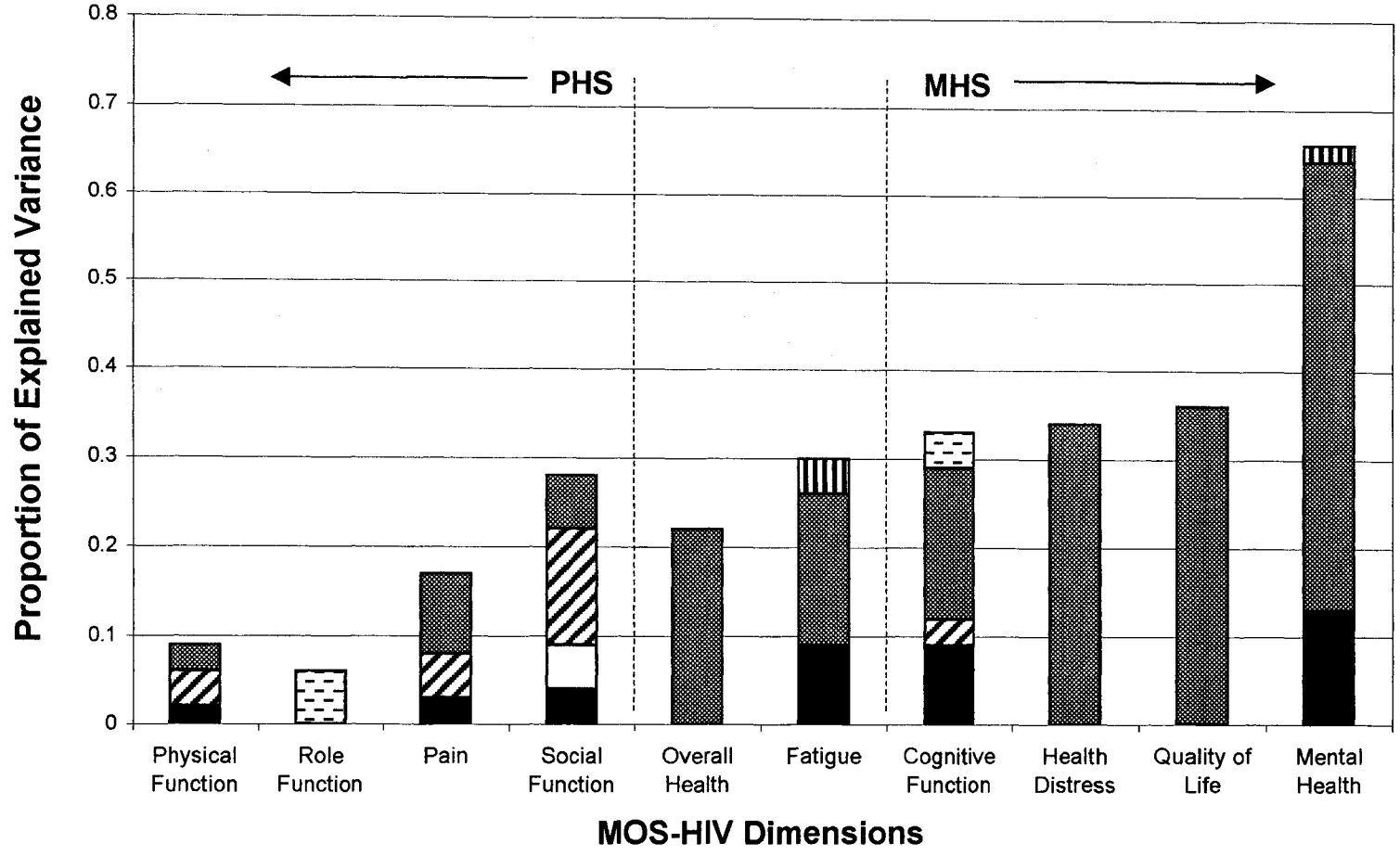


Figure 4. Proportion of Variance of MOS-HIV Item-Based Factors Predicted by Medical and Neurobehavioural Variables at Baseline

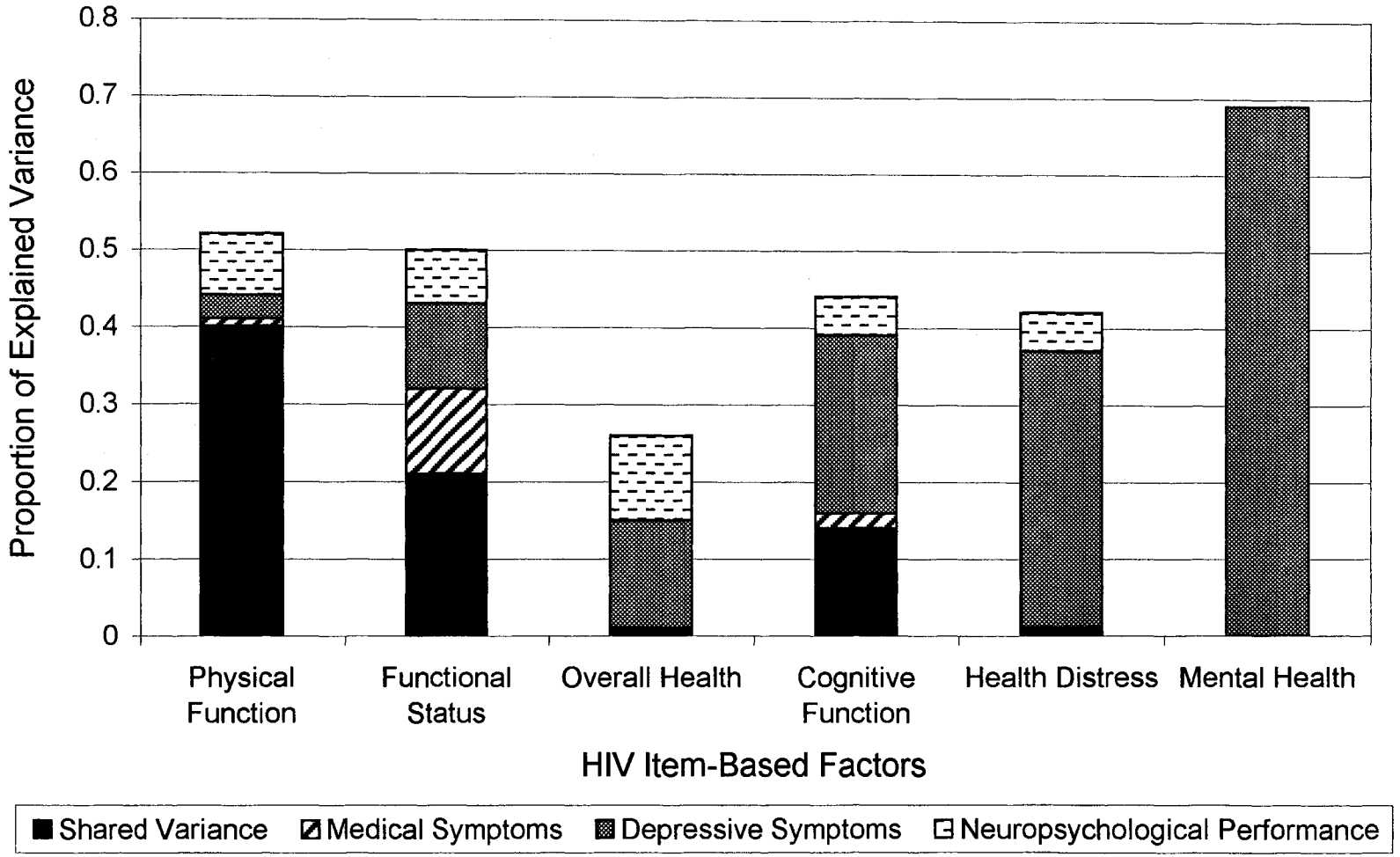


Figure 5. Proportion of Variance of MOS-HIV Item-Based Factors Predicted by Medical and Neurobehavioural Variables at Follow-Up

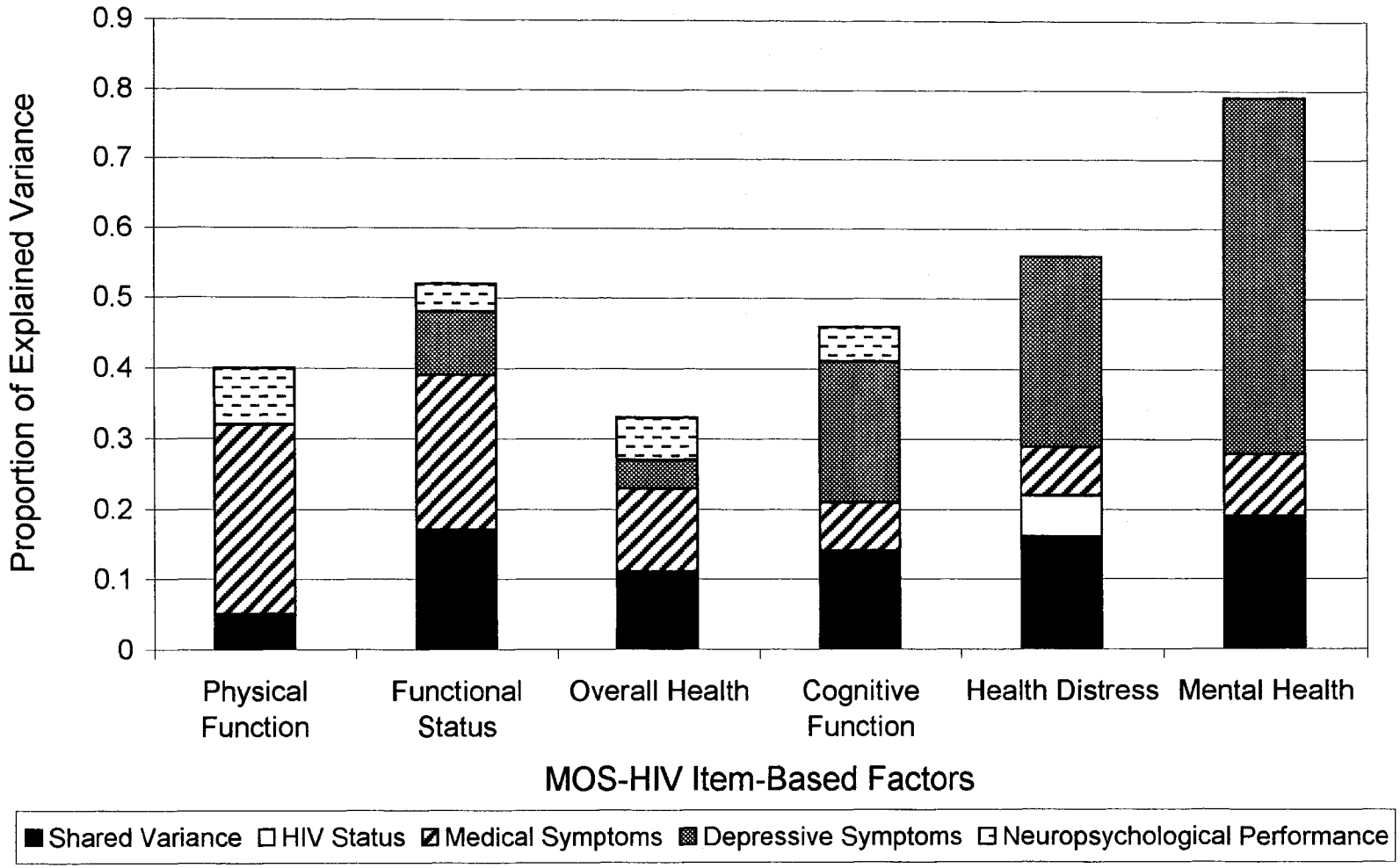


Figure 6. Proportion of Variance of MOS-HIV Item-Based Factor Change Scores Predicted by Age, Medical, and Neurobehavioural Variables

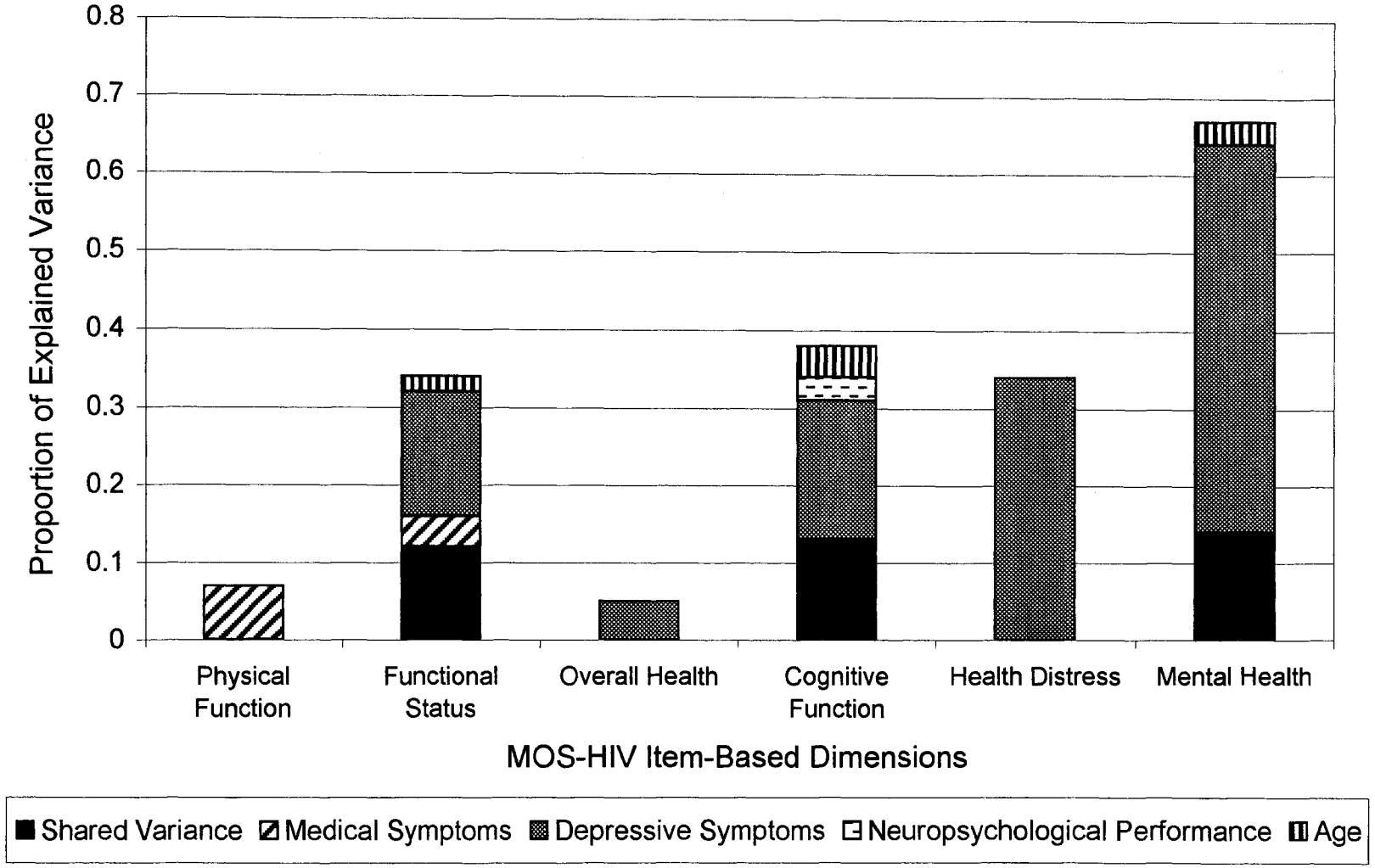
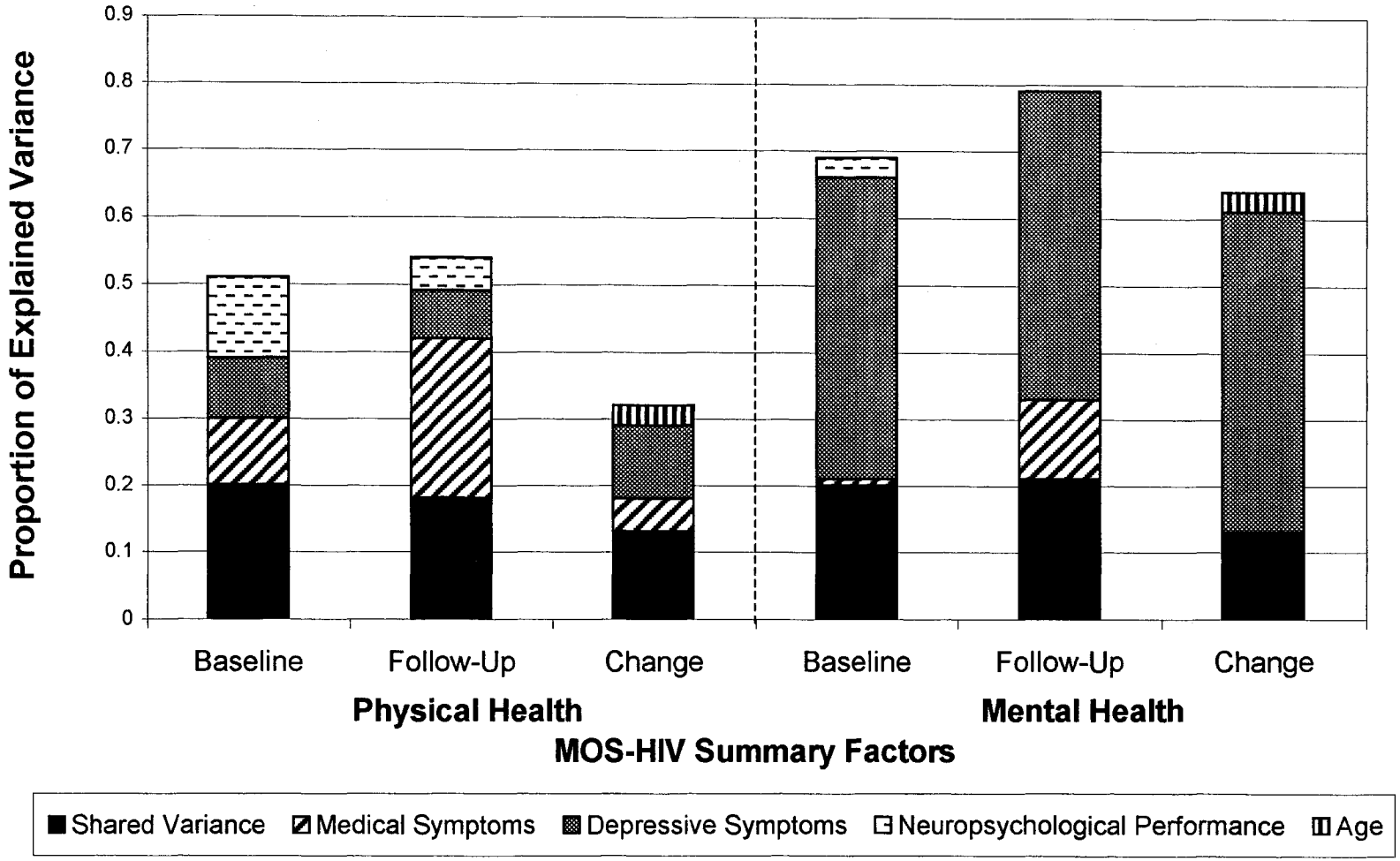


Figure 7. Proportion of Variance of MOS-HIV Summary Factors Predicted by Age, Medical, and Neurobehavioural Variables



only uniquely predicted 2 percent of the variance of the Mental Health dimension at follow-up. In the change score analysis, change in age scores (i.e., test-retest interval) uniquely predicted between 2 and 4 percent of the variance of the following MOS-HIV measures: Fatigue and Mental Health dimensions; Functional Status, Cognitive Function, and Mental Health item-based factors; and PHS and MHS. With increases in test-retest interval, declines in HRQOL were more likely to occur.

HIV Status. CD4 counts and a history of AIDS-defining conditions (i.e., AIDS-status) were inconsistent predictors of the Health Distress dimension and item-based factor, as well as the Role and Social Function dimensions. HIV status variables uniquely accounted for a maximum of 6 percent of the variance of these HRQOL domains.

Medical Symptoms. Medical symptoms were generally unique predictors of physical function dimensions of the MOS-HIV (Physical Function, Role Function, Pain, Social Function, Overall Health, and Fatigue). In addition, some mental health domains were also influenced by medical symptoms. At baseline, up to 11 percent of the variance of HRQOL dimensions and factors was uniquely predicted by medical symptoms. Medical symptoms had the largest impact on HRQOL at follow-up, when symptom scores uniquely predicted between 5 to 27 percent of all of the MOS-HIV dimensions and factors. Changes in medical symptoms were associated with changes in Physical Function dimension and factor scores, Pain, Social Function, and Cognitive Function dimensions, and the Functional Status factor (uniquely accounting for between 3 to 13 percent of the variance).

Depressive Symptoms. Depression scores generally contributed unique variance for all of the MOS-HIV dimensions and factors, with larger contributions for mental health than physical health domains. For example, the variance of the mental health dimensions (Mental Health, Quality of Life, Health Distress, Cognitive

Function, Fatigue, and Overall Health) uniquely predicted by BDI-Affective scores at baseline ranged from 17 to 70 percent. In contrast, depressive symptoms at baseline uniquely predicted only up to 8 percent of the variance of dimensions within the physical functioning realm (Physical Function, Role Function, Pain, and Social Function). Similar patterns in depression and HRQOL relationships can be observed with MOS-HIV dimension follow-up and change score data, as well as analyses using item-based and dimension-based factor scores. Depression scores were the strongest predictors of mental health MOS-HIV scales, and uniquely predicted between 45 to 70 percent of the Mental Health dimension and factor scores. As a result of this strong relationship, the Mental Health dimension and factor scores tended to have the greatest proportion of explained variance.

Neurocognitive Performance. Of the four neurocognitive measures used in this study, Digit Symbol raw score was the best predictor of HRQOL. Digit Symbol scores uniquely predicted up to 12 percent of the variance of MOS-HIV scales at baseline and follow-up. Grooved Pegboard performance and CVLT-Total recall were variable predictors of the Physical Function dimension and item-based factor, and the Social Function, Role Function, and Pain dimensions, uniquely accounting for a maximum of 4 percent of the variance. Neurocognitive measures were not significantly associated with many MOS-HIV change scores, with relationships only occurring for Grooved Pegboard with the Role Function dimension, and Digit Symbol with the Cognitive Function dimension or item-based factor. Overall, neurocognitive performance was more predictive of the physical function domains of HRQOL but was not a good predictor of MOS-HIV change scores.

DISCUSSION

Comprehensive evaluation of HIV disease progression and treatment effects requires psychometrically sound, responsive, and easily interpretable HRQOL instruments. The MOS-HIV is the most widely used HRQOL instrument for individuals with HIV-infection and provides information about 10 different domains of HRQOL. The purpose of this study was to provide additional empirical evidence demonstrating the psychometric properties and clinical utility of the MOS-HIV HRQOL instrument. Specifically, the factor structure and test-retest reliability of the MOS-HIV were obtained using a sample of adults with HIV-infection. In addition, the sensitivity of the MOS-HIV to variations in medical status (AIDS diagnosis, CD4 counts, medical symptoms) and neurobehavioural functioning (depression and neuropsychological performance) was delineated in order to determine its' clinical utility. The results of this study provide important information about measures of the MOS-HIV, conceptualizations of health status, and the relationships between clinical variables and domains of HRQOL. These findings are discussed in terms of their clinical and research implications.

MOS-HIV MEASURES OF HRQOL

HRQOL is a complex construct that is believed to be composed of psychological and physical health core components (Berzon et al., 1997). The MOS-HIV is able to provide both general and domain-specific information about HRQOL. Ten dimensions of functioning are examined by the MOS-HIV: Physical, Role, Social, and Cognitive Function, Pain, Overall Health, Fatigue, Health Distress, Quality of Life, and Mental Health. These 10 dimensions can be reduced to two summary indices of mental and physical health with factor analysis. In addition, factor analysis of MOS-HIV items produces 6 domains of HRQOL, Mental Health, Health Distress, Cognitive Function, Overall Health, Physical Function, and Functional Status. The 2-factor, 6-factor, or 10 dimension measures of the MOS-

HIV provide important information about HRQOL functioning. Selection of appropriate MOS-HIV measures is dependant on the purpose of HRQOL assessment as well as psychometric considerations. As such, knowledge of the advantages and disadvantages of MOS-HIV dimensions and factor scores is necessary to ensure that appropriate and useful HRQOL information can be obtained for the evaluation of treatment problems or disease processes (see Table 20). This is discussed in terms of the information that the measures provide and their psychometric properties.

10 MOS-HIV Dimensions

MOS-HIV dimension scores provide information about specific aspects of HRQOL that may not be directly assessed by factor scores. For example, research examining the impact of interventions on fatigue would require a specific measure of fatigue, such as the MOS-HIV Fatigue dimension, rather than more general indicators of physical functioning. The use of MOS-HIV dimensions may also be required when comparing findings to previous research, as these scores are most typically reported in the literature. However, the use of MOS-HIV dimensions should be limited to those dimensions with established psychometric properties, namely Overall Health, Mental Health, Cognitive Function, Fatigue, Health Distress, Quality of Life, Physical Function, and Social Function. Role Function and Pain dimensions had unacceptable test-retest reliability and may require the inclusion and/or modification of items to improve their psychometric properties.

Disadvantages of the MOS-HIV dimensions include the poor test-retest reliabilities of some dimensions. Only four of the 10 dimensions demonstrated high test-retest reliability, whereas two dimensions, Role Function and Pain, had unacceptable reliabilities (i.e., correlation coefficients <.50). Given the relatively long test-retest intervals used in this study, these poor coefficient scores may reflect sensitivity to changes in clinical status rather than poor reliability. However, similar results were obtained in a Spanish-speaking population for a two-week test-retest

Table 20. Comparisons of MOS-HIV Measures

	Composition	Structure/Stability	Test-Retest Reliability	Differential Utility
10 Dimensions: Physical, Role, Social, & Cognitive Function, Pain, Fatigue, Overall Health, Mental Health, & Health Distress	Measures composed of face valid items for HRQOL domains believed to be important for HIV	Some dimension items did not consistently load together in factor analyses (i.e., Physical Function, Fatigue, & Overall Health dimensions)	Poor reliabilities for Role Function & Pain; other dimensions were acceptable	Use when detailed HRQOL information is required
6 Item Factors: Physical Function, Functional Status, Overall Health, Cognitive Function, Mental Health, & Health Distress	Measures based on factor structure of 34 MOS-HIV items	Overall Health, Physical Function, & Mental Health appear stable; Health Distress, Cognitive Function, & Functional Status less stable	Generally good	Use when information about major domains of HRQOL is required
2 Summary Factors: Physical & Mental Health Status	Measures based on factor structure of 10 MOS-HIV dimensions	Factor structure consistently obtained across studies	Good	Use when summary scores of HRQOL are required

interval (Badia et al., 1999). Dimensions with a restricted number of items and/or range of item scores had the poorest reliability scores in the current and previous studies and may benefit from the inclusion of additional items to improve their reliability.

Factor analysis of the MOS-HIV dimensions scores indicated that the structure of some dimensions may be inappropriate. Although previous research has demonstrated the internal validity of MOS-HIV dimensions composed of more than one item (Badia et al., 1999; Burgess et al., 1993; Copfer et al., 1996; Holmes & Shea, 1999; Kaplan et al., 1997; Wu et al., 1997c), items within the same dimension did not consistently load together when factor analyses were performed in this study. For example, the "feeling bad lately" Overall Health item, the "feeling full of pep" Fatigue item, and the Quality of Life item consistently loaded with Mental Health items, suggesting that these items may be better indicators of mental health than their specified aspects of HRQOL. These findings indicate that the current configuration of some MOS-HIV dimensions may not be appropriate and modification of the structure of some dimensions may be necessary.

6 MOS-HIV Item-Based Factors

MOS-HIV item factors provide six summary indices of HRQOL that are composed of items with statistical similarities. Areas of HRQOL assessed by the 6 item factors are frequently comparable to the 10 MOS-HIV dimensions. Physical Function, Overall Health, Cognitive Function, and Health Distress dimension items loaded together and also formed item factors. This suggests that the Physical Function, Overall Health, Cognitive Function, and Health Distress dimensions have good stability because dimension items, with the exception of one Physical Function and one Overall Health dimension item, loaded on the same item factor. These item and dimension scores were comparable in terms of test-retest reliability and relationships with demographic, medical, and neurobehavioural variables. The other item factors, Mental Health and Functional Status, were composed of multiple

MOS-HIV dimension items and, although similar to related dimensions, were less directly comparable. The similarities between MOS-HIV dimensions and item-based factors are displayed in Table 21.

Overall Health, Physical Function, and Mental Health item factors were generally consistent with previous research (Holmes & Shea, 1990; Rourke et al., 2001), which provides support for their stability. The Cognitive Function, Functional Status, and Health Distress factors were not consistently obtained in other studies. A possible explanation for differences in factor analysis results between studies could be the restricted number and range of some of the MOS-HIV dimension items, such as Social Function, Pain, and Role Function. Items with reduced ranges tended to have more variable loadings between analyses (i.e., current study; Holmes & Shea, 1990; Rourke et al., 2001). MOS-HIV items assessing unique aspects of HRQOL may not form an independent factor but may have weak loadings on other factors or variable factor associations. This is seen with the Social Function item, which had weak loadings on all factors (<.32). The limited number of possible scores within items may also prevent the formation of stable associations with more broadly ranged items. For example, Role Function items are dichotomous; associations with related items could be more variable because a change in score by 1 value would have more of an impact when items are composed of 2 rather than 5 or 6 possible scores. Role Functioning items loaded with Fatigue and Pain items at baseline and Overall Health items at follow-up. Future research is required to verify the factor structure of the MOS-HIV item factors using larger samples. Future research is required to verify the stability of the Cognitive Function, Functional Status, and Health Distress item factors before they are used in intervention studies and other research evaluations. However, these factors may still provide important clinical information.

An advantage of the MOS-HIV item-based factors over MOS-HIV dimensions is that all 6 item factors had acceptable test-retest reliability. In addition, MOS-HIV item factors are composed of items with statistical similarities rather than items that

Table 21. Comparisons of MOS-HIV Dimensions and Item Factors

10 MOS-HIV Dimensions	6 MOS-HIV Factors	Psychometric Properties	Relationship with Predictor Variables
Physical Function	Physical Function	Good stability Good test-retest reliability	Medical Sx.: +/+++ Depression: 0/+ Cognitive Function: +
Role Function, Fatigue, Pain, & Social Function	Functional Status	Variable stability Need to verify factor structure	Medical Status: 0/+ Medical Sx.: + to +++ Depression: 0 to ++ Cognitive Function: 0/+
Overall Health	Overall Health	Good stability Good test-retest reliability	Medical Sx.: +/++ Depression: +/++ Cognitive Function: +/++
Cognitive Function	Cognitive Function	Good test-retest reliability Need to verify factor structure	Medical Sx.: + Depression: ++/+++ Cognitive Function: +
Health Distress	Health Distress	Good test-retest reliability Need to verify factor structure	Medical Status: 0/+ Medical Sx.: 0/+ Depression: ++/+++ Cognitive Function: 0/+
Mental Health & Quality of Life	Mental Health	Good stability Good test-retest reliability	Medical Sx.: 0/+ Depression: ++++++ to +++++++

R^2 values of predictors: 0=no relationship; + = ≤.10; ++ = .11 to .20; +++ = .21 to .30; ++++++ = .51 to .60; +++++++ = .61 to .70

are believed to assess the same HRQOL domains but which may not actually do so. Item factors are generally composed of a larger number of items than MOS-HIV dimensions, which increases the precision of HRQOL assessment. For example, the Functional Status factor combines information from a number of dimensions with restricted ranges, such as Role and Social Function. As such, the Functional Status factor has greater range than the dimensions composing it, and is likely a more sensitive measure of HRQOL than Role and Social Function dimensions.

A major disadvantage of the MOS-HIV item factors is the variation in factor structure in the current and previous analyses (Holmes & Shea, 1990; Rourke et al., 2001). Although Mental Health, Overall Health, and Physical Function factors were consistently obtained in all analyses, Health Distress, Functional Status, and Cognitive Function factors were not. These latter three factors should be used with caution until additional empirical support for the occurrence of these factors is obtained using large and diverse HIV-positive samples.

The variability of factors between studies and the lack of an established means of calculating factor scores prevents research from being easily compared across studies, which is a significant disadvantage. The use of factor scores may hinder interpretation of treatment effects for some factors because they are composite scores of multiple dimensions of HRQOL. For example, impairments in Functional Status may be difficult to interpret, as they may result from impaired role or social functioning, and/or physical symptoms that commonly occur with HIV-infection. Another disadvantage of MOS-HIV item factors is that they may not provide information about specific areas of HRQOL that could be obtained using MOS-HIV dimensions, such as pain, fatigue, or social function. In addition, item factors would not be appropriate for use when summary indices of HRQOL are desired.

2 MOS-HIV Dimension-Based Factors

Two general indicators of mental and physical health status are obtained

with factor analysis of MOS-HIV dimensions (i.e., MHS and PHS). Advantages of the mental and physical health summary scores include high test-retest reliability and factor stability, within the current study and previous research (Burgess et al., 1993; Gielen et al., 2001; Revicki et al., 1998; Rourke et al., 2001). MHS and PHS also provide easily understood summary scores of overall HRQOL. As such, they provide an efficient means of conveying information about health status when more detailed HRQOL information is not required. Finally, MHS and PHS can be used to generally compare the HRQOL of individuals with HIV-infection to other medical samples because these factors have been consistently obtained with generic MOS-based HRQOL instruments (e.g., Bing et al., 2000).

A disadvantage of using summary factor scores is that these measures do not provide information about more specific aspects of HRQOL. Also, interventions may have varying effects on different aspects of mental or physical health status. For example, treatment of medical symptoms may have a greater impact on physical function than pain, even though both aspects of HRQOL assess physical health status. Summary scores may not reflect increases in one aspect of physical health status (e.g., pain) because decreases in another aspect of physical health status (e.g., social function) may have occurred. As such, summary scores may not be sensitive to variations within sub-domains of mental or physical health.

In summary, both MOS-HIV dimensions and item factor scores provide psychometrically sound information within Physical Function, Overall Health, Cognitive Function, Health Distress and Mental Health domains. These dimensions and item factors were generally consistent, although the Mental Health item factor was composed of Quality of Life, Overall Health, and Fatigue dimension items in addition to the Mental Health dimension items. The MOS-HIV dimensions also provide measures of Quality of Life, Pain, Fatigue, Role Function, and Social Function. However, test-retest reliability of the Role Function and Pain dimensions is poor, and these dimensions should be avoided unless modification and/or

addition of items is performed to in order to improve their reliability. The final MOS-HIV item factor combines information from the Pain, Fatigue, Role Function, and Social Function dimensions and has good test-retest reliability. This functional status factor would be preferable over the individual MOS-HIV dimensions if a global score of functional status were required. However, this measure does not provide information about more specific aspects of HRQOL. For example, if information about fatigue or social functioning was of interest, the use of MOS-HIV dimensions would be required. The MOS-HIV also provides mental and physical health summary factors that are of use when global information about HRQOL is needed. These two summary factors are psychometrically sound and provide easily understood information about overall HRQOL.

DOMAINS OF HRQOL ASSESSED BY THE MOS-HIV

The results of this study have demonstrated that the MOS-HIV dimensions and item factors assess Physical Function, Overall Health, Cognitive Function, and Health Distress domains of HRQOL (see Table 21). In addition, indicators of Mental Health and Functional Status were also obtained which were composites of multiple MOS-HIV dimensions. For example, Functional Status was composed of items assessing reduction of social activities due to health status, feelings of fatigue, ability to perform vigorous physical activities, and limitations in work due to health status or symptoms of pain. All domains of HRQOL were interrelated; however, important distinctions between these domains can be made.

Mental Health and Health Distress were strongly associated and primarily associated with general mental health status. Mental Health was composed of items that primarily assess depressive symptoms (e.g., fatigue and happy, downhearted, or bad feelings) while Health Distress items assessed fear, discouragement, and despair related to health functioning. Both health domains had strong associations with depression. In fact, Mental Health was moderately to highly predicted by depressive status alone, indicating that it is largely a measure of mood status. This

is not surprising as both Mental Health and depression indicators were designed to assess the same construct. The presence of high associations between mental health functioning and depression suggests that there is a minimal distinction between these two measures. As such, mental health would be expected to provide similar information about health functioning as indicators of mood status, and only one of these measures would be necessary to determine mental health function.

Health Distress also had strong associations with depression but was also related to medical symptoms and cognitive status. Therefore, Health Distress appears to go beyond reflecting mood status alone. In addition, examination of the Health Distress items indicated these items tend to reflect worry and concern related to medical, psychological, and cognitive status rather than only depressive symptoms like Mental Health. It is not clear if Health Distress function is influenced by fluctuations in anxiety and/or represents more longstanding, ruminative personality traits. Further research examining the relationships between Health Distress and measures of state and trait anxiety is required to improve understanding about this factor.

Cognitive Function was another domain of HRQOL assessed by the MOS-HIV (see Table 21). Items composing Cognitive Function examined perceived difficulties with problem solving, memory, sustained attention, and concentration. Consistent with previous research (e.g., Moore et al., 1997; Rourke et al., 1999a; 1999b), Cognitive Function was associated with depressive and medical symptoms, such as fatigue, impaired attention, and feelings of sadness and helplessness. Neuropsychological performance was associated with Cognitive Function. However, only five percent of the variance of Cognitive Functioning was uniquely predicted by neuropsychological measures, which suggests that this relationship may not be clinically significant. Given the weak relationship between subjective and objective measures of cognitive functioning, the Cognitive Function factor may reflect a heightened sensitivity to cognitive concerns and may be related to depression and/or personality factors. The Cognitive Function item factor should not be used

in place of objective neuropsychological instruments when assessment of cognitive functioning is required. However, it can be used as an indicator of perceived cognitive impairment and concern related to cognitive status.

Overall Health was largely an indicator of physical health status and was composed of items examining general impressions of health functioning. Similar overall health questions are frequently used in research studies to assess HRQOL (e.g., Bergner et al., 1976b; Cleary et al., 1993; Ganz et al., 1994; Lorenz et al., 2001). Overall Health was predicted by depression, medical symptoms, and psychomotor efficiency. As such, it is likely impacted by symptoms within several domains of functioning and may provide an indicator of morbidity. It is interesting to note that the "quality of life" summary item of the MOS-HIV was associated with mental health functioning and mood status rather than Overall Health or other physical health status items. As such, the terminology used to determine overall HRQOL (i.e., ratings of overall health versus quality of life) may have a significant impact on the kind of health status information that is obtained.

Physical Function and Functional Status both strongly reflect physical health status and were highly interrelated. Both domains of HRQOL were strongly associated with medical symptoms, and to a lesser extent, depression and impairments in cognitive efficiency and psychomotor speed (see Table 21). Physical Function items assessed ability to perform physical tasks, such as walking, climbing stairs, lifting heavy objects, accomplishing moderate physical activities, and performing activities of daily living. In contrast, Functional Status was composed of items examining the occurrence of fatigue and pain, interference in work or social functioning due to health status, and impairment in the ability to perform vigorous physical activities. Therefore, Physical Function primarily reflects mobility and performance of basic activities of daily living whereas Functional Status provides an indication of an individual's ability to participate in more demanding physical, occupational, and social activities. As Functional Status examines a more comprehensive and diverse range of functioning than Physical Function, changes

in Functional Status may be more difficult to interpret. Therefore, use of the Physical Function measures may be preferred. However, if more detailed aspects of health functioning are of interest, such as fatigue or social function, specific dimensions of Functional Status may need to be examined.

Domains of HRQOL examined by the MOS-HIV can be reduced to physical and mental health summary domains (i.e., PHS and MHS, respectively). PHS and MHS were highly correlated, suggesting similarities between the constructs. Both HRQOL summary measures were significantly predicted by depression, medical symptoms, and psychomotor efficiency. However, MHS was more strongly associated with depression whereas PHS was more strongly associated with medical symptoms. Therefore, despite similarities between the two domains of HRQOL, distinctions between mental and physical aspects of health functioning are present.

HRQOL FOR INDIVIDUALS WITH HIV-INFECTION

Models of Health Status

Despite significant interest in HRQOL issues, few conceptual models of HRQOL and related clinical variables have been developed. Models provided by Wilson and Cleary (1995) and Bergner (1985) are presented in Table 22, along with information obtained from this study. Items at the top of the table represent specific biological and/or physiological variables. As health status levels progress down the table, they become broader in scope and represent more complex indices of health-related functioning.

Wilson and Cleary (1995) proposed five levels of health status: biological and physiological factors, symptom status, functional status, general health perceptions, and overall health quality of life. Personal and environmental factors are believed to have significant effects on the latter four levels of the model. This model appears to be primarily limited to medical and physical health aspects of functioning and minimizes psychological or mental health aspects of HRQOL.

Table 22. Comparison of HRQOL Models and Current Results

Wilson & Cleary (1995)	**Bergner (1985)**	**Current Study**
	Genetic Foundations	Demographic Variables
Biological/ Physiological Indices	Biological, Physiological, & Anatomical Conditions (Including disability status)	Medical Status Indicators
Symptom Status		Medical, Depression, & Cognitive Symptoms
Functional Status (Physical, role, social, & psychological)	Functional Status (Physical, social, & cognitive function)	Functional Status (Physical, role & cognitive function)
	Mental Condition	Mental Health & Health Distress
General Health Perceptions		Overall Health
Quality of Life	Health Potential	

A model by Bergner (1985) has also conceptualized health status into five levels, with similarities to and differences from the Wilson and Cleary model. At the most basic level of functioning is genetic foundations or inherited characteristics, which are believed to form the basis of all other aspects of health status. The next health status level consists of biochemical, physiological, and anatomical conditions which includes disease-related disability and, presumably, symptom status. Functional status is obtained in both models, but it does not include psychological function in the Bergner model. The mental condition health status level was included to reflect mood or emotional states. Finally, there is a health potential factor, which is related to the individual's functional potential, longevity, and disease prognosis. Health status was believed to be influenced by personal and societal views about health care (e.g., health habits, attitudes, and knowledge), extent and quality of available social networks, personal coping skills, access and use of resources (economic, educational, and psychological), and fulfillment of basic needs. Bergner's model is more comprehensive than Wilson and Cleary's (1995) model because of the inclusion indicators of both mental and physical heath status, rather than a primary focus on physical health status.

It appears that the models described above can be divided into two parts. The levels of health functioning presented in Table 22 that occur above the double horizontal line are important indicators of health status and have strong relationships with HRQOL but do not reflect aspects of HRQOL themselves. In contrast, levels of health functioning that occur below the double line represent frequently assessed HRQOL domains.

The findings of this study generally support the Wilson and Cleary (1995) and Bergner (1985) models of health status. As can be seen in Table 22, demographic, medical status, medical symptom, depression, and neuropsychological variables were used to predict HRQOL functioning. It appeared that variables that were closest to the level of HRQOL factors, namely indicators of symptom status, were the strongest predictors of HRQOL. Medical status indicators

had weaker and more variable associations with HRQOL factors whereas demographic variables had few relationships with HRQOL. Therefore, it appears that as predictor variables become more complex and move away from specific genetic, biological, or physiological indicators, they have a greater association with HRQOL domains. This provides some support for structure of health status levels presented in the upper portion of Table 22. It is possible that levels of health status have stronger associations with variables within bordering health status levels. For example, genetic factors may be more highly related to biological indicators than medical symptoms, whereas medical symptoms may have stronger associations with biological indicators and HRQOL measures than genetic factors. Additional research is required to confirm or reject this hypothesis.

Aspects of HRQOL examined in this study appeared to fall within three major domains of health status. Indicators of basic mobility and activities of daily living (Physical Function), participation in more demanding social and occupational activities (Functional Status), and perceived cognitive functioning (Cognitive Function) domains of HRQOL appeared to fit within the Functional Status health status level. Overall Health in this study was similar to the General Health Perceptions health status level of functioning described by Wilson and Cleary (1995). Finally, Mental Health and Health Distress appeared to fall within the Mental Condition factor described by Bergner (1985). The grouping of HRQOL domains of this study according to the health status levels described in Table 22 was generally supported by correlations between the HRQOL domains. The exception was Cognitive Function, which had similar associations with mental health and functional status, but was only included in the functional status domain of HRQOL. Mental Health and Health Distress were highly interrelated and together represented mental health status whereas Physical Function and Functional Status were highly interrelated and together represented physical/functional health status. Overall Health had moderate and equivalent correlations with other domains of HRQOL and remained a unique health status level in the Wilson and Cleary (1995)

and Bergner (1985) models.

It does not appear that HRQOL domains clearly fall within the hierarchical organization presented in Table 22. In the current study, HRQOL domains tended to differentially assess aspects of mental and physical health functioning. HRQOL domains would be expected to have various impacts on different aspects of functioning rather than represent various hierarchical levels within one primary aspect of functioning. Mental health status indicators, Mental Health and Health Distress, were more strongly predicted by symptom status (particularly depressive symptoms) than by functional status indicators, which does not support the hierarchy demonstrated in the Wilson and Cleary (1995) and Bergner (1985) models. In addition, the hierarchy of HRQOL displayed in Table 22 indicates that Overall Health should be more highly predicted by Mental Health and Health Distress than Functional Status. In this study, Overall Health demonstrated a stronger relationship with Functional Status than Mental Health and Health Distress (see Table 10). These results suggest that the HRQOL domains presented below the double lines in Table 22 should not be interpreted as representing a hierarchy of health status functioning.

Overall, the relationships between HRQOL and demographic, medical, and neurobehavioural variables obtained in this study were consistent with conceptual models of health status developed by Wilson and Cleary (1995) and Bergner (1985). These relationships will be examined in more detail below. Models of HRQOL generally represent a hierarchical structure of interrelationships between HRQOL domains, with functional status predicting mental health status, which predicts overall health functioning. However, the results of this analysis do not support the presence of a linear hierarchical relationship between HRQOL domains. Instead, mental health, overall health, and functional status are all interrelated and may represent equally important aspects of HRQOL functioning. As such, it is not surprising that they are all differentially associated with medical, depression, and

cognitive symptom status.

Impact of Clinical Variables on HRQOL Domains

HROQL domains were differentially associated with demographic, medical, and neurobehavioural variables at baseline and follow-up. Associations between clinical predictor variables and HRQOL were weakest when examining change scores. This likely occurred because of the reduced variance and range of change scores, as well as the lack of significant changes in medical symptoms, CD4 counts, AIDS status, and most neuropsychological variables between baseline and follow-up. As such, there was less impact of these variables on HRQOL change scores. Depression scores significantly improved between baseline and follow-up and, not surprisingly, had the greatest impact on MOS-HIV change scores. Change scores were occassionally predicted by the time interval between baseline and follow-up, with longer test-retest intervals weakly associated with greater declines in some aspects of health status. This is likely a result of a gradual decline in HRQOL over time, possibly as a result of HIV disease progression.

Depression and Medical Symptoms. The results from this study provided additional empirical evidence for the strong associations between medical symptoms (Justice et al., 1999; Kemppainen, 2001; Revicki et al., 1995; Vogl et al., 1999; Wilson & Cleary, 1996) and depression (e.g., Kaplan et al., 1995; Kemppainen, 2001; Osowiecki et al., 2000) with HRQOL. Mental health function was most strongly predicted in this study because of very high associations with depressive status. This suggests that an individual's level of mental health functioning can be reasonably determined from the extent of depressive symptoms reported by that individual. An individual with many symptoms of depression would be expected to have poor mental health whereas a person with no mood complaints would likely have good mental health. Strong relationships between medical symptoms and physical health functioning were also evident in this study. This

pattern of a stronger impact of depression on mental health and medical symptoms on physical health is consistent with predictions and previous research (e.g., Sherbourne et al., 2000; Wilson & Cleary, 1996). This study also demonstrated that changes in depressive symptoms over time were associated with changes in most aspects of HRQOL, particularly mental health domains.

It is not clear why medical symptoms had a greater impact on HRQOL at follow-up as compared to baseline. Total number of medical symptoms did not significantly change between the two time periods and examination of the individual medical symptom items revealed significant declines in persistent fatigue, but no differences for any other medical symptoms. Therefore, the greater impact of medical symptoms at follow-up as compared to baseline does not appear to be directly related to the incidence of medical symptoms. Depressive symptoms significantly declined between the two assessments. As a result of this decrease in depression scores and their variance, the relative impact of depression may have declined whereas the relative impact of medical symptoms may have become more apparent. Thus, medical symptoms scores may have been more likely to contribute unique variance to the prediction of HRQOL domains and remain in the final regression equations. It is important to realize that depression and medical symptoms are strongly associated with HRQOL. However, these clinical conditions may be overlooked by health care professionals primarily concerned with CD4 counts or viral load, which are important for HIV management but have minimal effect on HRQOL. Depression and medical symptoms are easily assessed and clinical interventions are well established. The occurrence of these symptoms is also significantly associated with reductions in medication adherence (Bartlett, 2002; Holzemer et al., 1999), which further points to the need to identify and treat these conditions.

Neuropsychological Variables. As expected, relationships between neuropsychological variables and primarily physical HRQOL domains were found

(Kaplan et al., 1995; Osowiecki et al., 2000). Neuropsychological performance likely is more related to physical than mental health functioning as the cognitive requirements of neuropsychological tests are also necessary for activities of daily functioning, such as work, social activities, shopping, cooking, and physical exercise. Performance on some neuropsychological tasks, particularly those requiring psychomotor speed and cognitive efficiency, may provide a crude indication of physical health functioning. Improvements in cognitive functioning would be expected to produce minor benefits in physical and functional status, overall impressions of health functioning, and perceived cognitive functioning.

Psychomotor efficiency (i.e., Digit Symbol performance) was the strongest predictor of HRQOL among the neuropsychological measures selected for this analysis. This measure has been demonstrated to predict HRQOL in a female sample using a different measure of HRQOL (Osowiecki et al., 2000). Thus, this appears to be a robust finding.

It is important to consider why Digit Symbol performance was the best neuropsychological predictor of HRQOL. It is possible that this task combines the skills required in the other tasks selected for analysis in this study. As a result, it may have accounted for most of the variance among the neuropsychological variables. Grooved Pegboard requires psychomotor speed and motor dexterity, Digit Span requires working memory and attention, and CVLT-Total recall requires the ability to learn information and use the memory systems. These skills are all necessary to perform the Digit Symbol task; psychomotor speed and motor dexterity are required as the task is timed and requires symbols to be written down quickly, whereas attention, learning, and memory skills are necessary to encode, store, and recall the number-symbol pairings and perform the task more efficiently.

Statistically significant associations between cognitive aspects of HRQOL and neuropsychological performance were obtained. However, neuropsychological variables were only able to predict a maximum of five percent of the variance of perceived cognitive status, which is not clinically significant. Overall, the results

from this study and previous research (Moore et al., 1997; Rourke et al., 1999a; 1999b) have clearly demonstrated that perceived cognitive status best reflects health status, particularly symptoms of depression, rather than objective cognitive performance.

HIV/AIDS Status. HIV/AIDS status variables (i.e., current CD4 counts and history of AIDS-defining conditions) were weak predictors of HRQOL, with variable relationships with health distress and functional status. These results partially supported the current hypothesis that HIV/AIDS status would be more strongly associated with physical health than mental health domains of HRQOL. Research results are mixed regarding the relationship between HIV/AIDS status and HRQOL domains, with some findings indicating associations between AIDS status and physical functioning (Burgess et al., 1993; Hughes et al., 1997; McDonnell et al., 2000), stronger relationships between CD4 counts and mental health than physical health (Chan & Revicki, 1999), or no relationship between HIV status and HRQOL variables (Badia et al., 1999; Copfer et al., 1996; Lenderking et al., 1997; Osowiecki et al., 2000). It is possible that these differences may result from variations in the severity of illness and other characteristics of HIV-infected samples as well as measures of HRQOL and HIV/AIDS status that are examined.

Current CD4 counts and a history of an AIDS-defining condition are medically important variables, but they had a relatively restricted impact on health status. As such, interventions for these variables would not be expected to significantly improve HRQOL. CD4 counts are relatively stable (as compared to depression and medical symptoms) and individuals may be able to adjust to changes in them more easily as they occur over a longer time period than changes in many other clinical variables. When an AIDS-defining condition first occurs and criteria for AIDS are met, HRQOL would likely be significantly impaired. However, after months or years following diagnosis of AIDS and remission of their illness, individuals' HRQOL would be expected to be less influenced by AIDS status and

more influenced by fluctuating clinical variables, such as variations in depressive or medical symptoms. Overall, changes in HIV/AIDS status would be expected to produce minimal changes in physical health aspects of HRQOL and no changes in mental health functioning, unless HIV/AIDS status changes were accompanied by depression or medical symptoms.

Demographic Variables. Contrary to the results of previous research (e.g., Hughes et al., 1997; Kemppainen, 2001; Lenderking et al., 1997; McDonnell et al., 2000; Holmes & Shea, 1999), demographic variables generally did not have a significant impact on HRQOL functioning in this study. In fact, age was the best demographic predictor of HRQOL and uniquely predicted only two percent of the variance of mental health status. Differences between the findings of this study and previous research are likely due to differences in sample composition. For example, our study was primarily composed of Caucasian males within a relative restricted range of age and education. In contrast, Holmes and Shea (1999) studied an ethnically diverse sample with a larger proportion of females and a greater range of education than the sample used in this study.

In summary, HRQOL demonstrated significant relationships with depression, medical symptoms, and cognitive impairments. These relationships have been observed using other instruments of HRQOL and clinical status (e.g., Bozzette et al., 1995b; Fanning & Emmott, 1993; Griffen et al., 1998; Justice et al., 1999; Kemppainen, 2001). HRQOL domains were differentially predicted by clinical variables; depression had stronger associations with mental health whereas medical symptoms had stronger associations with physical health. Neuropsychological functioning was more predictive of measures of physical health function. In contrast, HIV status and demographic variables were weak predictors of HRQOL. The results of this study indicate that treatment of depression and medical symptoms would likely result in the largest improvements in HRQOL. In

contrast, treatment of HIV status variables (e.g., CD4 counts) would be expected to produce minimal changes in health status.

IMPLICATIONS OF RESULTS

This research project was conducted with a sample of Caucasian, university educated, gay men. As such, the obtained results may not generalize to other populations with HIV-infection. The findings of this study need to be confirmed with other HIV-positive samples, such as women, children, heterosexual men, individuals with hemophilia, and intravenous drug users, with diverse ethnic and socioeconomic status backgrounds. Despite the limitations in sample, the results of this study have important implications for the evaluation of treatment interventions as well as recommendations for clinical practice.

Associations between clinical status variables and health status provide possible avenues for treatment interventions that improve HRQOL. A reduction in depression would be expected to produce a significant improvement in all aspects of HRQOL, with the greatest influence on mental health and health distress. It is likely that a reduction in mood symptoms would enable individuals to cope more effectively with their health impairments and improve physical health in addition to mental health function. Recent research has begun to examine these causal relationships. HIV-positive (Elliott, Russo, & Roy-Byrne, 2002) and HIV-negative (Kennedy, Eisfeld, & Cooke, 2001) individuals with clinical depression who respond to treatment have an associated improvement in HRQOL. Interventions for medical symptoms would likely benefit physical health and functional status, as well as impressions of overall health. This may lead to secondary benefits in health distress and mental health. Improvement of neuropsychological status, possibly as a result of antiretroviral medications, may provide modest improvements in physical functioning, functional status, health distress, and perceptions of overall health and cognitive status. Finally, treatment of HIV status variables, such as CD4 counts, would likely result in minimal changes in HRQOL. Future research is required in

order to verify these predictions.

Depression and medical symptoms were the strongest predictors of HRQOL, particularly measures of mental and physical function. These clinical symptoms are relatively variable over time and do not reflect the stability seen with HIV status indicators. Given their strong associations, variations in symptom status would likely be associated with variations in reported HRQOL. The impact of these symptoms is not consistent across HRQOL domains but has differential relationships with health status measures. For example, changes in mood were more highly associated with changes in mental health and health distress, and more weakly associated with physical health and functional status. In an intervention study, individuals may benefit from treatment but if they experience psychological distress due to non-experimental factors during post-treatment evaluations, the benefits of treatment may not be reflected in their HRQOL ratings. In this case, researchers would obtain a greater understanding of the impact of the treatment on health status if they also obtained measures of depressive symptoms and other indices of clinical status that could influence HRQOL in order to control for potentially confounding variables. It may also be beneficial to obtain average health status scores composed of HRQOL ratings over several time periods in order to reduce variability due to brief fluctuations in clinical symptomology.

Caution is required when interpreting improvements or declines in HRQOL domains. For example, physical health is strongly associated with medical symptoms, but increases in physical health should not be assumed to reflect changes in medical status. It is possible that medical symptoms have remained stable, but improvements in psychomotor efficiency and/or reductions in number of mood symptoms may have occurred due to primary or secondary effects of medication interventions. In addition, interventions for some domains of HRQOL may negatively affect other aspects of functioning. While antiretroviral medications may improve HIV status and cognitive efficiency, they may have significant adverse effects on physical and mental health status due to the occurrence of side effects

(e.g., lipodystrophy, fatigue, diarrhea, and nausea). As a result, these interventions may produce declines rather than improvements in HRQOL. It is important to tease apart these variables when making determinations about the impact of new antiretroviral medications on HRQOL.

In clinical trials, samples are typically selected that do not have significant depressive and/or medical symptomology. The strong impact of these clinical symptoms on HRQOL may not be detected by these studies as improvements in HRQOL may be more strongly attributed to medical status variables given the lack of variation of depression or medical symptoms. This may lead to the inaccurate conclusion that medical status is the most important indicator of HRQOL. In addition, possible interactions between medication effects and clinical status, such as depression, may not be identified. For example, individuals with depression may be prescribed a medication that has only been tested in non-depressed samples. This may result in unexpected outcomes in terms of the drug's effectiveness and the overall impact of these factors on HRQOL. Overall, the selective samples used in clinical trials limit the generalizability of the results of these studies to a large proportion of individuals with HIV, given the predominance of depression and medical symptoms that occur within this population.

Other aspects of functioning not examined in this study may significantly improve the prediction of HRQOL domains. For example, personality characteristics, coping strategies, availability of social support and other resources, non-HIV related stressors, current medications, and employment status factors would be expected to have some influence on HRQOL either directly and/or indirectly through changes in mood, physical status, or perceived cognitive function. Variations in HRQOL may also occur because of individual differences in health values. An individual who is unemployed may tolerate neuropsychological impairments relatively well whereas an employed individual may value cognitive function over physical, social, emotional, or sexual functioning. Given these individual differences as well as the large number of potential factors that could

impact upon HRQOL, it is important to determine the most important clinical, personal, and environmental variables for each HRQOL domain. This will enable treatment providers to individualize interventions in order to improve treatment efficacy and maximize HRQOL. For example, individuals with a strong support network and effective coping skills may require brief and focused interventions while individuals with a poor support network, an external locus of control, and a psychiatric diagnosis may require longer and more comprehensive assistance.

SUMMARY AND FUTURE DIRECTIONS

The study has provided important information about the underlying structure, reliability, and clinical utility of the MOS-HIV HRQOL instrument. The results of this study are limited by the use of a homogeneous sample that was primarily composed of highly educated, gay, Caucasian men. It is essential that this study be replicated with other HIV-positive populations from diverse socioeconomic backgrounds. These samples should include women, children, and individuals who obtained HIV-infection because of haemophilia or intravenous drug use.

The MOS-HIV is composed of 10 dimensions of HRQOL. Dimension scores are recommended for use when results need to be compared to previous research using these measures or research is focused on specific areas of functioning, such as fatigue. However, some of MOS-HIV dimensions have poor test-retest reliability and may require modification and/or addition of items to improve their psychometric properties. MOS-HIV items load onto six associated but independent aspects of HRQOL: mood status, anxiety related to health functioning, perceived cognitive status, overall health status, physical functioning, and more complex functional status. These HRQOL item factors need to be confirmed with additional research using larger and more diverse HIV-positive samples. However, most factors were stable over time and all factors had adequate test-retest reliability. Item factors can be used to monitor treatment interventions or the progression of HIV-infection. Stable and reliable overall mental and physical health status factors can also be

obtained when summary scores of HRQOL are desired.

MOS-HIV dimensions and factors demonstrated clinical utility. In general, depression and medical symptom scores were the strongest predictors of HRQOL, with depression more highly related to mental health domains and medical symptoms more highly related to physical health domains. Neuropsychological variables, specifically psychomotor efficiency, tended to predict physical rather than mental health domains. Age and medical status indicators (i.e., AIDS status and CD4 counts) were weak and inconsistent predictors of various HRQOL domains. These findings indicate that interventions for depression and medical symptoms would likely result in the greatest improvement in HRQOL. Domains of HRQOL identified in this study and their associations with medical and neurobehavioural variables were generally consistent with conceptualizations of health status developed by Wilson and Cleary (1985) and Bergner (1996). Future research is required to test these models of HRQOL using appropriate statistical techniques, such as path analysis.

The item factors obtained in this study need to be replicated in larger and more diverse samples of individuals with HIV-infection. Also, this study used relatively long test-retest intervals that ranged from 3 to 19 months in the test-retest reliability analyses. As such, changes in clinical status may have occurred between baseline and follow-up. A subset of subjects with minimal changes in depressive symptoms was used in the reliability analysis, to reduce the likelihood that reliability coefficients were influenced by changes in clinical status. However, defining clinical stability solely by mood status does not exclude changes that may occur in other areas of functioning (e.g., CD4 counts, viral load, non-HIV related medical symptoms or conditions, job loss or other environmental stressors, and drug or alcohol use) that could significant impact upon HRQOL. Future research is needed to determine the test-retest reliability of the MOS-HIV dimensions and factors using a shorter test-retest interval and/or clinically stable samples, as defined by measures of clinical status that are more comprehensive than the identification of

subjects with minimal changes in depressive symptoms.

Replication of this study using other HRQOL instruments and more diverse HIV-positive samples is required in order to identify clinical variables with the greatest and most consistent impact upon various domains of HRQOL. In addition, other measure of HRQOL may provide measures of health status functioning that are not assessed by the MOS-HIV, such as sexual function, disturbances in sleeping and eating behaviours, occupational status, medication adherence, non-HIV related medical status, or spirituality. It is also important to examine relationships between clinical and HRQOL variables in other medical and psychiatric samples to determine which relationships are universal (i.e., consistent across patient populations) as well as which relationships appear to be disease/condition specific. Together, this information would provide a better conceptualization of HRQOL.

MOS-HIV measures were differentially predicted by demographic, medical, and neurobehavioural variables in this study. Mental Health was highly predicted by these clinical variables while Overall Health was less strongly predicted by the same variables. Other clinical, personality, and environmental factors need to be examined in order to improve the prediction of HRQOL domains. These may include psychiatric diagnoses, non-HIV related medical history, antiretroviral medications, coping strategies, personal health values, social support networks, assistance with activities of daily living, and financial constraints. Identifying important predictors would enable the development of effective individualized treatment interventions.

Finally, additional research is required that progressively evaluates interventions that are developed to improve HRQOL, such as treatment of depression and medical symptoms. The identification of interventions that are most effective given specific clinical, personality, and environmental information would also be beneficial in order to maximize treatment efficacy and improve HRQOL within diverse medical and psychiatric populations.

APPENDIX A: MOS-HIV Health Survey

MOS-HIV HEALTH SURVEY

INSTRUCTIONS TO PATIENT: **Please answer the following questions by placing a "✓" in the appropriate box.**

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

Excellent	1 ☐
Very Good	2 ☐
Good	3 ☐
Fair	4 ☐
Poor	5 ☐

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

None	1 ☐
Very Mild	2 ☐
Mild	3 ☐
Moderate	4 ☐
Severe	5 ☐
Very Severe	6 ☐

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 ☐
A little bit	2 ☐
Moderately	3 ☐
Quite a bit	4 ☐
Extremely	5 ☐

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?

	(Check one box on each line.)	YES, limited a lot (1)	YES, limited a little (2)	NO, not limited (3)
a.	The kinds or amounts of **vigorous** activities you can do, like lifting heavy objects, running or participating in strenuous sports.	☐ (1)	☐ (2)	☐ (3)
b.	The kinds of **moderate** activities you can do, like moving a table, carrying groceries or bowling.	☐ (1)	☐ (2)	☐ (3)
c.	Walking uphill or climbing (a few flights of stairs).	☐ (1)	☐ (2)	☐ (3)
d.	Bending, lifting or stooping.	☐ (1)	☐ (2)	☐ (3)
e.	Walking one block.	☐ (1)	☐ (2)	☐ (3)
f.	Eating, dressing, bathing or using the toilet.	☐ (1)	☐ (2)	☐ (3)

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

(Check One)

Yes 1☐

No 2☐

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

(Check One)

Yes 1☐

No 2☐

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.

	All of the Time 1	Most of the Time 2	A Good Bit of the Time 3	Some of the Time 4	A Little of the Time 5	None of the Time 6
7. How much of the time, during the past 4 weeks, has your **health limited your social activities** (like visiting with friends or close relatives)?	☐	☐	☐	☐	☐	☐
8. How much of the time, during the past 4 weeks:						
a. Have you been a **very nervous person?**	☐	☐	☐	☐	☐	☐
b. Have you felt **calm and peaceful?**	☐	☐	☐	☐	☐	☐
c. Have you felt **downhearted and blue?**	☐	☐	☐	☐	☐	☐
d. Have you been a **happy person?**	☐	☐	☐	☐	☐	☐
e. Have you felt so **down in the dumps that nothing could cheer you up?**	☐	☐	☐	☐	☐	☐

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.

	All of the Time 1	Most of the Time 2	A Good Bit of the Time 3	Some of the Time 4	A Little of the Time 5	None of the Time 6
9. How often during the past four weeks:						
a. Did you feel full of pep?	☐	☐	☐	☐	☐	☐
b. Did you feel worn out?	☐	☐	☐	☐	☐	☐
c. Did you feel tired?	☐	☐	☐	☐	☐	☐
d. Did you have enough energy to do the things you wanted to?	☐	☐	☐	☐	☐	☐
e. Did you feel weighed down by your health problems?	☐	☐	☐	☐	☐	☐
f. Were you discouraged by your health problems?	☐	☐	☐	☐	☐	☐
g. Did you feel despair over your health problems?	☐	☐	☐	☐	☐	☐
h. Were you afraid because of your health?	☐	☐	☐	☐	☐	☐

	All of the Time 1	Most of the Time 2	A Good Bit of the Time 3	Some of the Time 4	A Little of the Time 5	None of the Time 6
10. How much of the time, during the **past 4 weeks:**						
a. Did you have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things?	☐	☐	☐	☐	☐	☐
b. Did you forget things that happened recently, for example, where you put things and when you had appointments?	☐	☐	☐	☐	☐	☐
c. Did you have trouble keeping your attention on any activity for long?	☐	☐	☐	☐	☐	☐
d. Did you have difficulty doing activities involving concentration and thinking?	☐	☐	☐	☐	☐	☐

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.)

	Definitely True 1	Mostly True 2	Not Sure 3	Mostly False 4	Definitely False 5
a. I am somewhat ill.	☐	☐	☐	☐	☐
b. I am as healthy as anybody I know.	☐	☐	☐	☐	☐
c. My health is excellent.	☐	☐	☐	☐	☐
d. I have been feeling bad lately	☐	☐	☐	☐	☐

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

APPENDIX B: HIV-Related Symptom Checklist Questionnaire

HIV- and AIDS-related symptoms:		≥2 weeks in past 6 months	In past week
(1)	Persistent fatigue (feeling tired all the time)	_____	_____
(2)	Oral Candida/thrush or white patches in the throat	_____	_____
(3)	Night sweats	_____	_____
(4)	Diarrhea	_____	_____
(5)	Persistent or recurrent fever over 100°F	_____	_____
(6)	Persistent/frequent or unusual headaches	_____	_____
(7)	Unintentional weight loss ≥10 lbs or ≥10% body weight	_____	_____
(8)	New skin rash	_____	_____
(9)	New or unusual cough	_____	_____
(10)	Persistent sore throat or mouth	_____	_____
(11)	Unusual bump, bruise, or skin discolouration	_____	_____
(12)	Persistent shortness of breath	_____	_____

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