Health related quality of life (HRQoL) of people living with HIV: A comparison with biomedical markers of HIV

by

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Dissertation Submitted in Partial Fulfilment of the Masters of Clinical Pharmacology Degree

University of Zimbabwe

November 2013

Declaration

I, **Blessing Dzingirai**, certify that this dissertation is my original work and has been prepared in accordance with guidelines of the Master of Clinical Pharmacology Program, University of Zimbabwe. I further attest that this work has not been submitted, in part or in full, for any other degree at any university and/or any publication.

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I, having supervised and read this dissertation, I am satisfied that this is the original work of the author in whose name it is being presented. I confirm that the work has been completed satisfactorily for presentation in the examination.

Name of Academic Supervisor_____

Signature_____Date_____

Chairman of the Department of clinical Pharmacology, University of Zimbabwe

Signature_____Date_____

Dedication

This work isdedicated to my wife Lourene and our son Akudzwe Joash (AJ)

Acknowledgements

All the glory be unto God the provider of life and grace.

My special gratitude to my supervisors Dr S Khoza, Dr R van Hulst and Mr N Mafirakureva for your guidance on development of the research topic and methods, execution of the study, and thesis write up.

Mr S Gavi helped me with the statistical analysis. God Bless you.I would like to thank Dr O Moyo, the CEO of Chitungwiza General hospital for allowing me to collect the data for the study. I am deeply moved by the participants who volunteered to contribute to this body of knowledge.

This project was funded by the NECTAR Mentored Research Scholars Programme under the NIH grant.

Abbreviations and Acronyms

3TC - Lamivudine

ABC- Abacavir

AIDS- Acquired Immuno Deficiency Syndrome

ART - Antiretroviral therapy

ARV - Antiretroviral

AZT/ZDV - Zidovudine

CCR5- Chemokine Receptor Five

D4T - Stavudine

DALYS - Disability Adjusted Life Years

ddC- Zalcitabine

DISWO- Disclosure Worries

EFV - Efavirenz

EQ-5D - European Quality of Life Five Dimensions

FAHI - Functional Assessment of Human Immunodeficiency Virus

FINWO- Financial Worries

FTC- Emitricitabine

HAT-QoL- HIV/AIDS Targeted Quality of Life Instrument

HIV - Human Immunodeficiency Virus

HIVMA- HIV Mastery

HRQoL- Health Related Quality of Life

HRQoL-HIV -Health Related Quality of Life –Human Immunodeficiency Virus

ICC- Intraclass Correlation

LISAT- Life Satisfaction

LPV- Liponavir

MEDWO- Medication Worries

MOS-HIV -Medical Outcomes Study –Human Immunodeficiency Virus

MRCZ- Medical Research Council Of Zimbabwe

NIH - National Institute of Health

NNRTI - Non Nucleoside Inhibitors

NtRTI - Nucleotide Analogues

NVP - Nevirapine

OI- Opportunistic Infections

OVFXN- Overall Function

PI - Protease Inhibitors

PROTR- Provider Trust

PTID- Participant Identification

QALYs- Quality Adjusted Life Years

QoL- Quality of Life

RT - Reverse Transicriptase

RT- Ritonavir

SG- Standard Gamble

SXFXN - Sexual Function

TDF - TenofovirDisproxilFumarate

TTO- Time Trade Off

VAS- Visual Analogue Scale

WHO - World Health Organisation

WHO-ICF - World Health Organization Classification of Functioning , Disability and Health

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ABSTRACT

Background: Health related quality of life (HRQoL) in HIV patients has become an important indicator of impact of disease and treatment outcomes. Linking CD4 count to HRQoL measures is necessary to determine if HRQoL can be predicted from CD4 count.

Methods: A cross sectional study was carried out at Chitungwiza Opportunistic Infections Clinic among HIV patients on ART. The HAT-QoL and EQ-5D-3L were used to measure HRQoL. Internal consistency of HAT-QoL and EQ-5D-3L was evaluated. Univariate and multivariable linear regression was used to identify predictors of HRQoL in HIV/AIDS patients.

Results: A total of 257 participants (mean age 39.7±8.9, 72% female) out of 351(73.4% response rate) consented to take part in the study. The overall mean HAT-QoL score was 69.3±16.9. The mean EQ-5D-3L index and VAS scores were 68.7± 29.4 and 73.3 ±18.9 respectively. The overall Cronbach's alpha for HAT-QoL and EQ-5D-3L was 0.76 ($p<0.001$) and 0.68 ($p<0.001$). The Cronbach's alpha between EQ-VAS and EQ-5D index was 0.68 ($p=0.004$). Income was a significant predictor of HRQoL scores [(HAT-QoL: $\beta=0.37$, $p<.001$), (EQ-5D index: $\beta=0.18$, $p=0.05$), (EQ-VAS :$\beta=0.19$, $p=0.04$)] . CD4 count was not correlated with HRQoL scores. Unadjusted coefficients and p-values were: ($\beta=0.09$, $p=0.26$), ($\beta=0.05$, $p=0.59$) and ($\beta=0.16$, $p=0.06$) for HAT-QoL, EQ-5D index and EQ-VAS respectively. Adjusted coefficients and p-values were ($\beta=0.02$, $p=0.82$),($\beta= 0.07$, $p=0.48$) and ($\beta=0.12$, $p=0.19$) for HAT-QoL, EQ-5D index and EQ-VAS respectively.

Conclusion: There was no correlation between CD4 count and HRQoL scores. HAT-QoL and EQ-5D-3L have good psychometric properties and potential for use in clinical settings.

Incorporation of HRQoL in the management of HIV/AIDS patients is essential to provide clinicians with accurate estimates of the quality of life patients.

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Chapter 1: INTRODUCTION

1.1: Problem Statement

More than three decades after the first case, the human immunodeficiency virus (HIV) remains a major public health problem in Zimbabwe. International and national scale up efforts have seen many HIV infected people being put on antiretroviral therapy. Scientific advancement in antiretroviral treatments and care have resulted in people living with HIV surviving longer and the disease is now considered a chronic illness[1]. Health outcomes from antiretroviral treatment have been based on increased length of life from the treatment[2]. Clinically, the surrogate indicators such as CD4 count, viral load and clinical evaluations remain the major pointers of disease progression and treatment outcome[3]. These clinical markers have been shown to provide an incomplete picture of the impact of disease and its treatment on an individual's life[4]. Health related quality of life (HRQoL) measures in the context of HIV/AIDS find relevance to complete this picture.

HRQoL is broadly defined as the value assigned to the duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy[5]. HRQoL in HIV takes into account the impact of the infection and the antiretroviral treatment on an individual's physical, psychological and social wellbeing as reported by the patient. HRQoL-HIV measures are important as an indicator of the efficiency and responsiveness of the HIV treatment and care programmes. HRQoL values play a pivotal role in resource allocation decisions as they are incorporated in economic evaluations[6]. This is critical for resource limited settings like Zimbabwe.

Zimbabwe has an estimated 1.2 million adults living with HIV, with close to 80% of them on antiretroviral therapy[7]. Data on the quality of life of the years added by effective treatment

programmes is missing from the picture of the epidemic. HRQoL weights available for people living with HIV in Zimbabwe are from the study by Sebit etal. in 2000 that explored the effect of traditional medicine on HRQoL[8]. The management of HIV has since changed significantly, therefore there is need for a new study to provide a more representative picture of the HRQoL in patients on ART. HRQoL scores are based on patient preferences, which are sensitive to social, economic, and political environments. Another study by Jelsma et al. in 2003 looked at quality of life weights in the Zimbabwean context in healthy respondents[9]. The study reported that the respondents valued their health status consistently[9].

There is need to explore the strength of the association between HRQoL scores and clinical biomarkers to establish if they can be used as proxies of each other. Although it is logical to predict that viral load and CD4 count are directly linked to HRQoL, evidence supporting this link is limited[10]. Understanding the link will involve determining the biomarker that is the stronger predictor of HRQoL and which domains of HRQoL are more sensitive to changes in clinical progression of the disease. A few studies that have tried to link the two yielded conflicting results[3,10-12]. Variations in the strength of the associations were observed in different populations and among different domains of HRQoL[3,10,11].Due to the subjectivity of HRQoL scores, evidence of the link from other populations may not be applicable to Zimbabwean population.

1.2 Study Significance

The study yielded HRQoL scores which are important in assessing how HIV/AIDS and its treatment affect the lives of people. As people infected by HIV live longer, the interest is no longer

in the lengthy of life only, but the quality of the years lived. Monitoring HRQoL help determine whether the effect of side effects outweigh the clinical benefit of treatments[13]. Side effects may result in reduced or non-adherence to drug treatment[14] and deterioration of HRQoL[15]. Monitoring and optimising HRQoL in clinical settings may help improve adherence.

This study also gave utilities which are used in economic evaluations. Economic evaluations are critical in rational resource allocation especially in resource-limited settings. HRQoL scores also serve as an important indicator of evaluating the success of HIV treatment programmes. HRQoL is useful as communication tool from the patient to the healthcare provider.

Assessing the association between HRQoL scores and clinical biomarkers is important to answer the questions, 'what change in HRQoL is clinically significant and what improvement in clinical biomarkers will result in significant improvement of HRQoL scores?'[16]. This helps clinicians and researchers to predict changes in HRQoL based on changes in clinical biomarkers. Given the conflicting results on the strength of the association in literature, this study provided further evidence on the nature of the relationship in the Zimbabwean context.

1.3 Purpose Statement

The main purpose of this study was to establish the strength of the association between HRQoL scores from two instruments and clinical biomarkers of HIV. The study aimed to determine the correlation coefficients between HRQoL scores from both EQ-5D and HAT-QoL and CD4 counts. HRQoL scores were also compared with viral loads. The associations were compared to determine the better predictor of quality of life between CD4 count and viral load.

The study also explored the effect of confounding factors on HRQoL scores such as education level, income, duration on ART, treatment regimen and WHO clinical stage. The performance of the EQ-5D and HAT-QoL instruments in the population under study was assessed and compared.

CHAPTER 2: LITERATURE REVIEW

2.1 HIV/AIDS

Globally HIV/AIDS remains a major public health problem, with more than 34 million people living with HIV at the end of 2011[7]. Southern African region contributes 69% to the number of the people living with HIV worldwide[7]. The countries mostly affected in Southern Africa are Botswana, South Africa, Lesotho, Malawi, Namibia, Swaziland, Mozambique, Zambia and Zimbabwe[7]. The overall prevalence rates are on the decrease but remain very high within high risk groups such as women, sex workers and men who have sex with men[7]. The prevalence of HIV among sex workers in Zimbabwe is as high as 49%[7].

In the past decade, global efforts have resulted in several milestones in the fight against the pandemic in Africa. The most celebrated successes include an805% increase in the people receiving treatment, 33% reduction in new infections, 24% reduction in infections among children and 32% reduction in AIDS related deaths[17]. Increased funding towards the programmes to combat the disease is one of the reasons for these successes. Although domestic spending on AIDS has doubled in Africa from 2005 to 2011, most countries still depend on donor funding[18]. Encouraged by the success, policy makers and researchers in HIV/AIDS are beginning to visualize the end of HIV/AIDS.

2.1.1 Economic Burden

The economic burden of HIV/AIDS can be divided into direct medical costs and indirect costs[19]. The direct costs include the treatment costs, hospital personnel and all other costs that impact the health budget of a nation. It is estimated that more than half of the admissions in Southern Africa are due AIDS-related conditions[20]. A South African study reported that HIV positive patients stay

in hospital upto four times longer than other patients[21]. The total cost for care of an HIV infected patient is estimated atUSD1100 per year in low income countries[22]. In Zimbabwe, the total cost of health related services in HIV patients is estimated to be 3.5% of GDP, about .34 billion USD per year[22]. Based on the new WHO treatment guidelines, the global annual budget for HIV treatment is projected to be 22-25 billion USD by 2015[23].

Indirect costs refer to loss of productivity and household income. The pandemic affects mainly the age group 15-49 which is the most productive age group. Households experience an estimated 48-78% decline in income when one member of the family dies of HIV- related illness. The impact of HIV on productivity is due to morbidity and mortality related costs[24]. Morbidity related costs include loss of productivity due to absenteeism, reduced performance and medical care and insurance. Mortality related costs include retraining of new staff and payouts. Some costs difficult to estimate include loss of workforce morale, loss of experienced staff, and lack of cohesion. One of the most affected labour force is the agriculture sector, which is projected to lose 22.7% of its workforce by 2020 due to HIV/AIDS[25].

2.1.2 Treatment

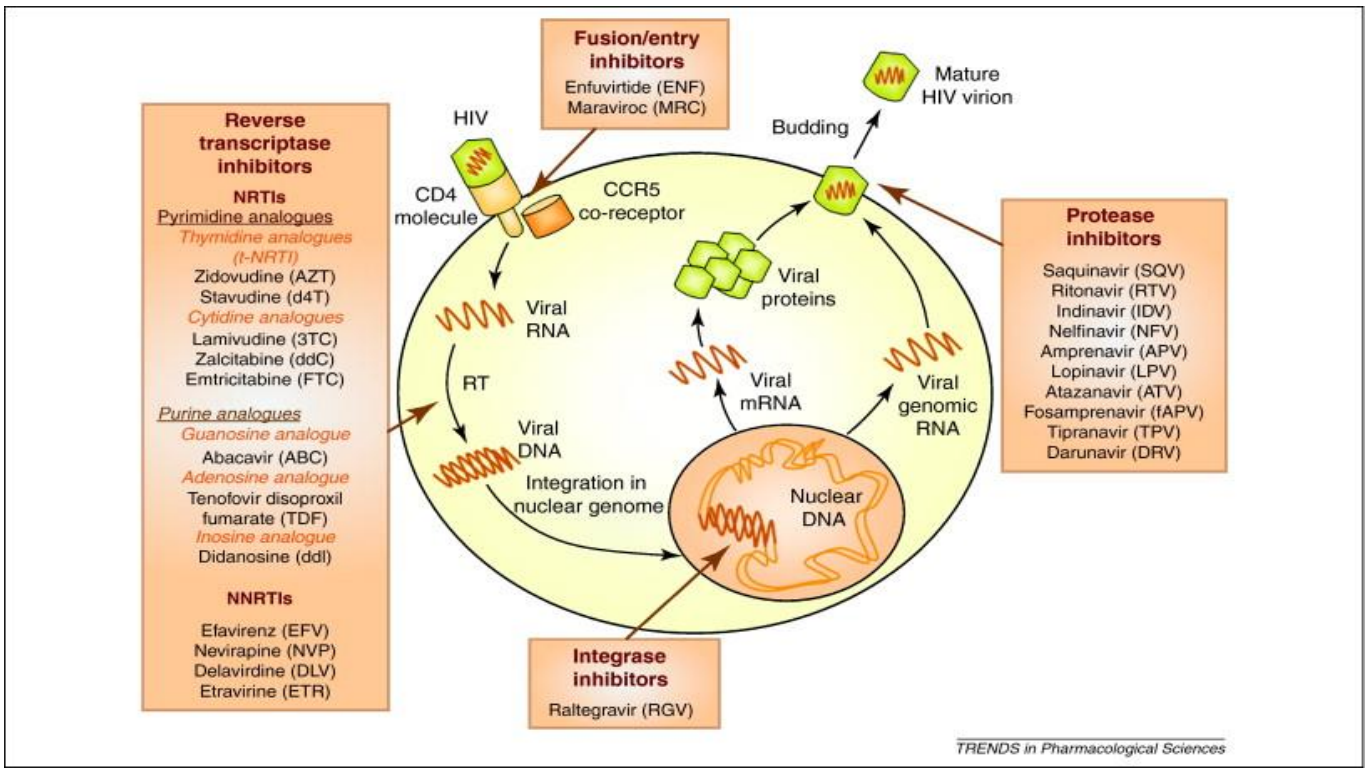
To date there is no cure for HIV/AIDS. Antiretroviral therapy has developed from zidovudine (AZT) monotherapy to 31 drugs approved by FDA that are combined in the management of people living with HIV[26,27]. Antiretroviral therapy suppresses replication of the virus and prolongs lives. The drugs are grouped into reverse transcriptase inhibitors, protease inhibitors, fusion/entry inhibitors, intergrase inhibitors and drug combination products. Maturation inhibitors are in development[26]. The points at which the drugs act are shown in Figure 2.1.

2.1.3 Clinical Pharmacology of Antiretroviral Drugs

Reverse transicriptase (RT) inhibitors consist of nucleoside and nucleotide analogues , (NtRTIs) and non nucleoside inhibitors (NNRTIs). NtRTIs include thymidine analogs stavudine(d4t) and zidovudine(AZT/ZDV), cytosine analogs lamivudine (3TC) and zalcitabine (ddC), guanosine analog abacavir (ABC), inosine analog didanosine (DDI) and adenosine analog tenovofir disproxil fumerate (TDF).NtRTIs undergo intracellular phosphorylation by cytoplasmic and mitochondrial kinases and competitively bind to active site of the RT, resulting in termination of viral DNA elongation. Side effects of NtRTIs include peripheral neuropathy, pancreatitis, lipoatrophy, myopathy, anemia and lactic acidosis. There is evidence for occurrence of resistance and cross resistance for all NtRTIs. NNRTIs bind non-competitively to RT and do not require cellular activation. Examples include efavirenz (EFV), delaviride and nevirapine(NVP). Side effects include rash and liver toxicity[28]. Single mutation is required for NNRTIs cross resistance[29].

Protease inhibitors (PIs) competitively inhibit the cleavage of gag-pol polyprotein , which is crucial for viral maturation[28]. PIs include fosamprenavir, atazavir, darunavir, indanavir, lopinavir, nelfinavir, ritonavir, saquinavir and tipranavir. Side effects include gastrointestinal disturbances, increased lipidsand insulin insensitivity[28]. Resistance to PIs require high build-up of multiple mutations[29].

Enfuvirtide is a synthetic 36 amino acid peptide that binds to gp41, inhibiting the binding of HIV to target cell. Administration of enfuvirtide is by subcutaneous injection[28]. Maraviroc is another fusion inhibitor that binds to chemokine receptor, CCR5 preventing viral entry into target cell.



Source: Trends of Pharmacological Sciences 2011[30]

Figure 2.1: HIV Life cycle and sites of action of drugs

2.1.4 Treatment Guidelines

Treatment guidelines are available in different geographical and economical regions. The guidelines help healthcare workers to make decisions on when to start antiretroviral therapy and algorithms on different combinations. Availability of resources determines the drug options included in guidelines for different settings. In resource limited settings, the WHO treatment guidelines are mostly adapted. The WHO issued new guidelines in July 2013[23,31]. The new guidelines recommend starting ART in adults at CD4 counts below 500 cells/mm^3 and children below 5 years regardless of CD4 count. The guidelines further recommend tenofovir (TDF), lamivudine or emtricitabine (FTC) and efavirenz (EFV) as first line agents and viral load testing as

the optimal way of monitoring first line therapy[31]. In Zimbabwe, recommendations from WHO guidelines are adapted and used to formulate national guidelines. The summarised guidelines are shown in Table 2.1.

Table 2.1: Treatment Regimens for Adults and Adolescents in Zimbabwe [32]

Level	Drugs	Alternative
1st Line	TDF 300mg od + 3TC 300mg od +NVP 200mg bd*	AZT 300mg bd + 3TC 300mg bd +NVP 200mg bd*
2nd Line	AZT 300mg bd** + 3TC 300mg bd*** + LPV/RTV 2 tabs bd	ABC 300mg bd / 600mg od + DI 400mg od**** + LPV/RTV 2tabs bd*****

*lead dose of 200 mg od to be given for first 2weeks

** If AZT was in first line give TDF 300mg

***may be replaced by FTC 200mg od

**** if weight greater than 60kg

***** may be replaced by ATV/RTV

2.2 Health Related Quality of Life.

WHO defines health as a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity[33]. Despite this concept being more than 50 years old, health is still being largely measured in terms of morbidity and mortality in resource limited settings. Advancement in medical options resulted in reduced mortality from many diseases and hence the logic of including health related quality of life outcomes in health assessments. HRQoL is defined by Patrick and Erickson "as the value assigned to the duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease,

injury, treatment or policy"[34]. HRQoL aspects include physical, social, emotional and cognitive functioning, patient perception of health and symptoms[35-37].

HRQoL measures have become important to researchers, healthcare professionals and healthcare policy makers[38]. HRQoL measures are important for the assessment of the impact of the chronic disease and its treatment on the patient. Healthcare practitioners are interested in HRQoL as treatment outcomes. HRQoL measures are also useful in cost effective analysis. Utility function in health is a product of health status and consumption of the good hence the use of HRQoL weights in calculation of cardinal utility scores[6]. Healthcare policy makers use HRQoL in allocation of resources.

2.2.1 Health related quality of life Models

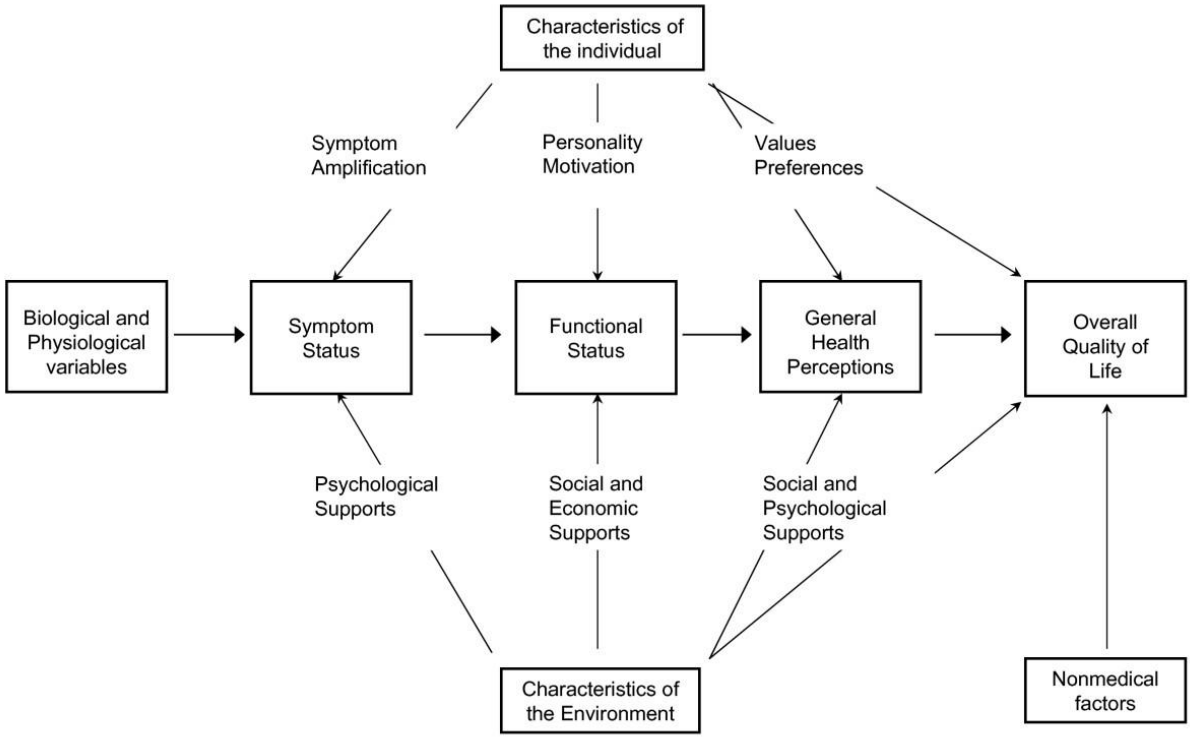
A model is a schematic representation of the theory to understand the concept of HRQoL[38]. The need for a model in understanding HRQoL is because of its multidimensional nature and application in different disease states and populations. Bakas et al. recently did a systemic review of models used in chronic diseases research for the past decade using the Bredow criteria. The three most frequently used models were the Wilson and Cleary, Ferrans et al. and the WHO [38].

2.2.2 Wilson and Cleary Model

Wilson and Cleary developed the model which combines the biological and the psychological aspects of health outcomes[39]. It consists of five main domains that influence the overall HRQoL. The five domains are biological and physiological function, symptom function, functional status, general health perceptions and overall HRQoL[39]. The other two factors, individual characteristics and environmental factors, are not well defined in the model but influence the overall HRQoL[39]. The model has been applied in cancer, Parkinson's disease, arthritis and HIV/AIDS[40]. Validation of

the model using structural equation modelling in people living with HIV showed that the data fitted adequately and the relationships between domains were all significant[40]

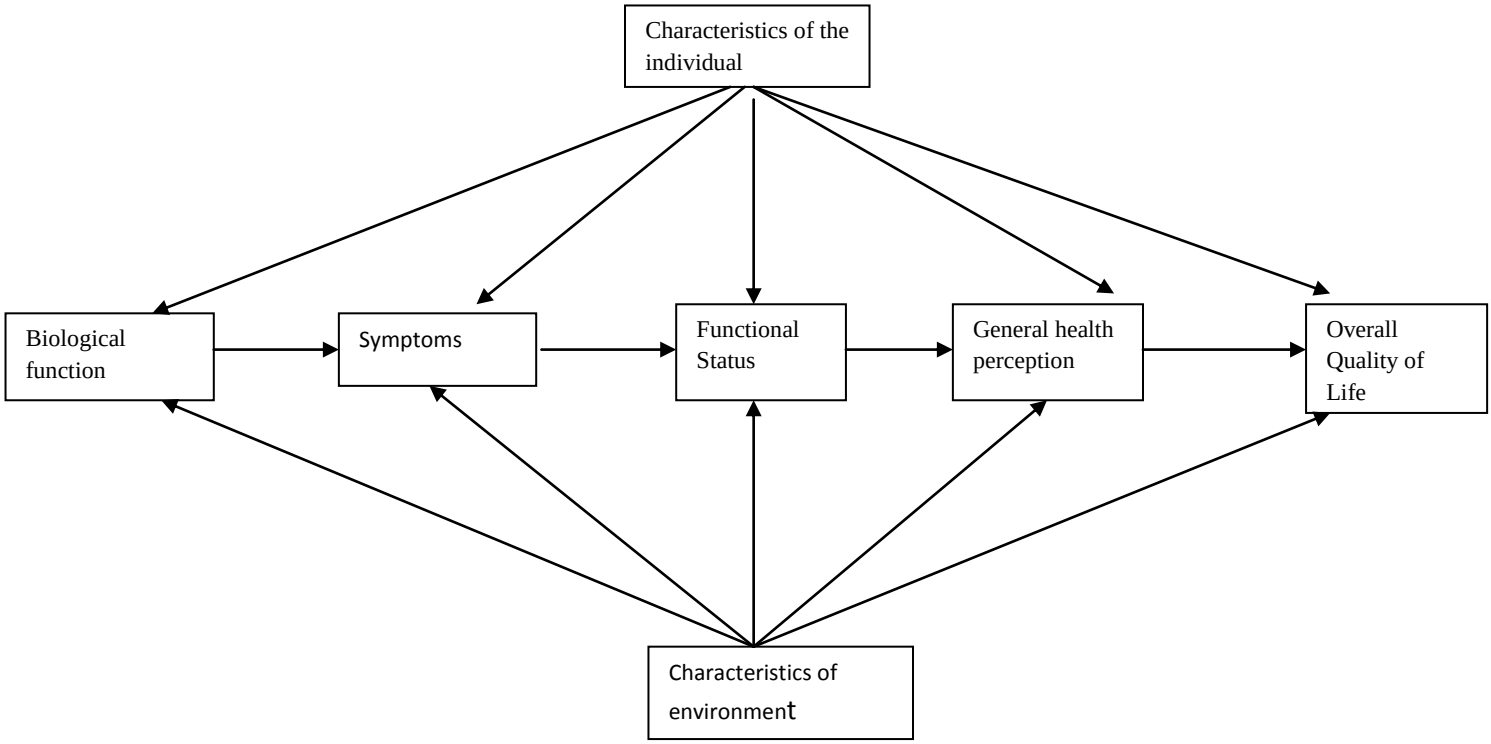
Figure 2.2 : The Wilson and Cleary Model 1995



2.2.3 Ferrans et al. Model (Revised WCM model 1995)

Ferrans et al. modified the Wilson and Cleary model. They retained the five main domains but further defined the environmental and individual domains. They also removed the confusing nonmedical factors and labels on the arrows[38].

Fig 2.3 : Ferrans etal. Model (Revised WCM 1995)

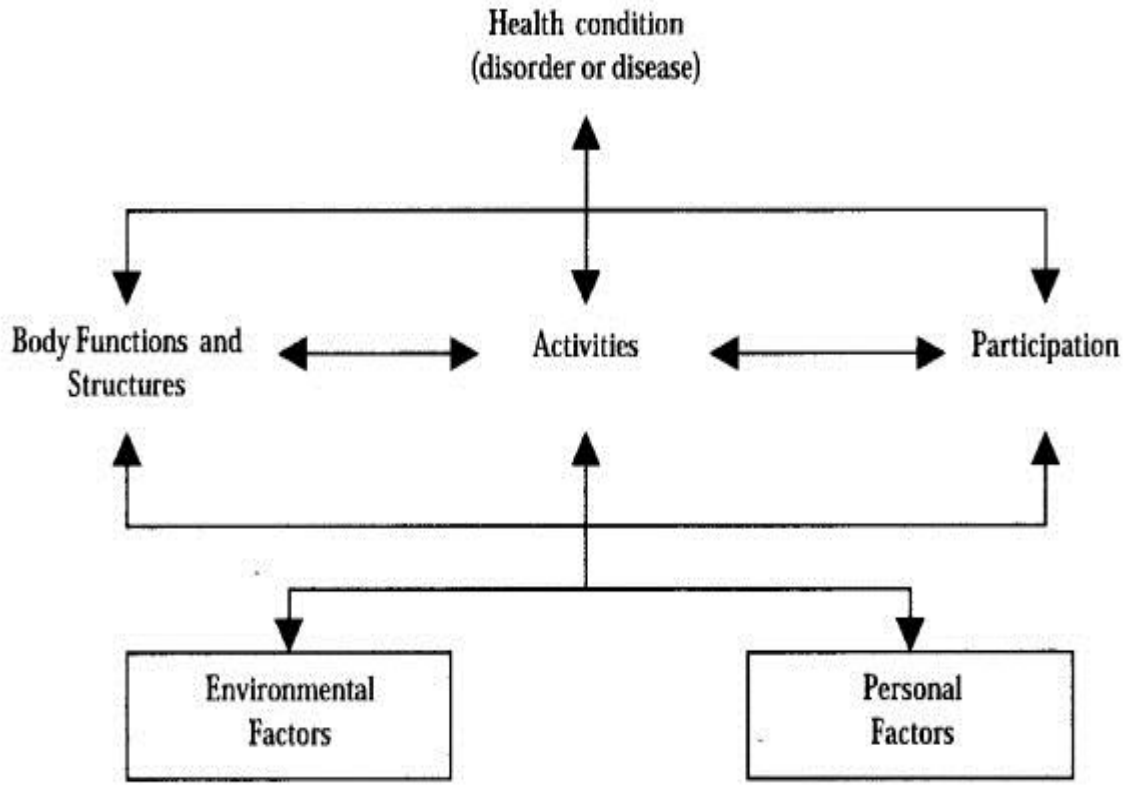


2.2.4 The WHO Classification of Functioning, Disability and Health (WHO-ICF)

The ICF is a classification of health and health related domains. The classification is done through the list of body function and structure, the list of activity and participation, the list of environmental factors. Although regarded as a model, the ICF also serves as standard tool for describing health status and disability. Body function refers to the physiological processes of individual and structure refers to body organs, together which directly influence the activities an individual can participate in. Participation entails to social interactions at personal and societal level. Interplay of these

domains determines the overall quality of life. The relationship between the domains is a source of hypotheses in HRQoL[38].

Fig 2.4 : WHO International Classification of Functioning,Disability and Health



Source: World Health Organization (WHO) (2001).

2.2.5 Health Related Quality of Life and HIV

HIV infection has been found to negatively affect the quality of life in different populations[12,35,41,42]. The diagnosis of HIV may result in psychological trauma, loss of productivity and limitations in social activity. Medical effects of HIV which include muscle wasting increased susceptibility to opportunistic infections, sexual dysfunction, chronic diarrhoea lymphadenopathy

and decrease in CD4 count decrease HRQoL.The advancement and improved accessibility of the treatment options for AIDS led to its transition into a chronic disease. This resulted in people with HIV living longer. Despite notable reductions in HIV-related morbidity and mortality, people living with HIV are still affected by side effects of the medications which affect their well-being[43]. Lipodystrophy syndrome consists of metabolic abnormalities that affect fat distribution resulting disfigured body shape. This may result in limitations in physical and social activities, reduced self-esteem and depression[44]. Patients with severe lipodystrophy are associated with impaired psychosocial functioning[45]. Diarrhoea (major side effect of protease inhibitors) may result in decreased functional ability, social functioning, mental health and general health perceptions[46]. HIV patients with peripheral neuropathy associated with lower scores in the physical and psychosocial domains[47].Studies that have assessed the impact of HAART on the quality of life have reported slight improvement, some marked improvement and some decrease in the quality of life[10,12,48].

2.2.6 Measurement of HRQoL in HIV

HRQoL measurement instruments can be classified as generic or disease specific[49]. Generic instruments find application in comparing HRQoL weights of different diseases and populations. Specific measuring tools are used in clinical settings and are very sensitive to treatment. HRQoL measurements are further classified into health status measures and preference based measures. Preference based measures are important in economic evaluations.

2.2.7 Assessment of HRQoL instruments

An ideal HRQoL instrument is one that

i. is reliable and valid,

ii. can be self administered ,

iii. is brief yet comprehensive,

iv. can evaluate relevant aspect of HIV,

v. is responsive to clinical changes ,

vi. is easy to understand for all literacy levels,

vii. is sensitive to a wide range of patient cultural and ethnic backgrounds,

viii. is available in appropriate translated versions,

ix. can have wide patient acceptance /adherence,

x. allows easy data collection, scoring and interpretation[50].

The commonly used tools do not fulfill all the requirements. Combination of the instruments will help overcome the weaknesses.

2.2.8 Reliability

Reliability refers to the consistency of an instrument over time, patients or observers. Establishing reliability of a health measure is a prerequisite for establishing its validity. Reliability is demonstrated by test-retest, internal consistency and interrater reliability[49]. Expression of reliability has changed from use of Pearson correlation coefficients to intraclass correlation (ICC), kappa coefficients and Cronbach's alpha coefficient. The alpha coefficient is an indicator on internal consistency[51].

2.2.9 Validity

Validity refers to the extent to which the different health status scores reflect the health status differences among the individuals. Validity is explored under content, criterion and construct validity[49]. Content validity refers to comprehensiveness of the questions selected in the instrument in covering the important aspects of the disease or health. Content validity is assessed by measuring sensibility using Feinstein checklist. Criterion validity seeks to establish if the scores from the instrument do agree to existing standard measurements. Criterion validity can be concurrent or predictive. Criterion validity is established under convergent, discriminant and known groups validity[51]. Construct validity assess how the instrument fits into a predefined conceptual framework.

2.3 Review of Instruments used in HIV

2.3.1 Disease-Specific

MOS-HIV (Medical Outcomes Study-HIV)

This instrument was developed from the MOS short form with 35 items and takes 5 minutes to complete[5,52]. It covers general health perceptions, physical functioning, role functioning, pain, social functioning, mental health, energy, health distress, cognitive functioning, QoL and health transition domains. The MOS-HIV is self-administered with subscales of 0-100, with 100 indicating perfect health status[5,52,53]. The Shona MOS-HIV was validated in the rural Zimbabwean HIV infected population[54]. The instrument exhibited good psychometric properties with a mean Chronbach's alpha coefficient of 0.7 across the domains. The MOS-HIV exhibit good construct validity and is sensitive to changes in QoL[54,55]. It has been widely used in research[52]. However, the MOS-HIV tool exhibit ceiling and floor effects and does not evaluate all the areas critical in HIV[54].

FAHI (Functional Assessment of HIV)

This instrument was developed from the Functional Assessment of Cancer Therapy FACT-G for cancer[52]. FAHI covers HRQoL in the physical wellbeing, function and global wellbeing, emotional well being, social well being and cognitive functioning domains. The assessment includes 42 lengthy and yields sub-scale scores and one overall score. The instrument has good internal consistency, construct validity and known groups validity[56]. FAHI has reported Cronbach's alpha of 0.72-0.94[57]. It contains aspects of the FACT-G for cancer and thus can be used for HRQoL comparison across diseases. However assessment takes long time to complete[56].

HAT-QoL (HIV/AIDS- Targeted Quality of Life Instrument)

This instrument covers nine domains of HRQoL in HIV/AIDS patients. It covers overall function, sexual function, disclosure worries, health worries, financial worries, HIV mastery, life satisfaction, medication concerns and provider trust[58]. The developers of this tool recommend combination with a HRQoL generic tool[52,58]. The tool was validated in the rural Zimbabwean population and showed robust psychometric properties [54,59]. The mean Cronbach's alpha for HIV infected adults in rural Zimbabwe was 0.78[54].The HAT-Qol tool exhibits low ceiling and floor effects, good internal consistency and construct validity[58]. The tool evaluates much of the aspects critical among HIV/AIDS patients. However the tool is lengthy and takes longer time to administer.

WHOQoL-HIV (World Health Organization Quality of Life –HIV)

WHOQoL-HIV is a 120 item-instrument covering physical, psychological, level of independence, social relationships, environment and spiritual/religion/personal domains[60]. The evaluation yields

scores for each domain and overall HRQoL score. This instrument exhibited good psychometric properties with alpha scores for all domains between 0.68 and 0.9 in different cultural settings and good discriminant validity[61]. The WHOQoL-HIV tool is lengthy and takes a lot of time to complete. However, there is revised version WHOQoL-HIV BREF whichhas 31 items[62].

2.3.2 Generic Instruments

MOS (Medical Outcomes Study-derived quality of life measures)

These assessments include SF-12, SF-20, SF-21, SF-36, SF-38 and SF-56, covering 2-11 health domains[52]. The number in the name of each tool indicates the number of items included that tool. Scores range from 0-100, with 100 indicating perfect health. MOS-SF-36 is the most commonly used in HIV/AIDS patients. The instrument shows high internal consistency, reliability and responsiveness[53,63]. It can be self-administered or by an interviewer. The instruments are not sensitive to age. Floor and ceiling effects reported with SF-36.

EQ-5D

The EQ-5D was developed by the EuroQol group[64]. The instrument has five items and a visual analogue scale (VAS). The items included are mobility, selfcare, usual activities, pain/discomfort and anxiety/depression. EQ-5D was designed to complement disease specific HRQoL tools[64,65]. The tool has demonstrated good psychometric properties in different populations including in Zimbabwe, with good construct validity. The kappa scores for the Zimbabwean population range from 0.695 to 0.893 among the items[66]. The Shona version reported even higher test-retest scores of 0.78-1.0[66].The EQ-5D is prone to ceiling effects and insensitive to clinical changes like CD4 counts and viral loads[53].

2.4 Studies on HRQoL in HIV

Very few studies have been done on the health related quality of life and HIV in Zimbabwe. Sebit et al. carried out a study in 1998 to investigate the impact of phytotherapy on the quality of life of HIV infected patients[8]. The study was a community based cohort design with a sample size of 105 HIV infected patients. The participants were followed up over a 2 year period and a generic tool, WHOQoL was used. Patients on phytotherapy yielded significantly lower QoL scores than those on conventional therapy[8]. In contrast, the study by Taylor et al. in 2001 concluded that traditional medicines lead to greater improvement in QoL in one month than conventional medication[67]. Talyor et al. used the Shona versions MOS-HIV and HAT-QoL in the rural population. Jelsma et al. did a study in 2000 to determine the HRQoL weights for healthy Zimbabwean urban population. The EQ-5D tool and the time trade off (TTO) method were used to determine health utilities. The major finding of the study by Jelsma et al. is that Zimbabweans can value their health in a consistent manner and determination of HRQoL weights is feasible and valid[9]. Only the study by Jelsma et al. yielded health preferences utilities that can be used to calculate QALYS[9,68].Most studies in Zimbabwe used the disease-specific tools in HIV patients. Disease specific instruments provide very important clinical data for monitoring treatment. However, the outcomes from specific instruments are of limited value in economic valuations[2].

Several other studies have been carried out in Southern Africa. Hughes et al. used EQ-5D tool in South Africa[69].The major finding of the study was that HRQoL was compromised in AIDS stage 3 and 4and mean VAS score of 60.4 compared to 80.1 of the general population[69]. Jelsma et al. explored the effect of antiretroviral treatment on HRQoL scores in the South African HIV patients[70]. The study reported mean VAS score improvement from 0.62 to 0.76 after 12 months of treatment[70]. Other studies on the South African population used similar methods and data collection

instruments but reported higher scores for patients on treatment. This maybe attributed to improvements on the antiretroviral therapy.

The study by Lara et al. explored the HRQoL weights among people living with HIV in Ugandan settings[71]. The study used the VAS, TTO and SG methods in assessing the patients' health preferences for predetermined AIDS stages. The conclusion from the study was that the VAS, TTO and SG had good psychometric properties and could be used in resource-limited settings. The VAS scores reported in the Ugandan patients ranged from 0.6 to 0.62[71].

Table 2.2 : Studies on generic HRQoL for HIV in Sub-Saharan Africa[2]

1st Author	Setting	HIV Population	HRQoL Measure	Conclusion
O'Keefe (1996)	SouthAfrica (Western Cape)	WHO stages 1-4 Outpatients	SF-36	HIV subjects scored significantly lower on all subscales to controls.The decline in function occurred early in disease by WHO stages 1 and 2.Insignificant differences in functioning between different CD4 strata[72].
Sebit (2000)	Zimbabwe (Harare)	Various stages excluding the most severely ill	WHOQoL	WHOQoL is a good measure of quality of life for patients with HIV infection. Phytotherapy has a role in improving Qol[8].
Kaaya (2002)	Tanzania(Dar es Salaam)	HIV positive women attending antenatal clinics	SF-36 and HS CL-25	Good correlation between SF-36 scores and HSCL-25. HSCL-25 is useful in screening depression[73].
Hughes (2004)	South Africa (Cape town)	WHO stage 3-4, or CD4 < 200, HAART	EQ-5D VAS	HRQoL is severely compromised in stage 3 and 4 including the four domains of mobility, usual activities, pain/discomfort and anxiety/depression.The domain self care is less affected. VAS score 0.60
Jelsm a(2005)	South Africa (Cape town)	WHO stage 3-4, or CD4 < 200, HAART	EQ-5D VAS	Even in resource poor settings HRQoL can be greatly improved by treatment and there seems to be a neglible impact from side effects of the drugs. Improvements were found for all the five domains of health. VAS score
Nuwagaba-Biribonwoha (2006)	Uganda (Kampala)	HIV-positive and negative women attending antenatal care	Dartmouth COOP	Dartmouth COOP was found to be acceptable and feasible and showed HIV adversely affects maternal QoL among pregnant women. HIV positive womenhad poorer scores on 6 of 9 domains
Louwagie (2007)	South Africa(Free State)	WHO stage 3-4, or CD4 < 200, HAART	EQ-5D VAS	EQ-5D was highly sensitive to HAART with improvements after initiation of treatment on all five dimensions. This supports its use in future evaluation of HIV/AIDS care. Results suggest that HAART is effectice in improving people's self reported HRQol
McInerney (2008)	South Africa (Kwazulu Natal)	>18yrs on ART	SF-36	Individuals who reported a greater length of time on medications, fewer comorbid health problems and greater social support had better physical functioning.

Very few studies have directly measured the association between biomedical indicators of HIV and HRQoL in the antiretroviral therapy era[3,10-12]. These studies have reported different results about the relationship. Venter et al carried out a study in South Africa to determine the relationship between CD4 count, nutritional status and HRQOL. CD4 counts were obtained from medical records and WHOQOL-HIV tool was used to measure HRQoL in 90 ART-naïve HIV infected adults. The study by Venter et al reported weak correlations between CD4 count and all the domains of HRQoL($r=0.27$, $p=0.01$)[11]. Igumbor et al.did a secondary analysis of 642 South African HIV patients with an aim to establish the relationship between CD4 count, viral load, and HRQoL. The CD4 counts used in the study were obtained from the medical records and the HRQoL were measured using WHOQOL-HIV. That study reported weak ($r= 0.19$-0.38, $p<0.001$) to no correlation between viral load, CD4 count and HRQoL scores[3].Gill et al.did a cross sectional study in USA to determine the relationship between CD4 count, viral load and HRQoL among 678 HIV infected adults. Participants in the Gill et al study had blood drawn for CD4 count and viral load. The HRQoL scores were measured using the HIV Patients Assessed Report of Status and Experience(HIV-PARSE). Gill et al. reported significant correlations between CD4 count, viral load and HRQoL scores across all health domains[10]. This can be explained by the subjectivity of HRQoL measures, different instruments and different socio-economic factors.

In summary very few studies have measured HRQoL in people living with HIV in Zimbabwe. In addition no study has measured preference based HRQoL in people living with HIV. There is therefore no literature upon which calculation of QALYs and DALYs can be based in the HIV-infected Zimbabwean population. Based on the literature reviewed, no study has directly measured the association between clinical biomarkers with HRQoL weights. The HRQoL measures are subjective and vary due to sociocultural and demographic differences. The HRQoL scores and the

correlations established among people living with HIV in other populations cannot be generalised to the Zimbabwean population.

2.4 Study Rationale

Current evidence linking clinical biomarkers and HRQoL measures among HIV infected people is inconclusive and only relevant to populations studied. Given the importance of HRQoL measures in HIV management, understanding the relationship is crucial for clinicians to be able to predict changes in quality of life based on clinical outcomes. Results from this study will provide evidence for the need to incorporate HRQoL measures in standard of care for people living with HIV. The subjectivity of HRQoL measures call for population specific evidence.

The reviewed literature has no evidence of preference based health utilities for the population under study. This study also serves a purpose to provide these preference based utilities, which can be used to calculate QALYS and DALYs. The QALYs and DALYs are useful in economic evaluations that affect people living with HIV. The results of this study will applied in implementing cost effective treatments and programmes.

2.5 Aims, Objectives, Hypotheses

Aim: To determine the relationship between HRQoL measures and HIV/AIDS biomarker (CD4 count) in patients on antiretroviral treatment.

Objectives

1. To determine the HRQoL scores for people living with HIV
2. To determine the association between the HRQoL scores and demographic characteristics(age, gender, income)of people living with HIV.
3. To determine the association between the HRQoL scores and clinical characteristics(CD4 count and type of ART regimen, time on ART) of people living with HIV
4. To determine internal consistency of HAT-QoL and EQ-5D instrument

Hypotheses

Objective 2

$H_{0(2a)}$: there is no association between HRQoL scores and age

$H_{0(2b)}$: there is no association between HRQoL scores and gender

$H_{0(2c)}$: there is no association between HRQoL scores and income.

Objective 3

$H_{\mathbf{0(3a)}}$**:**there is no association between HRQoL scores and CD4 count

$H_{0(3b)}$: there is no association between HRQoL scores and type of ART regimen.

$H_{0(3c)}$: there is no association between HRQoL scores and time on ART

Objective 4

$H_{o(4a)}$: the HAT-QoL instrument does not have acceptable Cronbach's alpha

$H_{0(4b)}$: the EQ-5D instrument does not have acceptable Cronbach's alpha

Chapter 3: METHODOLOGY

3.1 Study design

This was a cross sectional study in which demographics, CD4 count, and HRQoL scores are measured once and analysed.

3.2 Study population

Participants were drawn from a population of HIV infected adults, aged 18-60 years who are on antiretroviral therapy. To be included in the study participants were supposed to be attending Chitungwiza Central Hospital Opportunistic Infections (OI) clinic and willing to give informed consent.

3.3 Study setting

Recruitment and all study procedures were carried out at Chitungwiza OI clinic.

3.4 Sampling

The sample size was determined usingthe Pocock's formulafor sample size determination[74].Assuming HRQoL scores are normally distributed and given the summary of the measures are to be reported as mean,the formula used to calculate the sample size is

$$n = \frac{2[Z_{1-\propto/2} + Z_{1-\beta/2}]^2}{\Delta^2} \Delta = \frac{\mu_{hiv} - \mu_h}{\sigma}$$

Δ- standardised effect size

$Z_{1-\alpha/2}$ and $Z_{1-\beta}$ - values for normal distribution for 100(1-α/2) and 100(1-β) respectively

μ_{hiv}- mean HRQoL score in HIV- infected population

μ_{ht}- mean HRQoL score in health population

σ- standard deviation assumed to be the same in both populations.[75]

Using data from previous studies assuming σ=20, μ_{ht}-μ_{hiv} of 5 points or more practically relevant[9,68], with power of 80% and 5% significance level gives Δ of 0.25 and estimated sample size of 252.

3.5 Recruitment

Participants were recruited as they present at the OI clinic for care and treatment. Study staff gave an overview of the study to the patients in a group. Those willing to join the study and eligible underwent the informed consent process.

3.6 Procedures

3.6.1 Ethical Approval

Ethical approval for the study was obtained from the Joint Parirenyatwa Hospital and College of Health Sciences Ethical Committee (JREC), Medical Research Council of Zimbabwe (MRCZ), and Chitungwiza Central Hospital ethics committee.

3.6.2 Informed Consent

All participants provided written informed consent to participate in the study. The informed consent was administered either in English or Shona. The informed consent form contained information about the aims and objectives of the study. It also informed the participant of the procedures, risks and benefits of the study. The participant was given two copies of the informed consent to sign as study staff witnesses. The participant left one copy of the signed informed consent with study staff to be kept in the participant binder for verification. The other copy, the participant took home. No study procedure was commenced before signing of the informed consent.

3.6.3 Enrolment

After verification of signing of informed consent, the study staff assigned a unique participant ID (PTID) to the participant. The PTIDs were assigned chronologically from PTID list. The PTID list links the participant with his/her unique national ID number to avoid co-enrolment / double enrolment. Assignment of the PTID indicated enrolment into the study and all study documents for the participant were identified by the PTID.

3.6.4 Demographics

After enrolment, study staff administered the demographics (DF-1) form on the participant up to item 7. The demographics questionnaire covered gender, age, level of education, income and HIV–related aspects.

3.6.5 EQ-5D

After the demographics form, the participants were asked to complete the Shona EQ-5D-3L tool The EQ-5D-3L is a generic HRQoL instrument developed by the EuroQoL group. It consist of five dimensions , mobility (MO), self-care (SC), usual activities (UA), pain/discomfort (PD) and anxiety/depression(AD).The EQ-5DL also includes a visual analogue scale with endpoints from 0-100.The English version was validated in the Zimbabwean population. The completed tool will be filed in the participant binder.

3.6.6 HAT-QoL

After completing the EQ-5D, study interviewers administered the Shona HAT-QoL questionnaire. The HAT-QoL assesses overall function, health worries, financial worries, illness mastery, life satisfaction, medication worries, provider trust and sexual function. The assessment yields one score on a scale 0-100, with 0 being the worst scores possible and 100 being the best score possible. The completed HAT-QoL instrument was filed in the participant binder.

3.6.7 Reimbursement

After completion of the HRQoL assessments participant was reimbursed.

3.6.8 CD4 count and Viral load

The study staff reviewed participant records linked by OI number assigned by the clinic. Review of the records gave CD4 count and viral load from samples taken within 3 months from the date of study enrolment. The records review also gave information on date of testing positive and date ART was started. Participants whose CD4 count and viral load values were too old or missing in records were booked for bleeding.CD4 count and viral load results were entered in the study file for the participant.

3.7 Outcomes

For each participant in the study the following outcomes were obtained

i. Demographic data
ii. EQ-5D index scores
iii. EQ-VAS scores
iv. HAT-QoL scores
v. CD4 count

3.8 Data Analysis

Data was analysed using Statistics Package for SocialSciences17.0. Descriptive statistics were used to describe demographics and HIV related characteristics.

Objective 1

The HRQoL scores were reported as mean scores ± standard deviation from the HAT-QoL and the EQ-5D index and EQ-VAS.

Objective 2 and 3

Univariate regression analysis was done between CD4 count and the HAT-Qol, EQ-5D index and EQ-VAS scores. Multivariable linear regression was used to determine the association between predictor variables (age, gender, income, CD4 count, duration on ART and type of ART regimen)and HAT-QoL scores, EQ-5D index and EQ-VAS scores[76]. $H_{0(2a)}$-$H_{0(3d)}$ were rejected if $p<0.05$. The strength of association was determined by the numerical value of standardized β-coefficients of the regression model.

Objective 4

Dimension-specific psychometric evaluations were completed including corrected item total correlations and reliability coefficients. The general rule of thumb for accepting Cronbach's alpha was; $\alpha> 0.9$ (excellent internal consistency), $0.7<\alpha< 0.9$ (good internal consistency), $0.6<\alpha<0.7$ (acceptable internal consistency) , $0.5<\alpha<0.6$ (poor internal consistency) and $\alpha<0.5$ (unacceptable).The $H_{0(4a)}$ and $H_{0(4b)}$ was rejected if computed Cronbach's $\alpha>0.6$

Chapter 4: RESULTS

A total of 257 out of 351 potential participants consented to participate in the study, response rate of 73.4%.A total of 184 participants had their CD4 count figures obtained during the duration of the study. For 99 participants CD4 count values were obtained in the medical records and for 158 participants the values were either missing or too old (longer than 3months) to be included in the analysis. For 85 participants blood samples were drawn for CD4 count and viral load. Out of the 158 who had values missing, 73participants failed to come for the bleeding visit. Viral load results were not available at the time of analysis and were excluded from the evaluation.

4.1 Demographic and Clinical Characteristics

The demographic and clinical characteristics of the participants of the study are summarised in Table 4.1 and Table 4.2 respectively. The majority of the participants were female (72%), with a mean age of 39.7±8.9. More than half of the participants (54.1%) were married and had finished secondary school (65.4%). A greater proportion of the participants were unemployed (87.9%) with a median income of USD100.

The highest percentage of the participants were in stage III (42.8%), followed by stage II (34.3%) and least stage I(22.9%). The mean CD4 count was 423.6 (SD=288), IQR of 367. Close to half of the participants were taking stavudine based ART (49.1%), with 38.9% taking tenofovir –based regimen and 21% on zidovudine based regimen. The mean time on ART was 37.2 mo (SD=30.

Table 4.0 Demographic Characteristics of the study sample (N=257)

Characteristic	n	%
Age ±SD	39.7± 8.9	
Gender		
Female	185	72
Male	72	28
Marital Status		
Married	139	54.1
Single	23	8.9
Widowed	63	24.5
Level of Education		
Primary	81	31.5
Secondary	168	65.4
College or University	7	2.7
Employment		
Yes	31	12.1
No	226	87.9
Mean Income(USD) ± SD	146.5± 155.8	
House		
Rented	133	51.8
Owned	124	48.2

Table 4.1: Clinical Characteristics of participants

Characteristic	n	%
WHO Staging(N=187)		
I	43	22.9
II	64	34.3
III	80	42.8
Mean CD4 count(N=184)	423±288	
25Q	204.3	
50Q	343	
75Q	571.3	
Time on ART/mo±SD	37.2±30.3	
Drug regimen		
D4t-based[a]	86	49.1
AZT-based[b]	21	12
TDF-based[c]	68	38.9

a- d4T/3TC/NEV or d4T/3TC/EFV

b-AZT/3TC/NVP

c-TDF/3TC/NVP or TDF/3TC/EFV

4.2 HRQoL Scores: Objective 1

The mean HRQoL scores for ShonaHAT-QoL and EQ-5D-3L are shown in Table 4.3 and Table 4.4 respectively. The mean scores for most of the domains on the HAT-QoL are above 70. Lower scores were reported for sexual function (46.9) and financial worries (40.6) domains.

Very few of the participants reported 'some problems' (15.2%) on the mobility domain of the EQ-5D. In the usual activities domain 16% of the participants reported 'some problems' and 4.2% reported 'severe problems'. The most affected domain was the pain/discomfort with 54.9% reporting 'some problems' and 8.9% reporting 'severe problems' and the least proportion of participants who reported 'no problems'. The mean EQ-5D index and EQ-VAS were 68.7(SD=29.4) and 73.3(SD=18.9) respectively.

Table 4.2: HRQoL Scores –HAT-QoL (N=257)

Domain	Mean Score	SD
Overall Function (OVFXN)	77.0	24.7
Life satisfaction (LISAT)	74.4	28.8
Health worries (HEAWO)	79.4	25.2
Financial worries (FINWO)	40.6	32.9
Medication Worries(MEDWO)	86.5	20.5
HIV mastery (HIVMA)	75.5	35.3
Disclosure Worries (DISWO)	64.4	30.1
Provider Trust (PROTR)	68.5	32.5
Sexual Function(SXFXN)	46.9	40.0

Table 4.3: HRQoL Scores –EQ-5D-3L (N=257)

Domain	No problems (1)	Some Problems (2)	Severe Problems(3)
Mobility	218(84.8%)	39(15.2%)	0(0%)
Self care	247(96.1%)	9(3.5%)	1(0.4%)
Usual Activities	205(79.8%)	41(16%)	11(4.2%)
Pain /Discomfort	93(36.2%)	141(54.9%)	23(8.9%)
Anxiety/Depression	115(44.7%)	106(41.2%)	36(14%)

Mean VAS Score: 73.3± 18.9

Mean EQ-5D index: 68.7 ± 29.4

4.3 Determinants of HRQoL :Objective 2 and 3

The standardised β coefficients and p-values for the univariate and multivariable regression of the predictor variables and the HRQoL scores are shown in tables 4.5, 4.6, 4.7 and 4.8. Statistically significant association was obtained between income and HAT-QoL overall score, EQ-5D index and EQ-VAS. Significant association between ART regimen and EQ-VAS (β= -0.19; p=0.04). CD4 count, time on ART,gender and age had no significant associations with HRQoL scores. Based on the univariate and multivariable linear regression results the hypotheses$H_{0(2a)}$- $H_{0(2c)\ and}$ $H_{0(3a)-(3b)}$ were not rejected.$H_{0(2d)}$ and $H_{0(3c)}$hypotheses were rejected.

Table 4.4: Univariate regression analysis

HRQoL Score	βstandardised Coefficient	p- value
HAT-QoL	0.09	0.26
EQ-index	0.05	0.59
EQ-VAS	0.16	0.06

Table 4.5 :Determinants of HRQoL in HIV patients using HAT-QoL: Multivariable linear regression.

R^2 = 0.22 (p<0.001)*

Variable	β standardised Coefficient	p-value
Age	0.16	0.051
Gender	-0.07	0.43
Income	0.37	p<0.01*
CD4count	0.02	0.82
Time on ART	0.13	0.16
ART regimen	-0.08	0.38

* **Statistically significant**

Table 4.6: Determinants of HRQoL in HIV patients using EQ-VAS: Multivariable linear regression

R^2 = 0.108 (p=0.038)*

Variable	β standardised Coefficient	p-value
Age	0.06	0.49
Gender	-0.01	0.89
Income	0.19	0.04*
CD4count	0.12	0.19
Time on ART	0.16	0.09
ART regimen	-0.19	0.04*

* Statistically significant

Table 4.7: Determinants of HRQoL in HIV patients using EQ-5D index: Multivariable linear regression

R^2 = 0.085 (p =0.098)

Variable	β standardised Coefficient	p-value
Age	0.02	0.86
Gender	-0.03	0.77
Income	0.18	0.05
CD4count	0.07	0.48
Time on ART	-0.02	0.87
ART regimen	-0.2	0.03

*Statistically significant

4.4 Reliability of HAT-QoL and EQ-5D-3L: Objective 4

The Cronbach's alpha for HAT-QoL of 0.761(p<0.001) was acceptable according to the general rule of thumb set in the methodology section and statistically significant. All the domains had robust Cronbach's alpha except the provider trust domain which if deleted the overall Cronbach's alpha will rise to 0.815 and a low item correlation of 0.296.

The Cronbach's alpha for the EQ-5D-3L tool of 0.684 (p<0,001) was within the acceptable range. All the items of the tool are robust as indicated by alpha scores which are less than the overall if the items were to be deleted. The selfcare domain had the lowest total item correlation of 0.303. The decision to reject $H_{0(4a)}$ and $H_{0(4b)}$ was taken.

Table 4.8: Internal Consistency HAT-QoL

Overall Cronbach's alpha : 0.761 ($p<0.001$)

Domain	Cronbach's alpha if item is deleted	Corrected Total item correlation
Overall function	0.680	0.608
Life Satisfaction	0.685	0.601
Health Worries	0.659	0.776
Financial Worries	0.708	0.488
Medication worries	0.693	0.580
HIV mastery	0.704	0.612
Disclosure worries	0.740	0.360
Provider trust	0.815	0.296
Sexual function	0.736	0.371

Table 4.9: Internal Consistency EQ-5D-3L

Cronbach's alpha : 0.684 ($p<0.001$)

Domain/item	Cronbanch's alpha if item deleted	Corrected Total Item correlation
Mobility/1	0.563	0.517
Selfcare/2	0.645	0.303
Usual Activities	0.548	0.484
Pain/Discomfort	0.514	0.534
Anxiety/Depression	0.666	0.320

EQ-5D vs EQ-VAS: Cronbach's alpha: 0.676 ($p=0.004$), Intra class correlation 0.624, CI (0.519-0.706) , $p<0.001$.

Chapter 5: DISCUSSION AND CONCLUSIONS

The main purpose of this study was to establish the relationship between CD4 count and HRQoL scores in patients on antiretroviral therapy. Coupled to the main purpose of the study were the other objectives to determine the HRQoL scores for HIV infected people and determine the effect of demographic and clinical factors on HRQoL. The study also aimed at evaluating the psychometric properties of the Shona versions of the HAT-QoL and EQ-5D-3L.

The majority of the participants were women(72%) with an overall mean age of 39.7± 8.9. The prevalence of HIV is higher in women(18%) than men (12%) and in the general population the proportion of women is greater than men. Women have greater risk of being infected by HIV because of biological factors and cultural norms that give them less power to negotiate for safer sex[77]. The mean age was within the age group (15-49) mostly infected by HIV in the population under study[78]. Despite high levels of education, most participants were not formally employed. The mean monthly income was below the poverty datum line of USD 545[79]. This means that people living with HIV struggle to obtain basic needs of life. The higher levels of education helped the participants to comprehend the tools and value their health.

The mean CD4 count was 423cells/mm^3(SD=288), with most of the participants in WHO stage III and on stavudine based ART regimen. The lower acceptable CD4 count limit for patients on antiretroviral therapy at Chitungwiza Hospital laboratory is 410cells/mm^3. Based on the mean CD4 count the participants were responding well to ART.The stavudine based regimens have been associated with peripheral neuropathy and fat redistribution abnormalities. This led to switch in policy from stavudine to tenovofir (TDF) based regimens. Despite the toxicities some patients are still progressing well on stavudine based regimens as indicated by immunological indicators. The other reason for maintaining patients on stavudine based regimens is lack of resources. The TDF-

based regimens are more expensive. The CD4 count cut-off point for starting ART used to be at 200cells/mm^3. This meant that people would significantly deteriorate before they are enrolled on the national ART programme. This explains why most of the participants were WHO stage III.

The participants reported high scores on the HAT-QoL instrument over all the domains except the financial worries and sexual function domains. The domain scores in this study were higher than those in another study in rural respondents in 2000[67].During the period between the two studies new, more potent and safer antiretroviral drugs have been introduced. This may be the explanation for the differences in the HRQoL scores. The health delivery system was adversely affected by brain drain and lack of government funding from 2000 to 2009. This was characterised by lack of drugs and health personnel resulting in compromised health related quality of life in people living with HIV. The political and macroeconomic reforms in 2010 led to improved healthcare delivery which in turn translates into improved health related quality of life. The mean EQ-5D index and EQ-VAS scores were 68.7 ± 29.4and 73.3± 18.9 respectively. The mean VAS score was slightly lower than mean VAS reported in healthy population of 79.8[9].These scores are comparable to the scores(EQ-5D index 69.0 and EQ-5D 76.0) obtained in HIV infected population on ART in South Africa[36].

Income was positively associated with overall HAT-QoL score, EQ-5D index and EQ-VAS. However, the coefficients were very small signifying weak correlations. The positive correlation between income and HRQoL scores is in agreement with studies in other settings[80]. High income means ability to access better healthcare. Although CD4 count test, viral load test and antiretroviral drugs are provided for free by the government, people living with HIV still require money for liver

function tests, hospital charges and non-ARV medicines. Having low income will impact negatively on the access to these services and HRQoL. Low income affects negatively access to food, shelter and sanitation. Lack of basic needs of life may adversely affect health related quality of life.

There was no significant correlation between CD4 count and all the HRQoL domains for both instruments. This was in agreement with many other studies that found weak to no associations[3]. Theoretically an improvement in CD4 count should translate into an improvement of HRQoL. This relationship was not observed because of the subjectivity of HRQoL measures and CD4 count variations. The failure for CD4 count to predict HRQoL measures means monitoring CD4 count only as an indicator of disease progression may not be enough. The incorporation of HRQoL in management of HIV is critical. However the relationship between change in CD4 and change HRQoL scores over time may bring valuable insights. Monitoring HRQoL changes over the natural progression of HIV is critical. Studies that explored the relationship over at least 1 year of follow up found significant association between surrogate markers of HIV and HRQoL outcomes[10,81].

The overall Cronbach's alpha (0.761) for the HAT-QoL was robust and acceptable. The study by Taylor et al reported Cronbach's alpha for HAT-QoL of 0.781among rural HIV infected individuals in Zimbabwe[54].

This study has potential limitations that are important to consider for future research. All participants were drawn from one hospital which draws its patients from high density to peri-urban settlements. This hadan influence level of income, which would be very different from a sample drawn from low density areas. This may limit application of the results of the study in high income earners. The sample had an overrepresentation of women which can be overcome by recruiting from male-friendly sites. Viral load testing is the gold standard for monitoring disease progression

of HIV. Exclusion of the viral load figures from the analysis of the association of biomarkers with HRQoL scores is another possible limitation to this study. Following up the participants over at least a year was going to give valuable data of the relationship of the change in clinical biomarkers and changes in HRQoL scores.

Based on the findings of this study incorporation of HRQoL measures in the clinical management of HIV infected individuals is critical. The Shona EQ-5D-3L and HAT-QoL tools have psychometric properties and have potential to be used in clinical settings. For future research in the area recruitment from multiple sites, inclusion of viral load and following up participants over a long period of time is recommended.

Conclusion

In conclusion this study reported high HRQoL scores for people living with HIV. The significant predictor of HRQoL was income. CD4 count was not to HRQoL scores. The shona EQ-5D-3L and HAT-QoL instruments have good psychometric properties and can be used in measuring HRQoL in HIV infected individuals.

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APPENDIX 1

DEMOGRAPHICS (DF)

Participant ID : _ _ _- _ _ _ _ _**Date:** _ _ -_ _ - _ _

For now I will ask you about general information about yourself.

1. Sex Male ☐ Female ☐

2. What is your date of birth …… if unknown record Age in years ……

3. What is your marital Status? Married ☐ Single ☐ Widowed ☐ Divorced ☐

4. What is your highest level of education?

- ☐ Did not go to school
- ☐ Primary school
- ☐ Secondary school
- ☐ College or university

5. Are you employed? Yes ☐ No ☐

6. How much do you earn per month (USD)……

7. Do you own a house or you rent where you stay. Owned ☐ Rented ☐

HIV Related

CD4 count …….. Date taken……..

Viral load …… Date taken……..

W.H.O stage …… Time since testing positive……

Time on ART…….. ART regimen…….

APPENDIX 2
INFORMED CONSENT FORM-ENGLISH VERSION

PROJECT TITLE*:*Health related quality of life (HRQoL) of people living with HIV: A comparison with biomedical markers of HIV

Short title: HRQoL –HIV study

Principal Investigator: Blessing Dzingirai [B.Pharm .Hons]
Phone number: 0772 128 026

What you should know about this research study:

- We give you this consent so that you may read about the purpose, risks, and benefits of this research study.
- The main goal of research studies is to gain knowledge about health related quality of life of people living with HIV that may help future patients.
- You have the right to refuse to take part, or agree to take part now and change your mind later.
- Whatever you decide, it will not affect your regular care at the clinic.
- Please review this consent form carefully. Ask any questions before you make a decision.
- Your participation is voluntary.

PURPOSE

The purpose of the study is to compare the health related quality of life scores to CD4 counts and viral load. You are being selected together with other 350 participants to take part in this study.

PROCEDURES AND DURATION
If you decide to participate, you will undergo the following procedures that will take 30minutes.

Informed Consent
The study staff will give you this document to read and will ask questions to make sure you have understood it. You will be asked to sign two copies of the document. One copy you will be given to take home.

Demographics
You will be asked questions about your age, education, work and on other information about yourself on the demographics (DF-1) form of the study.

Health Related Quality of Life
Using the document HAT-QOL-1 of the study the study staff will ask questions about how things are going in different areas of your life as affected by the HIV infection and the medications. Some of the questions on the questionnaire will ask you about your job and your doctor or any health professional you normally visit for help.

CD4 count and Viral load
Your health records stored at the OI clinic will be reviewed by the study staff. Your CD4 and viral load and the figures will be documented in your study document. If no values taken within 3months are obtained in your records a total of 10mls of blood will be taken for viral load and CD4 testing. All of the blood will be used for laboratory tests. No blood will be stored for any other tests now or in the future.

RISKS AND DISCOMFORTS
There are no foreseeable risks you may encounter in this study. You may encounter mild pain during blood draw. The inconvenience you will encounter is the extra time you spend at the clinic.

BENEFITS AND/OR COMPENSATION
Although we cannot and do not guarantee or promise that you will receive any monetary benefits from this study, your participation will contribute to the management of people living with HIV. Your reimbursed USD $3 for the extra time you spend at the clinic.

CONFIDENTIALITY
If you indicate your willingness to participate in this study by signing this document, your study documents may be reviewed by MRCZ and JREC. Information that is obtained in connection with this study that can be identified with you will remain confidential and will be disclosed only with your permission.Any written information published about the study results will not include your name or make you known personally.

VOLUNTARY PARTICIPATION
Participation in this study is voluntary. If you decide not to participate in this study, your decision will not affect your future relations with University of Zimbabwe, its personnel, and Chitungwiza

OI clinic**.** If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without penalty.

OFFER TO ANSWER QUESTIONS

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

AUTHORIZATION

You are making a decision whether or not to participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

I do accept/decline to participate in the HIV-QoL study.

Name of Research Participant (please print)	Date
Signature of Participant or legally authorized representative	Time
Signature of Witness (*Optional*)	Signature of Staff Obtaining Consent

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research participant or research-related injuries; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Medical Research Council of Zimbabwe on telephone 791792 or 791193.

APPENDIX 3
GWARO RETENDERANO RINE RUZIVO RWAKAKWANA-SHONA VERSION

MUSORO WECHIRONGWA: Mhando yeuhupenyu maerarano nezvehutano muvanhu vanorarama nehutachiwana hweHIV, tichienzanisa nehuwandu hwemaCD4 nehwehutachiona muropa.

Musoro wechirongwa muchidimbu : Chirongwa che HRQoL-HIV

Mukuru wechirongwa : Blessing Dzingirai vane Bachelor of Pharmacy , vari kudzidza kuti vawane dzidzi yepamusoro yemasters pachikoro cheUniversity of Zimbabwe.

Nhamba Dzefoni dzavo: 0772 128 026

Zvakakosha kuti muzive zvinotevera

- Takupai gwaro iri kuti muzive zvinangwa zvechirongwa, njodzi dzamungasangana nadzo muchirongwa nerubatsiro mungawana nekuva muchirongwa.
- Chinangwa chikuru chechirongwa ndechekuwana ruzivo pamusoro pemhandu yehupenyu maererano nezvehutano hwe vanhu vanorarama nehutachiona hweHIV , zvichabatsira vamwe varwere mune ramangwana.
- Makasununguka kuramba kupinda muchirongwa, kana kubvuma izvezvi , kana kuzochinja pfungwa dzenyu munguva inotevera.
- Sarudzo yenyu haina zvainochinja pamabatirwo amunoitwa pano pachipatara.
- Torai nguva yenyu kuverenga gwaro rino , makasununguka kubvunza mibvunzo pamusinganzwisisi.
- Kupinda kwenyu muchirongwa isarudzo yenyu makasununguka.

CHINANGWA CHECHIRONGWA

Chinangwa chechirongwa ndechekuenzanisa mhando yehupenyu hwevanhu vanorarama nehutachiona hweHIV nema CD4 count nemaviral load. Muri kukumbirwa kupinda muchirongwa pamwe chete nevamwe 350.

ZVICHAITIKA MASARUDZA KUPINDA MUCHIRONGWA

Kana masarudza kupinda muchirongwa muchakumbirwa kuita zvinotevera zvichatora nguva yenyu ingaita maminitsi anoita makumi matatu(30).

Kusaina gwaro retenderano

Muchapiwa gwaro rino kuti muverenge murinzwisise. Vashandi vechirongwa vachakupai makopi egwaro rino ari maviri kuri musaine. Rimwe muchakumbirwa kuti musiye , rimwe motakura.

Demographics

Muchabvunzwa mibvunzo inechekuita nekuzvarwa kwenyu, kudzidza, kushanda , nezvimwe zvinechekuita nehupenyu hwenyu zviri pagwaro rechirongwa rinonzi demographics (DF).

Mhando yehupenyu maererano nehutano

Vashandi vechirongwa vachakubvunzai mibvunzo inoenderanda nehupenyu hwenyu sekupingaidzwa kwahungaitwa nehutachiona hweHIV nemishonga yamunotora. Vachakubvunzai vachishandisa gwaro rechirongwa rinonzi HAT-QOL. Imwe yemubvunzo ichakubvunzai nezvebasa renyu , nezvachiremba wamunogara muchiona mazuva ose.

CD4 neviral load

Magwaro enyu ezvehutano achaongororwa nevashandi echirongwa. MaCD4 count ne maviral load enyu achorekodwa mumapepa enyu echirongwa kuti agoshandiswa patsvagiridzo yechirongwa. Imi hapana zvamunokumbirwa kuita paongororo iyi. Kana maCD4 nemaviral load akashaikwa mumagwaro enyu ehutano muchakumbirwa kupa ropa rinoita 10mls rekuita viral load neCD4. Ropa rese richatorwa richashandiswa kulab kuita maCD4 neviral load .Hapana rimwe reropa renyu richachengetwa kuita dzimwe ongororo iyezvino kana munguva inotevera.

NJODZI MUNGASANGANA NADZO MUCHIRONGWA

Hapana njodzi dzatinotairisira mukasangana nadzo nekuda kwekuva kwenyu muchirongwa.Munogona kunzwa kurwadziwa kushoma nekuda kwekutorwa ropa.Munogona kuzopedza nguva yakareba muri pachipatara kudarika nguva dzemazuva ese.

MUBAIRO WECHIRONGWA

Hapana mubairo watinokuvimbisai wekupinda muchirongwa.Kupinda muchirongwa kuchabatsira chaizvo pakupamhidza ruzivo rwekurapa vane hutachiona hweHIV.Muchapiwa USD $3 yekuripa nguva yenyu yamuchapedza muri pachipatara.

KUCHENGETEDZWA KWEHUMBOWO HWEHUTANO HWENYU MUCHIRONGWA

Kana muchinge mabvuma kupinda muchirongwa humbowo hwehutano hwenyu hunogona kuzivakanwa chete nevashandi vachirongwa, vatariri vechirongwa vanoti, veMRCZ neve JREC. Humbowo hune zita renyu huchachengetedzwa pakabata uye hauna achahuudzwa pasina bvumo yenyu. Pachashambadzwa maresults echirongwa achenge asina zita renyu.

SARUDZO YEKUPINDA MUCHIRONGWA

Sarudzo yekupinda muchirongwa ndeyenyu musina kusundwa. Mukasarudza kusapinda muchirongwa hazvikanganisi hukama hwenyu neUniversity of Zimbabwe , vashandi vayo kana

kuchinja mabitirwo enyu pachipatara. Kana masarudza kupinda muchirongwa munogona kuzobuda pamadira pasina kupihwa mhosva.

MIBVUNZO

Kana mune mibvunzo bvunzai vashandi vechirongwa musati masaina gwaro rino.

TENDERANO

Mava kuita sarudzo yekupinda muchirongwa che HRQoL-HIV. Kana muchinge maverenga mukanzwisisa gwaro rino , mibvunzo yenyu ikapindurwa muchibvuma kupinda muchirongwa sainai pazasi apa.

…… ……..

Zita remunhu ari kuda kupinda muchirongwa Zuva

nyora mavara makuru

……... ……..

Sainecha yemunhu arikuda kupinda muchirongwa Nguva

……..... ……..

Sainecha nemunhu apa huchapupu Sainecha yemushandi Wechirongwa

MUCHAPIHWA IMWE KOPI YEGWARO RINO MUENDE NARO KUMBA

Kana mune imwe mibvunzo inechekuita nechirongwa, gwaro rino isiri mibvunzo yadavidzwa nevashandi vechirongwa, inosanganisira mibvunzo pachirongwa chino, kodzero dzenyu, kana kuti mafunga hamuna kubatwa zvakanaka muchirongwa chino fonerai veMRCZ panhamba dzefoni 791792 or 791193.

APPENDIX 4

MIBVUNZO YE

HAT-QOL*

Utachiona hunokonzero mukondombera/Mukondombera -- Mibvunzo iri maererano noutano nemararamiro © 1999, William C. Holmes, M.D., M.S.C.E
Adapted by Tonya N. Taylor, PhD

---------- **KUMURWERE**----------

Mibvunzo iri mupepa rino yakananganana nokutsvaka ruzivo maererano nezvakasiyana-siyana zvirikuitika muupenyu hwenyu. Musati matanga kupindura mibvunzo iyi pane mibvunzo miviri yamunotarisirwa kuva noruzivo rwakadzama pamusoro payo:

1. **Muchawana mibvunzo iri maererano nebasa renyu kana mamwewo mabasa amunoita zuva nezuva.**

Kana muine basa ramunoita, munotarisirwa kupindura mibvunzo iyi makanangana nebasa ramunoshanda iri.Asi kana musingashandi edzai kupindura mibvunzo iyi makanangana nemamwewo mabasa amunogara muchiita mazuva mazhinji.Mabasa acho munogona kusanganisira basa raunoita pamusha nezvimwe zvakasiyana-siyana zvakaita sekuenda kuchikoro kana kuti riya basa rekuzvipira kushandira mapoka akasiyana-siyana anoyamura vanhu.

2. **Muchawana mimwe mibvunzo ichibvunza nezvachiremba kana murapi wenyu.**

Kana muchigara muchiona mukoti, murapi kana mumwewo munhu anoona nezveutano asiri chiremba pindurai mibvunzo iri mugwaro rino makanangana nemunhu uyu.

---

1. Mibvunzo inotevera iri maererano nezvamainzwa kana zvamaiita muvhiki ina dzapfuura.

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handir
vi. Muvhiki ina dzapfuura ndaigutsikana nokusimba komuviri wangu ……					
vii. Muvhiki ina dzapfuura muviri wangu waisada kuti ndiite mabasa angu epamusha emazuva ose……					
viii. Muvhiki ina dzapfuura marwadzo akaderedza kukwanisa kwangu kuita basa kana zvinoda simba ……..					
ix. Muvhiki ina dzapfuura ndaishushikana nokutadza kushanda basa rangu/kana mamwewo mabasa andioita zuva nezuva					
x. Muvhiki ina dzapfuura ndakanzwa kuti kuva noutachiona hunokonzera mukondombera kwaindikanganisa uwandu hwebasa randinogona kushanda kubasa/randinoita mazuva ose……					
xi. Muvhiki ina dzapfuura ndakanga ndakaneta zvakanyanyisa zvokusagona kutandara nevamwe ……					

2. Mibvunzo inotevera iri maererano nokugutsikana kwenyu noupenyu muvhiki ina dzapfuura:

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handir
a. Muvhiki ina dzapfuura ndanga ndiri kufara nehupenyu hwangu ……..……					
b. Muvhiki ina dzapfuura ndainzwa kuti ndinogona kuita zvandinoda neupenyu hwangu ……					
c. Muvhiki ina dzapfuura ndakagutsikana zvekunzwa kuda kutandara nevamwe ……..……..					
d. Muvhiki ina dzapfuura ndanga ndichigutsikana nemamiriro eutano hwangu ……					

3. Mibvunzo inotevera iri maererano nokushushikana kwenyu nezvoutano hwenyu muvhiki ina dzapfuura:

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handi
a. Muvhiki ina dzapfuura handina kukwanisa kurarama hupenyu hwandaida nokuti ndaishushikana nehutano hwangu ……..……					
b. Muvhiki ina dzapfuura ndanga ndichishushikana nenyaya yekuti ndine utachiona honokonzera makondombera					
c. Muvhiki ina dzapfuura ndange ndichishushikana nekuti ndingangobate chirwere ……					
d. Muvhiki ina dzapfuura ndange ndichishushikana nenyaya yekufunga kuti ndingangofe …….					

4. Mibvunzo inotevera iri maererano nokushushikana kwenyu maererano nezvemari muvhiki ina dzapfuura:

	Nguva dzose	Nguva Zhinji	Dzimwe nguva	Rushoma rwenguva	Handi
a. Muvhiki ina dzapfuura ndaishungurudzwa nokurarama nemari shoma ……..……					
b. Muvhiki ina dzapfuura ndaishungurudzwa nokuti ndobhadhara zvikwereti zvangu sei ……					
c. Muvhiki ina dzapfuura ndange ndisina mari yakakwana yokuzviriritira nenzira yandinofunga kuti ndiyo yakakodzera …….					

5. Mibvunzo inotevera iri maererano nezvamakafunga pamusoro pemishonga ya makashandisa iri yokurapa utachiona hunokonzera mukondombera muvhiki ina dzapfuura:

<u>Makamboshandisa mishonga iri yokurapa utachiona hunokonzera mukondombera here muvhiki ina dzapfuura?</u>

KWETE -> -> -> ->Pindura mibvunzo iri muchikamu 6

HONGU -> -> -> ->Enderera mberi nokupindura mubvunzo 5a

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handin
a. Muvhiki ina dzapfuura kutora mushonga wanga uri mutoro					
b. Muvhiki ina dzapfuura kushandisa mushonga wangu kwakaita kuti ndiomerwe nekugara zvakanaka semazuva ose …….					
c. Muvhiki ina dzapfuura kutora kwandanga ndichiita mushonga kwakakonzera kuti ndive nemamwe marwadzo andanga ndisina ……..……					
d. Muvhiki ina dzapfuura ndaishushikana nezvingangoitika kumuviri wangu nokuda kokushandisa mishonga ……..					
e. Muvhiki ina dzapfuura ndainge ndisina chokwadi nekuti ndiri kushandisirei mishonga iyi ……..……					

6. Mibvunzo inotevera iri maererano nezvamaifunga pamusoro pokuva noutachiwona hwemukondombera muvhiki ina dzapfuura:

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handin
a. Muvhiki ina dzapfuura ndaidemba mararamire angu akaita kuti ndive neutachiona hunokonzera mukondombera ……..……..					
b. Muvhiki ina dzapfuura ndakange ndakatsamwa maererano nezvandakaita kutindibate utachiona hunokonzero mukondombera……					
c. Muvhiki ina dzapfuura ndakange ndakatsamwa maererano nezvandingadene ndakaita kuti ndisabate utachiona hunokonzera mukondombera ……					

7. Mibvunzo inotevera iri pamusoro pekushushikana kwako nokuzivisa vamwe pamusoro pourwere hwako:

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handir
5. Muvhiki ina dzapfuura ndanga ndisingataure zvakawanda-wanda kuvanhu pamusoro pezvangu ……..					
b. Muvhiki ina dzapfuura ndaitya kuudza vamwe vanhu kuti ndine utachiona honokonzera mukondombera …….					
d. Muvhiki ina dzapfuura ndaishushikana pamusoro pokuti hama dzangu vangangoziva kuti ndine utachiona hunokonzera mukondombera ……..					
e. Muvhiki ina dzapfuura ndanga ndiri kutyira kuti vanhu vapabasa pangu/vandinoita navo twakasiyana-siyana mazuva ese vachaziva kuti ndine utachiona honokonzera Mukondombera ……..					
f. Muvhiki ina dzapfuura ndaitya kuti basa rangu richapera kana vanhu vachinge vaziva kuti ndine utachiona Honokonzera mukondombera ……					

8. Mibvunzo inotevera iri maererano nezvamakafunga pamusoro pachiremba/murapi wenyu muvhiki ina dzapfuura:

	Nguva dzose	Nguva Zhinji	Dzimwe dzenguva	Rushoma rwenguva	Handir
a. Muvhiki ina dzapfuura ndainzwa kuti ndaikwanisa kuona chiremba/murapi wangu chero nguva yandaifanira ……					
b. Muvhiki ina dzapfuura ndakafunga kuti chiremba/murapi wangu anoda kunzwawo pfungwa dzangu pakuedza kundibatsira ……..					
c. Muvhiki ina dzapfuura ndanga ndichinzwa kuti chiremba /murapi kana murapi wangu anondichengetedza ……..					

Tinokutendai nokupindura mibvunzo iyi kwamaita.

Kana mune mibvunzo sunungukai kutaura ne munhu akupai mibvunzo iyi, kana kuti nomunhu anokubatsirai nezveutano.

Tinokutendai zvikuru!