Therapeutic and Virological Outcomes in Adults Living with HIV/AIDS at 6 and 12 Months after Initiation of First-Line Highly Active Antiretroviral Therapy in an Urban Population in Namibia.

By

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Therapeutic and Virological Outcomes in Adults Living with HIV/AIDS at Six and 12 Months after Initiation of First-Line Highly Active Antiretroviral Therapy in an Urban Health Centre in Namibia.

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Declaration

I declare that *Therapeutic and Virological Outcomes in Adults Living with HIV/AIDS at Six and 12 Months after Initiation of First-Line Highly Active Antiretroviral Therapy in an Urban Health Centre in Namibia* is my own work. It has not been submitted for any degree or examination at any other university. All sources used or quoted have been acknowledged and fully referenced.

Vivianne Inganai Gorova May 2010

Signed ……

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ABBREVIATIONS

AIDS	Acquired immune deficiency syndrome
AMIS	Antiretroviral Management Information System
ANC	Antenatal Clinic
ART	Antiretroviral therapy
ARV	Antiretroviral
CD4	Cluster differentiation 4
CI	Confidence interval
EPP	Estimation and Projections Package
HAART	Highly Active Antiretroviral Therapy
HIV	Human immunodeficiency virus
IQR	Inter-quartile range
MOHSS	Ministry of Health and Social Services
MPR	Medication possession ratio
NNRTI	Non-nucleoside reverse transcriptase inhibitor
RNA	Ribonucleic acid
WHO	World Health Organisation

DEFINITION OF TERMS

Adherence: Refers to compliance or obedience to a medication regimen exactly as prescribed by a health care provider (PAGAA, 2008).

Eligibility: Qualification for inclusion into study or initiation of ARV therapy

First-line therapy: One of four recommended combinations of non-nucleoside reverse transcriptase inhibitor based drug regimens used at the initiation of treatment of a drug naive HIV positive patient (MOHSS, 2007).

Self-reported dose adherence: This is a measurement of therapy dose compliance based on a patient recalling medicine taken in the last 3 days (Steel *et al*, 2007).

Start weight/CD4: This is the number of measured kilograms (weight) or count of cells/mm^3 (CD4) at the initiation of ARV therapy.

Tuberculosis: This is the medically reported presence of mycobacterium tuberculosis infection in the patient.

New Opportunistic Infection (OI): This is the medically reported presence of any previously unreported opportunistic infection in the patient.

Treatment supporter: This is the existence of a registered individual other than medical personnel who help a patient on ARV therapy.

WHO stage: These are any one of the four stages of HIV progression to AIDS published by the World Health Organisation.

ABSTRACT

Introduction: Antiretroviral regimens have side effects that can threaten adherence by patients resulting in evolution of viral resistance due to suboptimal drug levels. Studies have shown that drug adherence of at least 80% can result in viral load suppression. There is no literature on the association between the level of adherence to antiretroviral therapy and the degree of virological suppression in Namibia. The aim of the present study was to determine the therapeutic and virological outcomes in HIV/AIDS patients at 6 and 12 months after initiation of highly-active antiretroviral therapy (HAART) in an urban population in Namibia.

Materials and Methods: An observational cross-sectional retrospective review of patient care booklets for patients initiated on HAART at Katutura Health Centre, Namibia during the period January 1st - December 31st 2007. Viral load results were placed into categories of <40 copies/ml, 40-399 copies/ml, 400- 999 copies/ml and >1000 copies/ml at the 6 and 12 months time points. Self-reported dose adherence at 6 and 12 months was classified as good (≥ %95), fair (85 -94%) and poor (<85%). The prevalence of ≥95% adherence at 6 and 12 months of initiating therapy was calculated. Patients with viral load ≥400 copies/ml were then compared with those with a viral load <400 copies/ml at 6 and 12 months.

Results: Of 687 patients initiated on first-line HAART during the year under review, 508 (74%) patients met the eligibility criteria. At 6 months, 88% and 92% of patients had viral load <400 copies/ml and <1000 copies/ml, respectively. Whereas, at 12 months, 70% and 88% of patients had viral load <400 copies/ml and <1000 copies/ml, respectively. At 6 months the self-reported HAART dose adherence of≥95% adherence

was 84% and 88% at 12 months. Poor virological outcome (viral load ≥400 copies/ml) was significantly associated with poor self-reported prophylaxis adherence and self-reported ARV dose adherence at 6 and 12 months.

Conclusion: The distribution of viral load results showed a low uptake (35%) of virological monitoring at 6 month time point and even lower (12%) at 12 months. A conservative viral load threshold for virological response is required in the Namibian setting. The current adherence level of >80% encourage increased ARV therapy rollout. Poor virological outcome was associated with self-reported adherence.

1. INTRODUCTION

1.1 Background

Namibia is one of the seven countries most affected by HIV/AIDS in sub-Saharan Africa (MOHSS, 2004). According to the 2008 HIV Sentinel Survey, Namibia has an HIV prevalence of 17.8% (MOHSS, 2008). The Estimation and Projections Package (EPP) model that calculates national HIV prevalence based on ANC HIV prevalence and other information had results for Namibia that suggested adult (15-49 years) prevalence in 2007/2008 of 15.4% (MOHSSb, 2008). The EPP estimated 204 000 people to be living with HIV in 2007/2008 and this number is projected to grow as the total population size of the 15-49 year age group grows. According to the Namibian Spectrum model, linked to EPP model, in 2007/08 there were approximately 14100 new infections with 50600 individuals (adults and children) receiving ARV therapy and an estimated 63600 adults were in need of ARV therapy by end of March 2008 (MOHSSb, 2008). While the deaths due to AIDS were approximately 5400 persons (plausibility bounds: 3700-7300) (MOHSSb, 2008).

In order to curb the high mortality and adverse socioeconomic effects of the HIV/AIDS pandemic, in 2003 the MOHSS started providing ARV therapy to patients meeting defined clinical criteria (MOHSS, 2004). However, expanded ARV therapy came with the challenge of maintaining treatment adherence among a growing number of ARV patients and the need to improve patient management and care (Steel *et al*, 2007; Dyul *et al*, 2002; San Lio *et al*, 2008; Pierson *et al*, 2000).

Another challenge has been to minimize the emergence of drug-resistant HIV strains in HIV-patients receiving treatment.

Antiretroviral therapy clinics have been opened around the country through collaboration of the MOHSS and donor organizations and one such clinic is the Katutura Health Centre. The ARV clinics operate based on set guidelines and protocols such as the HAART protocol for patient management and the MOHSS circular stating the use of laboratory tests for patient monitoring (MOHSSa, 2007; MOHSS, 2005). According to these guidelines, there are four recommended combinations for first-line therapy and they are all NNRTI based drugs. The laboratory test panel includes the HIV viral load at six months and CD4 counts every three months. The optimal response to treatment has been given as a median CD4 cell rise of 100 to 200 cells within the first year (MOHSS, 2007).

The infrastructure for viral load testing is in place at the local parastatal referral laboratory. The challenge however is to ensure the use of the viral load and the CD4 results to make patient management decisions. The guidelines do not present any expected viral load values, thus an undetectable status of viremia has by default become the expectation. This study sought to determine the viral load levels that can be expected under the current adherence practice, monitoring techniques and other underlying factors. It is hoped this will aid clinicians in decision making in HAART patient management.

1.2 Research setting

Namibia is a vast country with a population of approximately 2 million most of who are relatively young with 43% under 15 years and 4% are over 65 years (MOHSSc, 2008). Namibia has very diverse ethnicity, there are 11 indigenous languages that are spoken but English is the official language. Although the country is classified as a middle income country, it has one of the largest differentials between rich and poor in the world (MOHSSc, 2008).

The health delivery system is under 13 regional directorates with 34 health districts. This structure has a national referral hospital (Windhoek Central Hospital), 3 intermediate/ referral hospitals (Oshakati, Rundu and Katutura Hospitals), 30 public district hospitals, 44 health centres, 265 clinics and 1150 outreach sites (MOHSSc, 2008). Katutura Health Centre is one of the 44 health centres around the country. The Centre is situated within the Khomas region in the proximity of the capital city, Windhoek and is located in the heart of Katutura, the largest high density settlement in Windhoek. The ARV clinic is a stand alone facility within the Katutura Health Centre grounds and is open from Monday to Friday with Tuesdays reserved for initiating new patients on ARV therapy. The current rate of initiating therapy is approximately 30 patients per week as of 15 July 2008, and prior to this date it was 15 patients per week. Due to increased uptake of the HIV care services at the Centre initiation of patients to HAART was doubled on 15 July 2008 to increase access to ARV therapy.

Based on ARV therapy guidelines, an HIV-positive person is evaluated for eligibility to begin ARVs at an ARV clinic such as this study's research site, Katutura Health Centre. The assessment includes medical history, HIV disease directed physical examination to determine WHO clinical staging, CD4 count and a review of social eligibility (MOHSS, 2007). At the first visit, all patients are registered into the AMIS. A patient care booklet (Appendix 1) is utilised to capture baseline and monitoring data for each individual patient enrolled for HIV care in the clinician cubicles. The data is then entered by a data clerk to update the patient AMIS record. The patient keeps a card with a unique identifier that is the file number for the patient care booklet and AMIS record. A patient on HIV care is then initiated on ARV therapy when they have:

- WHO clinical stage 3 or 4 HIV disease irrespective of CD4 count, or
- CD4 cell counts $\leq$ 200 cells/mm^3 ($\leq$ 250 cells/ mm^3 for pregnant women), irrespective of WHO clinical stage and
- Met social eligibility criteria, namely:

✓ Have a fixed address for the past 3 months

✓ Have a treatment supporter (but should not be the sole reason to deny treatment)

✓ Have ready access to a designated treatment centre for follow-up

✓ Not drink alcohol

✓ Have no untreated underlying psychiatric disorders

✓ Be committed to lifelong treatment with HAART, strict adherence to treatment, practising safe sex and allowing home visits (MOHSS, 2007).

Initiating a patient on ARV therapy requires > 2 visits at least 2 to 4 weeks apart to ensure readiness. Antiretroviral dose adherence is then measured through use of self-reporting of > 95% of medication taken within the previous three days. The laboratory monitoring of therapy includes the measurement of HIV viral load and this is performed by the reference laboratory, Namibia Institute of Pathology.

1.3. Problem statement

There is limited data available in Namibia on adherence of adult HIV-infected patients to HAART regimens as assessed by self-reporting at 6 months and 12 months after initiating ARV therapy. The proportion of these patients that have virological failure and their corresponding demographic, clinical and social characteristics is unknown. This information is vital for the assessment of drug efficacy and the virologic effect of therapy as well as determining the continuation or change of therapy.

1.4. Purpose

This study seeks to provide data on level of self-reported dose adherence, distribution of viral load levels and the characteristics of patients with viral load ≥400copies/ml after initiating ARV therapy at Katutura Health Centre. This information can assist clinicians in the management and care of patients when assessing the virological effect of therapy and provide insight for recommendations in future guidelines in terms of viral load assay result usage in therapy continuation or change.

1.5. *Aim*

The aim of the study was to determine the therapeutic and virological outcomes in adults living with HIV/AIDS at 6 and 12 months after initiation of HAART in Katutura Health Centre in Namibia in 2007.

1.6. Specific *Objectives*

1. To describe the proportion of adult patients who had viral load measures recorded in their patient record at 6 and 12 months after initiating first-line HAART in 2007.

2. To describe the recorded viral load levels of the adult patients at 6 months and 12 months after initiation of first-line HAART in 2007.

3. To assess the adult patient self-reported dose adherence levels to first-line HAART at 6 and 12 months after initiation of first-line HAART in 2007.

4. To characterize and compare adult patients who achieved < 400 copies/ml and ≥ 400 copies/ml virological suppression at 6 and 12 months after initiation of first-line HAART in 2007.

2. LITERATURE REVIEW

The literature review starts with a review of the use of medical records and the general background to ARV therapy. This is followed by a review of literature on treatment adherence, viral loads and their relationship in ARV therapy and patient management. The section further highlights the various methods used in the identified studies. Firstly however, the debate on the use of medical records shall be discussed.

2.1 Use of medical records in research.

The use of medical records for research has been debated in the international community, debating the need for individual patient consent when conducting studies (Wald, Law, Meade, Miller, Alberman and Dickinson, 1994; Robling, Hood, Pill, Fay and Evans, 2003; Al-Shahi and Warlow, 2000). The debate arose when the European Commission proposed guidelines for use of medical records in research (Wald et a, 1994). Wald et al, 1994 highlighted the value of systematic record reviews and record linkage studies in expanding knowledge and improving medical practice. Al-Shahi and Warlow, 2000 suggested that need for consent in observational studies would introduce systematic bias, caused by refusal of patients to use their data. Wald et al, 1994 recommended the use of the guidelines of the Royal College of Physicians working group that advocates for medical record use as long as a "confidential manner without causing harm" is practiced.

The use of medical records is an inexpensive and efficient way of gaining a comprehensive view of the health system's response to a particular medical problem (Merion& Cash, 2006). However, in

the past few years the debate was on issues of informed consent and confidentiality. Merion and Cash, (2006) argue that obtaining informed consent may cause breach of privacy, undue psychological or social harm to a former patient, introduce bias and financial strain for studies. They also however conclude that confidentiality issues are likely to gain importance.

International guidelines were formulated that require ethical clearance for all studies. In Africa the reality for the need of ethical review boards came with the increased collaborative studies based on the Millenium development goals (Kigira, Wambebe and Baba-Moussa, 2005). Kigira, Wambebe and Baba-Moussa, 2005 performed a descriptive study to determine which WHO African region member countries had ethical review boards. They found that of the 28/46 countries that responded only 64% (18/28) confirmed the existence of national research committee. Although Namibia is not sited in this article as a respondent, there is an ethical review board present in the country. This study sort ethical approval to conduct the study based on national requirements and international standards. The approval letters can be found in Appendix 4 and 5.

2.2 Background to antiretroviral therapy

The HIV pandemic has now evolved to an era of ARV therapy. As ARV therapy is becoming more accessible to the general population and with the rapid evolution of information, interest is shifting to the use, monitoring and challenges of treatment regimens and maintaining treatment adherence (Steel, Nwokkie and Joshi, 2007; Dyul *et al*, 2002; San Lio *et al*, 2008; Pierson *et al*, 2000). Antiretroviral regimens are complex with serious side effects that pose difficulty with

adherence resulting in evolution of viral resistance due to non-adherence and suboptimal drug levels (Dyul *et al*, 2002). Generally, adherence of greater than 95% is required for good results to NNRTI based regimen (San Lio *et al*, 2008). However, Bangsberg *et al* (2006) and Martin *et al* (2008) have shown that adherence levels of 80-90% to combination regimens will still result in viral load suppression. There is no literature on the association between the level of adherence to ARV therapy and the degree of virological suppression in Namibia.

The assessment of ARV treatment failure involves the initial consideration and assessment of patient adherence, tolerability and pharmacokinetic issues (PAGAA, 2008). This is then followed by assessment of clinical progression, immunological and virological failure. Clinical progression is defined as the occurrence and recurrence of HIV-events after at least 3 months on treatment (PAGAA, 2008). Immunological failure is when an adequate CD4 response is not achieved or maintained (PAGAA, 2008). Virological failure is the inability to suppress viral load below detectable levels and may manifest as incomplete virologic response or virologic rebound (PAGAA, 2008). The solution to clinical progression, immunological and virological failure is treatment change. Unfortunately ARV regimen change is not a decision to be taken lightly as the drugs can lead to serious side-effects. There is also the cost of switching regimen and a problem of limited further options that may be exacerbated by the possibility of adverse events and the chance of drug resistance.

The change of ARV regimen requires a thorough drug treatment history with review of results of drug resistance testing (Dyul et al 2002). The threat of drug resistance has resulted in a set of early warning indicators being published (WHO, 2006). Shiningavamwe (2008) however showed no detectable (< 5% threshold) resistance levels among treatment-naïve pregnant women in Namibia. The study highlighted the need to revert to initial assessment considerations of adherence, tolerability and pharmacokinetic issues as causes of ARV treatment failure. Descamps *et al* (2000) carried out a case-control study over a period of 10 months in 3 urban hospitals in France and showed that the early and late virologic failures during the maintenance phase are related more to problems of adherence and ARV treatment potency than to resistant mutant strains. Furthermore the superior nature of NNRTI based regimens over single protease inhibitor regimen has been closely associated with regimen potency over higher levels of adherence (Weiser, Guzman, Riley, Clark and Bangsberg, 2004).

The current study therefore sought to describe self-reported dose adherence and viral load patterns as background information that can be utilised in the initial assessment of ARV treatment failure. If the patterns are known, then the prevalence of adherence as a cause of ARV treatment failure is considered appropriately. Furthermore, the viral load patterns encompass the tolerability and pharmacokinetic issues, as the patterns reflect response rates that can be expected in the Namibian setting of ARV therapy and virological monitoring.

2.3 Adherence to ARVs

The measurement of ARV adherence is essential for targeting and rigorously evaluating interventions to improve adherence and prevent viral resistance (Berg &Arnsten, 2006). Harries, Nyangulu, Hargreaves, Kaluwa and Salaniponi (2001) and Stevens, Kaye and Corrah (2004) reported concerns for the rapid access to ARV therapy in Africa. They concurred that it may lead to transmission of resistant strains as they believed a high proportion of patients in Africa would poorly adhere to treatment regimens. However, this theory was contested by Mills *et al* (2006) when their meta-analysis on adherence patterns revealed that patients in Africa (resource-poor) had adherence levels of 77.1% (95% CI: 67.3%-85.6%) which is equal and possibly better than North America (resource-rich) with 54.7% (95% CI: 48.0-61.3%). The varied estimates of adherence reported in the meta-analysis reveal the lack of standardization for adherence measures, which shall now be reviewed in the following section.

2.3.1 Methods for measuring adherence to therapy

Adherence measures include the visual analogue scale or pill identification test where a patient is asked to identify their medication, self-reporting of medicine taken in the past 3 days, pill counts of medication left in the vial at a visit (and unannounced version) and the medication possession ratio (MPR) - a metric that correlates to virologic outcomes (Steel *et al*, 2007; Chi *et al*, 2009). The limited understanding of how to optimize existing adherence measures has delayed progress in adherence research (Berg &Arnsten, 2006).

Self-reporting is the most widely used adherence measure and the most promising for use in clinical care and resource limited settings (Berg &Arnsten, 2006). This method is currently in use in Namibia as it is inexpensive and simple to use in the clinical setting, however it grossly over estimates adherence (Liu *et al*, 2006). Liu *et al* (2006) recommended the evaluation of calibrated patients self-reporting with duration of ARV regime and attitudinal measures (patient attitude and psychological factors) as they impact on the level of adherence. Unfortunately, self-reported adherence is not a precise predictor of treatment success to substitute for viral monitoring (Garcia *et al*, 2006). Hence Namibia introduced the viral load at 6 months after initiation of therapy to predict treatment response.

Objective measures such as pill counts are not as widely used with one reason being poor understanding of the source and magnitude of error biasing the methods (Berg &Arnsten, 2006). The use of unannounced monthly pill counts with pillbox organizers has appeared to improve adherence and virologic suppression (Petersen *et al*, 2007). The visual analogue is considered to be simple and potentially useful in routine patient care (Giordano *et al*, 2004). However it has been found that the visual analogue scale and unannounced pill counts are not different from the 3 day recall (Giordano *et al*, 2004). The MPR is a pharmacy-based measure of adherence. The MPR is calculated by dividing the number of days of medication supplied within a refill interval with number of days in refill interval (Peterson *et al*, 2007). If the MPR is calculated over multiple refills it is also referred to as the continuous measure of adherence. The MPR has been correlated to clinical outcomes in both developed and developing country settings (Chi *et al*, 2009).

The current study utilised the self-reporting of medication taking behaviour as a measure of adherence as it is not only in use in Namibia but also widely adopted in other resource limited settings. Since the self-reporting of adherence does not replace virological monitoring in Namibia, the association between the two was also analysed.

2.3.2 Studies on adherence to ARV therapy

Since adherence to ARV therapy is a topical issue, studies are being carried out all over the world in both developed and developing settings. The studies on adherence to ARV therapy are designed in various formats. Some are prospective observational studies (San Lio *et al*, 2008; Amberbir, Woldemchael, Getachew, Girma and Deribe, 2008; Martin *et al*, 2008; Nilsson, Schonnesson, Diamond, Ross, Williams and Bratt, 2006 and Laniece *et al*, 2003). Other studies have used a cross-sectional approach and retrospective review of patient clinical history (Weiser *et al*, 2003; Uzochukwu *et al*, 2007 and Chi *et al*, 2008). The studies reviewed were carried out over various time frames. Sample population and size was based on predetermined eligibility criteria for the setting. Cross-sectional studies and retrospective record reviews are the preferred study designs in research settings where resource constraints and time are important considerations. When taking into account the various methods of measuring adherence mentioned in the above section, sample size, study setting and study design, comparison of study findings is a challenge. However, the following sections shall describe studies on ARV adherence and their findings, highlighting the various differences in methodology.

A 12 month prospective observational study in Mozambique of patients receiving first-line HAART utilized the pill count as an adherence measure (San Lio *et al*, 2008). Out of a total of 531 participants, 137 (25.8%) patients left the program or discontinued first-line therapy by the end of the 12 month period. Of the 394 patients remaining 284, 72.1% of their patients had >95% treatment adherence. Of these adherent patients 96.5% had a final viral load of < 1000 copies/ml. Amberbir *et al* (2008) in their prospective study in South- West Ethiopia using a self-reported dose adherence as a measure found adherence of 94.3% in the first month and this decreased by 2% by the third month. Another prospective study carried out in Sweden used self administered questionnaires and medical records in a two year period (Nilsson *et al*, 2006). The study cohorts were patients that completed at least six of the seven follow-up questionnaires. Their study revealed that 61% of the patients maintained full-dose adherence (Nilsson *et al*, 2006). These two studies though two years apart, suggest reduction in adherence overtime in both developed and developing countries.

Chi *et al* (2009) utilized the MPR method as a retrospective adherence measure for a large cohort of treatment naïve adults initiating and continuing ARV therapy for ≥ 12 months in Zambia. They found 62.9% of patients had optimal adherence (≥95%), 28.3% had sub -optimal (80-94%) and 8.8% had poor adherence. A cross-sectional study using pre-tested interviewer- administered questionnaires in Nigeria from randomly selected 174 patients on treatment over the past 12 months revealed that approximately 25% of patients had adhered to the treatment regimen (Uzochukwu, Onwujekwe, Ndu, Okoli and Onoka, 2007). With sample size and study design

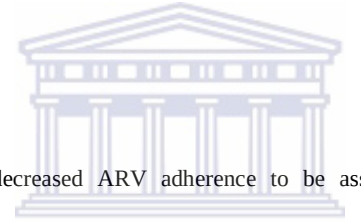
differences, the variation in adherence is hard to interpret. Other factors showing great variation in the studies reviewed are the determinants of adherence. This shall be the topic of the next section.

2.3.3 Determinants of adherence

The reported determinants of adherence to ARV therapy include social support, psychological and cognitive factors, use of memory aids, self-efficacy, age, number of doses a day and other sociodemographic variables such as the number of years of schooling, unemployment, alcohol use, self-reported adverse events, number of pills, financial constraints, stigma, travel/migration, switch of regime and increase lag time between HIV test result and first ARV prescription (Pinheiro, de-Carvalho-Leite, Drachler and Silveira, 2002; Amberbir *et al*, 2008; Gordillo, del Amo, Soriano and Gonzalez-Lahoz, 1999; Duong *et al*, 2001; Bonolo *et al*, 2005; Nilsson *et al*, 2006; Weiser *et al*, 2003; Laniece *et al*, 2003). These determinants and the direction of predictions in relation to ARV adherence shall now be reviewed in more detail.

Pinheiro *et al* (2002) carried out a cross-sectional study in a Southern Brazil referral service and concluded that the most important determinant of adherence is increased self-efficacy. Self-efficacy is a persons' conviction on successful execution of certain behaviour to produce a desired outcome, in this case taking prescribed medication. The other determinants reported in this study for increased adherence were decreased frequency of medicine taking and greater than 8 years of schooling. Bonolo *et al* (2005) carried out a prospective study in referral centres in Brazil over a 2 year period. The study confirmed an earlier finding by Pinherio *et al* (2002) when number of pills

per day increased risk of non-adherence. The study also found unemployment, alcohol use, >2 adverse reactions, switch of regimen and a longer time between HIV test result and first ARV prescription to be associated with increased risk of non-adherence. These two studies which were both conducted in Brazil show how determinants of adherence can vary even within country. Hence, a recommendation to incorporate feasible and reliable adherence indicators in routine monitoring of adherence in clinical practice (Bonolo *et al*, 2005). The patient care booklet used as a data source in this current study incorporates a section on the demographic and treatment profile of the patient.



A cross-sectional study in Spain showed decreased ARV adherence to be associated with depression, lack of self-perceived social support, intravenous drug users and younger individuals (Gordillo *et al*, 1999). These determinants in essence can be classified as psychological and behavioral which is in agreement with the findings of Duong *et al* (2001). Duong *et al* (2001) evaluated the Patient Medication Adherence Questionnaire in France and found that motivation to treatment, confidence in personal skills and an optimistic attitude to life as determinants of adherence. Thus they concluded that psychological and behavioral factors are central to adherence. They however excluded any association between lower medication adherence and sociodemographic background, social support, alcohol and illicit drug use and depression.

In the African setting, social support, use of memory aids and lack of depression were found to be positive predictors of adherence in Southwest Ethiopia (Amberbir *et al*, 2008). Interestingly, the

study demonstrated that the determinants also varied over time. Initially, social support and lack of depression were positive predictors, but at a 3 month follow-up, it was social support and use of memory aids that predicted adherence. In Botswana the principal barriers to adherence were financial constraints, stigma, travel/migration and side-effects, listed in decreasing order of negative determinants (Weiser *et al*, 2003). A cross-sectional study done in Senegal echoed the finding of cost as a barrier but also included the type of drug regimen (Laniece *et al*, 2003). In Namibia, therapy cost is subsidized due to funding organisations collaborating with the Ministry of Health. However, transport and other financial constraints are not subsidized.

The above review highlights the vast variation in the direction of prediction of ARV adherence determinants in different settings. It is therefore vital to assess determinants of adherence in a local setting. The within country variation in Brazil underscores this. Since adherence is a dynamic process that cannot be predicted with the use of a few characteristics, a recommendation to integrate adherence support into regular clinical follow-up was put forward (Bonolo *et al*, 2005; Amberbir *et al*, 2008). Although adherence support in the form of counseling and patient education has been integrated in the Namibian setting, the assessment of determinants of adherence is notably limited. The current study sought to describe the characteristics of patients with possible virological failure (viral load ≥400copies/ml) as an outcome of non-adherence to ARV therapy.

2.3.4 Adherence and clinical outcome

The goal of adherence to ARV therapy is to improve clinical outcome by achieving undetectable levels of HIV viral load and increasing immunological response (WHO, 2000). The overall outcome is to prevent disease progression from HIV infection to AIDS, hence reduce HIV morbidity and mortality within the HIV positive population. This prevention phenomenon has far reaching socioeconomic consequences in a population. The reported clinical outcomes from studies shall now be reviewed below.

San Lio *et al* (2008) assessed the risk associated with ≤ 95% treatment adherence having a viral load > 1000 copies/ml compared to those with an adherence of > 95 utilizing the Mantel-Haenszel procedure. The estimated odds ratio was found to be 5.11 (95% CI: 2.26- 11.54). The study also applied a Cox proportional hazard model to calculate the hazard ratios of having a viral load ≥ 1000 copies/ml in relation to adherence, CD4 cell count and age. The model found significant association with age <30 years, initial CD4 count <338 cell/mm^3 and having a viral load >1000 copies/ml. They explained that age < 30 years may be a behavioral marker that results in poor virological outcome. In terms of an initial CD4 count, San Lio *et al* (2008) suggested that it is a marker of disease progression and health status at initiation of ARV therapy. Thus a poorer level of health and more advanced disease progression at initiation of ARV therapy results in poorer clinical picture even after 12 months.

Chi *et al* (2009) in a cohort of patients in Zambia confirmed San Lio *et al* (2008) Mozambique findings when they reported that individuals >35 years of age or reported social support (an

adherence buddy) were less likely to exhibit poor clinical outcome. When they compared post-12-months mortality risk they found it to be similar for optimal and suboptimal adherence but higher in those with poor adherence. Unfortunately, their study findings on mortality risk may have been confounded by selection bias since their population was composed of patients that had survived the periods of highest mortality risk, first 90 days on ART or at least 12 months (Chi *et al*, 2009).

Ledergerber *et al* (1999) had earlier reported significant association with increases in CD4 count (immunological response) at 6 months with a favourable clinical stage at baseline of ARV therapy initiation. A South African work-based cohort also reported independent predictors of suboptimal virological outcome as <1 log decrease in viral load at six weeks, WHO stage 3 and 4, baseline viral load at baseline > 100000 copies/ml and site of ART delivery (Fielding *et al*, 2008). They suggested that poor virological outcome at 6 weeks (<1 log decrease in viral load) was more likely due to poor adherence than to transmitted resistance since their study population had very little prior ARV therapy. The poor outcome associated with site of delivery was interesting as all sites use the same guidelines, counseling protocols and drug regimens. Through their experience, they suggested long waiting times for clients, staff not being specially trained in HIV care, poor follow up of patients not attending the clinic or lack of communication between the pharmacy and clinic staff as possible causes (Fielding *et al*, 2008). Most resource limited settings do not assess baseline viral load, including Namibia.

The current study describes patient characteristics with virological outcome of ≥400 copies/ml at 6 and 12 months to identify factors that may be associated with poor outcome. It is hoped the findings will assist in patient management.

2.4 HIV viral load

The viral load is a quantification of circulating HIV ribonucleic acid (RNA) copies per milliliter (copies/ml) and can also be expressed as a log value. A change of 0.5 $\log_{10}$ is considered statistically significant (WHO, 2008). The viral load is a predictor of risk of HIV transmission, with it being rare at <1500 copies/ml, while a baseline viral load >100 000 copies/ml is related to increased mortality rates (Fielding *et al*, 2008; Quinn *et al*, 2000; Wood *et al*, 2006). HIV RNA is a surrogate marker for treatment response and is thus used for efficacy monitoring of ARV therapy (WHO, 2008; WHO, 2000). The goal of HAART is to reduce the viral load to undetectable levels (WHO, 2000). There are three Food and Drug Agency approved viral load assays with the following detection limits, the Amplicor (<40 copies/ml), Versant (<75 copies/ml) and the Nuclisens (<80 copies/ml). The Amplicor assay is currently in use in Namibia. The goal of undetectable levels should be achieved in 16- 24 weeks (WHO, 2008). Thus some studies have considered putting patients with undetectable viral load on maintenance regimes to reduce therapy costs and pill burden (Flandre *et al*, 2002 and Pia loux *et al*, 1998).

An audit of a clinical population in England revealed 92% of patients on therapy for more than 16 weeks had a viral load of <50 copies/ml (Madge *et al*, 2008). Thus they concluded that the

proportion of patients with viremia was low in their current clinical practice. In a study done in Mozambique, the findings were that 96.5% of patients had <1000 copies/ml at 12 months when adherence was > 95% (San Lio *et al*, 2008). This finding echoes the one in England in terms of viremic prevalence if >1000 copies/ml is used as the threshold. In Namibia there has been no study to find the association between adherence and virological outcome. This current study therefore seeks to provide insight.

Fielding *et al* (2008) reported the viral load at 6 weeks as the strongest predictor of suboptimal outcome at 12 months. Inexplicable increases in viral load have been observed and are referred to as "blips". The "blips" were found not to warrant change in treatment (Havlir *et al*, 2001; Lee, Keiffer, Siliciano and Nettles, 2006). These transient events only result in treatment failure in < 10% of cases kept on the same regimen (Garcia-Gasco et al, 2008). Thus, a conservative threshold of > 400 copies/ml is used to classify patients at risk of failing therapy to accommodate the "blip" phenomenon (Madge *et al*, 2008; Phillips *et al*, 2008). This conservative threshold of >400 copies/ml was also adopted in the current study. There are recommendations as to the frequency of viral load monitoring, as summarized in Appendix 2 (WHO, 2008). There are also guidelines for resource unlimited and resource limited setting for patients that have initiated HAART therapy (WHO, 2000, WHO, 2008). In the case of Namibia, a resource limited setting, a clinical review one month after initiating treatment, with assessments every 3-6 months is recommended. However in Namibia, due to the high cost of viral load testing, the viral load is only done at 6 months after initiating therapy and then thereafter as clinically indicated (MOHSS, 2005). Despite the

availability of recorded data of viral load, no study had been carried out in Namibia to determine viral load patterns of ARV therapy patients. Hence it is one of the objectives of this study.

2.5 Relationship between adherence and HIV viral load

The adherence to HAART is essential and closely associated with time on treatment and decrease in HIV viral load (Nieuwkerk & Oort, 2005; Bangsberg *et al*, 2003). The visual analogue scale and unannounced pill counts are not different from the 3 day recall although they are inversely correlated to HIV viral load (Giordano *et al*, 2004). A meta-analysis of studies on the relationship between self-reported adherence and viral load has shown that self-reported adherence measures can distinguish between clinically significant patterns of medication taking behavior (Nieuwkerk & Oort, 2005). Nieuwkerk & Oort (2005) indicate that confidentiality of responses, use of actual viral load measurements, an adherence level of lower than 95% and higher percentages of patients with intravenous drug use are significantly associated with the relation between adherence and virologic response. Increasing rates of viral suppression at high levels of adherence are balanced by increasing rates of drug resistance among viremic patients (Bangsberg *et al*, 2003). Bangsberg *et al* (2003) highlighted that exceptionally high levels of adherence will not prevent population levels of drug resistance. Discordant adherence-response relationship has been reported in Botswana, were very high rates of adherence were associated with virological failure (Bisson, Rowh, Weinstein, Gaolathe, Frank and Gross, 2008). Once again, there is no literature on the adherence-response relationship in Namibia.

2.6 Patient management

Patient management is one of the growing challenges of rapid ARV therapy scale up. In Sweden software for decision support called InfCare HIV was launched in 2004. Numerous functions are facilitated through structured data entry (Health Solutions, 2009). This software is now the largest common database and has also been launched internationally, in Denmark, Iceland, Russia and Finland. A structured patient booklet is used at Katutura Health Centre. This serves as the patient's record where the clinical history is captured. The use of a structured or pro forma format may improve completeness by≥ 50% and can be used easily and with speed by clinicians (Schmidt, Rizvi, Lee, Wood, Amisano and Fairley, 2005; Diver & Craig, 2005 ; Natha, Sheey, Pollard, Parkianathan and Prime, 2008). Since the lack of complete, timely and accurate data impacts on site monitoring and national planning the structured format may assist in these aspects (Makombe *et al*, 2008). Tierney *et al* (2007) state that "one major obstacle in HIV/AIDS care in developing countries is the lack of electronic medical record systems to collect, manage and report clinical data". They also aptly sited the various advantages of having such a system. Thus the Namibian MOHSS introduced AMIS an electronic medical record system at Katutura Health Centre in October 2008.

There is limited literature on patient data management in Africa and the situation is not different in Namibia. However at the time of data collection the AMIS electronic version was just starting to be used and patient records had been loaded. Another problem of patient management is the loss to follow up rates that are high ranging from 5-25% in resource-poor settings that are scaling up ARV

therapy (Yu *et al*, 2007). No literature is available on the loss to follow up rates in ARV therapy in Namibia.

3. METHODOLOGY

3.1 Study design

An observational, cross-sectional and analytic study that utilised retrospective review of clinical records. Patient care booklets for adult patients initiated on HAART at the Katutura Health Centre from 1st of January to 31st of December 2007 were reviewed for a period of up to 12 months from the date the adult patient initiated HAART.

3.2 Study population

The study population was all adult patients enrolled in 2007 on first-line HAART as retrieved from the electronic medical record system, using the time frame as a search criterion.

3.3 Sample size

The Katutura Health Centre initiated ARV therapy on approximately 15 patients per week during 2007, so total of 780 patient records was expected. To cover objectives 2- 4, the population comprised of records with a viral load result at 6 and/or 12 months. An assumption that at least 50% of the records were complete was made based on findings from other studies (Schmidt *et al*, 2005; Diver & Craig, 2005; Natha, Sheey, Pollard, Parkianathan and Prime, 2008). Unfortunately there are limited studies on data completeness and this is also true for Namibia. Then factoring in a maximum loss to follow up of 25%, then from 390 complete records only 293 were expected to also have a viral load result at 6 and/or 12 months. Madge *et al* (2008) have shown that 92% of

patients on HAART for more than 16 weeks have a viral load <50 copies/ml. San Lio *et al* (2008) revealed that 96.5% of patients on HAART had <1000 copies/ml at 12 months in Mozambique. Thus assuming a true value of 5% HAART failure within +/- 3% of the desired range a sample size of 212 would have been required as calculated on EpiInfo. Thus even factoring in maximum loss to follow up and completeness levels, the use of all expected records with a viral load at six and/or 12 months was assumed to be adequate.

3.4 Sampling procedure

All 687 patient booklets for patients initiated on ARV therapy from 1st January 2007 to 31st December 2007 were reviewed. Accordingly, a patient who was initiated on ARV therapy on 31 December 2007 was followed to January 2009 to have a full 12 months record. Below is the exclusion criteria applied.

Exclusion:

- All records with treatment switch/substitute within 12 month follow up period
- All records were a patient is reported pregnant within the 12 month follow up period.
- Prior ARV therapy

A therapy substitute or switch involves a drug change which impacts virological outcome. In pregnancy a CD4 cut-off of 250cells/mm^3 is used and this may result in a bias for outcome (MOHSS, 2007). Using the above criteria a total of 508 records were eligible for inclusion.

To fulfill objectives 2-4 the following inclusion criteria was applied on the 508 records:

- All records with viral load result at 6 months (5-7 month time frame)
- All records with viral load result at 12 months (11-13 month time frame)

The flexibility in the 6 and 12 month period was done to accommodate the laboratory turnaround time. A total of 178 records at 6 months and 61 records at 12 months were eligible for inclusion.

3.5 ***Data collection and processing***

The authorization letter provided from the MOHSS (Appendix 4) was presented to the manager at Katutura Health Centre. The purpose of the study was then explained to the staff members at the ARV clinic and a data collection schedule and data review location on site that suited the ARV clinic was adopted.

Key variables were defined and measured as follows:

Self-reported adherence-

Records of all patients initiated on ARV therapy from 1 January 2007 to 31 December 2007 were extracted from the AMIS electronic data management system using the time frame as a search criterion. The following variables were extracted:

a) Demographics: sex, age, date of birth and treatment support.

b) Treatment profile: prior ART, date confirmed, date initiated on therapy, entry WHO stage, eligibility, start ART date, start weight, start WHO stage and start CD4.

To fulfill objectives 2 to 4 each record was linked to a unique identifier. The data from the eligible record was extracted and entered into a customized Microsoft Excel spreadsheet linked to a unique identifier (Appendix 3). The following was data was extracted from each eligible record:

a) Treatment monitoring characteristics:
weight, WHO stage, tuberculosis, new opportunistic infection, adherence to prophylaxis, ARV adherence, viral load and CD4)

Data verification was carried out periodically to ensure correctness and completion by reviewing previously entered files. A data clerk was hired to code viral load results into the < 40 copies/ml, 40-399 copies/ml, 400- 999 copies/ml and > 1000 copies/ml categories for 10% of randomly selected eligible records from the study. The data clerk used the same data verification and data cleaning procedure as for the main study. The double coding task was done to assess the reliability of the study.

3.6 *Data cleaning and quality*

3.6.1 Data cleaning

There is growing importance on Good Clinical Practice for issues of data handling and quality in clinical epidemiology research (Broeck, Cunningham and Herbst, 2005). This study handled all its

data collection using a customized Microsoft Excel spreadsheet. The creation of a data collection tool before actual data collection was done to minimize data collection errors and assist in visual screening of data during collection and review. The process of data cleaning involves detecting, diagnosing and editing abnormalities (Broeck *et al*, 2005). Visual screening was done as a detection process through browsing of data tables searching for illogical results (biologically), outliers, date errors, classification errors, missing values and duplication. During the analysis phase frequency distributions and cross-tabulation were reviewed to identify data handling issues.

Once a data handling issue was noted, a diagnosis process followed. Previous stages of data flow were revisited for any information that could justify the data point. The patient record was also reviewed at the earliest chance to verify the data point. Some outliers, for example in the viral load results were solved this way before data coding. Thus, all eligible records with a viral load were included and all missing values were represented.

3.6.2 Data quality

Data quality assessment can be subjective, reflecting the needs and experiences of people involved or objective, task-dependent or task-independent metrics (Pipino, Lee and Wang, 2002). Objective data quality assessments involve the development of metrics utilizing simple ratio, minimum and maximum operation and weighted averages (Pipino *et al*, 2002). This study utilized a percentage of total outcomes over the desired outcomes to express the data quality dimension of completeness of data. A tabulation of this is included in the results section, Table 4.1.

3.7 Analysis

A summary table for completeness of data, Table 4.1, was created using percentage calculations of obtained number of records over the expected number of records. The proportion of patient records in the cohort that had viral load results was then calculated as a percentage.

First, the proportion of records with viral load at 6 months, 12 months, 6 and / or12 months and then finally the proportion of records with a result at both 6 and 12 months were calculated as a percentage. The distribution of viral load results at 6 and 12 months was then classified as proportions in the < 40 copies/ml, 40-399 copies/ml, 400- 999 copies/ml and >1000 copies/ml catergories. These categories were chosen due to the detection limit of the assay, viral load distribution variation in different settings and the "blip" phenomenon (WHO, 2000; Havlir *et al*, 2001; Madge *et al*, 2008 and Phillips *et al*, 2008). The Wilcoxon rank test was applied to check for significance in the viral load distribution.

The level of self-reported dose adherence at 6 and 12 months was classified as good≥(%95), fair (85-94%) and poor (<85%) based on the patient care booklets (HIV Care/ART cards). The prevalence of≥95% adherence at 6 and 12 months of initiating therapy was calculated as the

percentage of adherent patients (tally of all patients who self-reported ≥95% adherence at 6 or 12 months) over the total number of patients in the sample population. The further classification based on the patient care booklets HIV Care/ ART cards (Appendix 1) of fair (85-94%) and poor (<85%) adherence was reported in a similar manner. The Wilcoxon rank test was again applied to check for significance in the adherence levels at the two time points. Adherence and viral load categories were then cross-tabulated and findings summarized. The prevalence ratio was calculated for each category instead of the prevalence odds ratio as an effect measure because it was reported to be conservative, consistent and interpretable by Thompson, Myers and Kriebe, 1998). Furthermore, the ideal statistic of incidence rate ratio can not be calculated in a cross sectional study (Thompson, Myers and Kriebe, 1998). The multivariate estimation utilized the Mantel-Haenszel test to determine estimated odds ratios and 95% CIs for patients who had treatment adherence <95% having a viral load ≥ 400 copies/ml, compared with patients who had treatment adherence of >95%. Patients with viral load ≥400 copies/ml were then compared with those with a viral load <400copies/ml at 6 and 12 months of initiating therapy using the Chi-square or Fisher's exact test as appropriate. An alpha value of 0.05 was used in all statistical significance testing due to the recognition of small sample size in subpopulations analyzed (Peterson *et al*, 2007). All data was analyzed using SPSS version 8 statistical package.

3.8 Validity

The procedures have been well described to reflect a measurement that is as close to the true value as possible. Selection bias has been nearly negated with the use of all eligible records. The eligibility criteria have been minimal to ensure as great a number of records as possible are part of

the sampling frame. Unmeasured confounders may still affect the results since factors impacting adherence and viral load levels in this population have not been explored before to ensure inclusion of all relevant factors, however most potential confounders have been included in the data analysis.

3.9 Reliability

The reproducibility of measurement was done through use of the kappa coefficient for agreement of coding tasks. Inter-observer bias and measures of inter-observer agreement are important sources of measurement error in this study (Landis & Koch, 1977). As the study data elements were captured through data coding the recommendation to use the kappa coefficient over the traditional retest measures of change in mean, typical error and retest correlation was adopted (Landis & Koch, 1977; Bloch & Kraemer, 1989; Hopkins, 2000; Di Eugenio, 2000). The consistency of classification of patient records into the data collection tool was performed on 10% of randomly selected eligible records due to time and cost constraints by a data clerk. Random numbers were generated from Microsoft Excel. A kappa coefficient of 1, P=0.000 was obtained, indicating excellent coding agreement.

3.10 Generalisability

The results of the study are only expected to apply to first-line ARV therapy patients enrolled for 12 months at the Katutura Health Centre facility. The results however may have relevance in other similar settings.

3.11 Limitations

The limitations of this study include the use of medical records. The level of completeness of medical records is a challenge. There is also no method applied to confirm the medical self-report being done by the patients which may have resulted in recall bias. Those that experienced therapy failure and had a treatment substitution or switch may have been non compliant to their treatment. Thus exclusion of the patients who substituted or switched therapy during the follow up may have introduced a selection bias. The exclusion was however done as the therapy substitute and switch data was not well coded in the records and there was an intensive operational research study under way at the time of this study, following up all the treatment failure patients.

3.12 ***Ethical issues***

This study was based on record review. Ethical approval was obtained from the MOHSS Research and Ethical Review Board (Appendix 4) and the University of Western Cape Ethics Committee (Appendix 5). Permission was also sought from the Sister-in Charge at the Katutura Health Centre to carry out the study. Confidentiality of patient records was maintained throughout the study. All research data was kept in a password locked database with limited access. All record review was carried out in a room next to the filing room with access restriction. The findings and

recommendations of the study are hoped to assist the management and care of patients on HIV ARV therapy not only at Katutura Health Centre but in Namibia. The study findings will be reported to the MOHSS and a feedback session will be scheduled for the Katutura Health Centre staff.

4. RESULTS

A total of 687 patients were initiated on first-line HAART between January 1st and December 31st, 2007. All patients were followed-up for a period of up to12 months from the date of initiation of therapy through use of patient care booklet. Of the total population, 508 records were eligible.

4.1 Completeness of data

The completeness of the eligible records is shown below in Table 4.1.

Table 4.1: Completeness of baseline data collected

Table 4.1: Completeness of Baseline data collected			
Variable	**Study population N = 508 n (%)***	**6 month viral load population, N = 178 n (%)***	**12 month viral load population, N = 61 n (%)***
Sex	508 (100)	178 (100)	61 (100)
Age	508 (100)	178 (100)	61 (100)
Treatment supporter	508 (100)	178 (100)	61 (100)
Entry WHO stage	488 (96.1)	171 (96.1)	60 (98.3)
Eligibility criteria	467 (91.9)	167 (93.8)	55 (90.1)
Start Weight	453 (89.2)	161 (90.4)	54 (88.5)
Start CD4	460 (90.6)	165 (92.7)	56 (91.8)

(%)* The percentage completeness of the data in the specific population (for example: completeness of sex variable in the population with a 6 month viral load result (178/178= 100% completeness).

The percentage completeness baseline data of eligible records in the overall population and the population with viral load result at 6 and 12 months are comparable. The variables sex, age and treatment supporter had completeness levels of 100% across the study population and sub populations. The variables entry WHO stage, eligibility criteria, start weight and start CD4 had levels of completeness that were within +/- 2% of the main study population. The lowest level of

completeness was with the start weight variable in the sub population of 12 month viral load. The data on height measurements were missing in the records. Thus body mass index was not calculated.

4.2 Baseline characteristics of study participants

The baseline characteristics of 508 eligible patient records are summarized below. The baseline characteristics of the eligible patients at initiation of therapy showed that 53% were male. Their age had a median of 36 (IQR: 33-43) years. Most patients had a treatment supporter (72%), were at WHO stage 1 at initiation of treatment (37%) and were eligible for therapy based on CD4 count and clinical picture (68%). Their start CD4 count had a median of 460 (IQR: 80.3-192) cell/mm^3 while their start weight had a median of 57 (IQR: 50.5-62.1) kg.

Table 4.2: Baseline characteristics of study participants

Characteristic	Frequency
Sex n=508:	
Male	267 (53)
Female	241 (47)
Age (years) n=508:	
Median	36
IQR	33-43
Treatment supporter n=508:	
Yes	364 (72)
No	144 (28)
Entry WHO stage n=488	
1	189 (37)
2	101 (20)
3	118 (23)
4	80 (16)
Missing	20 (4)
Eligibility criteria n=467	
CD4 only	5 (1)
Clinical only	115 (23)
CD4 and Clinical	347 (68)
Missing	41 (8)
Start CD4 count cell/mm^{3}n=460	
Median	153.8
IQR	80.3-192
Start weight (kg) n=453	
Median	57
IQR	50.5-62.1

4.3 The distribution of viral load results at the two time points (6 and 12 months) after initiation of therapy

Table 4.3: Distribution of viral load at 6 and 12 months according to viral load categories		
Viral load (copies/ml)	**6 months n=178**	**12 months n=61**
<40, n (%)	101 (57%)	19 (31%)
40 – 399, n (%)	55 (31%)	24 (39%)
400-1000, n (%)	7 (4%)	11 (18%)
>1000, n (%)	15 (8%)	7 (12%)

Table 4.3 summarizes the distribution of viral load results at 6 months (n= 178) and 12 months (n=61). At 6 months, 101 (57%) patients had viral load counts less than 40 copies/ml, 55 (31%) had a count of 40-399 copies/ml. Counts of 400-999 copies/ml were observed in 7 (4%) patients and 15 (8%) had counts that exceeded >1000 copies/ml at 6 months. At 12 months, 19 (31%) patients had viral load counts less than 40 copies/ml, 24 (39%) had a count of 40-399 copies/ml. Counts of 400-999 copies/ml were observed in 11 (18%) patients and 7 (12%) had counts that exceeded >1000 copies/ml at 12 months.

Wilcoxon signed ranked test was applied and a P value of 0.092 for 12 months viral load being less than 6 months viral load was obtained.

4.4 The self-reported dose adherence levels to first- line ARV therapy at two time points (6 and 12 months) after initiation of therapy

Table 4.4 shows the distribution of self- reported ARV adherence at 6 and 12 months time points.

Table 4.4: Distribution of patient self reported ARV dose adherence at 6 and 12 months

Category	6 months n=176	12 months n=140
Good (≥95 %), n (%)	148 (84)	123 (88)
Fair (85- 94 %), n (%)	13 (7)	4 (3)
Poor (≤84 %), n (%)	15 (9)	13 (9)

Table 4.4 shows that at 6 months 84% of 176 patients self-reported a good (≥ 95%) ARV dose adherence, while 7% self-reported fair (85- 94 %) and 9% self-reported poor (≤84 %), ARV dose adherence. At 12 months 88% of 140 patients self-reported a good ARV dose adherence, while 3% self-reported fair (85- 94 %) and 9% self-reported poor (≤84 %), ARV dose adherence. Wilcoxon signed ranked test was applied and a P value of 0.179 was obtained.

4.5 The characteristics and comparison of patients with viral load < 400 copies/ml and ≥ 400 copies/ml at the 6 and 12 months after initiation of therapy.

Table 4.5 shows the characteristics and comparison of patients with viral load < 400 copies/ml and ≥400 copies/ml at 6 and 12 months.

Table 4.5: Tabulation of characteristics and a comparison of patients with viral load < 400 copies/ml and ≥ 400 copies/ml at the 6 and 12 months.

Characteristic	Viral load at 6 months		p value	Viral load at 12 months		p value
	< 400 copies/ml	≥ 400 copies/ml		< 400 copies/ml	≥ 400 copies/ml	
Gender:			0.323			0.243
Male	87	14		18	10	
Female	69	8		25	8	
Treatment supporter			0.551			0.279
Yes	115	16		31	15	
No	41	6		12	3	
WHO Stage			0.439			0.580
1	63	6		20	10	
2	35	4		11	2	
3	35	8		6	4	
4	17	3		5	2	
Eligibility			0.200			0.339
CD4 only	1	1				
Clinical and CD4	113	16		30	13	
Clinical only	33	3		7	5	
TB			0.089			
Yes	3	2		2	0	0.430
No	130	14		29	16	

*Fisher's exact test

Table 4.5: Tabulation of characteristics and a comparison of patients with viral load < 400 copies/ml and ≥ 400 copies/ml at the 6 and 12 months continued….

Characteristic	Viral load at 6 months			Viral load at 12 months		
	< 400 copies/ml	≥ 400 copies/ml	p value	< 400 copies/ml	≥ 400 copies/ml	p value
New OI						
Yes	7	0	0.444	0	1	0.340
No	126	16		31	15	
self-reported cotrimoxazole adherence			0.000			
Good ≥ 95%	112	11		28	7	0.001
Fair 85-94%	6	2		1	3	
Poor <85	3	5		0	4	
self-reported ARV adherence						
Good ≥ 95%	117	8	0.000	31	8	0.000
Fair 85-94%	9	2		0	3	
Poor <85	5	8		1	5	

*Fisher's exact test

Table 4.5 summarises the characteristics and comparison of patients with viral load <400 copies/ml and ≥ 400 copies/ml in the 6 months and 12 months categories. Poor virological outcome at 6 months was not significantly different according to gender (P=0.323), treatment supporter (P= 0.551), WHO stage (P=0.439), eligibility criteria (P=0.2), presence of TB (P=0.089) and presence of a new opportunistic infection (P=0.444). At 12 months, no statistically significant association was found with gender (P=0.243), treatment supporter (P= 0.279), WHO stage (P=0.58), eligibility criteria (P=0.339), presence of active TB (P=0.430) and presence of a new opportunistic infection

(P=0.340). Poor virological outcome at both 6 and 12 months was associated with self-reported cotrimoxazole adherence and self-reported ARV dose adherence, p<0.005 using the 95% confidence level.

Table 4.6: Cross tabulation of virological response using 400 copies/ml threshold and self-reported ARV dose adherence at 6 months

		Viral load copies/ml		
		<400	≥400	Total
Self-reported ARV Adherence	≥ 95%	117	8	125
	< 95%	14	10	24
	Total	131	18	149

The prevalence ratio = 1.60, probability of having a viral load less than 400 copies/ml is 1.60 times higher for those patients with ≥ 95% ARV adherence than those with < 95% ARV adherence. When Mantel-Haenszel test was applied at the six month time point, the odds of a viral load of >400 copies/ml and a self-reported dose adherence of <95% had a value of 2.346 (CI:1.264-3.429), P=0.000.

Table 4.7: Cross tabulation of virological response using the 1000 copies/ml threshold and self-reported ARV dose adherence at 6 months

		Viral load copies/ml		
		<1000	≥1000	Total
Self-reported ARV Adherence	≥ 95%	120	5	125
	< 95%	17	7	24
	Total	156	12	149

The prevalence ratio = 1.36, the probability of having a viral load less than 1000 copies/ml is 1.36 times higher for those patients with 95% and above ARV adherence than those with less than 95% ARV adherence. When Mantel-Haenszel test was applied at the six month time point, the odds of a viral load of >1000 copies/ml and a self-reported dose adherence of <95% had a value of 2.291 (CI: 1.036-3.546), P=0.000.

Table 4.7: Cross tabulation of virological response using 400 copies/ml threshold and self-reported ARV dose adherence at 12 months

		Viral load copies/ml		
		<400	≥400	Total
Self-reported ARV Adherence	≥ 95%	31	8	39
	< 95%	1	8	9
	Total	32	16	48

The prevalence ratio =7.15, the probability of having a viral load less <400 copies/ml is 7.15 times higher for those patients with ≥ 95% and above ARV adherence than those with < 95% ARV adherence. When Mantel-Haenszel test was applied at the 12 month time point, the odds of a viral load of >400 copies/ml and a self-reported dose adherence of <95% had a value of 3.434 (CI: 1.215-5.653), P=0.000.

Table 4.7: Cross tabulation of virological response using the 1000 copies/ml threshold and self-reported ARV dose adherence at 12 months

		Viral load copies/ml		
		<1000	≥1000	Total
Self-reported ARV Adherence	≥ 95%	36	3	39
	< 95%	5	4	9
	Total	41	7	48

The prevalence ratio =1.66, the probability of having a viral load <1000 copies/ml is 1.66 times higher for those patients with ≥95% ARV adherence than those with < 95% ARV adherence.

When Mantel-Haenszel test was applied at the 12 month time point, the odds of a viral load of >1000 copies/ml and a self-reported dose adherence of <95% had a value of 2.262 (CI: 0.497-4.027), P=0.023.

5. DISCUSSION

This study sought to determine viral load distribution and self-reported dose adherence to first-line HAART at two time points (6 and 12 months after initiation of HAART therapy). Futhermore, the study sought to characterize and compare adult patient virological outcome at 6 months and 12 months time points. The exclusion criteria was based on treatment substitute or switch and reported pregnancy. The completeness of data is the first topic of discussion in the following section.

5.1 *Completeness of data*

The completeness of baseline data variables for categorized eligible records ranged from 88.5% (CD4 count at the 12 months in records with a viral load result) to 100% for sex, age and treatment supporter variables. The completeness levels showed that the categorization of records into those with 6 months and 12 months viral load result did not introduce a selection bias based on level of completeness. The high level of completeness (>80 %) may also indicate rigor being placed in data completeness at initiation of ARV therapy. The rigor in completeness of data seems to have been lost in the treatment monitoring stage as indicated by the recommended follow up of a 6 month viral load only having 178 eligible records. This may be attributed to workload pressure on the healthcare worker despite use of the structured patient care booklet. Unfortunately, the level of completeness of data may impact negatively on site monitoring and national planning (Makombe *et al*, 2008).

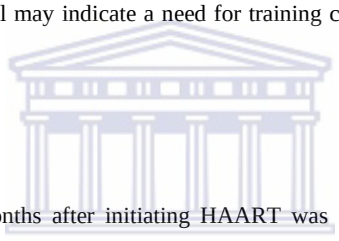
5.2 ***Baseline characteristics of study participants***

The baseline characteristics of the eligible patients at initiation of therapy showed that the uptake of the ARV therapy at Katutura Health Centre is balanced between the sexes (53% male). Most patients, 72% had a treatment supporter. However a clear population of 28% was initiated on ARV therapy despite lack of one. The initiation of patients without a treatment supporter is a reflection of the implementation of the ARV guidelines which recommend that lack of a treatment supporter should not be the sole reason for denying therapy (MOHSSa, 2008).

The WHO staging shows initiation of ARV therapy being most frequent at stage 1 (37%), but with stage 2 (20%) and stage 3 (23%) initiation being comparable. The WHO stage 4 has the lowest rate (16%) of initiation of ARV therapy. The reported WHO stages of initiation of therapy showed that most patients are initiated before they reach stage 4 is ideal for delay of HIV progression. While 4% did not have a WHO stage recorded, this may be an effect of medical record data completeness. When the eligibility criteria for initiation is analysed it is clear that most patients (68%) were HAART-initiated based on CD4 count and clinical picture (WHO staging). This may account for the comparable initiation of ARV therapy at WHO stages 2 and 3. The baseline CD4 count had a median of 154 (IQR: 80 to 192) cells/mm^3 which correlates well with the MOH guidelines of using 200 cells/mm^3 as a cutoff. Even though a median weight of 57 kg is reported, BMI would have been a better indicator as it takes into account gender variability of weight.

5.3 The distribution of viral load results at the two time points (6 and 12 months) after initiation of therapy

Of the 508 eligible records 35% had a viral load result at 6 months and only 12% had viral load results at 12 months. The majority of recorded viral load results were at 6 months which is in keeping with MOHSS guidelines to test for viral load at 6 months (MOHSSa, 2008; MOHSS, 2005). However, despite the MOH recommendations, the uptake of virological monitoring was only 35%. The low uptake of the viral load tool may indicate a need for training clinicians in the use of virological monitoring.



The distribution of viral load at 6 and 12 months after initiating HAART was summarized in categories. These categories were chosen due to the detection limit of the assay, viral load distribution variation in different settings and the "blip" phenomenon (Madge *et al*, 2008; Phillips *et al*, 2008; WHO, 2000;. San Lio *et al*, 2008). The viral load distribution showed 57% of records had undetectable copies/ml at 6 months versus 31% of records at 12 months. Then 88% of records had < 400 copies/ml at 6 months and 70% of records at 12 months. When the 1000 copies/ml cut off was applied, 92% of records had <1000 copies/ml at 6 months and 88% of records at 12 months. The viral load distribution findings in this study are different from an earlier report by Madge *et al* (2008) where 92% of patients on therapy for more than 16 weeks had a viral load of <50 copies/ml (Madge et al, 2008). It must be noted however that the study of Madge *et al* (2008) was carried out in a resource unlimited setting. The resource setting may account for the greater number of patients with suppressed viral load.

The viral load distribution findings indicate that the more conservative thresholds for viral load suppression of 400 copies/ml or 1000 copies/ml may need to be used in Namibia instead of the assay detection limit of 40 copies/ml. Madge *et al* (2008) and Phillips *et al* (2008) have already proposed the use of a conservative viral load threshold of 400 copies/ml to accommodate the "blip" phenomenon. Moreover other studies have already shown that the "blip" phenomenon does not warrant therapy change (Havlir *et al*, 2001; Lee, Keiffer, Siliciano and Nettles, 2006). In a study carried out in Mozambique the outcome of virological failure was placed at a viral load threshold of 1000 copies/ml (San Lio *et al*, 2008) versus the more stringent level of the detection limit of the assay. Thus, based on the current study findings and previous study findings there is evidence for the feasibility of using the more conservative thresholds.

There was at tendency for lower viral load results at 12 months compared to 6 months but the results did not reach statistical difference, P=0.092. Lower viral load results are expected in patients that are on successful ARV therapy as the goal of ARV therapy is undetectable viral load (WHO, 2000). A prospective study to follow the virological outcomes of patients on ARV therapy is required to determine possible confounders to obtaining undetectable viral load after initiation of therapy.

5.5 The self-reported ARV dose adherence levels to first line ARV therapy at two time points (6 and 12 months)

A high level of self-reported ARV dose adherence was observed at the two time points: 84% at 6 months and 88% at 12 months for ≥ 95% of medications taken in the past three days. The self-reported dose adherence findings dispel concerns of Stevens, Kay and Corrah, (2004), since rapid access to ARV therapy in Namibia did not led to poorly adhered to treatment regimens not clear what you mean. The high adherence levels of patients initiated on ARV therapy in 2007 is encouraging increased ARV therapy rollout using the current guidelines. The presence of good adherence levels are in agreement with findings from Mills et al, (2006) meta-analysis of adherences studies in Africa. Their study showed adherence levels of 77.1%. However, the higher adherence findings of the current study may be due to the overestimation of the self-reported dose adherence measure (Liu et al, 2006). Unfortunately the exact margin of overestimation is not known and thus highlights why adherence measurements are less objective than virological monitoring (Garcia *et al*, 2006).

The sustainability of good ARV dose adherence is a challenge with many determinants ((Pinheiro, de-Carvalho-Leite, Drachler and Silveira, 2002; Amberbir *et al*, 2008; Gordillo, del Amo, Soriano and Gonzalez-Lahoz, 1999; Duong *et al*, 2001; Bonolo *et al*, 2005; Nilsson *et al*, 2006; Weiser *et al*, 2003; Laniece *et al*, 2003). The determinants of adherence in the current study were only incorporated as far the scope allowed. Hence a comprehensive study of determinants of ARV therapy adherence in Namibia would be invaluable.

5.6 The description of patients with viral load ≥400 copies/ml at the 6 and 12 months.

The study showed that poor virological outcome of a viral load≥400 copies/ml was significantly associated at 6 months and 12 months with self-reported prophylaxis adherence and self-reported ARV dose adherence. Thus self-reported prophylaxis adherence and self-reported ARV dose adherence are predictors of poor virological outcome at both 6 and 12 months time points. The lack of change in determinants of adherence at the two time points is in disagreement with the findings by Amberbir *et al* (2008). The study findings agree with those of Chi *et al* (2009) and San Lio *et al* (2008) who reported that individuals >35 years of age or reported social support (an adherence buddy) were less likely to exhibit poor clinical outcome. However, it must be highlighted that the definition of poor virological outcome for San Lio *et al* (2009) was a viral load >1000 copies/ml.

Fielding *et al* (2008) reported poor virological outcome of a viral load ≥400 copies/ml at 12 months to be associated with older age, lower weight, <1 log decrease in viral load at six weeks, WHO stage 3 and 4, baseline viral load at baseline > 100000 copies/ml and site of ARV therapy delivery. The current study found no association with age. Unfortunately the other factors found to be associated with poor virological outcome by Fielding *et al* (2008), log decrease at 6 weeks and baseline viral load were not determined in this study as they are not accessed in the Namibian setting.

Cross-tabulation of virological response and self-reported dose adherence at 6 and 12 months was done. The prevalence ratio shows the probability of a viral load of <400 copies/ml with ≥95% self-reported adherence increasing from 1.66 times at 6 months to 7.15 times at 12 months. However the prevalence ratio does not show a dramatic increase when a threshold of <1000 copies/ml is used, with values of 1.36 times at 6 months and 1.66 at 12 months. The odds of a viral load >400 copies/ml or >1000 copies/ml, when self –reported ARV adherence is < 95% , shows significant association at 6 months and 12 months, P<0.05. Thus the study findings are consistent with those of San Lio et al (2008).

5.7 *Study limitations*

The measurement of adherence is difficult. Even though self-reporting of >95% of medication in the past three days is widely used it has been shown to overestimate adherence levels (Liu *et al*, 2006). The assessment of causal relationships was limited due to use of a retrospective approach that is associated with limitations such as selection bias, missing or incomplete information (Peterson *et al*, 2007). Though the completeness of the data was not guaranteed, based on the limited studies done an increased level of completeness was expected due to the use of a structured format for patient consultations. The quality of the data was expected to be of good quality since two senior clinicians are stationed at this site. The study findings are limited to the study setting.

6. CONCLUSION

The distribution of viral load results showed that 35% of the 508 eligible records initiated on ARV therapy in 2007 had a viral load result taken at 6 month time versus 12% of the 508 eligible records at 12 months. This reflects a low uptake of the virological monitoring tool recommended for an ARV therapy patient management at 6 months. Based on viral load distribution patterns a conservative viral load threshold of 400 copies/ml (or 1000 copies/ml) may need to be used for virological response assessment in the Namibian setting. The current adherence level of >80% self-reported dose adherence for patients initiated on ARV therapy encourages increased ARV therapy rollout using the current guidelines. Poor virological outcome of viral load ≥400 copies/ml was associated with lower self-reported prophylaxis adherence and self-reported ARV dose adherence at 6 and 12 months. Thus self-reported adherence is a predictor of poor virological outcome at both 6 and 12 months time points.

7. RECOMMENDATIONS

The following recommendations are drawn from this study:

- ✓ Due to poor uptake of virological monitoring as a tool, training of clinicians in the use of this tool is recommended.
- ✓ A conservative viral load threshold of 400 copies/ml or 1000 copies/ml should be used for virological response assessment in the Namibian setting.
- ✓ Self-reported ARV dose adherence may be used as a predictor of poor virological outcome at 6 and 12 months.
- ✓ A prospective study to determine predictors of poor virological outcome and adherence and possible confounders is encouraged.

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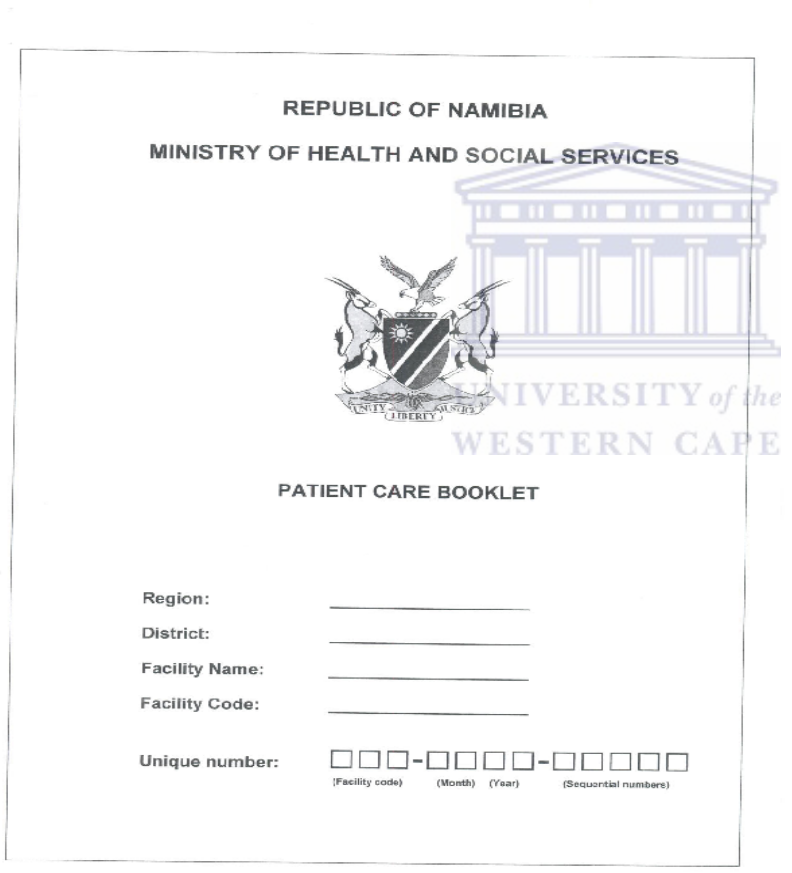
APPENDICES

Appendix 1: Patient Care Booklet



REPUBLIC OF NAMIBIA

MINISTRY OF HEALTH AND SOCIAL SERVICES

PATIENT CARE BOOKLET

Region: _____

District: _____

Facility Name: _____

Facility Code: _____

Unique number: ☐☐☐-☐☐☐☐-☐☐☐☐☐

(Facility code) (Month) (Year) (Sequential numbers)

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HIV CARE / ART CARD

Patient Unique # □□□-□□□□-□□□□□
(Facility code) (Month) (Year) (Sequential numbers)

Name _____ Health Passport # _____

Sex: M ☐ F ☐ Age _____ DOB _____ Marital status _____

Physical Address _____

Telephone (whose): _____

Prior ART:
- ☐ Transfer in with records
- ☐ Earlier ARV but not a transfer in
- ☐ PMTCT Date...../.../..... Regimen.....
- ☐ PEP
- ☐ None

Care entry point:
- ☐ PMTCT
- ☐ Medical
- ☐ Under5
- ☐ TB
- ☐ STI
- (Outpatient)
- ☐ Private/Co
- ☐ Inpatient
- ☐ IDU
- ☐ Adol
- ☐ Sex
- (Outreach)
- ☐ Self-refer
- ☐ CBO
- ☐ Other:

Treatment supporter/med pick-up if ill: _____

Physical Address: _____

Telephone (whose): _____

Home-based care provided by: _____

Names of close family members and partners (Relation)	Age	HIV +/- DK	HIV care Y/N DK	Unique no.

Medicine allergies:

ART treatment interruptions

Stop Lost (circle)	Date	Why	Date if Restart:
Stop Lost			
Stop Lost			
Stop Lost			
Stop Lost			
Stop Lost			

Date (dd/mm../y) — **Circle / tick**

_____ Confirmed HIV+ test — HIV 1 2 Ab / PCR (if < 18 mo)

_____ Enrolled in HIV care

COHORT:

ARV therapy

_____ Medically eligible Clinical stage____

Why eligible: ☐Clinical only ☐CD4_____ ☐Clinical & CD4_____

_____ Medically eligible *and* ready for ART

_____ Transferred in Facility Name: _____

_____ ART started

_____ **Start ART 1st-line initial regimen:** _____

At start ART: Weight _____ Function_____
Clinical stage_____ CD4_____

1st-line

Substitute within 1st-line:

_____ New regimen_____ Why_____

_____ New regimen_____ Why_____

2nd-line

Switch to 2nd-line (or substitute within 2nd-line):

_____ New regimen_____ Why_____

_____ New regimen_____ Why_____

_____ New regimen_____ Why_____

_____ **Transferred out** To where: _____

_____ If previous TB treatment within last two years: write **End Date**

_____ **Died**

Why STOP codes:
1 Toxicity/side effects
2 Pregnancy
3 Treatment failure
4 Poor adherence
5 Illness, hospitalization
6 Drugs out of stock
7 Patient lacks finances
8 Other patient decision
9 Planned Rx interruption
10 Other

Why SUBSTITUTE or SWITCH codes:
1 Toxicity/side effects
2 Pregnancy
3 Risk of pregnancy
4 Due to new TB
5 New drug available
6 Drug out of stock
7 Other reason (specify)

Reasons for SWITCH to 2nd-line regimen only:
8 Clinical treatment failure
9 Immunologic failure

HIV CARE / ART CARD

Patient Unique # □□□-□□□□-□□□□□

Name

Date Check if scheduled. Write in alternate pick-up if ill	Follow-up date	Duration in months since first starting ART	Duration in months since starting current regimen	Wt **If child write height**	If Pregnant EDD? PMTCT? FP/no FP If FP write method(s)	Function Work Amb Bed	WHO clinical Stage (Pre-ART=1,2,3,4, ART=T1, T2, T3, T4)	TB status (Use STOP if terminating Rx)	Possible Side Effects (Experienced & reported by patient)	New OI, Other Problems	Cotri-moxazole (Use STOP if terminating Rx)			Other meds prescribed	**ARV medicine** (Use STOP if terminating Rx)			Other Lab results	Refer or consult or link/ provide If hospitalized, # of days (include reason for hospitalisation)	Dr/Nurse Signature
											Adherence	Dose	No days prescribed		Adherence	Regimen	Duration			
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HIV CARE / ART CARD

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LABORATORY RESULTS

Date	/ /	/ /	/ /	/ /	/ /	/ /	/ /	/ /	/ /	/ /	/ /	/ /
CD4												
HB												
ALT												
Viral Load												

Pregnancy/family planning status if woman is of childbearing age:
P = Pregnant
If pregnant, give estimated due date (EDD) and write PMTCT if referred to PMTCT
FP= Not pregnant and on family planning
If using FP, note methods (note: more than 1 method may be recorded)
No FP = Not pregnant and not using FP

Codes for TB status (check on each visit):
No signs = no signs or symptoms of TB
TB refer = TB suspected and referred for evaluation
INH = currently on INH prophylaxis (IPT)
TB Rx = currently on TB treatment. Record TB card #
Sputums = TB suspected and sputum sample sent or record results

Codes for potential side effects or other problems:
Nausea
Diarrhoea
Fatigue
Headache
BN burning/numb/tingling
Rash
Anaemia
ABdominal pain
Jaundice
FAT changes
CNS: dizzy, anxiety, nightmare, depression
LD Lactic Acidosis
Other_____

Codes for new OI or other problems:
Zoster
Pneumonia
DEmential/**Enceph**
Thrush oral/vaginal
FEVER
COUGH
DB difficult breathing
IRIS Immune reconstitution inflammatory syndrome
Weight loss
UD urethral discharge
PID pelvic inflammatory disease
GUD genital ulcer disease
Ulcers–mouth
Other _____

Codes for why poor/ fair adherence:
1 Toxicity/side effects
2 Share with others
3 Forgot
4 Felt better
5 Too ill
6 Stigma, disclosure or privacy issues
7 Drug stock out—dispensary
8 Patient lost/ran out of pills
9 Delivery/travel problems
10 Inability to pay
11 Alcohol
12 Depression
13 Lack of food
14 Other_____

Codes for ART/CTX adherence. Estimate adherence for twice daily ART using the table below:

Adherence	%	Missed doses per month
G(good)	≥ 95%	≤ 3 doses
F(fair)	85-94%	4-8 doses
P(poor)	< 85%	≥ 9 doses

HIV CARE / ART CARD

	Follow-up education, support and preparation for ARV therapy		
	Date / Comments	Date / Comments	Date / Comments
Educate on basics, prevention and disclosure.			
Basic HIV education, transmission			
Prevention: abstinence, safer sex, condoms			
Prevention: household precautions, what is safe			
Post-test counseling: implications of results			
Positive living			
Testing partners			
Disclosure			
To whom disclosed (list)			
Family/living situation			
Shared confidentiality			
Reproductive choices, prevention MTCT			
Progression, Rx			
Child's blood test			
Progression of disease			
Available treatment/prophylaxis			
Follow-up appointments, clinical team			
ART preparation.....initiation.....support, monitor....			
CTX, INH prophylaxis			
ART -- educate on essentials (locally adapted)			
Why complete adherence needed			
Adherence preparation, indicate visits			
Indicate when READY for ART: DATE/result Clinical team discussion			
Explain dose, when to take			
What can occur, how to manage side effects			
What to do if one forgets dose			
What to do when traveling			
Nutritional information			
Adherence plan (schedule, aids, explain diary)			
Treatment supporter preparation			
Which doses, why missed			
ARV support group			
Home-based care, support			
How to contact clinic			
Symptom management/palliative care at home			
Caregiver booklet			
Home-based care -- specify			
Support groups			
Community support			

HIV CARE / ART CARD

Patient Unique # □□□-□□□□-□□□□□

Name_____

ADDITIONAL CLINICAL NOTES

DATE	NOTES

Appendix 2: Frequency and use of HIV viral load

CLINICAL INDICATION	INFORMATION	USE
Syndrome consistent with acute HIV infection	Establishes diagnosis when HIV antibody is negative or indeterminate	diagnosis
Initial evaluation of newly diagnosed HIV infection	Baseline viral load set point	Use as baseline information
Every 3-4 months in patients not on therapy	Changes of viral load	Use as continued monitoring or baseline value if therapy is to be initiated
2-8 weeks of initiation or change of therapy	Initial assessment of drug efficacy	Decision to continue or change therapy
3-4 months after start of therapy	Assessment of virologic effect of therapy	Decision to continue or change therapy
Every 3-4 months for patients on therapy	Durability of antiretroviral effect	Decision to continue or change therapy
Clinical event or significant decline in CD4 T-cells	Association with changing or stable viral load	Decision to initiate, continue or change therapy

Appendix 3: Data collection tool

Demographics

UNIQUE NUMBER	SEX	AGE	DATE OF BIRTH	Tx SUPPORTER

Treatment Profile

UNIQUE NUMBER	PRIOR ART	DATE CONFIRMED	DATE ENROLLED	ENRTY WHO STAGE	ELIGIBLITY	START ART DATE	START WEIGHT

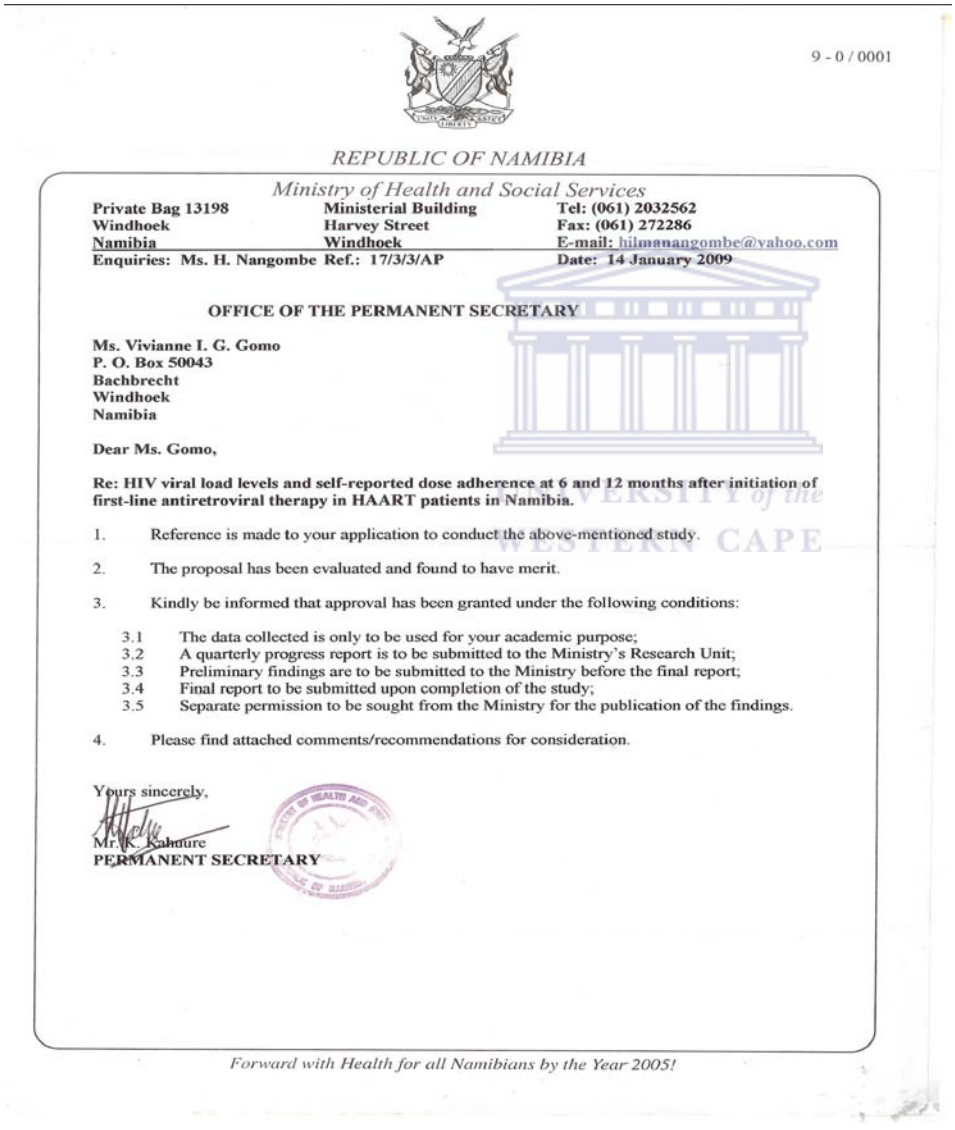
START WHO STAGE	START CD4	SUB IN IST LINE	SUB IN IST LINE CODE	SUB IN 1ST LINE DATE	SWITCH LINE	SWITCH DATE

Characteristics

UNIQUE NUMBER	Weight		WHO Stage		TB		New OI	
	6months	12months	6months	12months	6months	12months	6months	12months

ARV adherence		Viral load		CD4		Adherence Cotri Tx		Pregnancy	
6months	12months	6months	6months	12months	6months	6months	12months	6months	12months

Appendix 4: Namibian Ministry of Health and Social Services Ethical Clearance



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REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198 **Ministerial Building** **Tel: (061) 2032562**
Windhoek **Harvey Street** **Fax: (061) 272286**
Namibia **Windhoek** **E-mail: hilmannangombe@yahoo.com**
Enquiries: Ms. H. Nangombe Ref.: 17/3/3/AP **Date: 14 January 2009**

OFFICE OF THE PERMANENT SECRETARY

Ms. Vivianne I. G. Gomo
P. O. Box 50043
Bachbrecht
Windhoek
Namibia

Dear Ms. Gomo,

Re: HIV viral load levels and self-reported dose adherence at 6 and 12 months after initiation of first-line antiretroviral therapy in HAART patients in Namibia.

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. Kindly be informed that approval has been granted under the following conditions:

   3.1 The data collected is only to be used for your academic purpose;
   3.2 A quarterly progress report is to be submitted to the Ministry's Research Unit;
   3.3 Preliminary findings are to be submitted to the Ministry before the final report;
   3.4 Final report to be submitted upon completion of the study;
   3.5 Separate permission to be sought from the Ministry for the publication of the findings.

4. Please find attached comments/recommendations for consideration.

Yours sincerely,

Mr. K. Kahuure
PERMANENT SECRETARY

Forward with Health for all Namibians by the Year 2005!

Appendix 5: University of the Western Cape Higher Degrees Committee Ethical Clearance