

TITLE: A retrospective study to determine changes in quality of life over the first 6 months period of antiretroviral therapy, as measured by the MOS-HIV questionnaire.

Thesis Research in Partial Fulfillment of the Requirements for the Degree of M Phil (Palliative Care)

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CHAPTER 1

INTRODUCTION

There is currently no curative treatment for an HIV-infected person. The dream of eradicating and curing HIV infection had to be abandoned when it became evident that HIV remains detectable in latent infected cells, even after long-term treatment (Hoffmann, Kamps & Rockstroh 2006, p. 55). Instead it has become more realistic to consider lifelong management of HIV infection as a chronic disease, similar to that of diabetes mellitus. The management of the abovementioned condition is executed by using an individualized combination of at least three antiretroviral drugs, known as highly active antiretroviral therapy (HAART) (Hoffmann et al. 2006, p. 117; Miller S. 2002). HAART often requires significant lifestyle modifications, as well as adaptation of daily activities to the demands of prescribed treatment regimens. Adherence to HIV/AIDS treatment is required to be among the most rigid of any disease (Bosworth 2006). The reason is that there is potential for compromising the future effectiveness of these treatments, as well as the development of resistance to the prescribed medication(s) (Bosworth 2006).

New insights into mechanisms of resistance to HAART suggest that it happens when HIV continues to replicate in the presence of antiretroviral medication. Both less-active regimens and inadequate adherence to highly active regimens allow HIV to continue to replicate, creating selective pressure that increases the likelihood of resistance mutations. Full therapeutic benefit may require near-perfect adherence to the dosage, frequency, timing, and food requirements of many antiretroviral agents. Thus, imperfect adherence may be HAART's Achilles' heel (Friedman & Williams 1997; Bosworth 2006).

Bosworth (2006) reports that persons living with HIV/AIDS experience ongoing psychosocial stressors, both interpersonal (eg. stigma) and intrapersonal (eg. shame or guilt). This is due to the diagnosis of HIV/AIDS as a life-threatening chronic illness, treatment regimens that are complex to manage, and the uncertainty of the long-term benefit of these regimens. These multiple, severe and unrelenting stressors may profoundly affect the individual's quality of life (QOL) and tax existing coping resources. Thus, given the potential impact of HIV/AIDS, understanding the interaction and relationships among biological, psychological, social, and spiritual dimensions is imperative.

The success of HAART is often associated with dramatic health benefits. These include the observations that Cryptosporidia and Kaposi's sarcoma can disappear, progressive multifocal leukoencephalopathy (PML) can be cured completely, while secondary prophylaxis for cytomegalovirus can be stopped (Hoffmann et al. 2006). However, these clinical benefits may not accurately represent the effect of treatment on the patients' physical, psychological, and social functioning or their subjective sense of well-being.

The success of HAART can be evaluated using different criteria: virological indicators, immunological indicators or clinical success. Virological success, the earliest indicator of treatment success, is represented by a decrease in HIV viral load. The virus concentration in an infected person's blood can be measured, and is expressed as HIV virus copies per millilitre (c/ml). Most copies are segments of virus DNA or RNA, and counts indicate 'activity' more than 'absolute number of viruses per millilitre'. This is known as the viral load, and currently the test has a lower limit of detection of 25 - 50c/ml. A decrease to below the level of detection is normally reached after four months

of therapy, and a viral load above the level of detection after six months of treatment is generally seen as treatment failure.

Virological success is followed some time later by immunological treatment success. Immunological response to treatment is measured by the serial calculation of the infected person's CD4 T-cell count. An increase in the CD4 cell count represents treatment success.

Clinical treatment success is the absence of opportunistic infections, the absence of AIDS-defining illnesses and the presence of good health. This is detected by physical examination of the patient. Clinical treatment success, and even more so clinical treatment failure, usually becomes apparent only much later than changes detected in virological or immunological indicators. (Hoffmann, Kamps & Rockstroh 2006, p. 118).

Despite the increased use of highly active antiretroviral therapy and associated dramatic health benefits, the ultimate goal of antiretroviral therapy remains to prolong the patient's life, while at the same time maintaining the best possible quality of life (Hoffmann & Mulcahy 2006). This paradigm suggests that not only opportunistic infections and malignancies, but also side effects of therapy should be prevented. Ideally antiretroviral treatment should have little or no influence on daily life (Hoffmann, Kamps & Rockstroh 2006, p. 117).

A full appreciation of the impact of therapeutic regimens on patients with HIV disease requires the assessment of a comprehensive set of outcomes. These include clinical disease, laboratory markers, health-related quality of life (HRQL), economic outcomes, as well as the interrelationships of these variables (Berzon & Lenderking 1998). This creates a need for health-related quality of life measures. While traditional clinical

outcomes of HAART (such as an undetectable viral load, physiologic changes and adverse events) provide useful clinical and biological information, it is essential to understand the impact of HIV disease on different aspects of patients' lives. The toxicities and inconveniences associated with most regimens may outweigh the treatment benefits completely (Nieuwkerk et al. 2007, p. 600). It is important that the effects of drug treatment and other medical regimens translate into benefits that patients can experience. This means that the treatment must help patients to function, as well as feel, better (Nieuwkerk et al. 2007, Wu 1999).

A psychometric instrument, namely a Quality of Life Scale, can play an important role in distinguishing and highlighting subtle differences in treatment regimens of apparent equal clinical efficacy (Punpanich 2005). The purpose of a quality of life measurement tool is therefore not merely to measure the presence and severity of symptoms of disease, but also to show how the manifestations of an illness or treatment are experienced by an individual (Eiser & Morse 2001, p. 205, Nieuwkerk et al. 2007). Health status and health related quality of life (HRQOL) is of vital importance to patients and medical practitioners, as they assist both parties to assess daily functioning of patients and predict adherence to therapy (Berzon and Lenderking 1998).

Behaviour associated with adherence is complex. The prescribing clinician is a very important part of the adherence dynamic, together with the patient, the disease treated, the treatment regimen and the provider-patient relationship (Friedland & Williams 1997). Clinicians and patients alike have a range of beliefs about the efficacy of given pharmacologic agents and the importance of taking them as prescribed. These beliefs will ultimately contribute to patients' success or failure when integrating complex new behaviours into their daily lives, and thus ultimately influence adherence. Clinicians also make assumptions about a given patient's ability to follow a regimen (Friedland &

Williams 1997). The degree to which a regimen alters daily routines and lifestyle is extremely important and may only be evaluated using patients' assessments (Hoffmann et al. 2006, p. 56).

It was against this background that the present study evolved. Rapkin (2001) states that quality of life in people living with HIV/AIDS may directly influence treatment adherence. Medications may reduce quality of life for some patients by creating many side effects, by interfering with preferred routines, or by intruding upon desired activities and relationships. These quality of life factors may determine whether or not an individual is able to remain on medications for an extended period.

Based on the relevant literature the earliest criterion for treatment success, namely an undetectable viral load after six months of antiretroviral therapy, was chosen to compare with the patient's self-report on quality of life. If an improvement in quality of life can be seen at the same time as clinical benefit is evident it can serve as an additional motivational tool to improve adherence. One would be able to demonstrate a trade-off between treatment effectiveness, functional status and side-effects. Tracking changes in functional status over time, by routine assessment of the quality of life in persons with HIV infection, can improve overall care and enhance communication between patient and healthcare provider (Grossman, Sullivan and Wu. 2004). These quality of life factors may determine whether or not an individual is able to remain on medications for an extended period. A positive outcome of the study can help patients on HAART waver difficulties and side effects against the prospect of an improvement in their quality of life.

A positive outcome of the study can assist clinicians to obtain a better understanding of the holistic functioning of the people living with HIV/AIDS. This in

turn, by providing feedback and involving the patient in his/her therapy, is hoped to help improve adherence. Douaihy and Singh (2001, p. 451) report that improving the overall HRQOL of patients with HIV infection through the enhancement of positive general health perceptions represents an important area of therapeutic intervention.

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CHAPTER 2

LITERATURE REVIEW

2.1 Quality of Life

In spite of the fact that we all have some perception of what quality of life entails it is difficult to define. It is equally difficult and somewhat vague to establish what is meant by feeling good and being ill. The Ontario Council for Social Development sees quality of life (QOL) as the product of the interplay among social, health, economic and environmental conditions which affect human and social development ('Notes on Quality of Life' 2008).

The Quality of Life Research Unit at the University of Toronto ('Notes on Quality of Life' 2008) defines quality of life as the degree to which a person enjoys the important possibilities of his/her life. These possibilities result from the opportunities and limitations each person has in his/her life, and reflect the interaction of personal and environmental factors. Three major life domains are identified: Being, Belonging, and Becoming. The Being domain includes the basic aspects of "who one is" and has three sub-domains. Physical Being includes aspects of physical health, personal hygiene, nutrition, exercise, grooming, clothing, and physical appearance. Psychological Being includes the person's psychological health and adjustment, cognitions, feelings, and evaluations concerning the self, and self-control. Spiritual Being reflects personal values, personal standards of conduct, and spiritual beliefs which may or may not be associated with organized religions.

Belonging includes the person's fit with his/her environment(s) and also has three sub-domains. Physical Belonging is defined as the connections the person has with his/her

physical environments such as home, workplace, neighbourhood, school and community. Social Belonging includes links with social environments and includes the sense of acceptance by intimate others, family, friends, co-workers, the neighbourhood and community. Community Belonging represents access to resources normally available to community members, such as adequate income, health and social services, employment, educational and recreational programs, as well as community activities ('Notes on Quality of Life' 2008).

Becoming refers to the purposeful activities carried out to achieve personal goals, hopes, and wishes. Practical Becoming describes day-to-day actions such as domestic activities, paid work, school or volunteer activities, and seeing to health or social needs. Leisure Becoming includes activities that promote relaxation and stress reduction. These include games, neighbourhood walks, and family visits, or longer duration activities such as vacations or holidays. Growth Becoming activities promote the improvement or maintenance of knowledge and skills ('Notes on Quality of Life' 2008).

Ventegodt, Merrick and Andersen (2003, p. 1030) state that quality of life means a good life, where a good life is the same as living a life with a high quality. Quality of life, according to them, is therefore not one of many benefits of medical intervention, on par with other improvements, but belongs on the highest, most common level of life.

All great religions and philosophies have a perception of how to achieve a good life, ranging from saying that a good life is attained by practical codes of conduct (requesting one to engage in a certain positive attitude to life), to the search into the depths of your own being. Ideas about a good life are closely linked to the culture of which one is a part. When people in a Western culture, for example, view a good life, the

cultural conditioning makes them tend to include happiness, fulfillment of needs, and functioning in a social context (Ventegodt, Merrick & Andersen 2003, p. 1031).

Calman (1984, p. 124) defines quality of life as congruence between one's dreams, ambitions, hopes for the future, present lifestyle, and experiences. This definition of QOL largely parallels the World Health Organization (WHO) definition of health. The WHO has defined QOL as individuals' perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, standards, expectations and concerns (WHO 1997).

Jenaro et al. (2005, pp. 734 - 739) investigated the use of the quality of life concept internationally to test its etic (universal) and emic (culture-bound) properties. Similar profiles for respondents in different geographical groups indicated that the concept does have universal meaning, and differences across scores in groups indicated the emic (culture-bound) property of the QOL concept. In contrast to this Bullinger and Schmidt (Scottish Government Publications 2006, *Quality of life and well-being: Literature review and thinkpiece*) state that, even though researchers may desire a QOL assessment tool to be used globally, which will permit comparison of QOL of one culture with another, no such scale exists. Given the multiplicity of variables or domains comprising a culture, that goal is unrealistic, both theoretically and methodologically

Carr and Higginson (2001, pp. 1357 – 1359) indicate that quality of life is determined by:

1. The extent to which hopes and ambitions are matched by experience;
2. Individuals' perceptions of their position in life, taken in the context of the culture and value systems where they live and in relation to their goals, expectations, standards and concerns;

3. **Appraisal of one's current state against some ideal and the things people regard as important in their lives.**

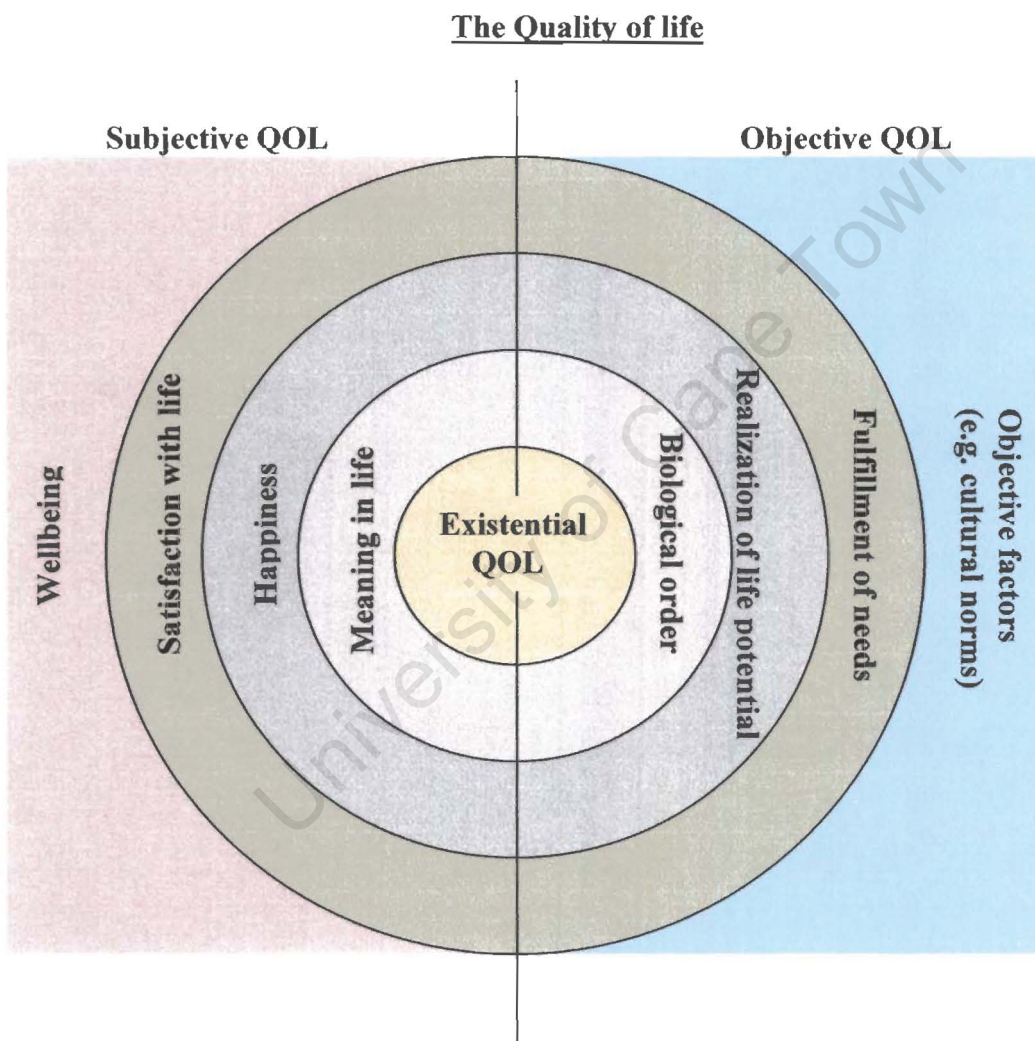
Ventegodt et al.. document that views about a good life can be divided into three loosely separate groups, each concerned with an aspect of a good life:

1. The *subjective* quality of life is how good a life each individual feels he or she has. Each individual personally evaluates how he or she views things as well as his or her feelings and convictions.
2. The *existential* quality of life means how good one's life is at a deeper level. It is assumed that the individual has a deeper nature that deserves to be respected, and that the individual can live in harmony with this nature. Included are the fulfillment of one's biological nature (like optimized growth), and to live in accordance with certain spiritual and religious ideals determined by the nature of our being.
3. The *objective* quality of life means how one's life is perceived by the outside world. This view is influenced by the culture in which people live. The objective quality of life reveals itself in a person's ability to adapt to the values of a culture and tells us little about that person's life. Examples may be social status, or the status symbols one should have to be a good member of that culture (2003, p. 1031).

Ventegodt, Merrick & Andersen place these opinions on a good life in a spectrum, ranging from the subjective to the objective with the existential element in the middle. They call this spectrum the integrative quality of life (IQOL) theory; since it incorporates a number of existing quality-of-life theories (cf. Figure 1). Wellbeing, satisfaction with life, happiness and meaning in life form part of the subjective spectrum, while cultural norms, fulfilment of needs, realising life potential and biological order constitute the objective side of IQOL. In the centre, between meaning in life and biological order, lies

an abstract nucleus that remains inexpressible and immeasurable. The subjective and objective unite in this nucleus, and it gives rise to the deepest subjective quality of life and the objective state of the organism, as we know it from health and sickness (Ventegodt, Merrick, Andersen 2003).

Figure 1: The integrative theory of the quality of life: (Ventegodt et al.)



The humanistic psychologist Abraham Maslow postulated in 1968 that quality of life is related to a progressive satisfaction of a hierarchy of needs. In ascending order they can be described as physiological needs (1), safety (2), love (3), esteem (4) and self-actualization (5) (Chang & Hsiao 2006)(cf. Figure 2).

Figure 2: Maslow's hierarchy of needs:



These five levels of the hierarchy of needs can be adapted to the palliative care setting, or the management of any debilitating diseases like HIV: The physiological needs are the desire to be free from distressing symptoms such as pain or dyspnoea. The need for safety is the need to be physically safe, the need not to be abandoned or even the desire not to die. The need for love and belonging equals the need for affection and acceptance in the face of a devastating disease, while the need for esteem translates as the need for dignity, respect and appreciation for the person. The need for self-actualisation includes the need to live on in the memory of loved ones and to leave some form of legacy behind (Raspa & Zalenski 2006).

The concept of fulfilment of needs is intuitively meaningful. The need is also closely linked with desires and the satisfaction we all achieve by having these needs or desires fulfilled. But fulfilment of needs can take the extreme stance that life is all about realizing one's biological information. That is clearly not the same as realizing one's life potential, and if one takes Maslow's need for self-realization in the abstract, the definition becomes vague and unclear. A need is no longer something the individual has to satisfy from an outside source such as food and shelter, but something the person has to contribute to and accomplish for him- or herself. Many researchers therefore suggest that we move away from focusing on *needs* (Ventegodt, Merrick & Andersen 2003).

2.2 Health-Related Quality of Life:

In a clinical or medical setting QOL includes those dimensions of life directly affected by the overall state of health and is often referred to as health-related quality of life. HRQOL is clearly a multidimensional concept that includes global health perceptions, symptom status, functional status, biologic and physiologic variables, individual and environmental characteristics, as well as overall quality of life (Douaihy and Singh 2001, p. 451). Non-health-related QOL domains include features of both the natural and the created environment (i.e. economic resources, housing, air and water quality, community stability, access to the arts and entertainment) and personal resources (i.e. the capacity to form friendships, appreciate nature, or find satisfaction in spiritual or religious life). These factors affect health-related quality of life, but unlike HRQOL domains, are less likely to improve with appropriate medical care (Albert 2002).

In 2005 the European Medicine Agency defined HRQOL as the patient's subjective perception of the impact of his/her disease and its treatment(s) on his/her daily life, physical, psychological and social functioning and general well-being. This definition

of HRQOL has as a common basis the definition of health given by the World Health Organisation (WHO) in 1948: "Health, is a state of complete physical, mental, and social well-being and not merely the absence of disease"... (European Medicines Agency 2005, p. 3)

Michalos (Scottish Government 2006), a critic of the terminology HRQOL, suggests that health-related QOL "...may be regarded as a particular species of the genus domain-related quality of life. Other species would include, for example, job-related quality of life and marriage-related quality of life..." (Scottish Government 2006). As with the wider term 'quality of life' there is no uniform definition of health-related QOL, merely competing views. The concept of health-related QOL also varies according to the focus of a specific investigation. It depends on whether the emphasis is placed on physical functioning or subjective well-being. As a result there are a wide range of different interpretations of health-related QOL, each tailored to specific purposes and resulting in an even wider range of measurements that relate to these.

HRQOL measures date back to the 1930s and 1940s with the New York Heart Association Classification and Karnofsky's Performance Status assessment, both of which described a patient's level of physical activity. These were early, standardized approaches for determining the patient's functional abilities as a result of a disease or treatment (Lin, Wu and Revicki 2002).

The approach to the measurement of the quality of life derives from the position that there are a number of domains of living. Each domain contributes to one's overall assessment of the quality of life. The domains include family and friends, work, neighbourhood (shelter), community, health, education, and spiritual. The purpose of a quality of life scale or index is to provide a tool which can be used to monitor key

indicators that encompass the mentioned domains. Quality of life scales can be used to comment on key issues that affect people and are intended to monitor conditions which affect the living and working conditions of people. Quality of life scales also focus action on ways to improve health ('Notes on Quality of Life' 2008).

Some HRQOL research is dominated by the psychological approach. It is about individual responses to the physical, mental, and social effects of illness on daily living. These influence the extent to which personal satisfaction with life circumstances can be achieved, even in the face of life-long antiretroviral medication.

The move from QOL to HRQOL is designed to emphasise an interest in the functional effects on patients of an illness and its consequent therapy. In this case 'quality of life' and 'health status' are interchangeable terms. Like HRQOL, health status defines function at either a generic or disease-specific level (Scottish Government 2006).

The debate around the definition of HRQOL centres upon two issues:

1. Different conceptions of health. It can be summarised as the medical definition (based on the absence of disease) as opposed to the 'positive' definition (which entails more than just the absence of disease) advanced by the WHO.
2. The relationship and distinction between 'health' and 'quality of life'.

These fundamental questions remain unresolved, resulting in contradictory definitions of the concept health-related quality of life.

HRQOL encompasses domains of life directly affected by changes in health and HRQOL domains are aspects of life that improve when a physician successfully treats a patient (Albert 2002). There is general agreement that HRQOL includes at least a

person's physical, social and cognitive functioning and subjective sense of well-being (Wu 1999; Hoffmann C., Kamps B., Rockstroh J. (ed.) 2006; Miller S. (chair) June 2002).

2.3 Quality of Life Scales:

The earliest uses of quality of life measures were in health research as part of natural history studies, documenting the problems and challenges faced by people living with arthritis and other chronic, debilitating diseases. Quality of life considerations began to enter into the treatment of AIDS during the late 1980s and early 1990s, as AZT and treatments for opportunistic infections came into use and length of survival after diagnosis began to increase (Rapkin 2001, *Who's Life is it Anyway?*).

Quality of life is measured by asking a series of questions about specific aspects of functioning and well-being. Rapkin (2001) divides QOL assessments into two main categories: the 'molecular' approach and the 'molar' approach. In the molecular approach QOL is determined by putting together answers to questions, similar to building an object by putting together different molecules.

The molecular approach relies on standard self-report scales that ask about different aspects of life, including physical symptoms, pain and fatigue, ability to carry out chores and care for oneself, mental health, work performance, social activities, and general health and well-being (Rapkin 2001).

With the 'molar' approach people are asked to put an overall value on their current health. QOL is looked at by using global assessments of life as a whole. One such an approach is the Standard Reference Gamble, designed by where people are presented with a range of bets, wagering time in their current health state against time in perfect

health. For example, most anyone would take the bet if the choice were one year in perfect health versus one year in current health. But, would you wager one year in current health to get eleven months in perfect health? (Rapkin 2001).

The molecular approach to QOL assessment has led to disease-specific sub-scales, addressing particular QOL concerns related to a specific diagnosis. HIV-specific sub-scales might include HIV stigma, experiences with disclosure, living with complicated medication regimens, or satisfaction with sexual function and intimacy in light of HIV transmission precautions. There are many molecular quality of life scales that differ in terms of the number of dimensions that they include as well as the number of separate items (questions) used to measure each dimension. Responses to items are usually made on numeric rating scales, where numbers stand for the frequency or severity of a problem or how strongly one agrees with a given statement (Rapkin 2001).

A claim about improvement in HRQL needs to be supported by data, collected by instruments validated for use in the corresponding condition. In theory both generic and disease specific questionnaires may be used for a given condition. In practice, it is very important to choose the questionnaire which contains/is adapted to explore the domains relevant for the disease and its treatment(s). 'HRQL improvement' as a claim implies that the most important and clinically relevant health-related domains of functioning, that impact patient's quality of life, are known and measured (European Medicines Agency 2005, p. 3).

In order to approve a global claim that a product "improves HRQL", it would be necessary to demonstrate robust improvements in all or most of these domains. There are situations where treatment improves specific domains of HRQL (such as physical or social functioning), which are considered important to patients. A company may seek

specific claim based on the subset (one or two) of domains of HRQL, if the analysis plan pre-specifies which domains will be targeted as endpoints in the study. In addition, the use of specific HRQL domains as study endpoints pre-supposes that the HRQL instrument was adequately developed and fully validated prior to measuring the subset of domains chosen (European Medicines Agency 2005, p. 3).

The most widely used measures of QOL in clinical research involving people living with HIV/AIDS are derived from the Medical Outcomes Study (MOS), conducted during the 1980s by the Rand Corporation. Several versions have been derived from the original MOS that differ somewhat in the number of items that they include and the aspects of quality of life that they assess. In the early 1990's researchers at John Hopkins University Hospital created a version of the MOS measure specifically for HIV/AIDS research and they named it the 'MOS-HIV' (cf. 2.4.3 The MOS-HIV Health Survey). Other quality of life measures that have been adopted for HIV/AIDS research include the Functional Assessment of HIV-Infection (FAHI), which was derived from a quality of life measure widely used in cancer research, and the HIV/AIDS Target Quality of Life measure (HAT-QOL) that includes areas of concern unique to AIDS (Rapkin 2001). All the HRQOL scales used in HIV/AIDS make use of patient-reported data.

The quality of life scale chosen for the study was the MOS-HIV questionnaire. It was chosen above other available scales for the fact that it has been validated for use in HIV/AIDS patients (validity, reliability, responsiveness and interpretability for the HIV setting)(European Medicines Agency 2005); it encompasses the most important and clinically relevant health-related domains of functioning; it integrates the positive and the negative effects of treatment to give a net effect in measurable areas; it can demonstrate changes in certain domains of HRQOL; it has been the questionnaire of choice of several drug companies developing new antiretroviral medication; and it is patient-reported.

2.3.1 Advantages of Patient-reported Data on Quality of Life:

Patient-reported data on quality of life give researchers access to information that is not available from any other source and which is of great importance to the patient. The most relevant and valid information about ability to function and quality of life must come from the person's own experiences. This position is supported by the fact that both clinicians' and family members' estimates of functioning are less reliable, and often do not agree with those of the patient (Wu 1999). The person's perception dictates how they perceive their situation, which is the most accurate way of determining QOL.

2.3.2 Disadvantages of Patient-reported Data on Quality of Life:

Patient reports of their quality of life are by their nature subjective. As such data obtained from patients often differ from data obtained from other sources. A pill count, for example, may reveal a different compliance to the compliance reported by the patient. In general patients tend to be more optimistic about their abilities than family members or physicians and thus judge their health to be better than others would.

Patient reported data can also be idiosyncratic in that there are sources of variability in patients' responses that are not related to the treatment they are receiving. If a woman, for example, gets evicted from her apartment, her mood may be depressed. This is a source of legitimate variability in a person's quality of life, independent of the disease and/or treatment, and will consequently be reflected in the answers she gives to the HRQOL questionnaire (Wu 1999).

2.3.3 The importance of HRQOL as a diagnostic tool:

Quality of life scales have the advantage of being able to integrate the positive effects of treatment on disease as well as the negative effects to give 'net' effects in measurable areas. Without such measures it can be difficult to interpret if a drug that both causes some symptoms and prevents others has a beneficial net effect. For example, it is difficult for a clinician to decide whether a patient should take a drug that is known to cause headache and anorexia, but decreases fatigue. This concept is of utmost importance in the treatment of HIV/AIDS.

It is essential to understand the impact of a disease on different aspects of patients' lives and it is important that the effects of drug treatment and other medical regimens translate into benefits that patients can experience. Although traditional outcomes, such as mortality, physiologic changes and adverse events provide useful clinical and biological information, they may not accurately represent the effect of treatment on the patients' physical, psychological, and social functioning, or their subjective sense of well-being. In addition, some of the effects of a drug or treatment may be in areas not accessible to physiologic measurement and may only be evaluated using patients' assessments. These areas include effects on energy, pain, or generally how patients feel. Although treatments frequently influence these parameters, a clinical setting is unlikely to demonstrate effects in these areas if patient-reported outcomes are not included. In this respect, quality of life measures capture patients' perspectives of their disease and treatment, their perceived need for health care, and their preferences for treatment and outcomes (Carr & Higginson 2001; Wu 1999).

2.4 Influences on Quality of Life:

The presence of symptoms, as well as side-effects of ARV medication, has the strongest impact on all measured dimensions of HRQOL in HIV-infected patients (Nieuwkerk et al. 2007). HRQL includes aspects of health and life that are experienced by the patient and are readily affected by disease and treatment. While many factors can influence the patient's quality of life, the more restricted concept of HRQL is the subjective perception of the impact of disease and treatment on the patient's health (Lin, Wu & Revicki 2002, p. 202). If, for the purpose of the study, subjects are chosen without present symptoms as a result of HIV disease, it leaves the impact and tolerability of antiretroviral regimens as the main determinant of health related quality of life, as well as of treatment success. It is therefore important to focus on the side-effects of antiretroviral medication. Some of the more common currently recognised side effects and complications of these agents are listed in Appendix B.

2.4.1 Antiretroviral Medication:

The following antiretroviral agents are currently available in South Africa for use in any HAART regimen: lamivudine, zidovudine, didanosine, nevirapine, efavirenz, stavudine, abacavir, tenofovir, nelfinavir, indinavir, ritonavir, saquinavir, lopinavir and atazanavir (MIMS Jan 2008). These agents are listed in Appendix A with the trade names and class of drug to which the agent belongs.

Gastrointestinal problems are the most common side effects of almost all antiretroviral drugs – nucleoside analogue reverse transcriptase inhibitors (NRTI's), non-nucleoside analogue reverse transcriptase inhibitors (NNRTI's) and particularly protease inhibitors (PI's) – and occur especially during the *early stages* of therapy (Buhk

& Schieferstein 2006). Typical symptoms include abdominal discomfort, loss of appetite, diarrhoea, nausea and vomiting. Heartburn, abdominal pain, meteorism and constipation may also occur. Nausea is a common symptom with zidovudine-containing regimens; diarrhoea occurs frequently with zidovudine, didanosine and all PIs, particularly with ritonavir and nelfinavir, as well as with saquinavir, lopinavir/r, atazanavir and tipranavir. Treatment with zidovudine rarely leads to a severe form of gastric pain, nausea and vomiting in the early phase of therapy, in which case it should be discontinued (Buhk & Schieferstein 2006).

There is an association between high plasma levels of efavirenz and the occurrence of central nervous system (CNS) symptoms. If the CNS side effects persist for more than two to four weeks, it is reasonable to prescribe 200 mg pills, so that the dose can be divided into a 400 mg night dose and a 200 mg morning dose (Buhk & Schieferstein 2006; Miller S. (chair) June 2002).

Peripheral neuropathy with NRTI's typically begins gradually after several months of therapy. (Buhk & Schieferstein 2006; Hoffmann C., Kamps B., Rockstroh J. (ed.) 2006).

Hypersensitivity reaction occurs mostly with abacavir, and happens within the first six weeks of treatment. (Criteria in favour of hypersensitivity reaction with ABC include gastro-intestinal side-effects, deterioration with each dose taken, and the development of symptoms within the first six weeks of treatment). Hypersensitivity to Nevirapine may also occur, and the time frames are similar to that of abacavir (Miller S. (chair) June 2002; Buhk & Schieferstein 2006).

Hepatotoxic reactions occur at different time points for different drug classes: nucleoside analogues lead to hepatic steatosis, which is probably caused by mitochondrial toxicity, and usually occurs after more than 6 months on treatment NNRTIs often cause a hypersensitivity reaction within the first 12 weeks (Buhk & Schieferstein 2006, Miller S. (chair) June 2002).

In up to 40 % of patients, treatment with efavirenz leads to CNS side effects such as dizziness, insomnia, nightmares; even mood fluctuations, depression, confusion, depersonalisation, paranoid delusions and suicidal ideation may occur. These side effects are observed mainly during the first days and weeks of treatment. Discontinuation of therapy becomes necessary in only 3% of patients. The side-effects of the classes of antiretroviral medication are tabled in Appendix B.

The timeframe of six months as a second evaluation for the quality of life seems appropriate in terms of possible side-effects of the treatment, which could influence the QOL. It appears as if most side-effects, related to a specific regimen or drug, will be resolved by six months, or only start after six months of therapy. In this way it is hoped that the generic effect of antiretroviral medication, and not specific regimens, will be measured in the changes in the quality of life.

CHAPTER THREE

AIM AND OBJECTIVES

3.1 Aim:

The aim of the research was to determine changes in quality of life over the first six months of anti-retroviral therapy.

3.2 Objectives:

3.2.1 To compare the results of the MOS-HIV survey done at initiation of antiretroviral medication to the survey completed after six months of therapy

3.2.2 To investigate a possible trend in the change in QOL as per the MOS-HIV surveys and whether this correlates with viral suppression

CHAPTER FOUR

METHODS

4.1 Study design:

The study was a retrospective study comparing the completed MOS-HIV questionnaires of thirty HIV-positive subjects. The MOS-HIV questionnaires formed part of clinical research studies that were completed previously at the study site. The questionnaires at two time points were compared: the MOS-HIV completed on the day of initiation of HAART was compared to the questionnaire completed after six months of treatment. A secondary analysis was done on the data which formed part of the clinic's record of the original clinical drug trials.

MOS-HIV questionnaires were used from subjects who had been treatment naïve, received their first antiretroviral regimen as part of the clinical drug trial, and had reached an undetectable viral load (less than 50 copies/ml) before or at 24 weeks of antiretroviral treatment.

4.2 Study Site:

The study site was the research office of Dr D R Malan at Triple M Research, 43 Parliament Street, Central, Port Elizabeth in South Africa.

4.3 Study participants:

MOS-HIV questionnaires were selected from subjects who came from resource poor areas in Motherwell, Walmer and Uitenhage in the Nelson Mandela Metropole. The

participants utilized in the study had sheltered living conditions with adequate ablutions and running water.

The nature of the study site is such that subjects are enrolled into clinical drug trials with CD4 counts of more than 200 cells/mm³ but less than 350 cells/mm³. This meant that MOS-HIV questionnaires chosen represented subjects who were relatively healthy.

4.3.1 Inclusion criteria:

MOS-HIV questionnaires were selected from study participants who met the following criteria:

1. Male or female subjects of at least 18 years of age
2. A subject was using his/her first antiretroviral regimen
3. A subject had completed two MOS-HIV questionnaires, the first one at initiation of HAART, and the second one after 6 months of therapy
4. A subject reached an undetectable viral load at or before 6 months of antiretroviral therapy
5. Subject was able to speak English and had an educational level of at least grade 8 at the time of completion of the MOS-HIV
6. Subjects agreed to participate in the research, and signed an informed consent document which included the use of quality of life data
7. Participants adhered to the required visit schedules and complied to the prescribed HAART regimen
8. Subjects had sheltered living conditions with ablutions and running water

9. **Subjects had disclosed their HIV status to at least one other person prior to starting on antiretroviral therapy, and this person in turn could render support the subject**
10. **Subjects' vital signs, physical examination and laboratory results did not show signs of any intercurrent illness, including an active AIDS-defining illness, within 30 days of initiation of antiretroviral medication**
11. **Subject did not experience any serious adverse event in the first 6 months of antiretroviral therapy (cf. 4.7 Serious adverse events).**

4.3.2 Exclusion criteria:

Data from study subjects were excluded from this study if the following exclusion criteria were present:

1. **Subject was unwilling to participate in a study investigating quality of life, or was not willing to sign an informed consent document pertaining to the use of quality of life data**
2. **Subject is considered by the investigator to be an unsuitable candidate for the study**
3. **Subject had obvious factors that influenced his/her quality of life (e.g. intercurrent illness, AIDS-defining conditions, unstable living conditions, recent mourning) other than the use of antiretroviral medication**
4. **Subject was unwilling or unable to adhere to the visit schedules**
5. **Subject did not comply with the treatment regimen**
6. **Subject did not achieve a viral load below the level of detection at or before 6 months of treatment**
7. **Subject did not disclose his/her HIV status to at least one person able to render support**

8. Subject developed a serious adverse event in the first six months of antiretroviral therapy.

4.4 Data collection:

The data were collected retrospectively from MOS-HIV questionnaires that had been completed as part of international pharmaceutical drug trials. These questionnaires formed part of the original study design of various antiretroviral drug trials, for which the participants had signed an informed consent document. The data were collected from the source note copies that forms part of the study site's records of the various clinical drug trials.

4.5 Measuring tool:

The measuring tool used in the collection of data was the MOS-HIV Health Survey (cf. Appendix D).

4.5.1 The MOS-HIV Health Survey:

The MOS-HIV Health Survey is a brief, comprehensive measure of health-related QOL used extensively in Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS). Questions in the MOS-HIV were drawn from a large pool of existing questions that had been extensively tested for use in the Medical Outcomes Study, a large multi-site study of the effects of different ways of delivering medical care. Developed in 1987, the MOS-HIV was one of the first disease-targeted measures available for these populations. The survey is widely used in clinical trials and other research and evaluation studies. The 35-item MOS-HIV assesses aspects of functioning and well-being

including physical function, social and role function (work), cognitive function, pain, mental health, energy, distress about health, quality of life and overall health (Wu 1999).

The MOS-HIV Health Survey consists of 35 questions which assess 10 dimensions of HRQOL, including general health perceptions, physical functioning, role functioning, pain, social functioning, mental health, energy, health distress, cognitive functioning and quality of life. In addition, one item assesses health transition.

The subscales of the MOS-HIV are scored as summated rating scales on a 0 – 100 scale, where higher scores indicate better health. For multi-item scales (two or more items), mean substitution is generally used for missing items if no more than 50% of the items are missing. In addition to these subscales, a Physical Health Summary score and a Mental Health Summary score can be generated. The instrument takes approximately five minutes to complete and can be self-administered using paper and pencil or a touch-screen personal computer. It can also be administered as a face-to-face interview or a telephone interview. A brief description of each dimension is presented below.

4.5.1.1 General Health Perceptions

This dimension utilizes a five-item scale adapted from the MOS Short Form 20-Item Health Survey (SF-20) which used a single-item rating of health, and four items from the Current Health scale from the Health Perceptions Questionnaire (Davies and Ware 1981; Ware 1976). This dimension retained the five items measuring current health from the SF-20. Individual items in the scale ask patients to report on their general health, resistance to illnesses and health outlook. Davies and Ware (1981) and Stewart and Ware (1992) have reported substantial empirical evidence of validity for this scale (Wu 1999).

4.5.1.2 Physical Functioning

This dimension consists of six items that assess a range of severe and minor physical limitations. These items represent different levels and kinds of limitations, which include lifting of heavy objects or participating in strenuous sports, walking uphill or climbing a few flights of stairs, bending, lifting or stooping, and walking a short distance. Limitations in self-care activities are measured with a single item assessing the ability to eat, dress, bath or use the toilet by oneself (Wu 1999).

4.5.1.3 Role Functioning

Two items are used to assess the impact of patients' health on their ability to perform adequately at work, around the house or in school. Patients are asked if their health keeps them from working at a job, doing work around the house or going to school. The second item in this scale asks if patients are unable to do certain kinds of work, housework or schoolwork because of their health (Wu 1999).

4.5.1.4 Pain

The MOS-HIV Health Survey assesses both the intensity of bodily pain and the degree of interference with normal activities due to pain (Wu 1999).

4.5.1.5 Social Functioning

This single item subscale asks patients to assess the extent to which their health in the past 4 weeks has limited their social activities. Precision is increased by specifically

assessing the impact of patients' health on social activities, thus eliminating the influence of non-health factors on social activity (Wu 1999).

4.5.1.6 Mental Health

The MOS-HIV Health Survey utilizes the same five-item Mental Health scale as found in both the SF-20 and MOS Short Form 36-Item Health Survey (SF-36). One or more items from each of the four major mental health dimensions (anxiety, depression, loss of behavioural/emotional control and psychological well-being) are included in the scale (Veit and Ware 1983). Items in this scale present a balance between favourably and unfavourably worded items thus controlling for response set effects (Wu 1999).

4.5.1.7 Energy/Fatigue

This four-item scale is included in the MOS-HIV Health Survey to measure differences in vitality. Items in this scale control for response set effects (Wu 1999).

4.5.1.8 Health Distress

This dimension assesses the degree to which patients are discouraged and afraid due to their health problems. The four-item scale also asks patients about the amount of time in the past four weeks that they have felt despair and weighed down by health problems (Wu 1999).

4.5.1.9 Cognitive Functioning

Consisting of four-items, this dimension measures the degree of difficulty patients have experienced in the past four weeks with respect to their cognitive abilities. Patients are asked to assess how much of the time they have had difficulty reasoning or solving problems, been forgetful, had difficulty in remaining attentive and concentrating on activities (Wu 1999).

4.5.1.10 Quality of Life

In this single item dimension patients are asked to assess the quality of their life during the past four weeks. The response categories range from very well, could hardly be better to very bad, could hardly be worse (Wu 1999).

4.5.1.11 Health Transition

This question asks patients about the amount of change in their physical and emotional health over a four week period. The health transition question has been found to provide useful information about actual changes in health status during the period prior to the administration of the MOS-HIV Health Survey (Wu 1999).

The table in Appendix D summarises the MOS-HIV Health Survey concepts.

4.5.2 Administration of the MOS-HIV:

Unlike laboratory data, the quality of questionnaire data depended in part on setting an appropriate context ('setting the stage') for the study participant. If a study

participant appreciated the importance of the data being collected, considered the questions carefully, and answered appropriately, the responses would be a more accurate reflection of the participant's self-perceived health and quality of life. Study participants would also be more likely to complete the questionnaire if they felt that it was important. The quality of data obtained from study participants could be improved if the survey was introduced and explained to study participants, and if completion of the questionnaire was explained when handing it out (Wu 1999).

4.5.3 Validation:

Paton et al. (2002) found significant differences in quality of life scores between Centres for Disease Control HIV stages, and significant correlations with CD4 count and symptom score. This serves to confirm the discriminant validity of the MOS-HIV. Factor analysis revealed two components corresponding to physical and mental health which were similar to those of studies in Western countries except that pain was more closely related to mental health than physical health.

The MOS-HIV questionnaire has been translated into twenty languages, including French, Spanish, German, Dutch, Italian, Lugandan, some Indian dialects, Thai, Polish, Danish, UK English and South-African English (Wu 1999). Internal consistency reliability was similar across translations and adequate for all scales with Cronbach's Alpha > 70 (Shinault et al. *A review of the statistical aspects of quality of life measurement tools for HIV/AIDS*). Multi-trait analyses supported structural validity of the MOS HIV scales in each translation (Scott-Lennox et al. 1999). The MOS-HIV has been cross-culturally validated in numerous countries, including South Africa (Wouters et al. 2007; Burgess et al. 1993; Paton et al. 2002; Punpinach 2005; Scott-Lennox et al. 1999; Tsai 2003).

4.5.4 Reliability:

The MOS-HIV has high test-retest reliability as well as high internal consistency reliability. Inter-rater reliability, which measures the degree of consistency between each rater measuring the same subject at two points in time, has not been done for the MOS-HIV (Shinault et al.; Revicki et al. 1998).

4.5.5 Data Entry:

Questionnaire responses should be recorded using the numbers coded on the questionnaire. Item recoding and scale scoring can then be completed (Appendix B) using standard data analysis software such as SAS or a statistics programme of preference. Prior to recoding or keypunching, completed surveys should be carefully edited for clarity and accuracy. Solutions for handling common coding problems include the following:

- If two adjacent responses are selected by the respondent, randomly select one to be entered.
- If two non-adjacent responses are selected, code the item as a missing value
- If more than one response is selected for a single item, code the item as a missing value (Wu 1999).

4.5.5.1 Missing Values:

For multi-item scales (two or more items), mean substitution is generally used for missing items provided no more than 50% of the items are missing. A scale score can be

calculate if the respondent answered at least half of the individual items in a multi-item scale for those scales consisting of four or more items. When an item is missing the author suggests substituting the respondent's average score across the completed items in the scale. For example, if a respondent leaves one item in the 5-item mental health scale blank, substitute the average score of the four completed items for the missing value (Wu 1999).

4.5.5.2 Item recoding:

Eleven items are reverse scored. These items are worded so that a higher pre-coded item value indicates a poorer health state. To ensure that a higher item value indicated better health on all MOS-HIV items and scales, these 11 items require recoding (Wu 1999)(cf. Appendix B).

4.5.6 Transformation of raw scale score:

The final step in scale construction involves transforming the raw scales to a 0 to 100 scale. This transformation permits comparisons among various dimensions which may have different response categories. A score of 0 is the lowest possible score and 100 the highest score. Formulas for linear transformation of each of the scales are detailed in Table 1.

Table 1: Transformation formulas for MOS-HIV raw scores:

<u>Scale:</u>	<u>Transformation formula:</u>
General Health Perception	$L_{genheal} = (100/(25-5)) * (\text{General health perception raw score} - 5)$
Physical functioning	$L_{phys} = (100/(18-6)) * (\text{Physical raw score} - 6)$
Role Functioning	$L_{role} = (100/(4 - 2)) * (\text{Role Functioning raw score} - 2)$
Social Functioning	$L_{social} = (100/(6 - 1)) * (\text{Social Function raw score} - 1)$
Cognitive Functioning	$L_{cognitiv} = (100/(24 - 4)) * (\text{Cognitive Function raw score} - 4)$
Pain	$L_{pain} = (100/(11 - 2)) * (\text{Pain raw score} - 2)$
Mental Health	$L_{mental} = (100/(30 - 5)) * (\text{Mental Health raw score} - 5)$
Energy / Fatigue	$L_{vitalit} = (100/(24 - 4)) * (\text{Energy/Fatigue raw score} - 4)$
Health Distress	$L_{distres} = (100/(24 - 4)) * (\text{Health Distress raw score} - 4)$
Quality of Life	$L_{quality} = (100/(5 - 1)) * (\text{Quality of Life raw score} - 1)$
Health Transition	$L_{trans} = (100/(5 - 1)) * (\text{Health Transition raw score} - 1)$

4.6 Ethical Considerations:

4.6.1 Informed consent:

Participants gave written, informed consent for the collection of data through the MOS-HIV questionnaire. The informed consent documents formed part of the original clinical drug trial, in which participants agreed to the use of quality of life data as reflected by the MOS-HIV questionnaires. Full informed consent was obtained from every participant according to Good Clinical Practice guidelines. During the informed consent process there was no coercion of any participant, nor any perverse incentives offered. Participants were given the reassurance that if the individual chose not to take part in, or withdrew from the study that they will still receive standard care. The informed consent procedure was done with the realization that the eligible individuals are part of a vulnerable population, and as a result might feel more obligated to take part in research.

4.6.2 Ethics approval:

The Research and Ethics Committee of the University of Cape Town gave approval for this study on the basis of a proposal submitted in 2007. Approval for the clinical drug trials, of which the MOS-HIV questionnaires formed part, was granted by Pharma-Ethics as well as the Medicines Control Council.

4.6.3 Ownership of data:

The QOL data collected at Triple M Research in the Eastern Cape, South Africa form part of the comprehensive trial data and belong to the pharmaceutical company conducting a specific trial. Permission was obtained from the various pharmaceutical companies to use the QOL data recorded at Triple M Research, collected at Baseline (the day of initiation of antiretroviral therapy) and visit Week 24. Pfizer Laboratories (Pty) Ltd refused permission for the use of data collected during the maraviroc A400-1026 study, and no data from subjects in the A400-1026 study were used.

4.7 Serious adverse events:

A serious adverse event is any adverse drug, biologic or device experience occurring at any dose that results in any of the following outcomes:

- death
- life-threatening adverse event
- persistent or significant disability/incapacity
- requires in-patient hospitalization, or prolongs hospitalization
- congenital anomaly or birth defect.

For the purpose of this retrospective analysis of QOL questionnaires completed in primary studies no adverse events were allowed, and any participant who experienced a serious adverse event in the first 6 months of antiretroviral therapy was excluded from the analysis. Constitutional symptoms, especially those associated with an SAE, have been proven to cause a dramatic change in a subject's quality of life, and choosing data from subjects who had experienced a serious adverse event would have distracted from the influence of antiretroviral therapy on HRQOL (Berzon and Lenderking 1998; Cowdery and Pesa 2002; Douaihy and Singh 2001).

University of Cape Town

CHAPTER FIVE

RESULTS

5.1 Introduction:

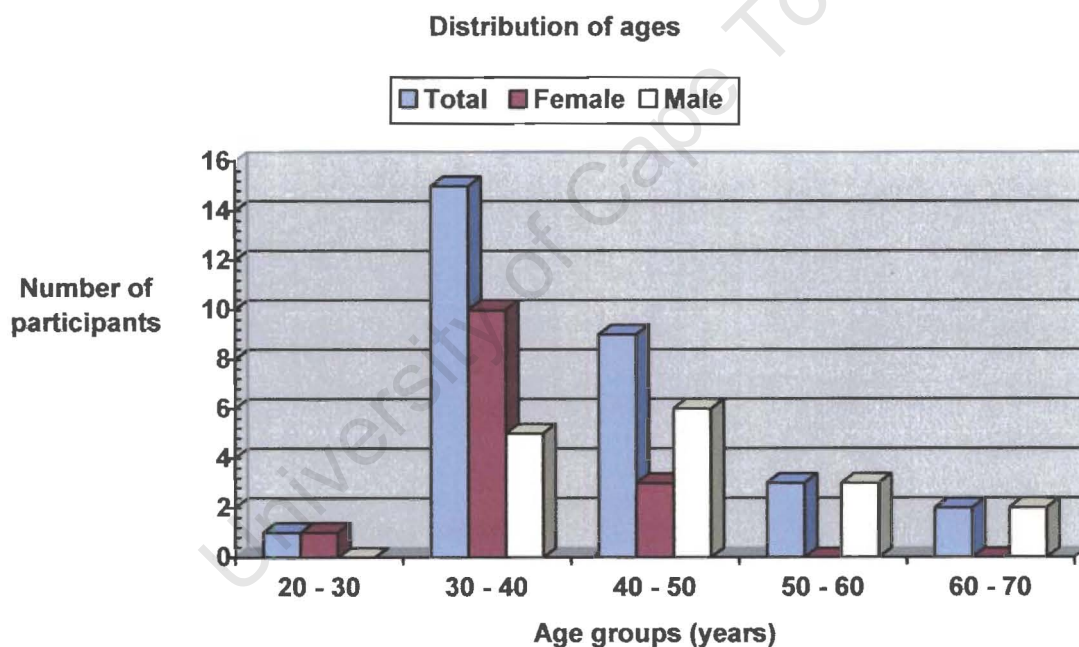
The overall aim of the study was to compare the quality of life in HIV positive patients between the day of initiation of antiretroviral medication and 6 months after the initiation. The results presented in this chapter reflect changes in the total MOS-HIV score, as well as changes in eleven sub-scores as discussed in chapter three. The subscales of the MOS-HIV are scored as summated rating scales on a 0 – 100 scale, where higher scores indicate better health.

The study does not attempt to reflect all the variables associated with quality of life, and focuses on the introduction of antiretroviral medication as the major consideration in influencing the quality of life. QOL surveys of thirty participants were selected for the study, of which 16 were male and 14 female participants. All participants had consented to the QOL data being used for the current study, and the informed consent procedure was initiated before the start of the primary study from which the surveys were utilised. The participants came from resource poor areas in Motherwell, Walmer and Uitenhage in the Nelson Mandela Metropole, and all participants had achieved a minimum qualification equal to Grade 8. All participants were all able to speak English. A nursing sister from Hope International assisted in translating from English into Xhosa all information when asked by a participant. The participants utilized in the study had sheltered living conditions with adequate ablutions and running water.

5.2 Distribution of ages:

The distribution of participants' ages were: one participant (female) between the ages of 20 and 30 years of age, 15 participants between 30 and 40 years of age (10 female and 5 male), 9 participants between 40 and 50 years of age (3 female and 6 male), three male participants and no females between 50 and 60 years of age, and two males with no females older than 60 years of age.

Figure 3: Graph indicating the distribution of participants' ages:



The participants' ages ranged from 26 to 65 years of age, with the mean age of the participants 42 years and 7 months. The female participants ranged in age between 26 and 46 years of age, with the mean age of the female participants 36 years and 1 month. The male participants ranged between 32 and 65 years of age, with the mean age of the male participants 46 years and 6 months.

5.3 Standardised scores:

All items and scales in the MOS-HIV Health Survey are scored so that a higher score indicates better health status. The following table reflects the standardised scores obtained from the study subjects at baseline and after six months of treatment with the *p*-value calculated in the last column.

Table 2: Standardised MOS-HIV scores from all participants:

	<u>Baseline</u> (Mean ± standard deviation)	<u>6-months</u> (Mean ± standard deviation)	<u>p-Value</u>
Total MOS-HIV score	143.6 ± 35.4	171.2 ± 17.2	0.0001
General health perceptions	42.2 ± 28.5	59.3 ± 19.1	0.0043
Physical functioning	84.7 ± 25.1	92.8 ± 23.1	0.1312
Role functioning	73.3 ± 38.8	100 ± 0	0.0008
Social functioning	83.3 ± 27.3	91.3 ± 21.5	0.1296
Pain	75.9 ± 25.1	88.5 ± 14.1	0.0105
Mental health	58.8 ± 26.5	80.7 ± 15.0	0.0001
Cognitive functioning	83.3 ± 27.3	91.3 ± 24.6	0.1615
Vitality	60 ± 28.4	81.2 ± 12.5	0.0003
Health distress	61.8 ± 29.1	79.7 ± 14.1	0.0013
Quality of life	58.3 ± 28.1	70 ± 17.9	0.0698
Health transition	60.8 ± 23.4	72.5 19.0)	0.0323

p-Values of <0.05 indicated significant differences in the total MOS-HIV score, general health perception, role functioning, pain, mental health, vitality, health distress

The following table reflects the scores obtained by male participants in the trial:

Table 4: Standardised MOS-HIV scores from male participants:

	<u>Baseline</u> (Mean ± standard deviation)	<u>6-months</u> (Mean ± standard deviation)	<u>p-Value</u>
Total MOS-HIV score	149.8 ± 36.0	177.9 ± 18.0	0.0172
General health perceptions	43.4 ± 27.4	65.0 ± 21.1	0.0150
Physical functioning	88.5 ± 21.3	96.4 ± 20.2	0.2437
Role functioning	78.1 ± 31.5	100 ± 0	0.0140
Social functioning	80.0 ± 32.7	91.3 ± 21.9	0.1440
Pain	82.0 ± 25.0	91.7 ± 10.3	0.1352
Mental health	66.3 ± 26.5	84.5 ± 14.1	0.0126
Cognitive functioning	76.6 ± 25.9	85.3 ± 18.9	0.2011
Vitality	61.9 ± 27.6	83.4 ± 11.2	0.0088
Health distress	63.4 ± 31.7	84.1 ± 12.3	0.0141
Quality of life	57.8 ± 29.9	70.3 ± 22.8	0.2396
Health transition	57.8 ± 23.7	75.0 ± 20.4	0.0519

p-Values <0.05 indicated significant differences in the total MOS-HIV score, general health perception, role functioning, mental health, vitality and health distress between baseline and month 6 of treatment for the male study population.

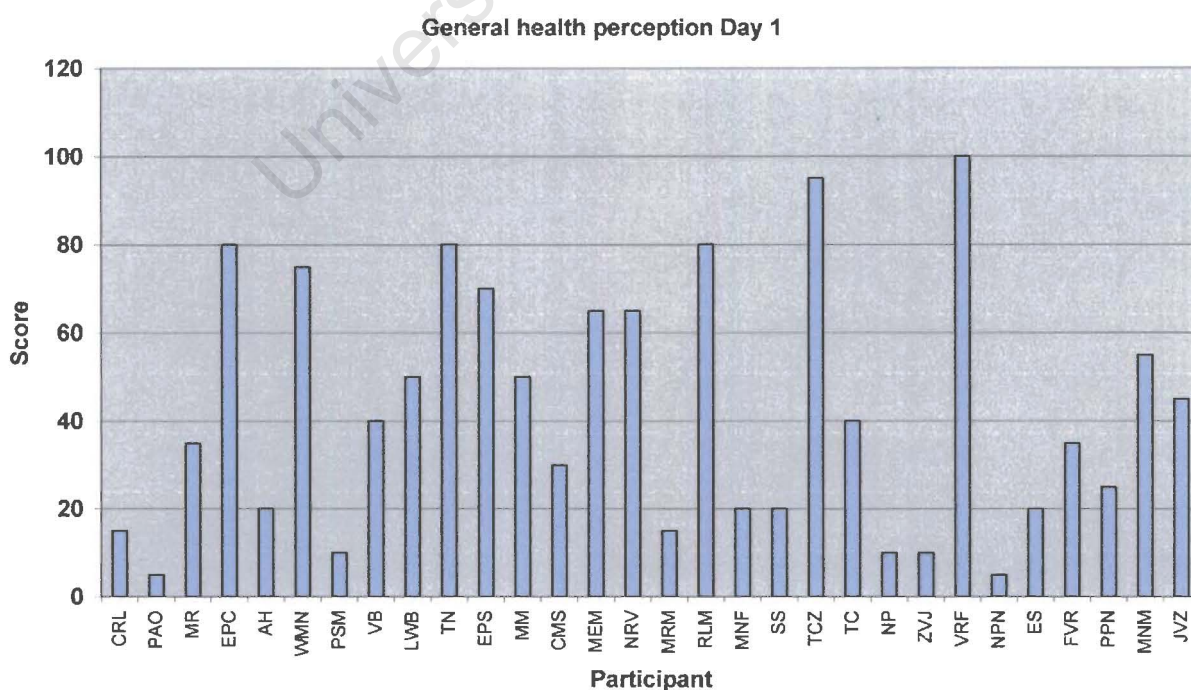
5.4 General health perception:

This score represents how participants viewed their own health, with a low score indicating views of a poor health, and high scores representing views of excellent health.

5.4.1 General health perception day 1:

The general health perception of the participants at baseline varied between 5 and 100 with a mean health perception raw score of 42,2. 18 of the 30 participants (60%) scored less than 50 on the general health perception rating at baseline, indicating that they viewed their health as poor when therapy was initiated. Six participants (20%) scored more than 75 at initiation of therapy, of which one scored 100, indicating views of good to excellent health.

Figure 4: Graph indicating standardized general health perception scores for day 1:



5.4.2 General health perception month 6:

The general health perception at month 6 varied between 25 and 100 with a mean score of 59,3. Ten participants (33%) scored less than 50, indicating that they viewed their health as poor. Eight participants (29%) scored more than 75 at six months of therapy, of which one scored 100, indicating views of good to excellent health.

Figure 5: Graph indication the standardized general health perception score for month 6:

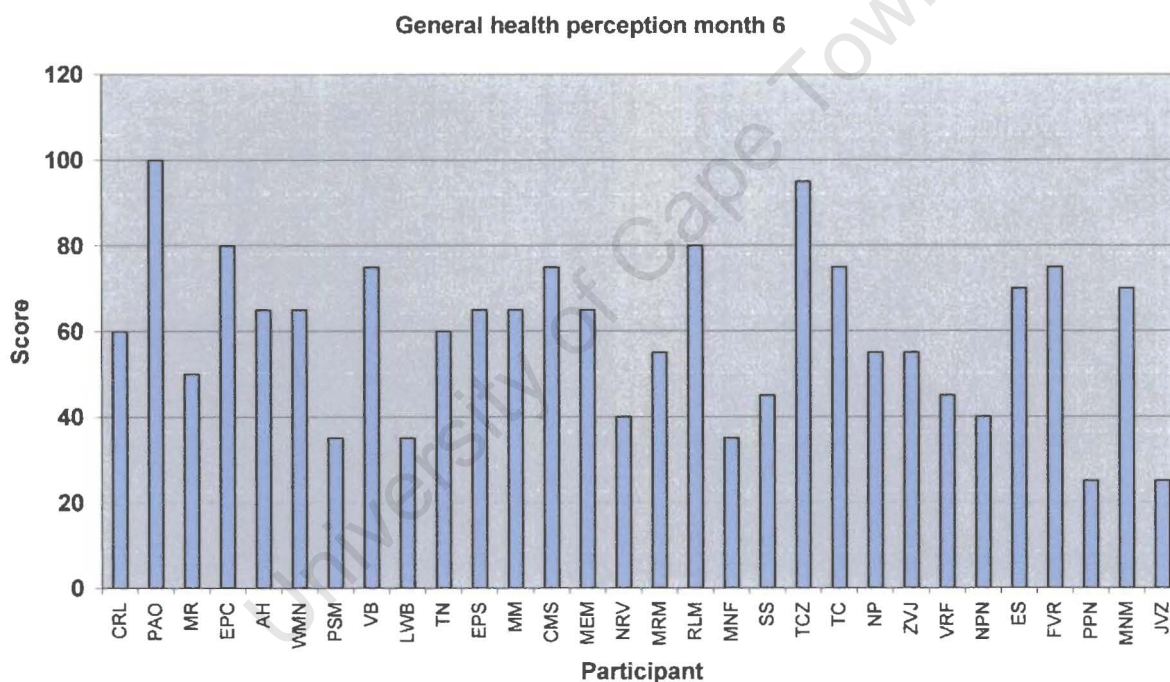
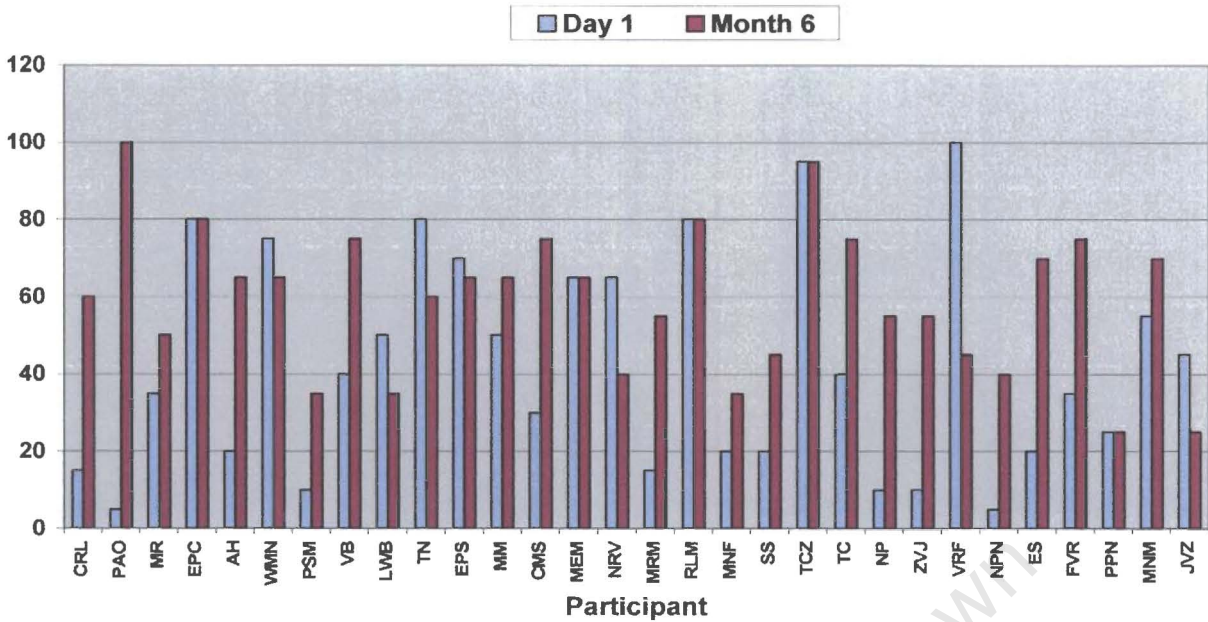


Figure 6: Graph indicating the standardised general health perception scores of participants:

$p=0.0043$

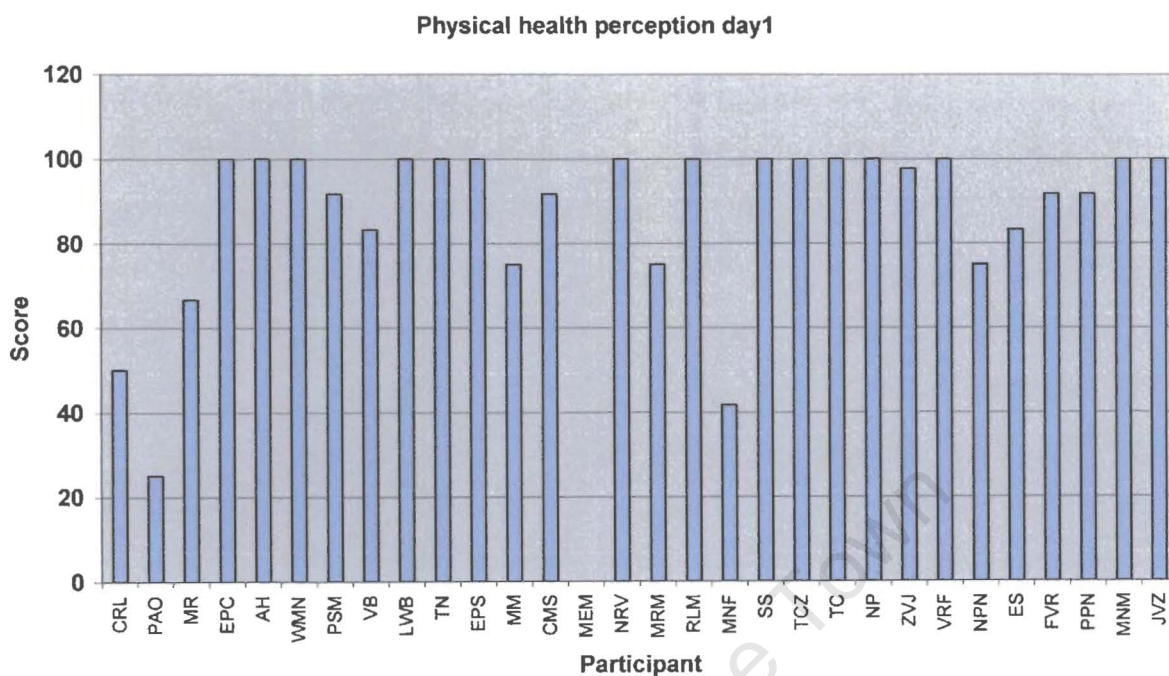
5.5 Physical Health Perception:

The physical functioning score indicates the degree in which the participant's disease limited them from performing physical activities like eating, dressing, bathing or using the toilet.

5.4.1 Physical health perception day 1:

The physical health perception score at Baseline varied between zero and 100, with a mean score of 84,7. 15 participants (50%) experienced no limitations in their physical activities due to HIV disease as indicated by scores of 100. 4 Participants (13,3%) experienced severe limitations due to HIV disease at initiation of therapy.

Figure 7: Graph indicating the standardised physical health perception score of participants on day 1:



5.5.2 Physical health perception month 6:

The physical health perception score after six months of anti-retroviral therapy varied between 8,3 and 100 with a mean physical health perception score of 92,8. 23 Participants (76,7%) experienced no limitations in activities after 6 months of therapy, while 3 participants (10%) experienced more limitations after 6 months of therapy.

Figure 8: Graph indicating the standardised physical health perception of participants at month 6:

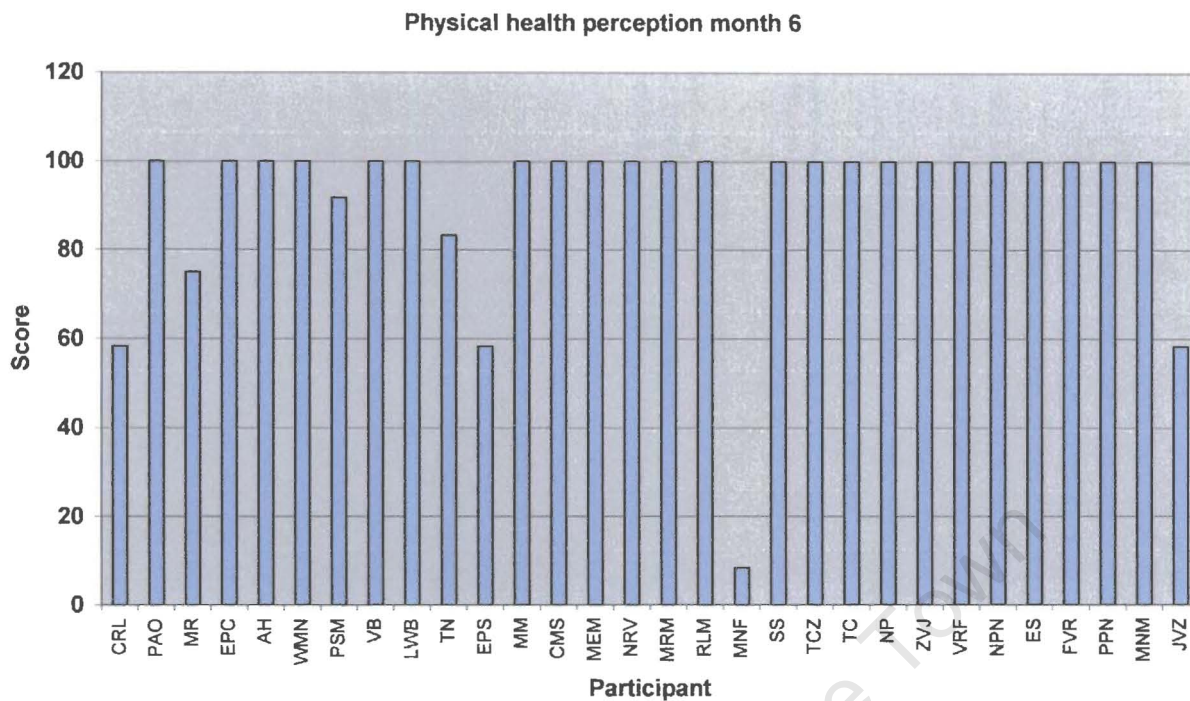
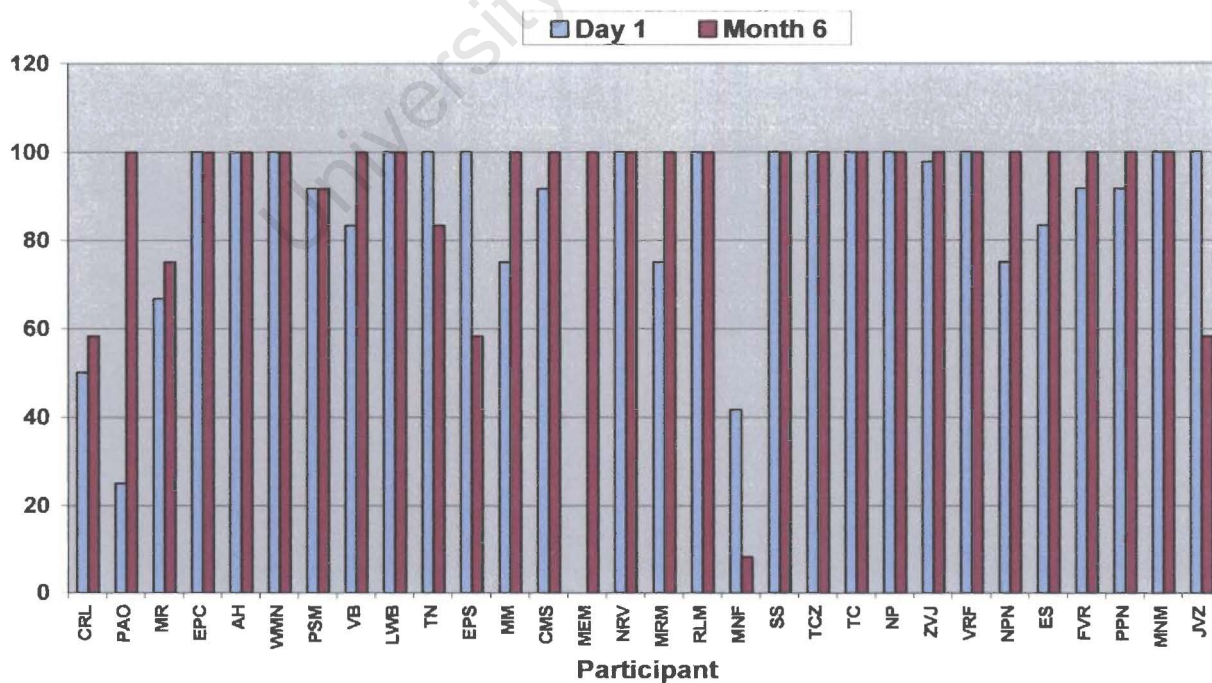


Figure 9: Graph indicating the standardised physical health perception scores of participants:



$p=0.1312$

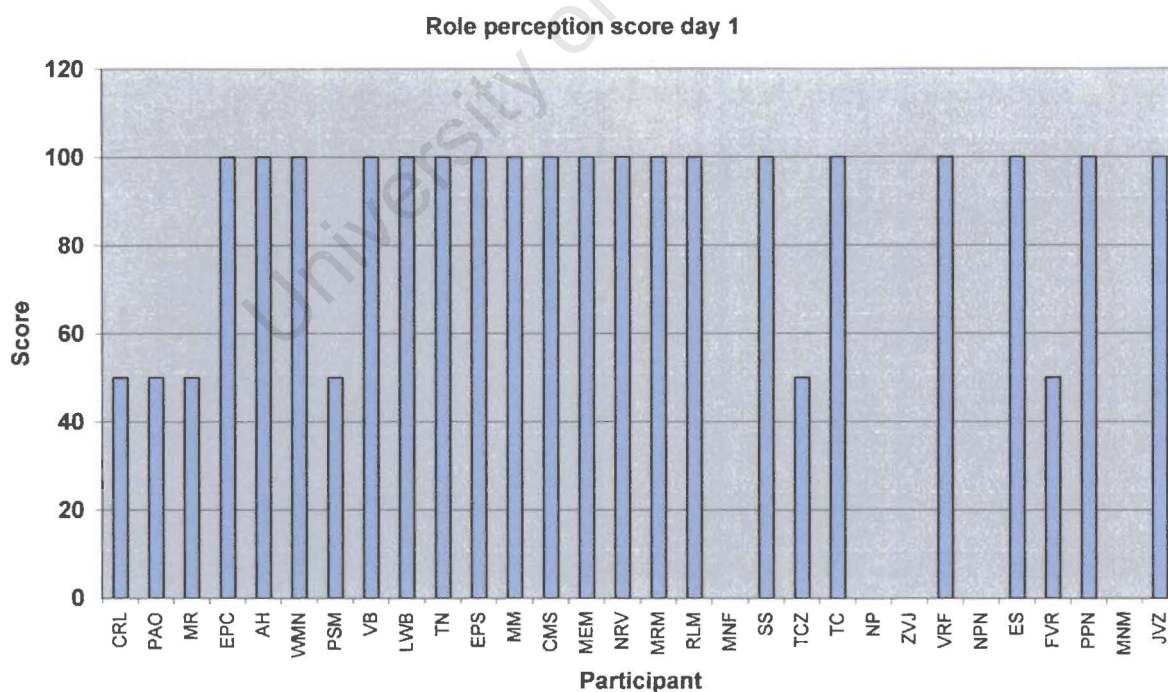
5.6 Role functioning:

The role functioning score indicated to what degree participants experienced that their disease caused problems with work or daily activities, with a low score indicating problems and a high score indicating no problems.

5.6.1 Role functioning day 1:

At baseline five participants (17%) scored zero, indicating severe problems in performing their daily activities. Six participants (20%) scored 50 and 19 participants (63%) scored 100. The mean score at baseline was 73,3.

Figure 10: Graph indication the standardized role functioning score for participants on day 1:



5.6.2 Role functioning month 6:

At six months of therapy all thirty participants (100%) scored 100, which indicated that no participant experienced problems as a result of HIV disease in performing their work or daily activities after six months of antiretroviral therapy. The mean role functioning score as a result was also 100.

Figure 11: Graph indicating the standardized role functioning score at month 6:

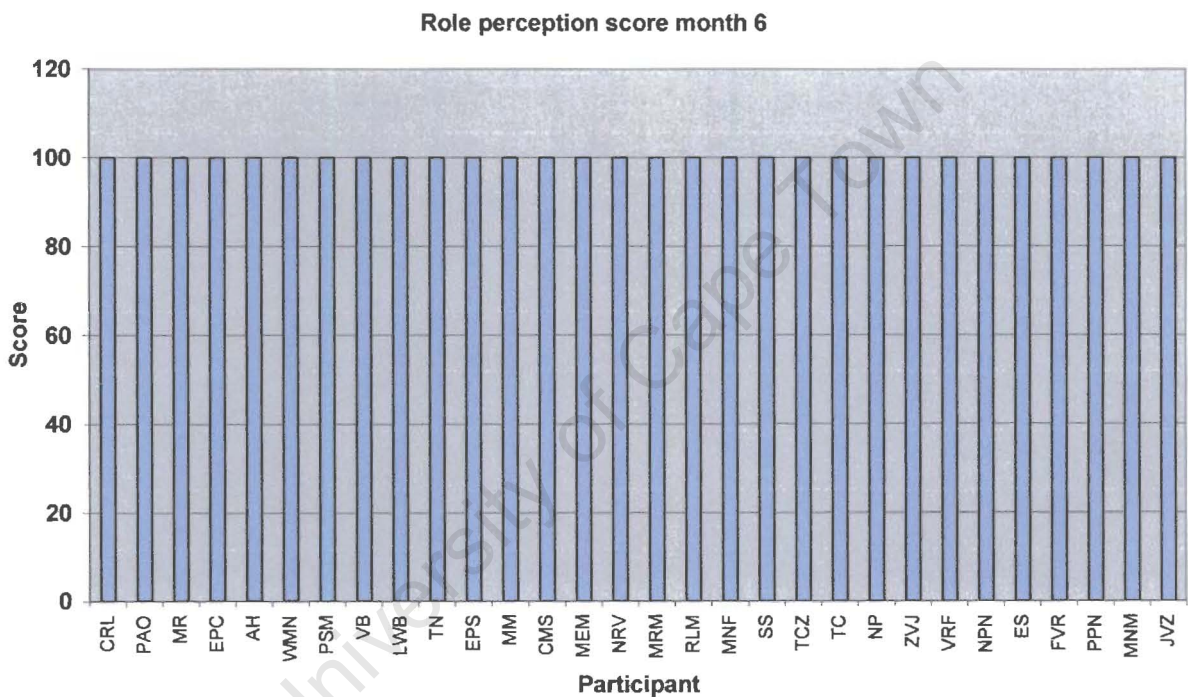
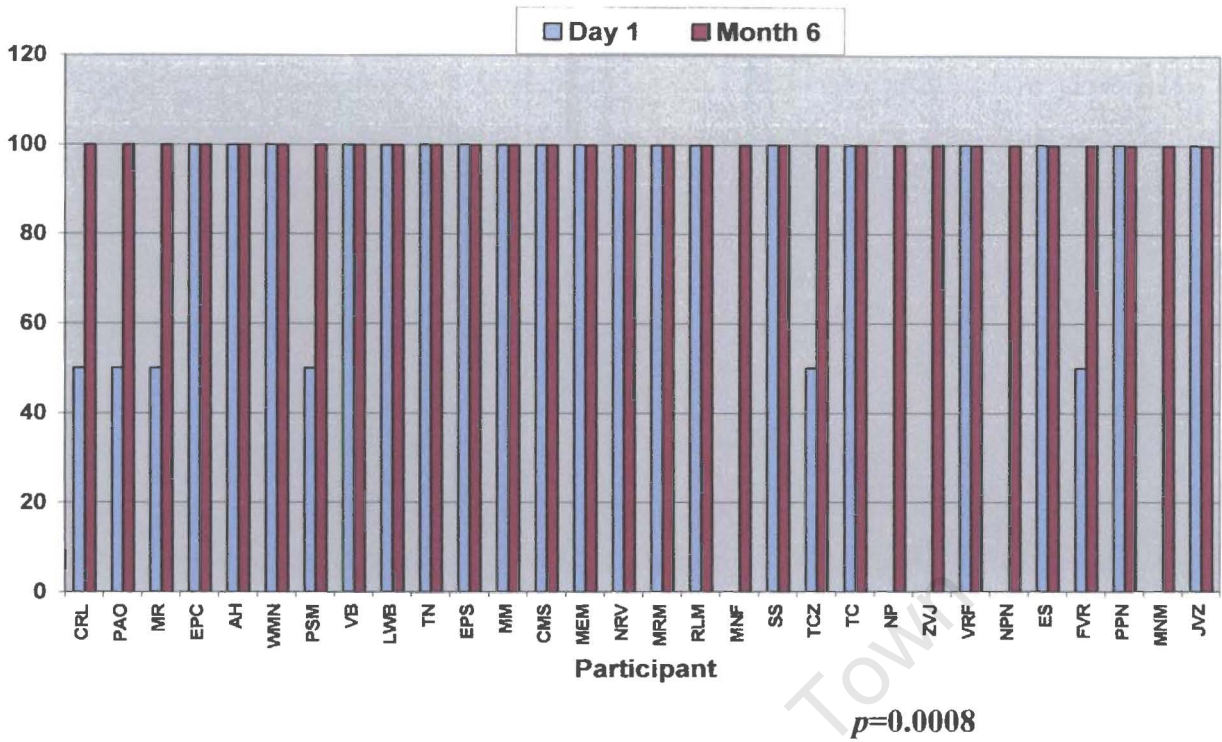


Figure 12: Graph indicating standardised role function scores of participants:



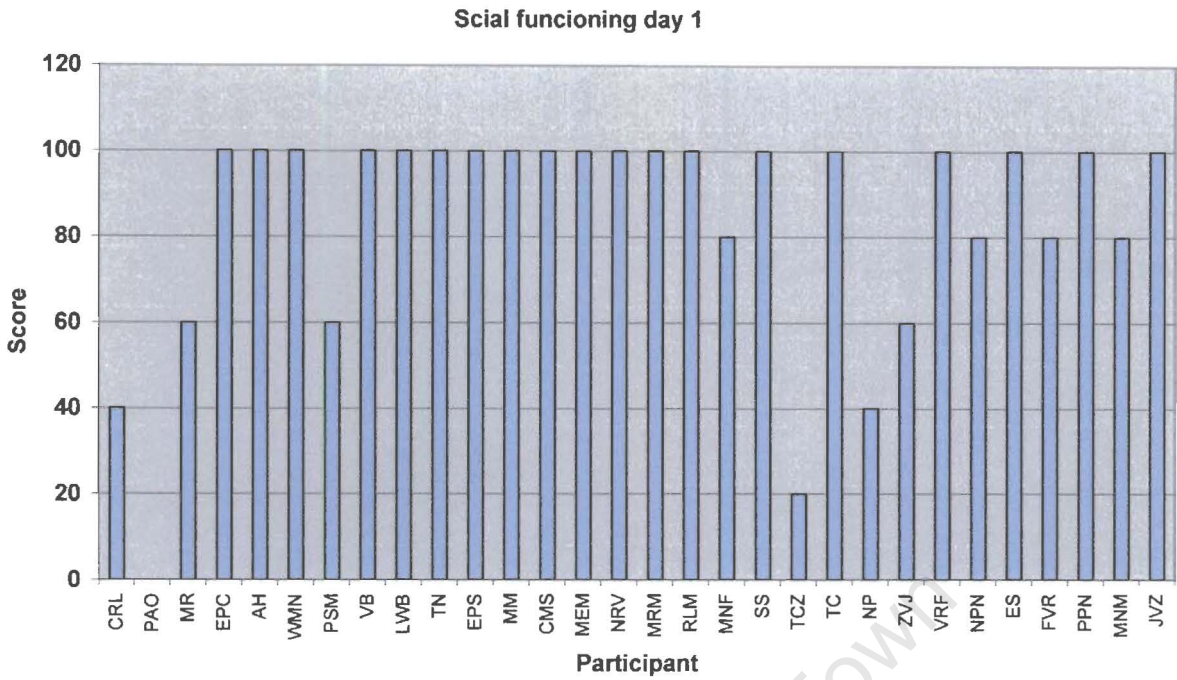
5.7 Social functioning:

A low score on the social functioning rating meant that participants experienced limitations in their social activities as a result of HIV disease, while a high score indicated little limitation in social activities.

5.7.1 Social functioning day 1:

At baseline the mean social functioning score was 83,3 with four participants (13%) scoring below 50 and 19 participants (63%) scoring 100.

Figure 13: Graph indicating standardised social functioning score of participants on day 1:



5.7.2 Social functioning month 6:

At month 6 the mean social functioning score was 91,3 with 24 participants (80%) scoring 100. Only two participants (7%) scored less than 50 at month 6, both with a score of 20.

Figure 14: Graph indicating standardised social functioning score of participants at month 6:

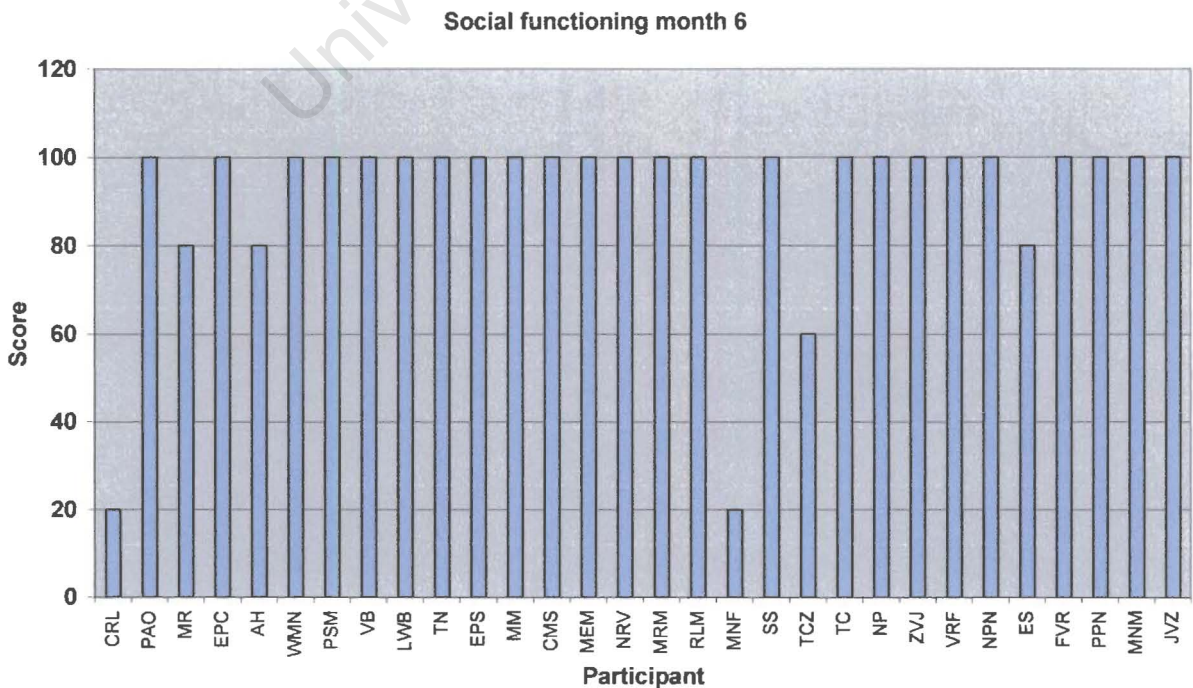
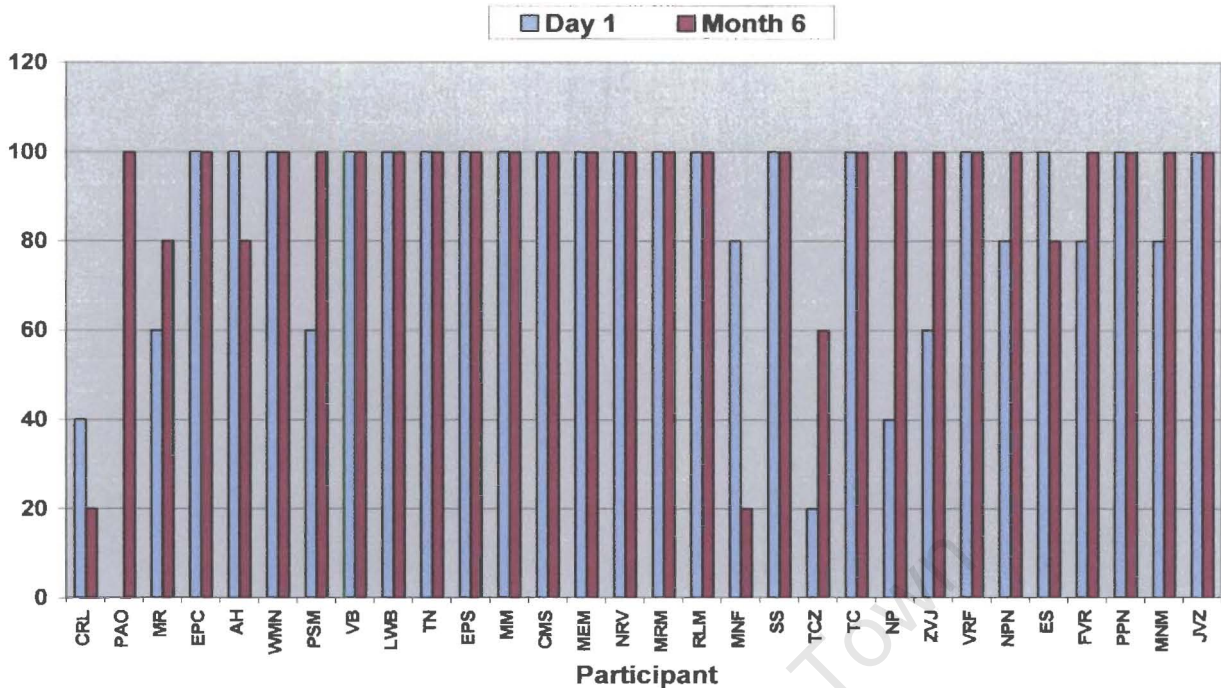


Figure 15: Graph indicating standardised social functioning scores of participants:



$p=0.1296$

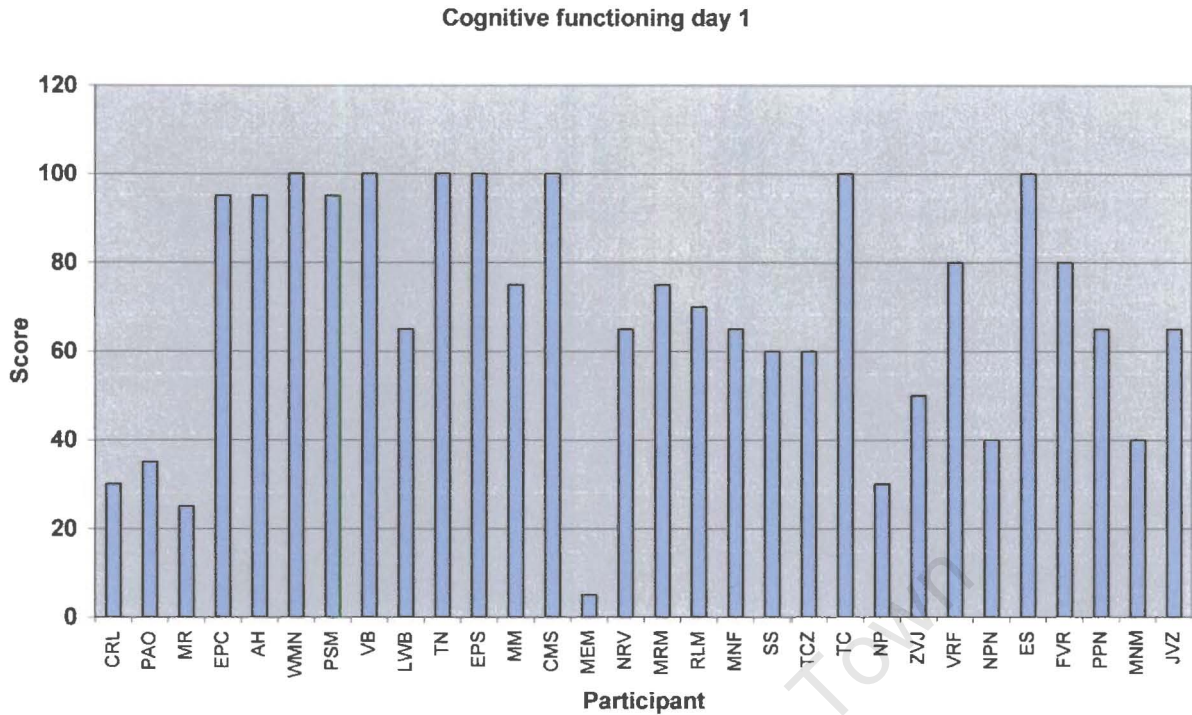
5.8 Cognitive functioning:

A low score on the cognitive functioning sub-scale means that a participant has difficulty in concentrating, reasoning and remembering all of the time, while a high score indicates no problems.

5.8.1 Cognitive functioning day 1:

At baseline the mean score was 68,8 with eight participants (27%) scoring less than 50. Five participants (17%) with scores of 100 indicated that they experienced no cognitive impairment, while 14 of the participants (47%) had scores of equal to or more than 75.

Figure 16: Graph indicating standardised cognitive functioning score of the study participants at day 1:



5.8.2 Cognitive functioning month 6:

At month 6 the mean cognitive functioning score was 77,3 and 11 participants (37%) had scores of 100. 18 Participants (60%) with scores more than 75 indicated that they had little problems to concentrate, reason and remember. Four participants (13%) had scores less than 50, indicating marked difficulties in cognitive functioning.

Figure 17: Graph indicating the standardised cognitive functioning score of participants at month 6:

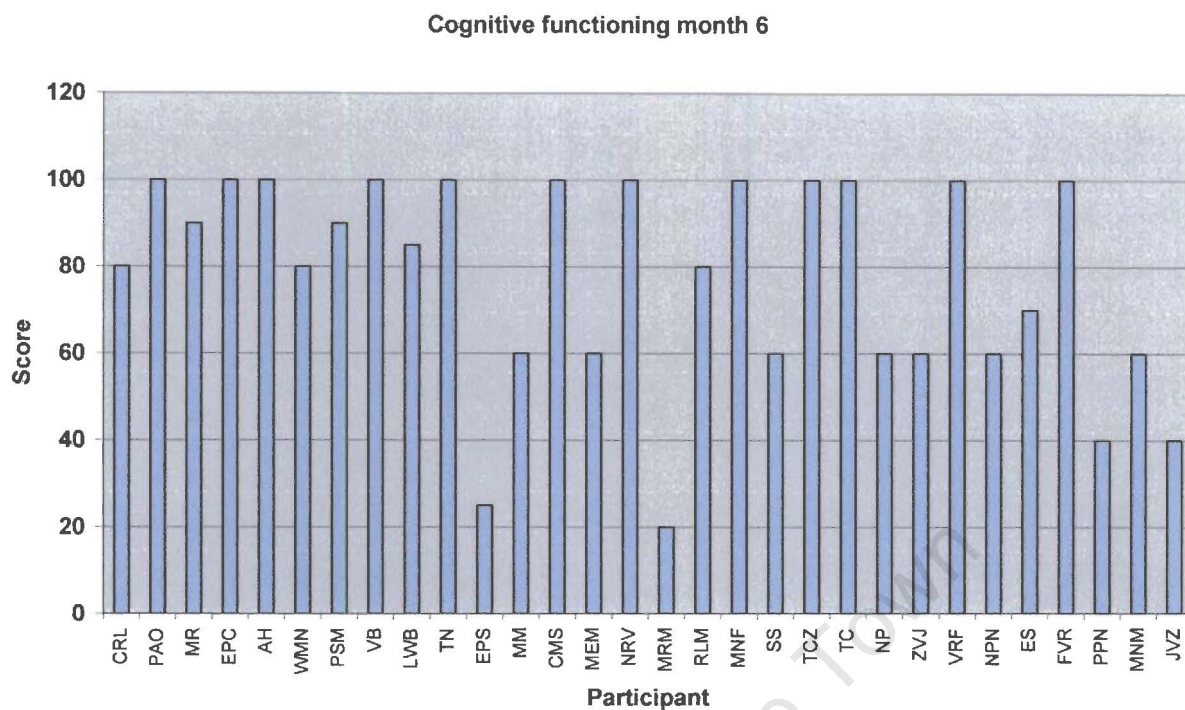
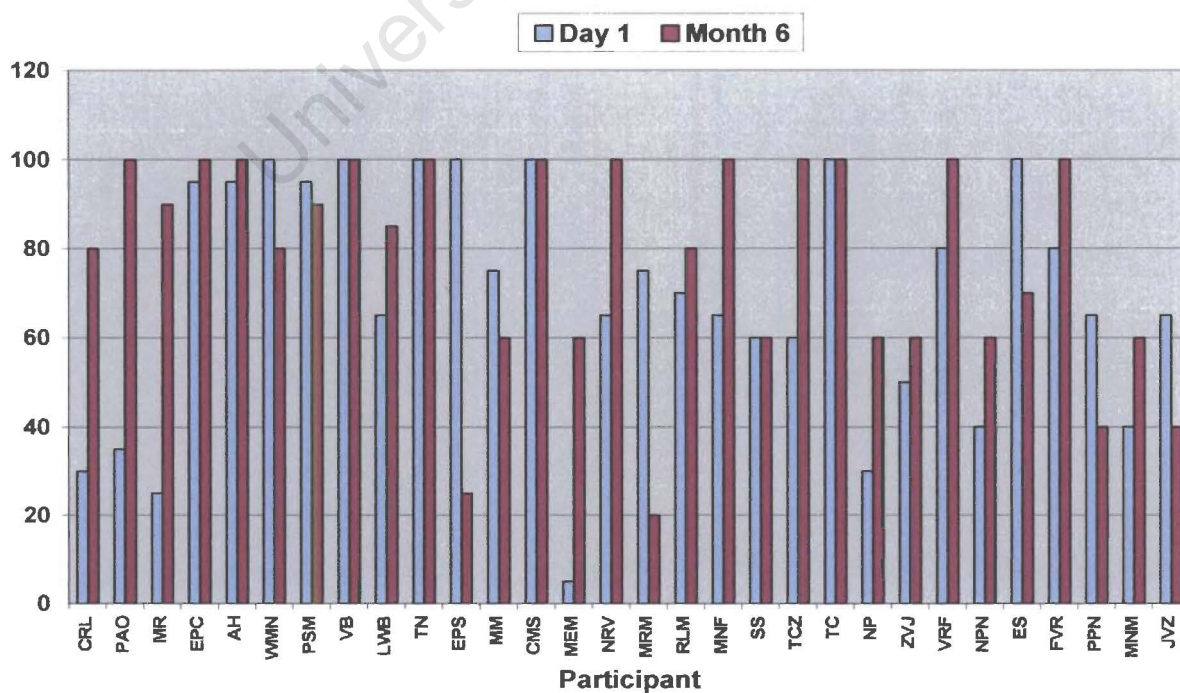


Figure 18: Graph indicating the standardised cognitive functioning scores of participants:



$p=0.1615$

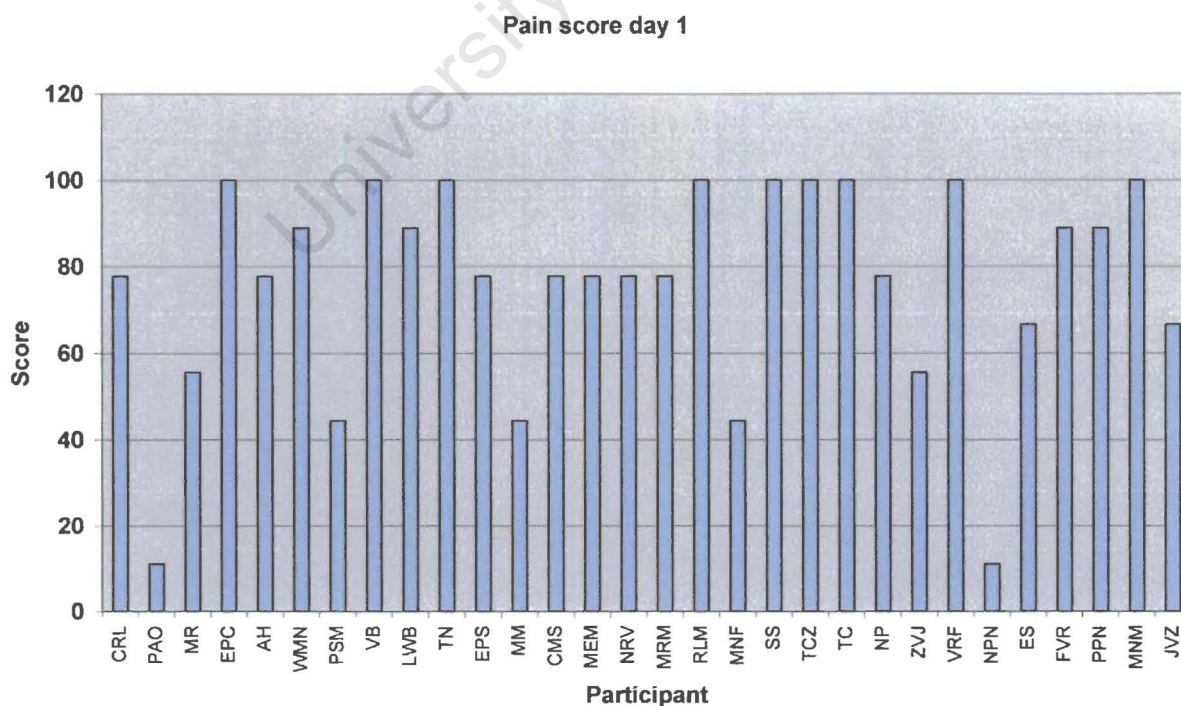
5.9 Pain:

The pain sub-scale indicates pain experienced by participants in the previous 4 weeks, with a low score indicating severe and limiting pain, and a high score indicating no pain or limitations due to pain.

5.9.1 Pain day 1:

The mean pain score at baseline was 75,9. Five participants (17%) indicated limitations as a result of pain with a score lower than 50. 21 Participants (70%) had scores of 75 or more, indicating no pain or limitations due to pain, and seven participants (23%) had scores of 100.

Figure 19: Graph indicating the standardised pain score of participants at day 1:



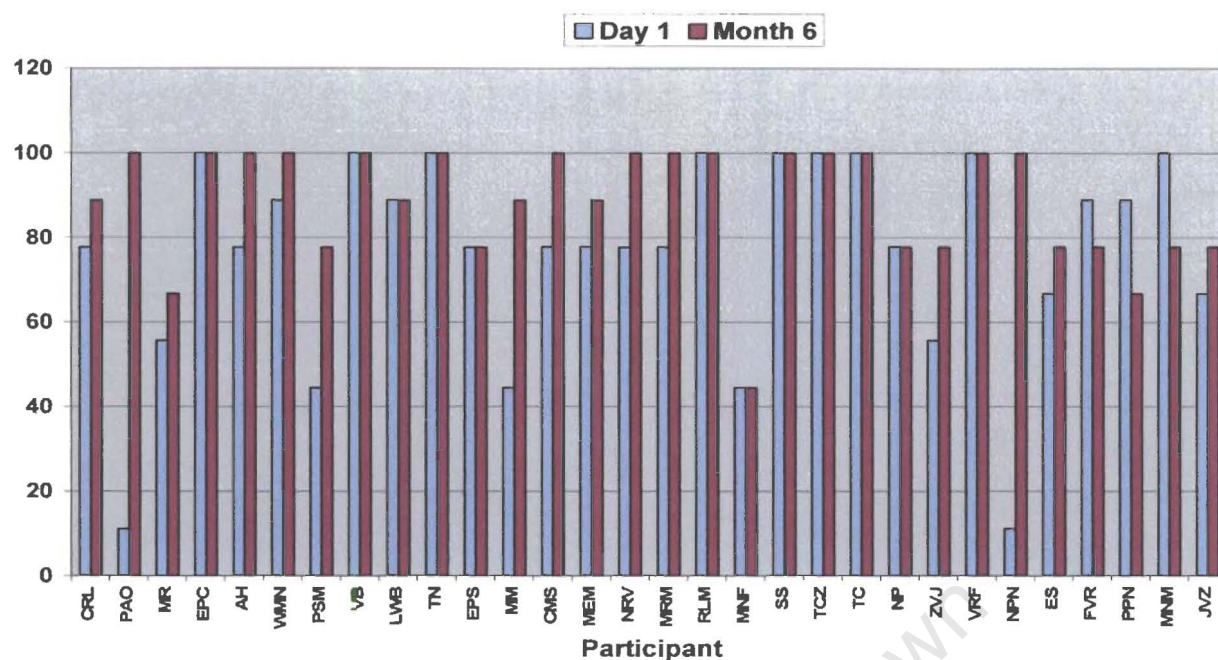
5.9.2 Pain month 6:

After six months of treatment the mean pain score was 88,5 and 15 participants (50%) with scores of 100 indicated that they had experienced no pain or limitations from pain in the previous 4 weeks. 27 Participants (90%) scored more than 75, indicating mild pain or limitations due to pain. One participant had a score lower than 50, unchanged from baseline at 44,4.

Figure 20: Graph indicating the standardised pain scores of participants at month 6:



Figure 21: Graph indicating the standardised pain scores of participants:



$p=0.0105$

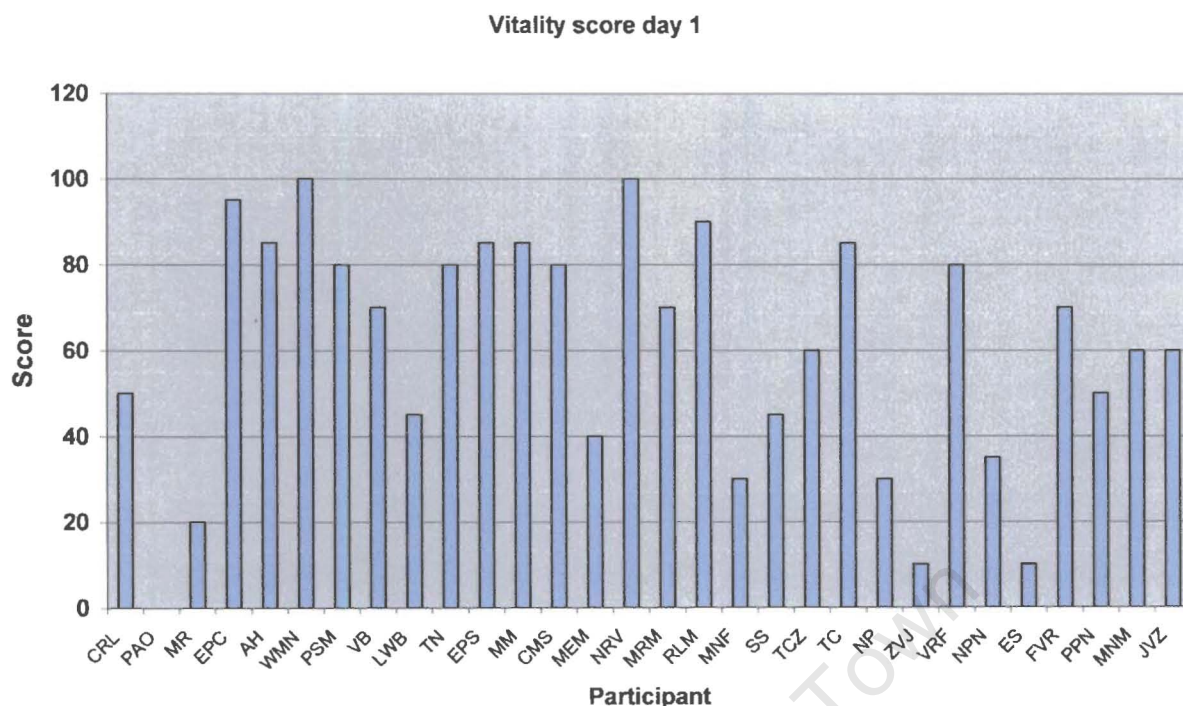
5.10 Vitality:

This score indicates the subject's energy level, with high scores indicating high energy levels and feeling full of vigour, and low scores feeling tired and worn out.

5.10.1 Vitality day 1:

The mean vitality score at baseline was 60. Eleven participants (37%) scored 50 or lower at baseline, of which one scored zero. This indicates that these participants felt tired and worn out most of the time. 12 Participants (40%) indicated that they felt energetic and full of vigour most of the time, as indicated by scores higher than 75.

Figure 22: Graph indicating the standardised vitality score of the participants at day 1:



5.10.2 Vitality month 6:

At month six of treatment the vitality scores varied between 55 and 100 with a mean score of 81.2. 24 Participants (80%) with scores of 75 and more indicated energy and vitality most of the time. There was no score less than 50 at month 6, and the lowest score was 55. This indicates that all participants felt more energetic than tired at 6 months of treatment.

Figure 23: Graph indicating the standardised vitality score of participants at month 6:

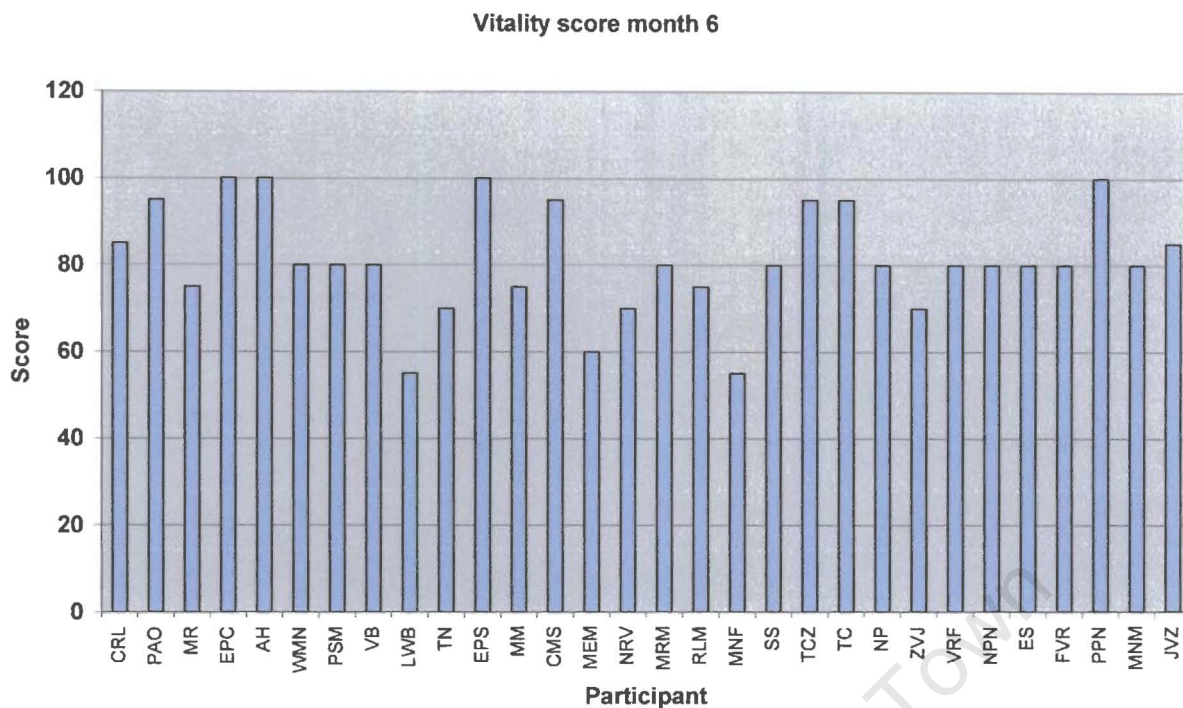
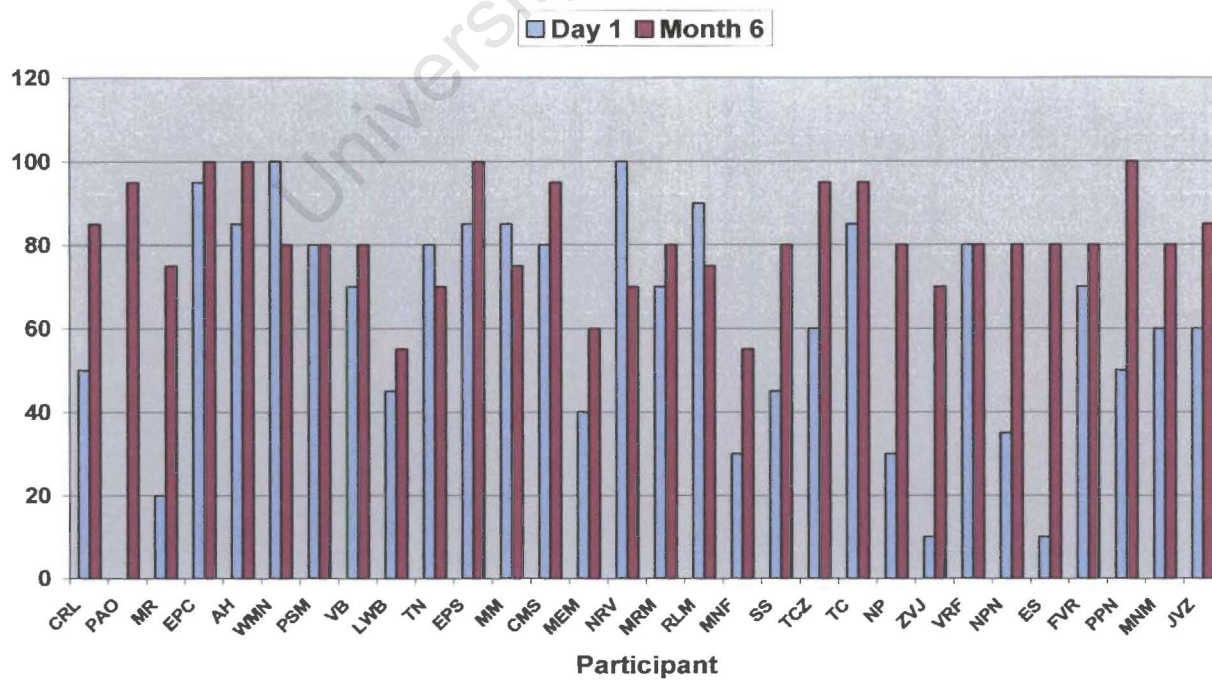


Figure 24: Graph indicating the standardised vitality scores of participants:



$p=0.0003$

5.11 Mental health:

The items included in the mental health sub-scale include one or more items from each of the four major mental health dimensions (anxiety, depression, loss of behavioural or emotional control and psychological wellbeing). A low score indicates that the participant feels nervous and depressed most of the time, while a high score indicates that the participant feels calm, peaceful and happy most of the time.

5.11.1 Mental health day 1:

The mean mental health score at baseline was 58,8, with 12 participants (40%) scoring less than 50. Four participants (13%) with scores of 100 indicated that they felt calm, peaceful and happy all of the time.

Figure 25: Graph indicating the standardised mental health score of participants at day 1:



5.11.2 Mental health month 6:

At month 6 the mean mental health score was 80,7 and seven participants (23%) with scores of 100 indicated that they felt happy all of the time. 21 Participants (70%) had scores of more than 75 which indicated that they felt calm, peaceful and happy most of the time.

Figure 26: Graph indicating the standardised mental health score of participants at month 6:

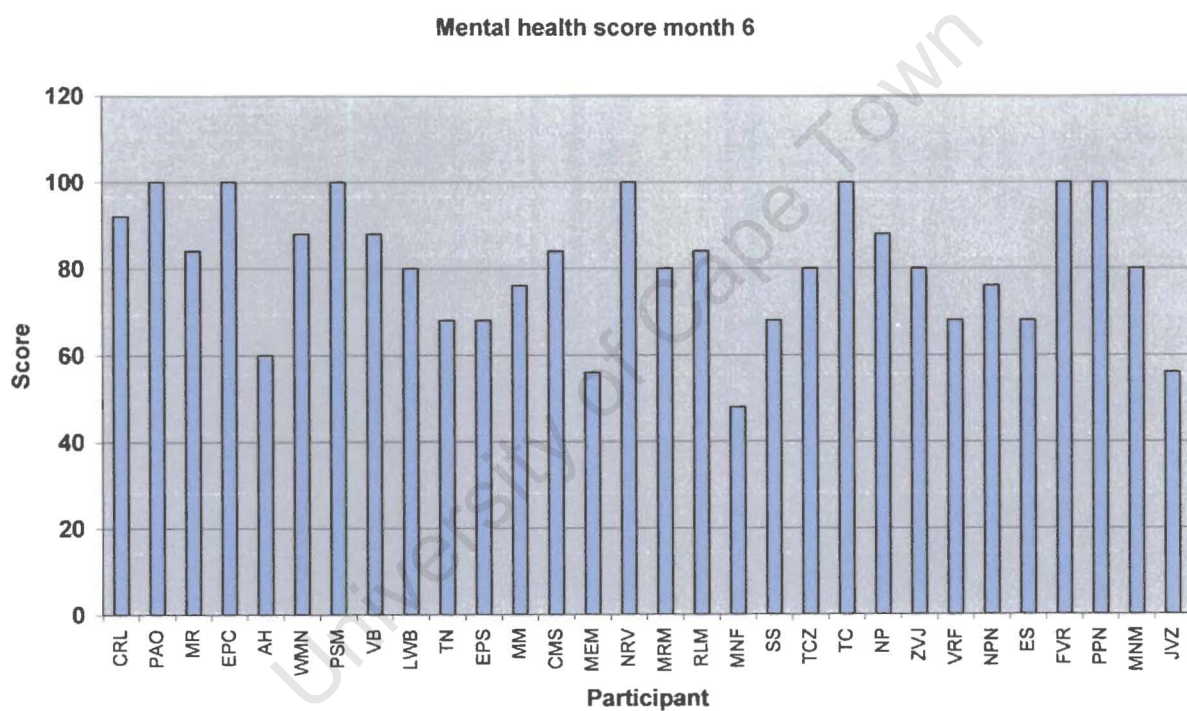
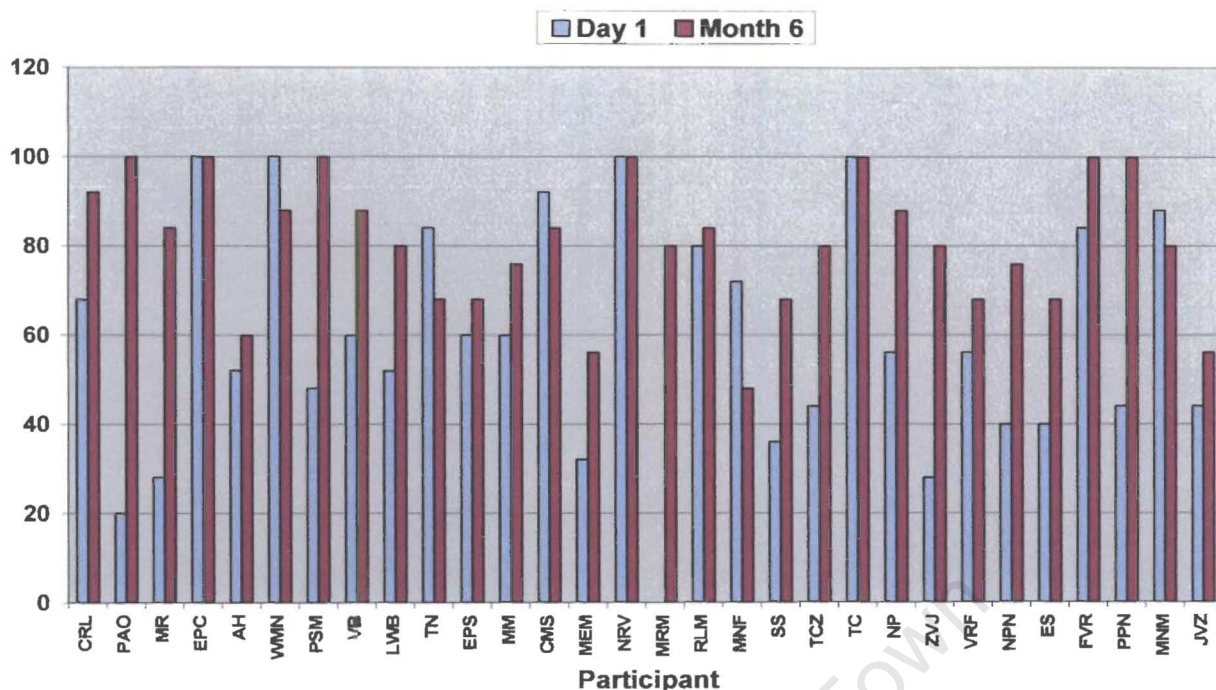


Figure 27: Graph indicating the standardised mental health scores of participants:



$p=0.0001$

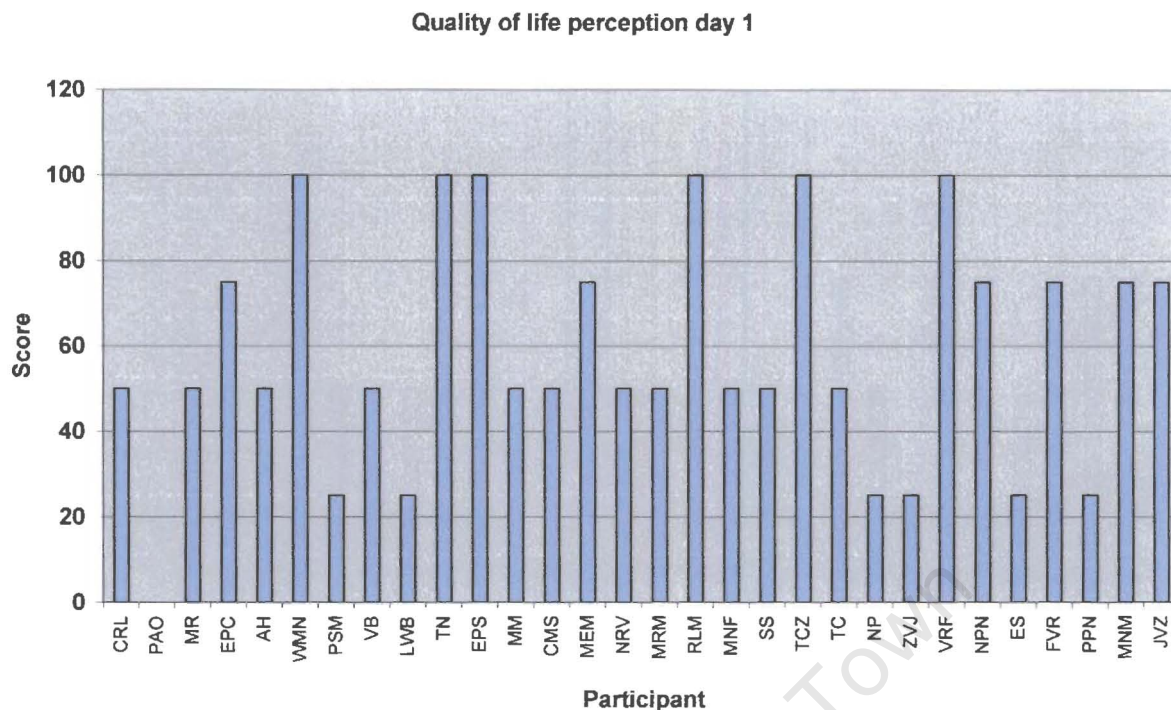
5.12 Quality of life:

This subscale indicates the subject's perceived quality of life, with high scores indicating a good quality of life, and low scores a poor quality of life.

5.12.1 Quality of life day 1:

The mean quality of life score at baseline was 58,3 and 18 participants (60%) with scores of 50 and lower felt that life had been bad. 6 Participants (20%) had scores of 100 and felt that life had been very good and could hardly be better.

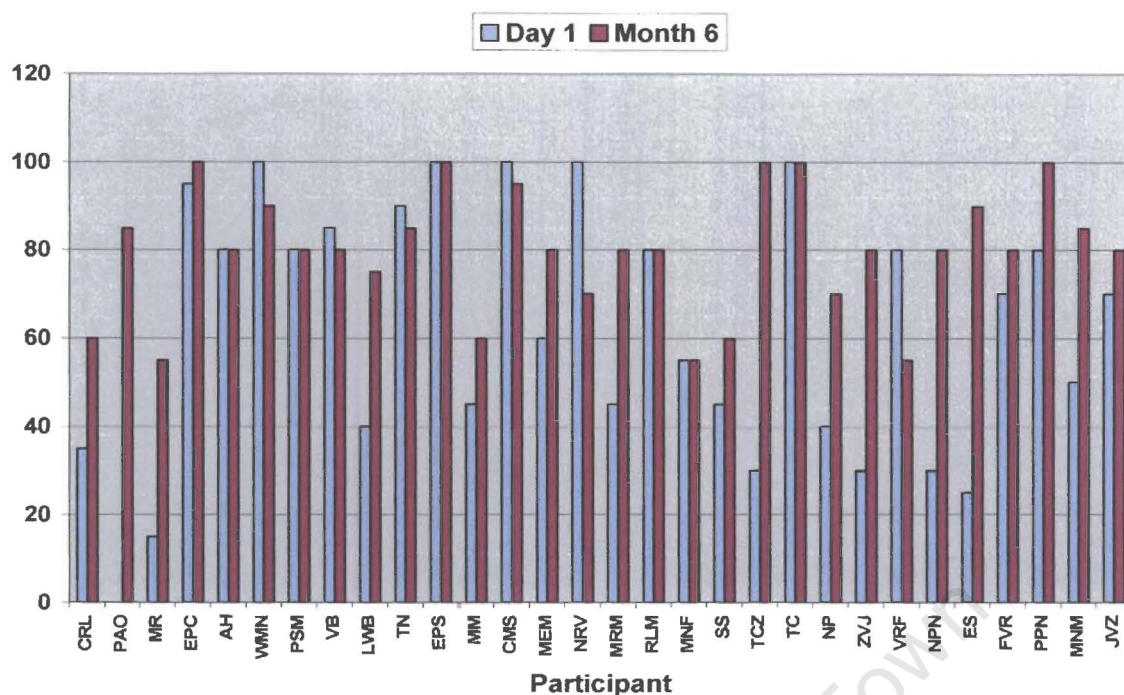
Figure 28: Graph indicating the standardised quality of life scores of the study participants at day 1:



5.12.2 Quality of life month 6:

At months 6 the mean quality of life score increased to 70. 24 Participants (80%) had scores of 75 or more and only one participant (CRL) had a score lower than 50. The majority of participants at month 6 felt that life had been good.

Figure 33: Graph indicating the standardised health distress scores of the study participants:



$p=0.0013$

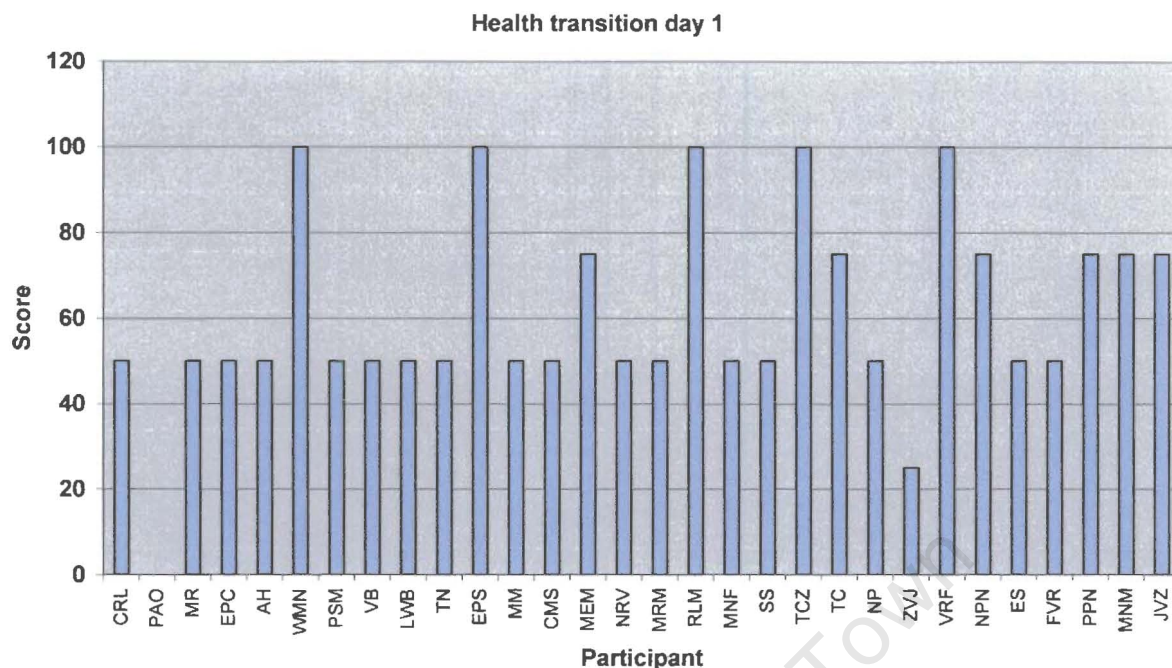
5.14 Health transition:

This sub-scale investigates the physical and emotional condition of the participant over the past four weeks. A low score means that the physical and emotional condition at the time of the questionnaire is far worse than 4 weeks ago, and a high score that it is much better than 4 weeks ago.

5.14.1 Health transition day 1:

At baseline the mean health transition score was 60,8. Two participants (7%) felt that their condition had been far worse than 4 weeks before, and 17 participants (57%) with scores of 50 felt that their conditions had been the same. 11 Participants (37%) indicated that their health was better at baseline than 4 weeks before.

Figure 34: Graph indicating the standardised health transition scores of the study participants at day 1:



5.14.2 Health transition month 6:

At month 6 the mean health transition score was 72,5. Nine participants (30%) with scores of 50 indicated that their health had not changed in the last 4 weeks. Seven participants (23%) with scores of 100 indicated that their condition had improved greatly since four weeks before.

Figure 35: Graph indicating the standardised health transition scores of the study participants at month 6:

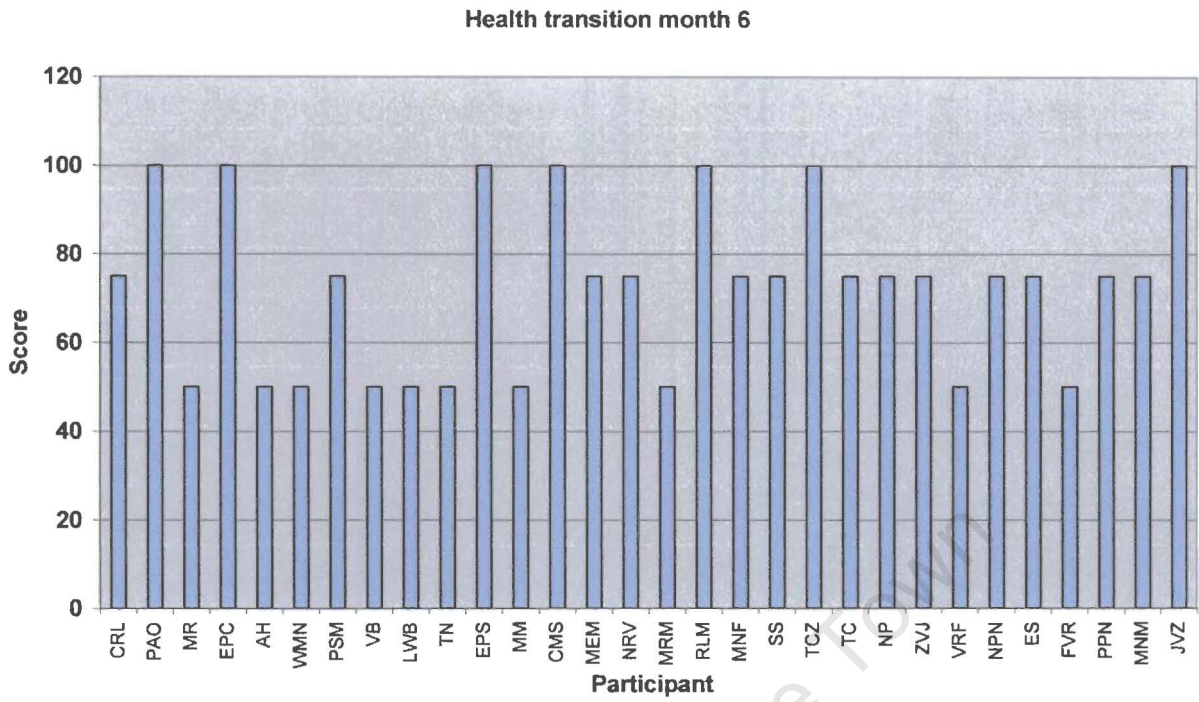
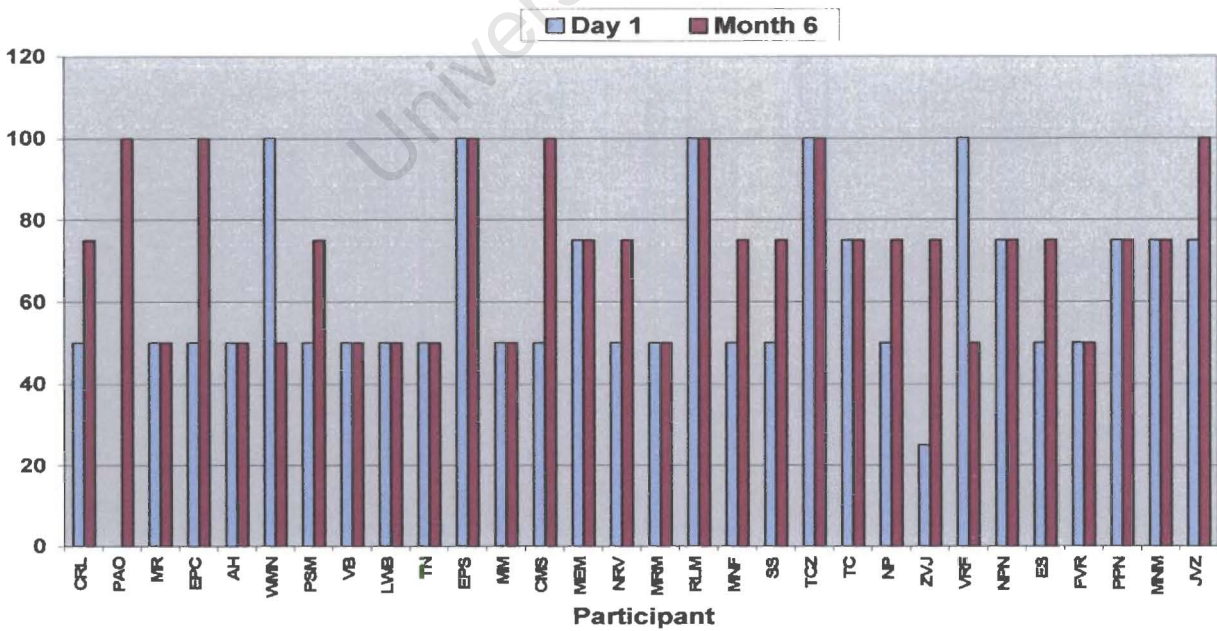


Figure 36: Graph indicating the standardised health transition scores of participants:



$p=0.0323$

CHAPTER SIX

DISCUSSION

6.1 Introduction:

This chapter discusses the study results obtained from the MOS-HIV Health Survey completed by 30 participants on the day antiretroviral medication was started (day 1; baseline) and 6 months after the initiation of medication. The results obtained on day 1 of antiretroviral treatment are compared to the results obtained after 6 months of treatment, and the differences in scores obtained interpreted to investigate changes in quality of life affected by the main variable, namely the introduction of antiretroviral therapy. The study did not make use of any therapy other than pharmaceutical intervention.

Tracking changes in functional status over six months, by routine assessment of the quality of life in persons with HIV infection, one would be able to demonstrate a trade-off between treatment effectiveness, functional status and side-effects (Grossman, Sullivan and Wu 2004). These quality of life factors may determine whether or not an individual is able to remain on medications for an extended period, like in the case of antiretroviral medication.

Although specific alternate hypotheses are not stated in each subset, the null hypothesis is statistically represented by H_0 : Value day 1 = Value month 6. Descriptive statistics and inferential statistics are used in the discussion of the total MOS-HIV score as well as the standardised score of each sub-scale of the MOS-HIV survey.

6.2 Total MOS-HIV score:

The total MOS-HIV score of the participants was high at initiation of therapy. Recent studies of the MOS-HIV demonstrated higher total MOS-HIV scores compared to the validation surveyed by Revicki et al. in 1994. This is mainly due to dramatic advances in HIV management during the past decade (Berman 2003).

Results of the present study indicate similar results to other studies conducted in Africa. Examples of studies include a study by Osahon and Erah (2007), which investigated the changes in QOL of 150 HIV-positive subjects in Nigeria during the first three months of antiretroviral treatment. They similarly reported a high initial total MOS-HIV score of 78.2 ± 11.2 on a scale of 0-100. Medina Lara et al. (2006) interviewed 159 HIV-positive adults from the Entebbe Cohort clinic in Uganda and also found the initial total MOS-HIV score to be high. The initial high scores on the total MOS-HIV measure in the current study were therefore not unexpected.

Homes, Bix and Shea (1996) stated that the MOS-HIV will not be sensitive to improvements in patients who are functioning at a relatively high level to begin with. In spite of this high initial total MOS-HIV score at the start of antiretroviral therapy 73,3% of the participants indicated an improvement in the score after 6 months of treatment. The improvement in the mean standardised total MOS-HIV score was statistically significant for the total population, as well as for both subsets of male and female participants. This indicated an improvement in the quality of life of the study participants after six months of antiretroviral therapy. The perceived improvement in QOL after six months of antiretroviral medication is important in motivating subjects to adhere to the HAART regimen.

The absence of constitutional symptoms or HIV-related symptoms in the current study, as per the inclusion criteria, was the major contributing factor to the initial high total MOS-HIV score. Cunningham et al. (1998) found a strong correlation between constitutional HIV symptoms and the total MOS-HIV score, with especially myalgia, exhaustion, anorexia, nausea, vomiting, night sweats and fever leading to a low total MOS-HIV score. Weight loss, T-lymphocyte counts, duration of illness and demographic characteristics did not influence the total MOS-HIV score or the quality of life outcome in their study (Cunningham, Shapiro, Hayes et al., 1998). Kohli et al. (2005) reported that regular medical intervention as well as regular psychological support may improve HRQOL. The current study was done on health surveys of participants who were followed up monthly as per the pre-determined visit schedules of the primary studies, and this regular follow-up was another contributing factor in the improvement in QOL of the participants. The regular completion of and attention given to the QOL questionnaires also clearly placed the focus on the participants' needs, which could have improved the perceived quality of life.

Three participants (10%) had no change in their total MOS-HIV score after 6 months of therapy, and four participants (13,3%) had a lower total MOS-HIV score at month 6. Revicki, Sorensen and Wu (1998) investigated QOL reports of 2 253 HIV-positive patients receiving their first HAART regimen, and compared the baseline HRQOL scores to those done after three- and six months of therapy. They found that patients reporting worsening health status over the first six months of therapy were significantly lower than scores of patients reporting stable or improving health status. This demonstrates the net positive impact antiretroviral treatment has on patient functioning and well-being as well as quality of life (Revicki, Sorensen and Wu 1998).

6.3 General health perception:

The mean standardised general health perception score of the study population at baseline was the lowest mean score of all sub-scales in the study. This can be seen as the sub-measure level at which participants perceived their health to be poorest. Arpinelli et al. (2000) reported in a study on the HRQOL of 214 Italian subjects with HIV that those with a CD4 count between 200 and 499 cells/mm³ scored lowest on the general health perception measure. No correlation with physicians' findings on these subjects' health was seen, and the low scores were related to the psychological impact of the HIV disease stage between a normal functioning immune system, represented by a CD4 count of 500cells/mm³ or more, and the initiation of HAART when the CD4 count falls below 200 cells/mm³. Subjects in the current study were chosen with CD4 counts between 200 and 350 cells/mm³, and since no evidence existed of intercurrent pathology, the same psychological factors are accepted as the explanation of the low mean standardised general health perception score.

The mean general health perception of the participants increased over the 6 months of therapy, and the increase in this score reached statistical significance for the total population as well as the male sub-population. The mean standardised general health perception score in female participants increased from baseline to month 6, but the increase was not statistically significant. Significant variance of the measure was also seen, once more indicating psychological more than physical differences.

The mean standardised baseline health perception score of female participants was lower than that of the male participants. Kohli et al. (2005) studied the changes in QOL of HIV infected persons in India, enrolled in an ongoing longitudinal prospective study of clinical progression, and reported that women had significantly lower health

perception scores compared to men, often in spite of more advanced disease. A study conducted in South Africa assessed the QOL in women and men using eight different QOL scales. In addition to assessing gender, differences in race were also explored. Findings concluded that black females in South Africa possessed the lowest scores on all scales except for physical functioning (O'Keefe and Wood 1996).

Vosvick et al. (2003) reported that HIV-positive women may have a more rapid decline in health than HIV-positive men, based on an observed faster disease progression and CD4 T cell count depletion. They regard this as a reason for lower health perception scores in women. Lenderking et al. (1997) investigated the QOL of 1 700 subjects with early HIV disease at initiation of antiretroviral medication, and stated that women indicated a lower QOL than men on all scales, while ethnicity was related to differences in health perceptions and physical and psychological functioning. In a discussion of assessment tools for QOL in persons with HIV, Grossman, Sullivan and Wu (2003) listed the following factors that could also have contributed in creating the lower health perception scores in females in the current study: low income, disclosure, decision making regarding privacy issues, the negotiations of safer sex and the fear (real or perceived) of violence resulting from disclosure of HIV status. At the end of the study period it seemed as though the introduction of antiretroviral medication improved the general health perception of male participants significantly, but that of female participants marginally.

6.4 Physical functioning:

The standardised physical functioning score increased in number from baseline to month 6 in the total study population, as well as in both the female and male populations separately, but it did not reach statistical significance in any of the groups mentioned.

O'Leary et al. (1998) examined the relation between the MOS-HIV questionnaire and the more detailed HIV Overview of Problems-Evaluation System (HOPES) in 318 HIV-infected subjects, and regarded the following problems in everyday life to correlate with a lower MOS-HIV physical measure: poor ambulation, restriction in activities of daily living, fewer recreational activities, loss of weight, difficulty working, pain, lack of clothing and physical symptoms of disease. It is feasible that subjects in the current study experienced some of these problems, and since they were not addressed specifically, caused the absence of a meaningful increase in physical functioning.

The language as well as the examples used in the questionnaire had an influence on the results: participants frequently asked the meaning of concepts like "strenuous sport", "bowling" or "stooping" and had little experience in climbing a flight of stairs or walking one hundred paces (cf. Appendix C question 4). Lin, Wu and Revicki (2002) warned that many QOL surveys were developed with educated, Caucasian populations in mind, and in the early days also focused mainly on homosexual men. The population of HIV/AIDS has shifted to other ethnicities, women, injection drug users as well as their partners. These hard-to-reach disadvantaged populations often encounter literacy level challenges, cultural expression variances and different terminology norms. Care should therefore be taken to ensure the instrument is a reliable and valid measure in the study setting (Lin, Wu and Revicki 2002).

Mast et al. (2000) reported on a study done in Uganda in 1998 where the MOS-HIV survey was translated from English to Luganda using two forward and three backward translations. This made it possible to use the MOS-HIV questionnaire in rural areas, but also made the questions generally more understandable. As an example the expression "moderate activities" was translated with "washing clothes, moving a jerrican

of water or bundle of firewood". Medina Lara et al. (2006), using the Luganda version of the MOS-HIV, reported a 100% response and good acceptability of the adapted survey.

One participant scored zero at baseline for physical functioning. This 35 year old female participant had no physical finding that could explain this low score, and the zero score reflects the floor effect of the MOS-HIV survey as reported by Revicki, Sorensen and Wu (1998) and Grossman, Sullivan and Wu (2003) in domains which include the physical functioning. The floor effect artificially restricts the lower limit of detection of the scale, and is an inherent flaw in the measure (Grossman, Sullivan and Wu 2003).

The use of antiretroviral medication did not make a meaningful difference in the physical functioning of participants in the first 6 months of therapy.

6.5 Role functioning:

Answers to the two questions in the role functioning subscale leads to a raw score which varies between 2 and 4, and this translates to a standardised score having one of only three possibilities: zero, 50 or 100. At baseline 4 female participants and 1 male participant (16,7% in total) had a score of zero, indicating severe problems in performing daily activities. Shahriar et al. (2003) reported significant floor effects of the role functioning subscale after investigating 39 published studies that used the MOS-HIV health survey. The mentioned floor effect explains the scores of zero in the current study, mostly due to few items in the role functioning domain. In contrast to this 9 female and 10 male participants (63% in total) had a score of 100 at baseline, which indicates the ceiling effect reported by Shahriar et al. (2003) and Badia et al. (2000) in the role functioning measure. The ceiling effect artificially restricts how high a participant can

score in a particular measure, and is, like the floor effect, an undesirable measurement outcome (Grossman, Sullivan and Wu 2003).

The mean standardised role functioning score at baseline was 73,3. Badia et al. (2000) reported on the HRQOL changes of 296 HIV-infected patients in Spain, starting or switching antiretroviral treatment, and found similar results with a mean standardised role functioning score at baseline of 73,1. The increase in mean standardised role functioning score between baseline and month 6 of all participants, the female participants as well as the male participants was statistically significant. The results have to be interpreted with caution, since all 30 participants (100%) had a standardised role functioning score of 100 (maximum score) at month 6. This can be interpreted that no participant experienced any problems as a result of his/her disease in terms of work or daily activities. It is not an accurate deduction, but rather confirms the ceiling effect in MOS-HIV subscales mentioned in previous studies (Holmes and Shea 1999; Badia et al. 2000; Shahriar et al. 2003, Revicki, Sorensen and Wu 1998). The ceiling effect in the role functioning domain is especially noticeable in the score of 100 (maximum score) at month 6 of a female participant with partial paralysis of the lower limbs due to peripheral neuropathy caused by tuberculostatic medication 9 months prior to the start of the study. The participant was in fact unable to do certain kinds of homework due to her disability, which meant that her health did prevent her from working at a job or doing work around the house. A maximum score in the role functioning domain does not reflect this restriction. It is possible, however, that she saw no additional restriction on her abilities after using the antiretroviral medication for 6 months and that she reflected this absence of change in her role functioning score at 6 months.

6.6 Social functioning:

The participants scored high on the standardised mean social functioning subscale (mean 83,3) at baseline. This meant that patients experienced few limitations in their social activities as a result of HIV disease. These results are in contrast to the findings of Badia et al. (2000) who reported a lower baseline standardised social function score of 60,9. The initial high score in this measure could be due to the fact that every participant had revealed his/her HIV status and had established social support before the initiation of the antiretroviral medication. This was required in terms of the inclusion criteria of the clinical trial(s) of which the MOS-HIV Health Survey formed part (cf. 4.3.1 Inclusion Criteria). A correlation between disclosure of a person's HIV status and higher social functioning was reported by Chandra et al. (2003) as well as Grossman et al. (2003). The pre-requisite of disclosure of HIV status to at least one person before the initiation of HAART, laid down by the South African Department of Health for the public sector ARV roll-out, is also based on the above-mentioned studies. This places the focus on the whole person, and not just the suppression of viral load, the CD4 count or specific symptoms.

The mean standardised social functioning score increased in value at month 6, but the increase was not statistically significant. Vosvick et al. (2003) reported that poor social functioning may be associated with greater use of avoidance coping strategies such as withdrawal and conflictual social interactions, leading to an increase in stress. Although it may adequately explain the absence of a significant improvement in the social functioning score in the current study, an investigation into the coping strategies and social interactions of participants fell outside the scope of this study. The MOS-HIV survey may also not be sensitive enough to reflect improvements in this sub-scale since participants were functioning at a high level to begin with (O'Leary et al. 1998). The

participants' perception of their social functioning was thus not dependent on the antiretroviral medication they had received, and the addition of HAART did not improve participants' social functioning over a period of 6 months. The influence of stigma and discrimination was not investigated in study participants, but it could have been another contributing factor in the perception that their social functioning did not improve in the first six months of antiretroviral use (Kohli et al. 2005).

6.7 Pain:

At day 1 the mean standardised pain score of all participants at baseline was 75,9, which indicates that participants did not experience much pain or significant limitations due to pain. Murri et al. (1997) reported a significant correlation between high MOS-HIV pain scores (indicating less pain) and higher CD4 counts. The initial high pain scores in this study can therefore be linked to the fact that participants were chosen with relatively high CD4 counts, even though this correlation had been challenged in subsequent studies investigating the reliability and validity of the MOS-HIV questionnaire in different translations (Scott-Lennox et al. 1999; Lau et al. 2006).

The high pain scores at baseline contradict the common belief that pain is generally associated with HIV disease. Even though pain may be a feature of symptomatic HIV disease, most pain in HIV can be attributed to an underlying treatable cause (Larue, Brasseur, Musseault 1994). The findings of the current study are in keeping with a HRQOL study done in Europe where a sample size of 534 HIV-positive subjects reported an incidence of only 22% of pain reaching a moderate level or higher (Savoye 2004). Hart et al. (2000) reported an increase in the experience of pain (and subsequent lower MOS-HIV pain scores) in subjects who used denial as a coping

strategy. In this regard the disclosure of HIV status assisted in increasing the MOS-HIV pain score, and lessened the perception of pain.

Female participants experienced more pain at baseline than the male participants. This is in keeping with the findings of Savoy (2004) where 38% of females vs. 16% of male participants reported pain of any kind. Savoy (2004) as well as Gray and Berger (2007) state that women experience pain differently from men due to biological, psychological, and social factors. These factors were not explored in the current study. The results also once more confirms the findings of Lenderking et al. (1997) that women report lower scores on all sub-scales of the MOS-HIV questionnaire, including the sub-scale of pain.

The higher pain score for the male population at baseline could be the reason that the increase in standardised pain score did not reach statistical significance (O'Leary et al. 1998). The increase in mean standardised pain score at month 6 did reach significance for the total study population as well as for the female population, which means that the antiretroviral medication was strongly associated with pain perception of these populations.

Participant MNF (with lower limb paralysis) had a standardised pain score of less than 50 at month 6: unchanged from baseline at 44,4. This low score was validated by the fact that she was the only participant who took pain medication, namely Paracetamol, on a regular basis during the first 6 months of antiretroviral therapy. Although MNF verbalised that her pain was controlled by the regular use of Paracetamol, the results of the pain scores may indicate that her pain was not adequately controlled.

6.8 Mental health:

In contrast to Maslow's theory, where he states that fulfilment of basic needs is necessary for effective functioning, most of the participants reflected above average mental health in spite of physiological malfunction (cf. figure 2: Maslow's hierarchy of needs). The standardised mental health score increased significantly after 6 months of antiretroviral therapy. This improvement in the mental health score was also the most significant increase of any sub-scale measured. The management of HIV as a chronic disease, the infusion of hope as participants responded to HAART, the reduction of fears associated with HIV disease as well as the support rendered by the study site to the participants contributed to this observation (Kohli et al. 2005, Grossman, Sullivan and Wu 2003). It further means that the management of participants with the introduction of antiretroviral medication was a strong contributing factor to the mental health perceptions of the participants over the period of 6 months.

The mental health findings in the current study is in stark contrast to a study of changes in QOL of 916 matched female participants where the introduction of HAART did not improve the participants' mental health score over a six month period (Liu et al. 2006). The differences in the South African context and unique factors in the South African setting have not been explored in the current study.

O'Leary et al. (1998) compared the MOS-HIV survey to the HIV Overview of Problems-Evaluating System (HOPES) and found that a range of emotional symptoms are involved in the rating of the very concise MOS-HIV Mental health scale. Important emotional aspects underlying the MOS-HIV mental health score were reported to be stigma, psychological distress, cognitive problems, difficulty communicating with friends or relatives, problems in sleeping and worry (O'Leary et al. 1998). These themes were not

investigated in the current study, but were found to be of significant importance in other studies investigating quality of life themes in South Africa (Jacobs-Jokhan 2004, Peltzer K. and Phaswana-Mafuya N. 2008). Lenderking et al. (1997) as well as Kohli et al. (2005) reported lower mental health scores in women, which was the same when compared to the current study.

6.9 Cognitive functioning:

The low mean standardised cognitive functioning score of participants at baseline indicated problems in concentrating, reasoning and remembering most of the time, although 46,7% indicated few problems in this regard, or being able to concentrate, reason and remember most of the time. Twelve participants (40%) had a maximum score at month 6, indicating no problems with concentration, reasoning and remembering immediately or over a period of time. These maximum scores confirm a ceiling effect in the cognitive functioning sub-scale, previously reported by Shahriar et al. (2003) as well as Revicki, Sorensen and Wu (1998). Wilkie et al. (2003) reported that cognitive impairment in persons with HIV was very common, and was the indirect effects of viral neurotoxins (viral proteins gp120 and tat) and neurotoxins released by infected or activated microglia, macrophages, and astrocytes. These cognitive disorders therefore do not respond well to the use of HAART (Wilkie et al. 2003). The results of the current study also saw no significant improvement in the cognitive functioning of participants in the first 6 months of HAART.

In addition to this were 8 participants (26,7%) who had a lower standardised cognitive functioning score at month 6, indicating that the introduction of antiretroviral medication caused more problems in cognitive functioning. Revicki (1999) found that the use of certain combinations of antiretroviral medication, or the inclusion of certain

antiretroviral agents in a HAART regimen, caused a decrease in cognitive scores from baseline. Osahon and Erah (2007) found that the introduction of antiretroviral medication had the biggest positive impact on patients' cognitive functioning. They concluded that QOL domain was strongly associated with the type of medication used in the HAART regimen, and not with sociodemographic variables. Burgoyne, Rourke, Behrens and Salit (2004) stated that the cognitive and mental aspects of quality of life remained consistently lower than reference norms in spite of the introduction of antiretroviral medication.

The CNS effects of certain antiretroviral medication were discussed in Chapter 2 and the deterioration in cognitive ability could be ascribed to certain components of the highly active antiretroviral regimen of participants in the current study. This association fell outside the scope of the study, but it was clear that antiretroviral medication did not improve the cognitive functioning of participants in the current study.

6.10 Vitality:

David and Pathak (2001) warned that the MOS-HIV survey does not demonstrate ideal psychometric properties, and can therefore not accurately reflect participants' vitality in the era of HAART. They reported that published data for the MOS-HIV questionnaire had common limitations of sample size, study design, as well as population demographics, and they doubted the reliability and validity of psychometric data reflected by the MOS-HIV.

The increase in the mean standardised vitality score between day 1 and month 6 is statistically significant for the total study population, and also significant for the female and male sub-populations. The management of HIV as a chronic disease through the use

of HAART, the hope brought on by the response to HAART, the reduction of fears associated with HIV disease, the absence of major side-effects of HAART as well as the support rendered by the study personnel was linked to this observation (Kohli et al. 2005, Grossman, Sullivan and Wu 2003). Similar results were seen in a study of 1 015 participants using the combined data from two randomised, open label phase III antiretroviral studies, although the results reflected the changes in QOL scores at more time points than just baseline and month 6 (Wu et al. 2006).

Twenty-one participants (70%) had a standardised vitality score of 80 or more at 6 months of antiretroviral medication, indicating high energy levels and feeling full of vigour. In contrast to this, 5 participants (16,7%) had a drop in mean standardised vitality score at 6 months of therapy, indicating poorer energy levels since starting the antiretroviral medication. The specific combination of drugs used in these participants' HAART regimens could explain this finding, but was not investigated in the current study. The mean standardised vitality score at month 6 was 81,2, indicating high energy levels. Scott-Lennox, Mills and Burt (1998) found that the use of antiretroviral medication generally improved the standardised vitality score over a period of 6 months, but that the combination of antiretroviral medication in the HAART regimen had an influence on this outcome. The data in the current study were not stratified according to HAART regimen used, but while on the HAART regimen did improve vitality over a period of six months.

6.11 Health distress:

The mean standardised health distress score at day 1 of antiretroviral therapy was 61,8, which reflected participants feeling hopeful, encouraged and not afraid due to health most of the time. Wu et al. (2006) found a correlation between health distress

scores and physical symptoms. The positive feelings in the study at day 1 of therapy can therefore be ascribed to the absence of physical symptoms as per the inclusion criteria, as well as relative good health due to a higher CD4 count.

The increase in mean standardised health distress scores for the total population, female population as well as the male population reached significance at month 6. The younger female population experienced more distress about their health (mean standardised distress score 74,6) than the male population (mean standardised distress score 84,1) at month 6 of treatment. In a study of 1 262 Canadian subjects affected by HIV infection, Lamping et al. (1991) reported that gender had no correlation with health distress, but that a younger age was strongly related to higher health distress (and lower scores on the MOS-HIV sub-scale). Although some studies reported female subjects to score lower on all MOS-HIV subscales than men (Kohli et al. 2005; Vosvick et al. 2003), the differences in health distress in the current study between the male and female populations may be due to age and not gender.

No participant scored lower than 55 on the health distress measure at month 6 of antiretroviral medication. This meant that all participants were feeling more optimistic most of the time, and that the use of antiretroviral medication positively affected the health distress measure.

6.12 Quality of life:

A ceiling effect in the quality of life perception measure was noted with six participants (20%) scoring 100 (maximum score) on the standardised quality of life measure at day 1. In spite of this 60% of participants had a standardised quality of life perception score at day 1 that indicated the perception of a poor quality of life. There

was an increase in number of the mean standardised quality of life score at month six, but it was not statistically significant for the total population, the female population or the male population. Liu et al. (2006), as well as Grossman et al. (2003), observed that subjects' perception of QOL remained stable over a period of 6 months after the introduction of HAART. They stated that this was mainly due to the trade-off between the prospect of longevity and the incorporation of ARV regimens into their lives. The perception of QOL changed negatively, however, when patients experienced side-effects due to the medication, or developed HIV-related symptoms. This observation is confirmed by one participant who scored zero on the quality of life measure at month 6 of therapy. He experienced an oculogyric crisis in the second month of antiretroviral treatment, not related to the antiretroviral medication and not regarded as a serious adverse event. As a result of the oculogyric crisis he was unable to read or drive for several months, and this led to a perceived poor quality of life.

The absence of existing or new constitutional symptoms in the current study population, as per the inclusion criteria, may therefore explain why six months of HAART did not change the quality of life perception measure.

6.13 Health transition:

Bastardo and Kimberlin (1998) studied HIV-positive subjects in Venezuela and found that the presence of symptoms was the most important factor influencing the health transition score. In the current study 56,7% of participants at day 1 and 33,3% of participants at month 6 of therapy indicated (with a score of 50 on the standardised health transition score) that they were uncertain if their physical and emotional health had been better than 4 weeks before. This can be explained once more by the absence of symptoms in the current study population. Although the increase in the mean

standardised health transition score at 6 months of antiretroviral therapy was statistically significant for the total study population, it was not significant for the female population or for the male population. Women once more scored lower on this MOS-HIV subscale.

6.14 Limitations of the study:

There were several limitations of the study noted. The study population was small ($n=30$) and was not powered adequately to correctly reject a false nil hypothesis. The study was also done retrospectively, and was therefore not designed with QOL as a primary endpoint.

The use of the English version of the MOS-HIV health survey in the current setting had limitations in terms of cultural expression variances and different terminology norms, while the survey itself had limitations in terms of floor- and ceiling effects. The MOS-HIV does not demonstrate ideal psychometric properties (David and Pathak 2001) and as a QOL tool may not have been the ideal choice for the study population. The MOS-HIV survey does not cover some aspects pertinent to HIV infection, such as somatic symptoms, sleep abnormalities, sexual dysfunction, eating behaviour or body image (Grossman, Sullivan and Wu 2003). Bruce (2001) reported that the MOS-HIV survey may provide a numerical rating of quality of life, but offers no insight or information into how people arrive at their scores. This has serious implications for our ability to interpret quality of life research. The study population was not well balanced in terms of gender, age or race, and was also not stratified according to different HAART regimens. The inclusion of participants with CD4 counts between 200 and 350 cells/mm³ limited the observational value of the study.

A possible limitation was that the information gathered and conclusions made from this study were based on the time-efficient MOS-HIV questionnaire, which, although validated, produced essential information only. More information could have been obtained and better conclusion drawn if longer, more detailed QOL measures were used. Better deductions could have been made if the MOS-HIV was accompanied by a biographical questionnaire, which could have added more in-depth information regarding aspects tapped by the quantitative measure.

Validation of the MOS-HIV health survey for different cultural settings in the South African context has not been done, and is a major limitation of the current study. The mere translation of the questionnaire into one of the eleven official languages is not enough, and should ideally be adjusted to a specific cultural idiom.

CHAPTER 7

CONCLUSION:

After 6 months of antiretroviral medication the increase in total MOS-HIV score indicated an improvement in quality of life in HIV-positive participants in this study. The increase was statistically significant. Although individual variation, personal factors and the choice of drugs played an important role in the perception of quality of life, the two major medical events that all participants experienced were the introduction of antiretroviral medication, and reaching an undetectable viral load. It is clear that, in spite of side-effects of antiretroviral medication, the therapy effected a net improvement in quality of life. A noticeable improvement in quality of life coincides with the moment when viral replication is suppressed maximally.

Participants indicated, by means of the MOS-HIV questionnaire, that the use of antiretroviral medication for six months improved their general health perception, role functioning, pain level, mental health, vitality, health distress and health transition. The difference in participants' physical functioning, social functioning, cognitive functioning or quality of life perception over the six month period was not highly significant, even though the mean scores of these measures increased in number. There were differences in the sub-scale scores for female and male participants.

RECOMMENDATIONS:

The study was done retrospectively, taken from trials where HRQOL was a secondary endpoint. The trials were therefore designed with the primary endpoint in mind, and not for a HRQOL endpoint. The sample size was randomly chosen in this

study, but for a HRQOL outcome the sample size should be calculated based on a HRQOL outcome. Better results can be obtained if a matched sample is used.

Unclear research questions can be eliminated by translating the questionnaire in the participant's idiom.

To increase the power of a HRQOL study it should be checked if sample size calculations are sufficient. Consultation with a statistician should be done during the design stage of the trial.

Future studies could complete the second MOS-HIV questionnaire at the moment an individual reaches undetectable viral levels, and not at a pre-destined time point. This could reflect a better relationship between maximal viral suppression and quality of life.

Future studies could investigate the MOS-HIV results in different age groups, different CD4 counts, different socio-economic strata, ARV medication used, or even race. For this each sub-group should have an acceptable number of participants, and such a study requires far more participants. Studies could be done in which matched variables (such as age and gender) are measured and compared between participants in a third- and first world country.

The MOS-HIV was developed over a decade ago when HIV disease and its treatment were very different from today. At that time, rapid health deterioration from HIV disease and its associated sequelae was prevalent. With rapid progression into the late stages of HIV disease, monitoring the HRQOL of patients who were developing HIV-associated sequelae such as cancers, opportunistic infections and AIDS dementia was imperative. Currently, however, with the availability of HAART, HIV disease is a chronic

rather than acute condition for the majority of patients, and as such may require an instrument to assess HRQOL that was designed for chronic rather than acute diseases (Shahriar J., Delate T., Hays R. D., Coons S. J. 2003).

Koole, Noestlinger and Colebunders (2007) reported that sexual health and sexual dysfunction constitute an important part of health-related quality of life. Sexual dysfunction is only reflected by one HRQOL survey, namely the WHO QOL-HIV questionnaire. The growing market for drugs that increase sexual performance in persons using antiretroviral medication is an indication that it is an aspect of HRQOL not accounted for in the MOS-HIV questionnaire. Future studies could therefore include other health surveys to include more variables linked to QOL.

REFERENCES:

- Albert S. M. 2002, *Quality of Life, Definition and Measurement*, Retrieved on 11 Jan 2008 from <http://www.AGIS.com>
- Arpinelli F., Visona G., Bruno R., Decarli G., Apolone G. 2000, *Health-Related Quality of Health in Asymptomatic patients with HIV*, *PharmacoEconomics*, Vol. 18, No. 1, pp. 63 - 72
- Badia X. et al. 1999, *A randomized study comparing instruments for measuring health-related quality of life in HIV-infected patients*, *AIDS*, Vol. 13, No. 13(Sep 1999), pp. 1727 – 1735
- Badia X, Podzameczer D, Casado A, Lopez-Lavid C, Garcia M. 2000, *Evaluating changes in health status in HIV-infected patients: Medical Outcomes Study-HIV and Multidimensional Quality of Life-HIV quality of life questionnaires. Spanish MOS-HIV and MQOL-HIV Validation Group*, *AIDS*, Vol. 14, No. 10, pp. 1439- 1447
- Bastardo Y. M., Kimberlin C. L. 1998, *Relationship between quality of life and social support in HIV-infected persons in Venezuela*, *International Conference on AIDS*, Geneva, abstract no. 14344
- Berman B. A. 2003, *What a Difference a Decade Made: Quality of Life in Adults Living with HIV/AIDS*, Retrieved on 23 Aug 2008 from <http://www.ACRIA.com>
- Berzon R. A., Lenderking W. R. 1998, *Evaluating the Outcomes of HIV Disease: Focus on Health Status Measurement*, Retrieved on 12 Feb 2007 from <http://www.outcomes-trust.org/monitor/nov98/4.html>
- Bosworth H. B. 2006, *The Importance of Spirituality/Religion and Health-Related Quality of Life Among Individuals with HIV/AIDS*, *Journal of General Internal Medicine*, Vol. 21, no. 5, Retrieved on 24 Jan 2007 from <http://www.blackwell-synergy.com>
- Bruce D. R. 2001, *Who's life is it anyway?*, Retrieved on 11 May 2007 from <http://ssl.thebody.com/content>
- Buhk T., Schieferstein C. 2006, *HIV Medicine 14th Edition 2006: Side-effects*, in “HIV Medicine 2006 (Hoffmann et al.)”, Flying Publisher, Paris
- Burgess A., Dayer M., Catalan J., Hawkins K., Gazzard B., 1993, *The reliability and validity of two HIV-specific health related quality of life measures: a preliminary analysis*, *AIDS*, vol. 7, pp. 1001-1008
- Burgoyne R. W, Rourke S. B., Behrens D. M., Salit I. E. 2004, *Long-term quality-of-life outcomes among adults living with HIV in the HAART era: the interplay of changes in clinical factors and symptom profile*, *AIDS and Behavior*, Vol. 8, No. 2, pp. 151-163
- Calman K. C. 1984, *Quality of life in cancer patients – an hypothesis*, *Journal of Medical Ethics*, Vol. 10, pp. 124 – 127
- Carr A. J., Higginson I. J. 2001, *Measuring quality of life: Are quality of life measures patient centered?*, *BMJ*, Vol. 322, pp. 1357 – 1360, Retrieved on 12 February 2007 from bmj.com

- Chang Y., Hsiao S. 2006, *Quality of Life: Scaling with Maslow's Need Hierarchy*, Gerontology, Aug 2006, Vol. 52, pp. 376
- Cohen C., Revicki D. A., Nabulsi A., Sarocco P.W., Jiang P. and The Advanced HIV Disease Ritonavir Study Group 1997, *Quality of life in advanced HIV disease patients: results of an international, randomized placebo-controlled clinical trial of ritonavir*. Manuscript in preparation.
- Copfer A. E , Ampel N. M., Hughes T. E., et al. 1996, *The use of two measures of health-related quality of life in HIV-infected individuals: a cross-sectional comparison*, Quality of Life Research, vol. 5, pp. 281-286
- Cowdery J. E., Pesa J. A., 2002, *Assessing quality of life in women living with HIV infection*, AIDS Care, No. 14, pp. 235-45.
- Cunningham W. E., Shapiro M. F., Hays R.D. et al. 1998, *Constitutional symptoms and health-related quality of life in patients with symptomatic HIV disease*, American Journal of Medicine, Vol. 104, pp. 129-136
- Davis E. A., Pathak D. S. 2001, *The annals of Pharmacotherapy*, Vol. 35, No. 5, pp. 546 - 552
- Douaihy D., Singh N. 2001, *Factors Affecting Quality of Life inpatient with HIV Infection*, AIDS Read, Vol. 11, No. 9, pp. 450 – 461
- Eiser C., Morse R. 2001, *A review of measures of quality of life for children with chronic illness*, Arch Dis Chil 2001, Vol. 84, No. 3, pp. 205 – 211
- European Medicines Agency 2005, *Reflection paper on the regulatory guidance for the use of health-related quality of life (HRQOL) measures in the evaluation of medicinal products*, Doc. Ref. EMEA/CHMP/EWP/139391/2004
- Friedland G., Williams A. 1997, *Adherence, Compliance and HAART*, AIDS Clinical care, July 1997. Retrieved on 13 November 2007 from <http://aids-clinical-care.jwatch.org>
- Gaede B. M., Majeke S. J., Modeste R. R. M., Naidoo J. R., Titus M. J., Uys L. R. 2006, *Social support and health behaviour in women living with HIV in Kwa-Zulu Natal*, Journal of Social aspects of HIV/AIDS, Vol. 3, No. 1(May 2006), pp. 362 – 368
- Gray G., Berger P. 2007, *Pain in women with HIV/AIDS*, Pain, Vol. 132, p. 161
- Grossman H. A., Sullivan P. S., Wu A. W. 2003, *Quality of Life and HIV: current assessment tools and future directions for clinical practice*, AIDS, Vol. 13, No. 12, pp. 583 - 590
- Hart S., Gore-Felton C., Maldonado J., Lagana L., Blake-Mortimer J., Israelski D., Koopman C., Spiegel D. 2000, *The relationship between pain and coping styles among HIV-positive men and women*, Psychology & Health 2000, No. 15, pp. 869–879
- Hoffmann C., Kamps B., Rockstroh J. (ed.) 2006, *HIV Medicine 2006*, Flying Publisher, Paris
- Hoffmann C., Mulcahy F. 2006, *Goals and Principles of Therapy*, Retrieved on 13 November 2007 from <http://www.hivmedicine.com>

Holmes W., Bix B., Shea J. 1996, *SF-20 score and item distribution in a human immunodeficiency virus-seropositive sample*, Medical Care, No. 34, pp. 562 – 569

Holmes W. C., Shea J. A. 1999, *Two approaches to measuring quality of life in the HIV/AIDS population: HAT-QoL and MOS-HIV*, Quality of Life Research, Vol. 8, No. 6, pp. 515 – 527

Jacobs-Jokhan D, 2004, *Research on the quality of life of HIV positive mothers in south africa with regards to infant feeding and early diagnosis*, 15th International Conference on AIDS, Bangkok, abstract no. MoPeD3805

Kohli R. M., Sane S., Kumar K., Paranjape R. S., Mehendale S. M. 2005, *Modification of medical outcome study (MOS) instrument for quality of life assessment & its validation in HIV infected individuals in India*, Indian Journal of Medical Research, Retrieved on 10 August 2008 from

Koole O., Noetslinger C., Colebunders R. 2007, *Quality of Life in HIV Clinical Trials: Why Sexual Health Must Not Be Ignored*, PLoS Clinical Trials, Vol. 2, No. 3, e8 doi:10.1371

Lampind D. L., Sewitch M., Clark E., Ryan B., Gilmore N., Grover S. A., Williams J. I., Meister C., Hamel M., Di Meco P. 1991, *HIV-related mental health distress in persons with HIV infection, caregivers, and family members/significant others: results of a cross-Canada survey*, International Conference on AIDS, abstract no. M.D.4050

Larue R., Brasseur L., Musseault P. et al. 1994, *Pain and HIV infection: a French national survey*, Journal of Palliative Care, No. 10, p. 95

Lau J. T. F., Hi Y. T., Patrick L. C. K., Rita C. W. Y., Molassiotis A. 2006, *Validation of a Chinese version of the Medical Outcomes Study HIV Health Survey (MOS-HIV) among Chinese people living with HIV/AIDS in Hong Kong*, Quality of life research, Vol. 15, No. 6, pp. 1079 - 1089

Lenderking W. R., Testa M. A., Katsenstein D., Hammer S. 1997, *Measuring quality of life in HIV early disease, the modular approach*, Quality of Life Research, Vol. 6, pp. 515-30

Lin M. K., Wu A. W., Revicki D. A. 2002, *Incorporating Quality of Life Measures in HIV Clinical Trials*, HIV Clinical Trials, Vol. 3, No. 3, pp. 202 – 208

Liu C., Weber K., Robison E., Hu Z., Jacobson L. P., Gange S. J. 2006, *Assessing the effect of HAART on change in quality of life among HIV-infected women*, AIDS Research and Therapy, Vol. 3, No. 6

Lubeck D. P., Fries J. F., 1997, *Assessment of quality of life in early stage HIV-infected persons: data from the AIDS Time-Oriented Health Outcome Study (ATHOS)*, Quality of Life Research, No. 6, pp. 494-506

Mannheimer S. B. & co 2005, *Quality of life in HIV-infected individuals receiving antiretroviral therapy is related to adherence*, AIDS Care, Vol. 19, No. 1, pp. 10 – 22

Mast T. C., Kigozi G., Wabwire-Mangen F., Makumbi F., Sewankambo N. K., Serwadda D., Gray R. H., Wawer M. J., Black R. E., Wu A. W. 2000, *Cultural adaptation, reliability,*

validity and feasibility of the MOS-HIV health survey to measure quality of life in rural Uganda, International AIDS Conference, Durban, Abstract No. MoOrD201

Mayo M., 2002, *Gender Differences In Quality Of Life In Persons Infected With HIV*, Retrieved on 21 August 2008 from <http://indigo.lib.uic.edu:8080>

Medina Lara A., Nyanzi Wakholi B., Kasirye A., Watera C., Gilks C.F., Grosskurth H. 2006, *Assessment of quality of life in HIV infected Ugandans using the Visual Analogue Scale (VAS) and the MOS-HIV Health Survey*, International Society of Quality of Life 13th Annual Conference, Lisbon, Portugal, 10-14 October 2006, Lisbon, Portugal. Oral presentation 1673

Miller S. (chair) June 2002, *Southern African HIV Clinicians Society Clinical Guidelines: Antiretroviral therapy in adults*, Retrieved on 03 Oct 2007 from <http://www.hst.org.za>

Murri R., Ammassari A., Fantoni M., Scoppettuolo G., Cingolani A., De Luca A., Damiano F., Antinori A. 1997, *Disease-related factors associated with health-related quality of life in people with nonadvanced HIV disease*, Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology, Vol 16, No. 5, pp. 350 - 356

Nieuwkerk P., Hillebrand-Haverkort M. E., Vriesendorp R., Frissen P. H., Jos M. D., de Wolf F., Sprangers M. 2007, *Quality of Life After Starting Highly Active Antiretroviral Therapy for Chronic HIV-1 Infection at Different CD4 Cell Counts*, JAIDS, Vol. 45, no. 5, pp. 600 – 601

Nunnally J. C. 1978, *Psychometric Theory*, 2nd ed., McGraw-Hill, New York

O'Keefe E. A., Wood R. 1996, *The impact of human immunodeficiency virus (HIV) infection on quality of life in a multiracial South African population*, Quality of Life Research, No. 5, pp. 275-280.

O'Leary J. F., Ganz P., Wu A. W., Coscarelli A, Petersen L. 1998, *Toward a better understanding of HealthRelated Quality of Life: A Comparison of the Meical Outcomes Study HIV Health Survey (MOS-HIV) and the HIV Ovrview of Problems-Evaluation System (HOPES)*, Journal of Acquired Immune Deficiency Syndrome and Human Retrovirology, Vol. 17, No, 5, pp. 433 - 441

Osahon P. T., Erah P. O. 2007, *Quality of life of HIV positive patients being managed in HIV/AIDS treatment centre in Benin City, Nigeria*, Abstract from the Fourth IAS Conference on HIV Pathogenesis, Treatment and Prevention, Sydney

Paton N. I., Chapman C. A. T., Chan S., Tan K. M., Leo Y., Aboulhab J., Soh C. 2002, *Validation of the Medical Outcomes Study HIV Health Survey as a measure of quality of life in HIV-infected patients in Singapore*, International Journal of STD and AIDS, vol. 13, no. 7, pp. 456 – 461

Peltzer K., Phaswana-Mafuya N. 2008, *Health-related quality of life in a sample of HIV-infected South Africans*, African Journal of AIDS Research, Vol. 7, No. 2, pp. 209-218.

Punpanich W. 2005, *Development of a culturally appropriate quality of life measure for HIV-infected children in Thailand*, PhD Dissertation, University of California, Los Angeles, School of Public Health, July 2005

Rapkin B. D. 2001, *Who's Life Is It Anyway? The Measurement and Meaning of Health Related Quality of Life*, Retrieved on 11 Jan 2008 from <http://ssl.thebody.com>

Raspa R., Zalenski R. J. 2006, *Maslow's Hierarchy of Needs: A Framework for Achieving Human Potential in Hospice*, *Journal of Palliative Medicine*, 2006, Vol. 9, No. 5, pp. 1120 – 1127

Revicki D. A. 1999, *Quality of life outcomes of combination zalcitabine-zidovudine, saquinavir-zidovudine, and saquinavir-zalcitabine-zidovudine therapy for HIV-infected adults with CD4 cell counts between 50 and 350 per cubic millimeter*, *AIDS*, Vol. 13, No. 7, pp. 851 - 858

Revicki D. A., Sorensen S., Wu A. W. 1998, *Reliability and validity of physical health and mental health summary scores from the MOS HIV Health Survey*, *Medical Care*, Vol. 36, No. 2, pp. 126-137

Revicki D. A., Swartz C. 1997, *Quality of life outcomes of saquinavir, zalcitabine, and combination saquinavir- zalcitabine therapy for advanced HIV- infection*, *Abstracts of 4th Conference on Retroviruses and Opportunistic Infections*, 27:266.

Revicki D. A., Wu A. W., Brown R. 1995, *Change in clinical status, health status and health utility outcomes in HIV-infected patients*, *Medical Care*, vol. 33. No. 4, AS173-AS182

Savoie E. 2004, *European HIV Quality-of-life Revue*, Presented at the 3rd IAS Conference on HIV Pathogenesis and Treatment

Scottish Government Publications 2006, *Quality of life and well-being: Literature review and thinkpiece*,

Scott-Lennox J. A., Wu A. W., Boyer J. G., Ware J. E. 1999, *Reliability and Validity of French, German, Italian, Dutch, and UK English Translations of the Medical Outcomes Study HIV Health Survey*, *Medical Care*, Vol. 37, No. 9, pp. 908 – 925

Scott-Lennox J. A., Mills R. J., Burt M. S. 1998, *Impact of zidovudine plus lamivudine or zalcitabine on health-related quality of life*, *The Annals of Pharmacotherapy*, Vol. 32, No. 5, pp. 525 - 530

Shahriar J., Delate T., Hays R. D., Coons S. J. 2003, *Commentary on using the SF-36 or MOS-HIV in studies of persons with HIV disease*, *Health and Quality of Life Outcomes*, Vol. 1, pp. 25

Sherbourne C. D., Stewart A. L. 1991, *The MOS social support survey*, *Social Science and Medicine*, Vol. 32, No. 6, pp. 705-714

Shinault K., Carabin H., Sonleitner N. K., Keese M., *A review of the statistical aspects of quality of life measurement tools for HIV/AIDS*, Retrieved on 12 Mar 2008 from [casr.ou.edu/rec/presentations/12-2005 APHA Review.ppt](http://casr.ou.edu/rec/presentations/12-2005%20APHA%20Review.ppt)

Tsai Y. 2003, *Validation of a Chinese version of the Sign and Symptom Checklist for Persons with HIV disease*, *Journal of Pain and Symptom Management*, Vol. 25, No. 4(Apr 2003), pp. 363 – 368

Ventegodt S., Merrick J., Andersen N. J. 2003, *Quality of Life Theory I: An Integrative Theory of the Global Quality of Life Concept*, The Scientific World JOURNAL, Vol. 3, pp. 1030 – 1040

Vosvick M., Koopman C., Gore-Felton C., Thoresen C., Krumboltz J., Spiegel D. 2003, *Relationship of Functional Quality of Life to Strategies for Coping With the Stress of Living With HIV/AIDS*, Psychosomatics, No. 44, pp. 51 - 58

Ware J. E. 1993, *SF-36 Health Survey: Manual and Interpretation Guide*, Boston: The Health Institute, New England Medical Center.

WHOQOL-Measuring quality of life. WHO/MSA/MNH/PSF/97.4, 1997

Wilkie F. L., Goodkin K., Khamis I., Van Zuilen M, H., Lee D., Lecusay R., Concha M., Symes S., Suarez P., Eisdorfer C. 2003, *Cognitive functioning in younger and older HIV-1-infected adults*, Journal of acquired immune deficiency syndromes, Vol. 33, Sup. 2, pp. S93 – S105

Wouters E., Meulemans H., Van Rensburg H. C. J., Heunis J. C., Mortelmans D. 2007, *Short-term physical and emotional health outcomes of public sector ART in the Free State province of South Africa*, Quality of Life Research, Vol. 16, no. 9, pp. 1461 - 1471

Wu A. W. 1999, *MOS-HIV Health Survey Users Manual*, Retrieved on 13 April 2007 from <http://chipts.ucla.edu/assessment/pdf/assessments/MOS-HIV.pdf>

Wu A. W., Jacobson D., Grant D., Scott-Lennox J. 1997, *Quality of life scores predict clinical trial attrition and mortality*, Abstracts of 4th Conference on Retroviruses and Opportunistic Infections, 31:298

Wu A. W., Lichter S. L., Richardson W., et al. 1992, *Quality of life in patients receiving clarithromycin for mycobacterium avium complex infection and AIDS*. VIII International Conference on AIDS/III STD World Congress. Amsterdam, The Netherlands B178(#PoB3550)

Wu A. W., Rubin H. R., Bozzette S. A. et al., 1991, *A Longitudinal Study of Quality of Life in Asymptomatic HIV Infection*, Seventh International Conference on AIDS, Florence, [abstract MC3200]

Wu A. W., Huang I., Thijs H., Finnern H. W., Kraft M., Gathe J. C., Fairclough D. L. 2006, *Health-related quality of life and tolerability of patients treated in RESIST*, 8th International Congress on Drug Therapy in HIV Infection, Glasgow, [Poster P25]

Appendix A:

Antiretroviral agents:

GENERIC NAME	TRADE NAME	CLASS OF DRUG
zidovudine (AZT)	Retrovir®	NRTI ¹
didanosine (ddI)	Videx®	NRTI
lamivudine (3TC)	3TC®	NRTI
stavudine (d4T)	Zerit®	NRTI
abacavir	Ziagen®	NRTI
tenofovir (TDF)	Viread®	NRTI
tenofovir/emtricitabine (TDF/FTC)	Truvada®	NtRTI ²
nevirapine	Viramune®	NNRTI ³
efavirenz	Stocrin®	NNRTI
nelfinavir	Vira-cept®	PI ⁴
indinavir	Crixivan®	PI
ritonavir	Norvir®	PI
saquinavir (hard gel formulation)	Invi-rase®	PI
saquinavir (soft gel formulation)	Forto-vase®	PI
amprenavir	Preclir®	PI
Lopinavir/ritonavir	Kaletra®	PI
Atazanavir	Reyataz®	PI

NRTI¹ : Nucleoside reverse transcriptase inhibitor

NtRTI² : Nucleotide reverse transcriptase inhibitor

NNRTI³ : Non-nucleoside reverse transcriptase inhibitor

PI⁴ : Protease inhibitor

Appendix B:

Side-effects of classes of antiretroviral drugs:

<u>SIDE EFFECT / COMPLICATION</u>	<u>NRTI</u>	<u>NNRTI</u>	<u>PROTEASE INHIBITORS</u>
Myelosuppression	Yes	No	No
GI Intolerance	Yes	Yes	Yes
Pancreatitis	Yes	No	No
Peripheral Neuropathy	Yes	No	No
Allergic Reaction	Rare; potential for hypersensitivity reaction with abacavir	Yes	Rare
Lipoatrophy	Yes	Unknown*	Unknown*
Lactic acidosis	Yes	No	No
Lipodystrophy	Yes	Unknown*	Yes
Raised cholesterol & triglyceride	Unknown*	Yes: Efavirenz	Yes
Insulin resistance	No	No	Yes
Neuropsychiatric manifestations	No	Yes: Efavirenz	Yes

(Miller S. 2002 (chair))

Appendix C:

MOS-HIV 35-ITEM INSTRUMENT

INSTRUCTIONS TO PATIENT: Please answer the following questions by placing a “ v ” in the appropriate box.

1. In general, would you say your health is:

Excellent.....	1	<input type="checkbox"/>
Very good	2	<input type="checkbox"/>
Good	3	<input type="checkbox"/>
Fair	4	<input type="checkbox"/>
Poor	5	<input type="checkbox"/>

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

None	1	<input type="checkbox"/>
Very mild	2	<input type="checkbox"/>
Mild	3	<input type="checkbox"/>
Severe	4	<input type="checkbox"/>
Very Severe	5	<input type="checkbox"/>

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

Not at all	1	<input type="checkbox"/>
A little bit	2	<input type="checkbox"/>
Moderately	3	<input type="checkbox"/>
Quite a bit	4	<input type="checkbox"/>
Extremely	5	<input type="checkbox"/>

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 At All 3
a. The kinds or amounts of <u>vigorous activities</u> you can do, like lifting heavy objects, running or participating in strenuous sports.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. The kinds or amounts of moderate activities you can do, like moving a table, carrying groceries or bowling.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Walking uphill or climbing a flights of stairs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Bending, lifting or stooping.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Walking one hundred paces.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Eating, dressing, bathing, or using the toilet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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

Yes 1

No 2

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

Yes 1

No 2

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	<input type="checkbox"/>
Pretty good	2	<input type="checkbox"/>
Good and bad parts about equal	3	<input type="checkbox"/>
Pretty bad	4	<input type="checkbox"/>
Very bad; could hardly be worse	5	<input type="checkbox"/>

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

Much better	1	<input type="checkbox"/>
A little better	2	<input type="checkbox"/>
About the same	3	<input type="checkbox"/>
A little worse	4	<input type="checkbox"/>
Much worse	5	<input type="checkbox"/>

THANK YOU VERY MUCH

Appendix D:

Summary of MOS-HIV Survey Concepts:

Concepts	No of items	Meaning: low scores	Meaning: high scores
General health perceptions	5	Views personal health as poor	Views personal health as excellent
Physical functioning	6	Very limited in performing physical activities due to poor health including eating, dressing, bathing or using the toilet	Performs all types of physical activities due to poor health including vigorous or strenuous activities without limitations
Role functioning	2	As a result of physical health, experiences problems with work or daily activities	No problems with work or other daily activities as a result of health
Pain	2	Very severe and limiting pain	No pain or limitations due to pain
Social functioning	1	Social activities limited due to Health	No limitations on social activities as a result of health
Mental health	5	Feels nervous and depressed all of the time	Feels calm, peaceful and happy all of the time
Energy	4	Feels tired and worn out all of the time	Feels energetic and full of pep all the time
Health distress	4	Feels despair, discouraged and afraid due to health all of the time	Does not feel despair, discouraged and afraid due to health
Cognitive functioning	4	Has difficulty concentrating, reasoning and remembering all of the time	Has no problem concentrating, reasoning and remembering
Quality of life	1	Life has been very bad; could hardly be worse	Life has been very good; could hardly be better
Health transition	1	Physical health and emotional condition much worse than 4 weeks ago	Physical health and emotional condition much better than 4 weeks ago

Appendix E:

MOS-HIV Scoring information:

GENERAL HEALTH PERCEPTIONS: Five items: 1, 11 a-d

VERBATIM ITEMS

1. In general, would you say your health is:

11 a. I am somewhat ill.

11 b. I am as health as anybody I know.

11 c. My health is excellent.

11 d. I have been feeling bad lately.

Items 1, 11 b and 11 c need to be recoded.

<u>Response choice</u>	<u>Questionnaire Item Value</u>	<u>Final Value</u>
Excellent	1	5
Very good	2	4
Good	3	3
Fair	4	2
Poor	5	1

Items 11a and 11d

<u>Response choice</u>	<u>Questionnaire Item Value</u>	<u>Final Value</u>
Definitely true	1	1
Mostly true	2	2
Not sure	3	3
Mostly false	4	4
Definitely false	5	5

Scale Scoring: The score from item 1 is summed with the scores for items 11 a-d to form a 5-item General Health Perception scale. The range of scores for this scale before it is standardized is then 5-25.

PHYSICAL FUNCTIONING: Six items: 4 a-f

VERBATIM ITEMS

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities?

4a. The kinds or amounts of vigorous activities you can do, like lifting heavy objects, running or participating in strenuous sports

4b. The kinds or amounts of moderate activities you can do, like moving a table, carrying groceries or bowling.

4c. Walking uphill or climbing (a few flights of stairs).

4d. Bending, lifting or stooping.

4e. Walking one block.

4f. Eating, dressing, bathing or using the toilet.

ITEM SCORING

Items 4 a-f

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
Yes, limited a lot	1	1
Yes, limited a little	2	2
No	3	3

Items in the Physical Function scale are simply summed. The range of possible scores for the Physical Function scale before it is standardized is 6-18.

ROLE FUNCTIONING: Two items: 5, 6

VERBATIM ITEMS

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

to school?

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

ITEM SCORING

Items 5, 6

<u>Response choice</u>	Questionnaire	
	<u>Coded Value</u>	<u>Final Value</u>
Yes	1	1
No	2	2

Scores are now summed for the Role Function scale. The range is of scores for Role Function before it is standardized is 2-4.

SOCIAL FUNCTIONING: One item: 7

VERBATIM ITEM

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)?

ITEM SCORING

Item 7

<u>Response choice</u>	Questionnaire	
	<u>Coded Value</u>	<u>Final Value</u>
All of the time	1	1
Most of the time	2	2
A good bit of the time	3	3
Some of the time	4	4
A little of the time	5	5
None of the time	6	6

The Social Function item is scored as coded before it is standardized with a range from 1-6.

COGNITIVE FUNCTIONING: Four items: 10 a-d**VERBATIM ITEMS**

How much of the time during the past 4 weeks:

10 a. Did you have difficulty reasoning and solving problems, for example making plans, making decisions, learning new things?

10 b. Did you forget, for example, things that happened recently, where you put things, appointments?

10 c. Did you have trouble keeping your attention on any activity for long?

10 d. Did you have difficulty doing activities involving concentration and thinking?

ITEM SCORING

Items 10 a-d

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
All of the time	1	1
Most of the time	2	2
A good bit of the time	3	3
Some of the time	4	4
A little of the time	5	5
None of the time	6	6

Items in the Cognitive Function scale are scored 1-6. None of the items need to be recoded. When the values of the 4 scale items are summed, the range for the Cognitive Function scale before it is standardized is 4-24.

PAIN: Two items: 2, 3

VERBATIM ITEM

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

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

ITEM SCORING

Item 2 - This item must be recoded.

	Questionnaire	
<u>Response choice</u>	<u>Coded Value</u>	<u>Final Value</u>
None	1	6
Very mild	2	5
Mild	3	4
Moderate	4	3
Severe	5	2
Very Severe	6	1

ITEM SCORING

Item 3 - This item must be recoded.

	Questionnaire	
<u>Response choice</u>	<u>Coded Value</u>	<u>Final Value</u>
Not at all	1	5
A little bit	2	4
Moderately	3	3
Quite a bit	4	2
Extremely	5	1

Note that these items are recoded so that a higher score corresponds to less pain. The range of possible scores for this Pain item before it is standardized is 2-11.

MENTAL HEALTH: Five items: 8 a-e

VERBATIM ITEMS

How much of the time, during the past 4 weeks:

8 a. Have you been a very nervous person?

8 b. Have you felt calm and peaceful?

8 c. Have you felt downhearted and blue?

8 d. Have you been a happy person?

8 e. Have you felt so down in the dumps that nothing could cheer you up?

ITEM SCORING

Items 8 a, 8 c, 8 e

Questionnaire		
<u>Response choice</u>	<u>Coded Value</u>	<u>Final Value</u>
All of the time	1	1
Most of the time	2	2
A good bit of the time	3	3
Some of the time	4	4
A little of the time	5	5
None of the time	6	6

Items 8 b, 8 d - These items need to be recoded.

Questionnaire		
<u>Response choice</u>	<u>Coded Value</u>	<u>Final Value</u>
All of the time	1	6
Most of the time	2	5
A good bit of the	3	4
Some of the time	4	3
A little of the time	5	2
None of the time	6	1

Items in the Mental Health scale are scored 1-6. The range is 5-30 for the Mental Health scale before it is standardized.

ENERGY/FATIGUE: Four items: 9 a-d

VERBATIM ITEMS

How often during the last 4 weeks:

9 a. Did you feel full of pep?

9 b. Did you feel worn out?

9 c. Did you feel tired?

9 d. Did you have enough energy to do the things you want to do?

ITEM SCORING

Items 9 a and 9 d - These items need to be recoded.

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
All of the time	1	6
Most of the time	2	5
A good bit of the time	3	4
Some of the time	4	3
A little of the time	5	2
None of the time	6	1

Items 9 b and 9 c

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
All of the time	1	1
Most of the time	2	2
A good bit of the time	3	3
Some of the time	4	4
A little of the time	5	5
None of the time	6	6

Items in the Energy/Fatigue scale are scored 1-6. The range for the Energy/ Fatigue scale is 4-24 before standardization.

HEALTH DISTRESS: Four items: 9 e-h

VERBATIM ITEMS

How often during the last 4 weeks:

9 e. Did you feel weighed down by your health problems?

9 f. Were you discouraged by your health problems?

9 g. Did you feel despair over your health problems?

9 h. Were you afraid because of your health?

ITEM SCORING

Items 9 e – 9 h

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
All of the time	1	1
Most of the time	2	2
A good bit of the time	3	3
Some of the time	4	4
A little of the time	5	5
None of the time	6	6

Items in the Health Distress scale are scored 1-6. None the items in this scale are recoded.

The range for the Health Distress scale is 4-24 before standardization.

SCORING INFORMATION: Quality of Life: One item: 12

VERBATIM ITEM

12. How has the quality of your life been during the past 4 weeks? i.e., How have things been going for you?

ITEM SCORING

Item 12 - This items needs to be recoded.

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
Very well: could hardly be better	1	5
Pretty good	2	4
Good and bad parts about equal	3	3
Pretty bad	4	2
Very bad: could hardly be worse	5	1

The Quality of Life item is scored 1-5 before standardization.

HEALTH TRANSITION: One item: 13

VERBATIM ITEM

XIII. How would you rate your physical health and emotional condition now compared to 4 weeks ago?

ITEM SCORING

Item 13 - This item needs to be recoded.

<u>Response choice</u>	<u>Questionnaire Coded Value</u>	<u>Final Value</u>
Much better	1	5
A little better	2	4
About the same	3	3
A little worse	4	2
Much worse	5	1

The Health Transition item is scored 1-5 before standardization.

Appendix F: Approval of study by the Research Ethics Committee of the Health Sciences Faculty, University of Cape Town

UNIVERSITY OF CAPE TOWN



Health Sciences Faculty
Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
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18 December 2007

REC REF: 512/2007

Dr DR Malan
c/o Dr L Gwyther
Public Health & Family Medicine

Dear Dr Malan

PROJECT TITLE: A RETROSPECTIVE STUDY TO DETERMINE CHANGES IN QUALITY OF LIFE OVER THE FIRST 6 MONTHS PERIOD OF ANTI-RETROVIRAL THERAPY, AS MEASURED BY THE MOS-HIV QUESTIONNAIRE

Thank you for submitting your study to the Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above-mentioned study.

Please ensure that data confidentiality is maintained. Ideally data needs to be collected and analysed anonymously. We also suggest that you are certain that 30 participants will provide sufficient sample size to undertake valid scientific analyses.

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC. REF in all your correspondence.

lemjedi

Yours sincerely

Lesley Hendley

PROF M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

University of Cape Town