CORRELATION BETWEEN CD4 CELL COUNTS AND ADHERENCE TO
ANTIRETROVIRALS IN TREATMENT EXPERIENCED PATIENTS AT
KATUTURA INTERMEDIATE HOSPITAL, WINDHOEK, NAMIBIA

by

Ms Dinah Jorokee Tjipura

Submitted in fulfilment of the requirements
for the

Master of Public Health (MPH)
in the
Department of Health Studies
at the

UNIVERSITY OF SOUTH AFRICA

SUPERVISOR: Dr VJ EHLERS

JOINT SUPERVISOR: Dr JH ROOS

November 2006
Student number: 349-663-07

DECLARATION

I declare that CORRELATION BETWEEN CD4 CELL COUNTS AND ADHERENCE TO ANTIRETROVIRALS IN TREATMENT EXPERIENCED PATIENTS AT KATUTURA INTERMEDIATE HOSPITAL, WINDHOEK, NAMIBIA is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any other degree at any other institution.

........................................
DINAH JOROKEE TJIPURA (MS)

........................................
DATE

616.9792096881 TJIP
The study analysed and compared data from patients' medical and pharmacy refill records to identify correlations between CD4 cell counts and adherence to antiretroviral drugs at Katutura Intermediate Hospital (KIH) in Windhoek, Namibia. The study investigated whether the pharmacy refill adherence measurement methodology could predict immunological recovery through increased CD4 cell counts. There was a positive but weak relationship between adherence and CD4 cell counts. Although the pharmacy refill records could predict immunological response it was not sensitive enough and should be used in combination with other adherence measurement tools.

Key words
Adherence to anti-retrovirals (ARVs), ARV pharmacy records, barriers to ARV adherence, CD4 cell counts, highly active anti-retroviral treatment (HAART), HIV/AIDS treatment, measurement of adherence.
ACKNOWLEDGEMENTS

First and foremost, I praise God the Almighty for giving me the strength and wisdom to complete this study.

I would also like to give my appreciation to the following people for their invaluable and unending support:

- Prof VJ Ehlers and Dr JH Roos, for their tireless guidance, support and the knowledge and skills they passed on to me. I am immensely indebted to both of you.
- The Permanent Secretary of the Ministry of Health and Social Services (Namibia) for allowing me to use the data from the hospital, the Senior Medical Superintendent of the KIH, staff of the KIH ART clinic and ARV pharmacy.
- My family for their encouragement, support and believing in me.
- My colleagues and friends for their invaluable contributions.
- Professor Mahindi for his assistance with data analysis and interpretation of statistics.

To you all please accept my sincere gratitude, appreciation and love and I wish you all strength in your endeavours.
DEDICATION

I dedicate this dissertation to my dear parents Samuel Adam (late) and Godfriedine Tjipura, my lovely sons Vekondja and Metarere.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>CHAPTER 1</th>
<th>INTRODUCTION AND BACKGROUND</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>INTRODUCTION</td>
</tr>
<tr>
<td>1.2</td>
<td>BACKGROUND INFORMATION</td>
</tr>
<tr>
<td>1.3</td>
<td>RESEARCH PROBLEM</td>
</tr>
<tr>
<td>1.4</td>
<td>RESEARCH QUESTIONS</td>
</tr>
<tr>
<td>1.5</td>
<td>PURPOSE OF THE STUDY</td>
</tr>
<tr>
<td>1.6</td>
<td>RESEARCH PURPOSE AND OBJECTIVES</td>
</tr>
<tr>
<td>1.7</td>
<td>ASSUMPTIONS UNDERLYING THE STUDY</td>
</tr>
<tr>
<td>1.8</td>
<td>SIGNIFICANCE OF THE STUDY</td>
</tr>
<tr>
<td>1.9</td>
<td>RESEARCH METHODOLOGY</td>
</tr>
<tr>
<td>1.9.1</td>
<td>Study design</td>
</tr>
<tr>
<td>1.9.2</td>
<td>Research setting</td>
</tr>
<tr>
<td>1.9.3</td>
<td>Research population</td>
</tr>
<tr>
<td>1.9.4</td>
<td>Data collection instrument</td>
</tr>
<tr>
<td>1.9.5</td>
<td>Data collection</td>
</tr>
<tr>
<td>1.9.6</td>
<td>Data analysis</td>
</tr>
<tr>
<td>1.9.7</td>
<td>Ethical considerations</td>
</tr>
<tr>
<td>1.9.7.1</td>
<td>Anonymity and confidentiality</td>
</tr>
<tr>
<td>1.9.7.2</td>
<td>Ethical approval</td>
</tr>
<tr>
<td>1.10</td>
<td>SCOPE AND LIMITATIONS OF THE STUDY</td>
</tr>
</tbody>
</table>
CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

2.2 ADHERENCE TO ARVs

2.2.1 Defining adherence

2.2.2 Scope of the problem

2.2.3 Role of adherence to ARVs in HIV/AIDS

2.2.4 The relationship between adherence and treatment outcomes

2.2.5 Factors affecting adherence to ARVs

2.2.6 Measuring adherence

2.2.6.1 Self reports

2.2.6.2 Pill counts

2.2.6.3 Pharmacy refill records

2.2.6.4 Electronic devices
CHAPTER 3
RESEARCH METHODOLOGY

3.1 INTRODUCTION

3.2 STUDY DESIGN

3.2.1 Descriptive

3.2.2 Retrospective

3.2.3 Quantitative

3.2.4 Cohort

3.3 RESEARCH METHOD

3.3.1 The research population

3.3.2 Research setting

3.4 DATA COLLECTION

3.4.1 The research instrument

3.4.2 Data collection procedures

3.4.3 Data management

3.4.4 The use of routine data

3.4.4.1 Advantages of using routine data
CHAPTER 4
DATA ANALYSIS AND DISCUSSION OF RESEARCH RESULTS

4.1 INTRODUCTION 63

4.2 DEMOGRAPHIC DATA 64

4.2.1 Gender 65

4.2.2 Age at previous birthday 67

4.2.3 Educational levels 70

4.2.4 Type of employment 72

4.2.5 Residence type 74
4.2.6 Persons chosen to support the patient with ART

4.3 CLINICAL DATA

4.3.1 Current use of TB medicines

4.3.2 CD4 cell count values

4.4 ANTI-RETROVIRAL THERAPY DATA

4.4.1 WHO HIV/AIDS status

4.4.2 Current ARV therapy

4.5 ADHERENCE LEVEL

4.6 CORRELATION BETWEEN ADHERENCE AND CD4 CELL COUNTS

4.7 ASSESSMENT OF THE PHARMACY REFILL ADHERENCE MEASUREMENT METHODOLOGY

4.8 CONCLUSION

CHAPTER 5
CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

5.1 INTRODUCTION

5.2 OBJECTIVES

5.3 LIMITATIONS OF THE STUDY

5.4 RECOMMENDATIONS FOR IMPROVING ADHERENCE TO ARVS AT KIH
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table 4.1</th>
<th>Baseline characteristics and profile of patients</th>
<th>64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 4.2</td>
<td>Gender versus adherence</td>
<td>66</td>
</tr>
<tr>
<td>Table 4.3</td>
<td>Relationship between adherence and age</td>
<td>69</td>
</tr>
<tr>
<td>Table 4.4</td>
<td>Level of education attained</td>
<td>71</td>
</tr>
<tr>
<td>Table 4.5</td>
<td>Type of employment</td>
<td>73</td>
</tr>
<tr>
<td>Table 4.6</td>
<td>Type of residence</td>
<td>75</td>
</tr>
<tr>
<td>Table 4.7</td>
<td>Baseline CD4 cell count versus most recent CD4 cell count</td>
<td>82</td>
</tr>
<tr>
<td>Table 4.8</td>
<td>Adherence levels</td>
<td>87</td>
</tr>
<tr>
<td>Table 4.9</td>
<td>Correlations between adherence, age, baseline CD4 cell count, most recent CD4 cell count</td>
<td>89</td>
</tr>
<tr>
<td>Table 4.10</td>
<td>Relationship of adherence to most recent CD4 cell count</td>
<td>91</td>
</tr>
<tr>
<td>Table 4.11</td>
<td>Post treatment adherence versus CD4 cell count</td>
<td>91</td>
</tr>
<tr>
<td>Table 4.12</td>
<td>Adherence versus mean most recent CD4 cell count</td>
<td>96</td>
</tr>
<tr>
<td>Table 4.13</td>
<td>Validity for predicting CD4 ≥200</td>
<td>96</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Figure 4.1</td>
<td>Relationship between adherence and gender</td>
<td>66</td>
</tr>
<tr>
<td>Figure 4.2</td>
<td>Relationship between adherence and age</td>
<td>70</td>
</tr>
<tr>
<td>Figure 4.3</td>
<td>Relationship between adherence and level of education</td>
<td>72</td>
</tr>
<tr>
<td>Figure 4.4</td>
<td>Relationship between adherence and type of employment</td>
<td>74</td>
</tr>
<tr>
<td>Figure 4.5</td>
<td>Relationship between adherence and type of residence</td>
<td>76</td>
</tr>
<tr>
<td>Figure 4.6</td>
<td>Relationship between adherence and treatment supporter</td>
<td>77</td>
</tr>
<tr>
<td>Figure 4.7</td>
<td>Patients currently using TB medicines</td>
<td>79</td>
</tr>
<tr>
<td>Figure 4.8</td>
<td>Scattergram: CD4 cell count baseline versus most recent CD4 cell count</td>
<td>81</td>
</tr>
<tr>
<td>Figure 4.9</td>
<td>Relationship between adherence and WHO HIV/AIDS stage</td>
<td>83</td>
</tr>
<tr>
<td>Figure 4.10</td>
<td>ARV regimen changes</td>
<td>84</td>
</tr>
<tr>
<td>Figure 4.11</td>
<td>Reasons for change of ARV regimens</td>
<td>86</td>
</tr>
<tr>
<td>Figure 4.12</td>
<td>Relationship of adherence to CD4 cell count</td>
<td>90</td>
</tr>
</tbody>
</table>
List of annexures

Annexure A: Letter to the MoHSS requesting permission to conduct the study
Annexure B: Letter of approval from the MOHSS granting permission to conduct the study
Annexure C: Ethical clearance from UNISA
Annexure D: Map of Namibia
Annexure E: Checklist used for data collection
Annexure F: Completed checklist
Annexure G: Letter from statistician
CHAPTER 1
INTRODUCTION AND BACKGROUND INFORMATION

1.1 INTRODUCTION

Acquired Immune Deficiency Syndrome (AIDS) was recognised in 1981 and it is caused by the Human Immune-deficiency Virus (HIV). HIV can be spread through sperm cells, blood, breast milk and vaginal secretions. Unprotected sexual intercourse is the most common route of HIV transmission (WHO 2006a:23). According to Grossman, Meier-Schellersheim, Paul and Picker (2006:289), untreated HIV infection leads to a gradual decline in the number of circulating CD4 T lymphocytes and then culminates in AIDS. Therefore, AIDS is viewed as a tale of two infections: the acute infection in which the virus depletes the mucosal CD4 cells and the chronic infection where the wounded immune system slowly dies.

According to the WHO (2006a:23), AIDS can kill because the infected individual’s immune system is unable to fight infections. The effect of the human immune deficiency (HI) virus on an individual can be detected by measuring the number of CD4 cells in the blood stream or the viral load. Viral load is defined as the number of the HI virus in the blood stream. A healthy individual has a CD4 cell count of about 1000 cells/mm$^3$ and once it falls, the individual is likely to suffer from various infections unless he/she is treated with anti-retrovirals
(ARVs). There are many types of ARVs and they attack the virus in different ways. Therefore treatment involves a combination of ARVs (WHO 2006a:26). The standard treatment for HIV infection was changed from single and dual therapies, to treatments containing three or more ARVs in order to reduce the possibility of HIV becoming resistant to ARVs. These combination therapies are referred to as highly active anti-retroviral therapy (HAART) (Population Briefs 2005). At the end of 2001, it was estimated that 40 million people in the world had HIV/AIDS. Of this estimate, 70% were from Sub-Saharan Africa (SSA), where only 10% of the world’s population lives (Buve, Bishikwabo-Nsarhaza & Mutangadura 2002:2011). According to Asamoah-Odei, Calleja and Boerma (2004:35), antenatal clinics have been the main source of data for national estimates in SSA since the 1980s.

In 2005 the epidemic appeared to have slowed down globally but new infections continue to increase. An estimated 38.6 million people are living with HIV/AIDS of which approximately 4.1 million became newly infected with HIV while about 2.8 million died during 2005 (The Body 2006). The estimate of people living with HIV in the 14 member states of the Southern African Development Community (SADC) was 15 million in 2005 and represented about 38% of the total number of people living with HIV in the world. There were 1.5 million new infections in 2005 in the SADC countries, representing 36.5% of all new HIV infections globally (SADC 2006:4).
The first four cases of HIV/AIDS in Namibia were recorded in 1986 and by December 2003 a cumulative number of 136,068 HIV/AIDS cases had been recorded (Ministry of Health and Social Services (MoHSS) 2004a:1). In 1992, the MoHSS started with the sentinel surveys among pregnant women who visited antenatal clinics to get an estimate of HIV infected people and the prevalence rate was 4.2% (MoHSS 2004b:10). This bi-annual sentinel survey has been showing steady increases but in 2004 the HIV prevalence rate dropped from 22.2% in 2002 to 19.7%. The average prevalence rate at Katutura Intermediate Hospital (KIH) in Windhoek was 22% in 2004 and that was a decrease from 27% recorded in 2002 (MoHSS 2004b:11).

The Government of the Republic of Namibia (GRN) established the National AIDS Control Programme (NACOP) to coordinate and manage the first medium term plan (MTP 1) (MoHSS 2004a:10). During 2006 the MTP III has been developed and implemented with various strategies to reduce the epidemic. In order to achieve the objective of component three ("Access to treatment, care and support services") of the national strategic plan on HIV/AIDS (MoHSS 2004a:55), the MoHSS introduced the provision of HAART at Katutura and Oshakati Intermediate Hospitals as pilot sites, during 2003. By the end of November 2005, HAART had been scaled up and was provided at four referral hospitals and all 30 district hospitals during April 2007 (when data were collected for this study), an increase from only seven health facilities in 2003. Utilisation of HAART has been on the increase since its inception with a monthly enrolment
currently exceeding 1,200 new patients during 2006. By the end of November 2005, about 14,400 HIV/AIDS patients had been put on HAART in the public sector in Namibia (MoHSS 2005a:19). Of that total, approximately 2,600 patients were receiving HAART at KIH at the end of November 2005 (MoHSS 2005b:6).

Fogarty, Roter, Larson, Burke, Gillespie and Levy (2002:95), indicated that the introduction of HAART in 1996, qualitatively changed the HIV clinical landscape. HAART proved to be highly effective in clinical trials by decreasing HIV viral loads often to undetectable levels and substantially reducing HIV related morbidity and mortality rates. The goal of HAART therefore is to suppress the viral load to an undetectable level for as long as possible and significantly elevate the CD4 cell counts (Fogarty et al 2002:93; Katzenstein, Lyons, Molaghan, Ungvarski, Wolfe & Williams 1997:48; Palela, Delaney, Moorman, Loveless, Fuhrer, Satten, Aschman & Holmberg 1998:853; Splete 2005). The most commonly used ARVs are from these three classes: the nucleoside analogue reverse transcriptase inhibitors (NRTIs), the non-nucleoside analogue reverse transcriptase inhibitors (NNRTIs) and the protease inhibitors (PIs) (MoHSS 2003:2; WHO 2006a:24).

Although ARVs do not cure HIV/AIDS, they are effective in controlling the virus and can even reduce the level of the virus to a point where it is no longer detectable in the blood. ARVs prevent HIV from multiplying rapidly and also boost the body’s immune system, increasing the length and quality of HIV
positive persons’ lives and enable people to lead full and productive lives (WHO 2006a:26).

While HAART is responsible for significant reductions in morbidity and mortality statistics among HIV/AIDS patients, these therapies are complicated and require high levels of adherence by individual patients (BHIVA/BASHI 2003; Trotta, Ammassari, Melzi, Zaccarelli, Ladisa, Sighinolfi, Mura, Monforte & Antinori 2002:S128). According to Jani (2004:4), since the introduction of ARVs in the early 1990s, experts in this field had already recognised the significance of adherence to treatment and the limitations of HAART due to its complexity in administration and the implications of drug resistance. Altice and Friedland (1998:503), stated that adherence was used interchangeably with compliance and was referred to as the action or quality of being consistent with prescribed medications. Non-adherence might mean not taking medications at all, taking reduced amounts, not taking doses at prescribed frequencies or intervals or not matching medication to food requirements. They argued that there were many factors that have been associated with adherence such as patient characteristics, type of disease, treatment regimen, clinician-patient relationship and clinical setting. Patient characteristics may include knowledge and beliefs about medication, depression, social support and stable living conditions.

According to Ickovics and Meade (2002:S98), adherence is very critical to obtain the full benefits of HAART, including maximal and durable suppression of viral
replication, reduced destruction of CD4 cells, prevention of viral resistance, promotion of immune reconstitution, and slowed progression to AIDS.

When the viral load is high, as is normally the case at the beginning of the therapy, high adherence to ARVs is required. If a patient misses a few doses at this stage, the danger of developing drug-resistant organisms is much higher than it would be after six months of regular treatment because by that time the person is expected to have a lowered viral load than at the commencement of therapy. Adherence to HAART is crucial for the successful treatment of HIV infection and sustained viral control. Adherence rates of 95% or higher are required for optimum viral suppression in order to prevent viral mutation and thus drug resistance (BHIVA/BASHH 2003; Fairly, Permana & Read 2005:368; Jani 2004:9; Ostenberg & Blaschke 2005:488; Paterson, Swindells, Mohr, Brester, Vergis, Squier, Wagener & Singh 2000:27; Saple 2005; Simone, Frick, Pantalone & Turner 2003:185). If an individual develops resistance to ARVs, there are two possible consequences. Firstly, the first line ARVs will become ineffective and the individual will start to suffer from multiple opportunistic infections. Secondly, the individual may transmit the drug-resistant virus to their contacts and when those individuals go for treatment it would be discovered that the virus does not respond to the first line therapy. Once individuals develop resistance to first line ARVs, the only alternative is to change to the second line ARVs which are more expensive and have more serious side effects. (Fogarty et al 2002:93; WHO 2006a:26-27). Therefore, every effort should be made to ensure a high level of
adherence (at least 95%) to the first line ARVs in order to delay the emergence of drug resistance and enable individuals to be treated for many years with first line ARVs.

To test the effectiveness of ARVs in a specific patient, plasma viral load is the test of choice used for monitoring in high income countries but it is very expensive and therefore not routinely used in developing countries. In Namibia, routine viral load (VL) testing is not being carried out, therefore CD4 cell counts and general clinical observations are the cornerstones of determining treatment outcomes. CD4 cell counts are taken at baseline and at six monthly intervals to test the effectiveness of ARVs and/or detect adherence problems (MoHSS 2003:12). Treatment effectiveness is usually noted with immunological recovery. When the virus is sensitive and there is adherence to the treatment, notable improvements in immune functions are usually observed within the first six months of treatment.

This study therefore looked at patients’ medical records to determine if there was a relationship between adherence as determined by pharmacy refills and immunological recovery as reflected in the increases in the CD4 cell counts of patients on HAART at KIH.
1.2 BACKGROUND INFORMATION

When the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) launched the three by five ("3 by 5"-treating three million people by 2005) strategy in December 2003, the baseline data of people receiving ARVs in low and middle income countries was 400,000 and by the end of December 2005, there were about 1.3 million people receiving treatment (WHO 2006b:19).

There was a serious concern about the long-term effectiveness of HAART in resource poor countries of which Namibia is one, because of their high potential for inadequate adherence due to the complexity of treatment regimes resulting in non-adherence and thus the development (mutation) of HIV strains resistant to ARVs. But a study conducted by Weiser, Wolfe, Bangsberg, Thior, Gilbert, Makhema, Keababetswe, Dickenson, Mompati, Essex and Marlink (2003:285) in Botswana (developing country) revealed that adherence rates to ARVs among patients were comparable to those in the developed world. It subsequently became evident that rates of adherence to HIV treatment and therapeutic outcomes were not that different from those seen in developed countries (Friedland, Abdool-Karim, Abdool-Karim, Laloo, Jack, Gandhi & El Sadr 2004:S423).
According to the Namibian anti-retroviral therapy (ART) guidelines (MoHSS 2003:6), adult HIV/AIDS patients are eligible to be put on HAART when they meet the following medical criteria:

- WHO stage IV HIV disease (clinical AIDS), irrespective of CD4 cell counts or
- WHO stages I, II or III HIV disease, with a CD4 cell count below 200 cells/mm³

A patient is not started on HAART on the first hospital visit because the patient should undergo education to maximise adherence. The counselling includes a review of the expected benefits, potential side effects, drug interactions, patient/caregiver partnership and the importance of lifelong commitment to the HAART regimens. The patients are required to come with a treatment supporter who can be a family member, a friend or a peer (MoHSS 2003:7). After the counselling session by the community counsellor, the patients are given appointments to visit the pharmacy for the final counselling session and collection of the ARVs. Though the prescription is for three months, only one month's supplies of ARVs are dispensed at each visit but the patient is informed about the date for his/her next pharmacy visit for ARV supplies. During the first refill, the patient is required to bring back the containers of the ARVs that were issued during the first month. This will assist the pharmacist to count the remaining pills in order to determine if ARVs were indeed taken as prescribed. If
there are problems, counselling is repeated again by the pharmacist or referred either to the community counsellor or social worker (Tenga 2006).

Measurement of adherence to the prescribed regimen is very challenging because information obtained about how well a patient has taken prescribed medicines is usually subjective. There are various methods that have been shown to be of great use in the measurement of adherence. Examples of these methods are patient self reports, pill counts, pharmacy refill records and medication event monitoring systems (MEMS) (Goudge, Ngoma & Schneider 2004:6). The pharmacy records require the patients to use the same pharmacy, which might not be possible at all times because patients travel and/or migrate.

A review of patients’ records in Botswana revealed that there was an average monthly adherence of 83.6%. This adherence rate was found be below the optimal adherence rate of at least 95%, and there was a need to develop strategies to improve adherence to ARVs (WHO 2005:12).

Kangudie, Judman and Van der Veen (2006) reviewed patients’ records on HAART enrolled between September 2003 and December 2005 in Rehoboth Mission Hospital in Namibia. Out of a total of 246 records reviewed, 30 (12.2%) patients defaulted for follow up visits to the pharmacy and the reasons cited were substance abuse and side effects of ARVs.
The researcher wanted to know the accuracy of the pharmacy refill records in measuring adherence to ARVs and how well that correlated with CD4 cell counts. Though various methods are generally available to measure adherence, at KIH the pharmacy refill records are used to identify defaulters. The pill count adherence measurement tool is recommended but it is not routinely used except during the first month of treatment. MEMS are not available and self report forms are also not being used to estimate patients’ adherence to their treatment regimes. Since all patients receive ARVs free of charge, if pharmacy refill is found to be a reliable measure of adherence, it will be a simple tool for use in public health facilities providing HAART in Namibia and possibly also in other SADC and/or resource poor countries.

1.3 RESEARCH PROBLEM

The ART guidelines stipulate that if a patient on HAART misses two consecutive follow up appointments, HAART should be discontinued and these patients are termed as defaulters (MoHSS 2003:7). Between December 2003 and December 2005, 181 patients defaulted at KIH (MoHSS 2005b:11) and in January 2006 more than 300 patients did not collect their ARVs from the pharmacy (KIH ARV pharmacy 2006). By the end of 2005, two years after the implementation of HAART, there were still no documented ways of educating patients on adherence to HAART (MoHSS 2005b:9). There are no standardised ways to
communicate during adherence counselling and no standardisation on interventions that are effective for improving adherence.

1.4 RESEARCH QUESTIONS

The researcher reviewed the patients’ records with the following questions in mind:

- Are pharmacy refill records good predictors of CD4 cell counts?
- Is pharmacy refill an accurate ARV adherence measuring tool?

1.5 PURPOSE OF THE STUDY

The purpose of the study is to determine the relationship between adherence to ARVs as measured by pharmacy refills and immunological recovery as indicated by an increase in CD4 cell counts in treatment experienced patients (aged 18 and older) at KIH.

1.6 RESEARCH PURPOSE AND OBJECTIVES

The overall purpose of the research was to determine the effectiveness of the adherence measurement practices at KIH in predicting CD4 cell counts.
Specific objectives of this study were to:

- determine if there is a correlation between adherence to ARVs as measured by pharmacy refill and CD4 cell counts
- determine if ARV pharmacy refills are effective adherence measurement tools at KIH
- recommend a simple adherence measurement tool at KIH

1.7 ASSUMPTIONS UNDERLYING THE STUDY

The study’s objectives are based on the assumptions that adherence to HAART will be predicted by increases in the CD4 cell counts and adherence is measured by regular collection of ARVs from the pharmacy. The patients who collect their refills regularly and maintain high adherence rates are expected to show immunological recovery as reflected in the increases in the CD4 cell counts. The study will use routinely collected data recorded on patients’ medical records and pharmacy refills as stipulated in the ART guidelines. Thus the results of this study will be dependent on the quality of these two data sources.

1.8 SIGNIFICANCE OF THE STUDY

Since the introduction of the HAART programme in Namibia, various data have been collected routinely. When the researcher discussed the possibility of
conducting the study with the clinician (Katjita 2006), who oversees the HAART programme at KIH, he welcomed the idea and indicated that the findings could assist healthcare workers in the improvement of this important programme. Therefore the need to look at the available data as part of programme evaluation cannot be overemphasised.

The researcher found it necessary to use the available routine data and assess adherence to ARVs that can be used as baseline information before further studies can be conducted to determine the reasons for non-adherence to HAART at KIH.

1.9 RESEARCH METHODOLOGY

The research methodology outlines the process of the research and what tools are needed to achieve the research objectives (Mouton 2001:56). The research methodology followed in this study is discussed in detail in chapter 3 of the dissertation.

1.9.1 Study design

This researcher used a cohort study which was quantitative, retrospective and descriptive in nature. These design concepts will be addressed in chapter 3 of the dissertation.
1.9.2 Research setting

The researcher conducted the study at KIH one of the two public health facilities where HAART was piloted during September 2003. The patients who received HAART at KIH were from diverse background in terms of race, gender, education and income.

1.9.3 Research population

The study population can be organisations, groups or human beings (Welman & Kruger 2001:46). The study population comprised adult patients who were started on HAART at KIH from 1 February 2006 until 31 March 2006 and who completed at least 12 months of treatment by 31 March 2007.

1.9.4 Data collection instrument

The checklist was developed specifically for this study and data were transcribed manually from the electronic ARV dispensing tool and the manual patients' medical records to a checklist for each patient.
1.9.5 Data collection

Data were collected by the researcher from the patients' medical records that are available manually at ART clinic and also from the electronic ARV dispensing tool at the ARV pharmacy.

1.9.6 Data analysis

Collected data were analysed using the Statistical Package for Social Science (SPSS) version 13. The researcher was assisted by a statistician in analysing and interpreting the data. (See the statistician's letter to this effect in Annexure G).

1.9.7 Ethical considerations

According to Babbie and Mouton (2001:521), ethics is associated with morality which deals with issues of right and wrong. The data in this study were not collected by interviewing patients and therefore most of ethical concepts were not applicable to this study. However, confidentiality and anonymity were considered relevant to this study.
1.9.7.1 Anonymity and confidentiality

The most serious concern is the protection of the identity of the patients (Babbie & Mouton 2001:523). Though the names of the patients were reflected on the patients' medical records, the researcher only recorded the ART clinic reference numbers as well as the ARV pharmacy reference numbers. From the collected data, neither the researcher nor any other person could identify the patient.

1.9.7.2 Ethical approval

All health research conducted in Namibia's public health facilities should request written permission from the Permanent Secretary (PS) of the MoHSS (see annexure A). Approval has been sought from the PS as well as from the Research and Ethics Committee of the Department of Health Studies of the University of South Africa (UNISA), and permission was granted before data collection commenced (see annexures B and C).

1.10 SCOPE AND LIMITATIONS OF THE STUDY

Approximately 308 patients were initiated on HAART at KIH during February and March 2006 but only 176 patients were recruited who met the inclusion criteria. The patients who were included in the study had to be adults (aged 18 or older), on HAART for at least twelve months and recipients of at least two CD4 cell
count results. The review covered demographic characteristics, clinical data, ART data and pharmacy refills.

The characteristics of the patients who do not default could be different from those who default and these findings cannot be generalised to all the ARV experienced patients.

KIH is one of the hospitals where specialist physicians are employed who oversee the HAART programme. It could be that these patients are advantaged in the sense that they might receive better clinical care compared with patients at other public health facilities. Thus it could be assumed that patients at KIH might have better adherence rates than patients acquiring ARVs from other sites in Namibia.

KIH is situated in the urban area of Windhoek, the capital city of Namibia (annexure D, map of Namibia), and only a few kilometres from the Central Medical Store (CMS). Therefore problems with out-of-stock supplies might be minimal because medicines can be delivered to KIH, or collected from the CMS, much faster than in any other areas in Namibia.

Treatment failure is mainly indicated by low CD4 cell counts and high viral loads. However, these results may not necessarily mean that the patient is non-adherent, but the virus might be resistant to the treatment and therefore the
patient will not experience immunological recovery. The investigation of this possibility falls beyond the scope of the current study, as only the patients’ records will be available for conducting the survey.

1.11 DEFINITIONS OF KEY CONCEPTS

The following terms have been used throughout this dissertation and their meanings are defined so that the researcher and the readers can share the same understanding of those concepts.

Adherence: It refers to the ability of the person living with HIV/AIDS to be involved in choosing, starting, managing and maintaining a given therapeutic combination medication regimen to control viral (HIV) replication and improve immune function (Jani 2004:3). Effective use of ARVs requires an adherence of at least 95%. In this study adherence is measured as the regular and consistent collection of ARVs from the pharmacy.

Adult patient: Any patient 18 years and older who is HIV positive and on HAART at KIH.

Anti-retroviral drugs: These are medications that are used in the treatment of infections caused by HIV. There are different classes of anti-retroviral drugs and they act at different stages of the HIV life cycle (WHO 2006a:24).
**CD4 cell:** These are immune system cells which fight infections.

**CD4 cell counts:** This is one of the useful and reliable methods to assess if an HIV positive patient should start ART as well as assessing the effectiveness of ART. An increase of more than 100 CD4 cells/mm³ during the first six to twelve months of treatment is typically seen in adherent ARV treatment-naïve patients, implying that they were using ART for the first time (MoHSS 2003:13).

**Descriptive study:** It is a type of a survey which quantifies the extent of a problem (Katzenellenbogen, Joubert & Abdool Karim 1997:66).

**Highly Active Anti-retroviral Therapy (HAART):** HIV/AIDS treatment containing three or more anti-HIV medicines (Population Briefs 2004).

**Treatment-experienced patients:** Patients who have been receiving HAART for more than six months. In this study only patients who had been using ARVs for at least twelve months were included.

**Treatment naïve patients:** Patients who have been started on HAART for the first time and have not been on HAART for at least 6 months.

**Viral load:** This is the term used to describe the amount of HIV in the blood. If there is an increase of the virus in the blood, then the patient loses CD4 T-cells.
The result of a viral load test is described as the number of copies of HIV RNA per millilitre (copies/ml). Usually, 10,000 copies/ml or less is generally considered to be low, and 50,000 copies/ml or more is considered to be high (Aidsmap 2004).

1.12 LIST OF ABBREVIATIONS

The following abbreviations have been used several times and though they were initially written out, all subsequent use appeared in abbreviated forms only.

AIDS Acquired Immune Deficiency Syndrome
ART Anti-retroviral therapy
ARV Anti-retroviral
BASHH British Association for Sexual Health and HIV
BHIVA British HIV Association
CMS Central Medical Store
DAART Directly Administered Anti-retroviral Therapy
DOT Directly Observed Treatment
GRN Government of the Republic of Namibia
HAART Highly Active Anti-retroviral Therapy
HI Human Immuno
HIV Human Immunodeficiency Virus
KIH Katutura Intermediate Hospital
MEMS  Medication Events Monitoring System
MoHSS  Ministry of Health and Social Services (Namibia)
MTP  Medium Term Plan
NACOP  National AIDS Control Programme
NRTIs  Nucleoside Reverse Transcriptase Inhibitors
NNRTIs  Non-Nucleoside Analogue Reverse Transcriptase Inhibitors
PI  Protease Inhibitor
PIs  Protease Inhibitors
PS  Permanent Secretary
RNA  Ribonucleic Acid
SADC  Southern African Development Community
SPSS  Statistical Package for the Social Sciences
SSA  Sub-Saharan Africa
UNAIDS  United Nations Joint Programme on HIV/AIDS
UNISA  University of South Africa
USA  United States of America
VL  Viral load
WHO  World Health Organization
1.13 ORGANISATION OF THE REPORT

This dissertation has been organised according to five chapters.

Chapter 1 introduced the study and provided background information about HIV/AIDS in the world, Sub-Saharan Africa, SADC and Namibia. It also highlighted on the provision of HAART in Namibia.

Chapter 2 discusses the literature reviewed on adherence to ARVs.

Chapter 3 describes the research methodology used in collecting data for the study.

Chapter 4 presents the results, analysis and discussions of the findings.

Chapter 5 discusses the conclusions and limitations of this study and provides recommendations for increasing adherence to ARVs and for conducting similar studies in future.
1.14 CONCLUSION

This chapter gave background information on HIV/AIDS internationally, continentally, regionally and at country level (Namibia). The following areas were discussed: the research problem, research questions, purpose of the study, research objectives, assumptions underlying the study, significance of the study, research methodology, scope and limitations of the study, definitions of key concepts, organisation of the report and conclusion.

Chapter 2 presents a discussion on the relevant literature reviewed in terms of the research questions.
CHAPTER 2
LITERATURE REVIEW

2.1 INTRODUCTION

The literature review will cover published and unpublished reports within the context of HIV/AIDS, HAART, adherence measurement methodologies, pharmacy refills and factors affecting adherence to HAART. Reviewed documents on adherence were obtained from websites as cited in the list of references, the MoHSS of Namibia (published and unpublished) and articles from journals. The literature review covered the period from 1996 to 2006.

2.2 ADHERENCE TO ARVS

Key words used in the search were: adherence to anti-retrovirals (ARVs), HIV/AIDS treatment, ARVs’ pharmacy records, barriers to ARV adherence, highly active anti-retroviral treatment (HAART), CD4 cell counts and measurement of adherence.

2.2.1 Defining adherence

There is no universal definition of medication adherence and various researchers defined medication adherence in the treatment of HIV differently.
The terms adherence and compliance are sometimes used interchangeably but compliance has been used to describe the patient’s ability to take medications as prescribed but the term has numerous connotations. Compliance is seen as connotating a paternalistic relationship between the physician and patient and that noncompliant patients perform deviant behaviours or exhibit weakness of character. Adherence is better seen to represent the more complex web among patient, provider and medication and reflects the fact that following a medication regimen is not necessarily a simple choice (AIDS Read 2000; Ostenberg & Blaschke 2005:487).

Jani (2004:1) defined medication adherence in HIV/AIDS care as “the ability of the person living with HIV/AIDS to be involved in choosing, starting, managing and maintaining a given therapeutic combination medication regimen to control viral (HIV) replication and improve immune function”.

According to Mehta, Moore and Graham (1997:1665), adherence relates to the extent an HIV/AIDS patient follows a prescribed regimen. They further cited Young et al (1986) who reported adherence in terms of a default rate from following up or any significant deviation from a prescribed regimen. The specifics of what the adherence or default rate measures depend on the prescribed regimen. For example adherence may apply to medication-taking behaviours, dietary intake or physical therapy.
Goudge et al (2004:5) defined adherence as the proportion of prescribed doses actually taken. They also cited William (1999) who used a range of cut off points dividing those that are adherent (80-90% of doses) from the poorly adherent (60-70%) to the non-adherent (below 60%).

Fogarty et al (2002:95) reviewed 20 articles and 74 conference abstracts to explore the nature of adherence research. One study defined adherence as the ratio of days of drug supply to days between drug dispensing and subsequent refill of greater than 90%. Another study described adherence as when a patient filled a prescription less than seven days from an expected refill date.

In this study adherence to ARVs is defined as to how regularly the patient collected the prescribed ARV from the pharmacy. The collected ARVs are assumed to have been taken as prescribed. The adherence level for each patient was then calculated and assessed whether it was 95% or lower.

2.2.2 Scope of the problem

According to the WHO (2006a:28), there were challenges in dealing with the long-term adherence to medication especially in chronic diseases other than AIDS and a review of 500 studies done over 50 years showed that adherence ranged from as low as 4.6% to 100% while only eight articles were on the treatment of AIDS and the mean adherence in these studies was 88%. This was
below the required adherence level of >95% to derive the maximum benefit from ARVs as stated in the study by Paterson et al (2000:21).

Research on medication adherence to ARVs has only started recently but studies of adherence to other chronic diseases like diabetes, hypertension and tuberculosis found adherence levels to average 50% irrespective of illness or setting (Westerfelt 2004). ARVs require lifelong daily treatment like hypertension or diabetic treatment but unlike the latter diseases, failure to adhere to the ARV treatment regimes could endanger the life of the patient by increased viral loads and decreased CD4 cell counts. When ARV regimens are compared to other therapies, these regimes require extraordinary lifelong high levels of adherence to achieve optimal viral suppression (Linsk 2004; Simone et al 2003:185). Therefore non-adherence to ARVs has more serious implications than non-adherence to medications for other chronic diseases because non-adherence to ARVs can lead to resistance and compromise future treatment options unlike with hypertension and diabetics. Thus, it is a potentially life-threatening decision to discontinue, or even not to adhere fully, with ART. Ostenberg and Blaschke (2005:487) argued that adherence in clinical trials can be higher owing to the attention the study subjects receive but the reported average adherence in real life are 43% to 78% among patients receiving medications for chronic conditions.

Goudge et al (2004:4) and AIDS Read (2000) reported that non-adherence to treatment regimens was not unique to HIV/AIDS patients. Adherence to medications in other chronic diseases such as TB which has simpler regimens
has been a thorny problem for a long time especially in low and middle income countries. It has been found that in those countries 20-50% of patients do not complete treatment in a two year period and that has been a subject of study for a range of modern medical science and social science disciplines.

WHO (2006a:29) cited Gill et al (2005) that the experience from Senegal was that 95% of patients had adherence levels exceeding 80% after one month of therapy but after 18 months, only 80% remained above that level. The 80% level of adherence would not be sufficient to prevent treatment failure or the development of drug resistance, because the percentage of patients with undetectable viral loads fell from 80% to 59% over that time.

Unfortunately, non-adherence is common among individuals treated with HAART. More than 10% of patients reported missing one or more medication doses on any given day, and more than 33% reported missing doses in the past two to four weeks due to non-adherence. Studies have also shown that HAART failed in approximately half of patients for whom it had been prescribed (Ickovics & Meade 2002:S98). This high failure rate could be attributed to non-adherence to HAART, at least to some extent.

Adherence to HAART in Namibia might be approximately the same (50%) as experienced in other chronic diseases, but there are no data on the level of adherence to HAART in Namibia. There have been concerns that in Namibia
patients, like their counterparts all over the world, have problems with strictly complying with treatments. However, no published studies could be identified that have estimated the magnitude of the problem in Namibia.

2.2.3 Role of adherence to ARVs in HIV/AIDS

Adherence to ARVs is the main determinant of the success of HAART. The use of HAART in the treatment of HIV/AIDS has led to complex drug regimens which present challenges to both patients and health care providers with respect to adherence. Without adequate adherence, ARVs are not maintained at sufficient concentrations to suppress HIV replications in infected cells nor to reduce the viral load (Chesney 2000:S171).

The importance of adherence has been demonstrated in various chronic diseases and it is known that patients tend to tell health care providers what they want to hear. Patients may therefore overestimate their level of adherence.

Unlike treatment for many other chronic diseases which may respond to only a portion of the prescribed medication, HAART requires a patient to take nearly 100% of prescribed doses. If medications are not taken as prescribed, the virus can mutate and become resistant to the ARVs and drug resistance is the major threat to the effectiveness of HAART. If a patient develops resistance to a particular drug, the health provider may switch the patient to another drug in the
same class but this strategy may not work because the patient may have developed resistance to every drug in that class (Jones 2004). The emergence of drug resistance during therapy and transmission of drug resistant HIV underscores the role that adherence plays in controlling HIV in the individual, as well as preventing a larger public health problem (Jani 2004:9; Wu, Ammassari & Antincri 2002:S96). Viral suppression with HAART reduces the infectiousness of an individual but does not eliminate the risk of transmission. Replication competent virions have been obtained from the secretions of patients on HAART who had undetectable viral loads (Jani 2004:9). Drug resistance is not only a problem to the individual but it is a public health concern with serious social and economic consequences. Changing regimens from first to second line can be very costly. The available funds for ART will then be used to treat fewer people with more expensive ARVs. For example, in Namibia the GRN spends about US$107 on HAART per year per patient who is on first line ARVs while the same patient, if treated with second line ARVs, will require about US$633 (Central Medical Store’s tender price list 2006).

According to Goudge et al (2004:4-5), patients taking less than 85% of doses have an 83% probability of virological failure. Out of patients who were 90-100% adherent, only 60% had an undetectable viral load. Paterson et al (2000:29), reported that missing as few as 5% of doses was associated with a loss of viral suppression.
Studies of PIs mono-therapy demonstrated that the drug resistant HIV virus was most likely to emerge in patients with suboptimal adherence and this relationship almost certainly held true for combination therapy as well (AIDS Read 2000). This has been challenged by Bangsberg, Moss and Deeks (2004:696), because they indicated that studies have shown that patients who were on PIs and NRTIs and highly adherent also developed resistance. This shows that non-adherence is not the only predictor of drug resistance and other factors should be excluded first before a conclusion is made that drug resistance in an individual was due to non-adherence.

2.2.4 The relationship between adherence and treatment outcomes

Adherence to HAART is crucial for the successful treatment of HIV infection and sustained viral control. Adherence rates of 95% or higher are required for optimum viral suppression in order to prevent viral mutation and thus drug resistance (Jani 2004:9; Fairly et al 2005:368; Ostenberg & Blaschke 2005:488; Paterson et al 2000:26; Saple 2005; Simone et al 2003:185).

Several studies have demonstrated that lapses in adherence decrease the likelihood of suppressing vireamia below detectable levels. Adherence measured with MEMS among patients with a viral load of less than 400 copies/ml varied from 33% to 100%. This broad range of adherence suggested that while an undetectable viral load may be a clinically satisfying response to HAART it
was not always a marker of adequate adherence. A detectable viral replication may occur because of pre-treatment resistance, poor drug absorption, drug drug interaction, or other factors (AIDS Read 2000). A number of these patients may require interventions to improve adherence and increase the likelihood of maintaining durable suppression.

Friedland et al (2004:424) studied 20 patients who were administered HAART through directly observed treatment (DOT) in South Africa. The outcome indicated enhanced immunological and virological responses among the 17 patients who completed the study. They achieved a viral load of <50 copies/ml and a mean increase in CD4 cell counts of 148 cells/mm³. This was in agreement with other studies indicating that adherence correlated with immunological and virological responses (Ickovics & Meade 2002: S98; Palela et al 1998:853; Paterson et al 2000:27).

Another study in South Africa has shown that individuals on HAART had a major reduction in mortality, though the benefits were only seen after several months of treatment. Very few treatment failures occurred during the first six months of treatment if the patient adhered to a good HAART regimen (Colebunders, Moses, Laurence, Shihab, Semitala, Lutwama, Bakeera-Kitaka, Lynen, Spacek, Reynolds, Quinn, Viner & Mayanja-Kizza 2006:54). Where CD4 cell count tests are not available, clinical manifestations might be useful to predict treatment
success or failure, possibly indicating whether patients are adhering to the ART regimen or not.

A study in Barbados followed 158 adult patients who were on HAART in a non clinical setting and after 12 months there were significant immunological and virological responses. Of the 158 patients, 79.9% had virological success (viral load <50 copies/ml) and 71.7% had an increase of CD4 cell counts of at least 100 cells/mm³ over baseline value. Those with greater than 90% adherence to HAART were significantly more likely to achieve virological success (Kumar, Kilaru, Sippy, Carter & Roach 2005:114). In a similar project Palela et al (1998:858) also followed 1255 HIV/AIDS patients who were receiving ARVs at nine outpatient clinics in the USA from 1994 to 1997. The data showed dramatic reductions in morbidity and mortality rates among patients with CD4 cell counts of less than 100 cells/mm³.

Paterson et al (2000:25) studied 99 HIV infected patients who were prescribed a protease inhibitor (PI) in the USA. Adherence was significantly associated with successful virological outcome and an increase in CD4 cell counts. The study revealed that only 22% of patients with adherence of 95% or greater had virological failure, while 61% of patients with adherence between 80% and 94% had virological failure and 80% of patients with adherence of less than 79% or less. In this study, virological failure was defined as the detection of viral load of more than 400 copies/mL. There was a significant association between
adherence and duration of acute care hospital stays during the study period. Though the study used a sophisticated electronic adherence measurement (MEMS) and it was in a clinical setting, later studies on adherence also agreed that increased adherence leads to virological and immunological improvement as shown by fewer hospitalisations of study participants. This study concluded that more than 95% adherence to ARVs was required for optimal treatment outcomes (Gulick 2006:942).

Patients on HAART at a military hospital in Nigeria were interviewed to recall missed doses during the last three days of the preceding month and showed that 92.5% of patients who reported not having missed a pill had undetectable viral loads compared to 8.8% of those reported to have missed pills. None of the patients who reported to have missed pills in the last three days had undetectable viral loads. As many as 64.2% of the “never missed pill” group had CD4 cell counts above 500 cells/mm³ compared to 25% in the “ever missed pill” category (Ezech, Onwujekwe, Odunnukwe, Adewole, Aboweyere, Ezecobi, Gbajabiamilla, Hebertson, Adu, Musa, Rabiu, Audu, Lemoh, Idigbe & Ekong 2005).

Ammassari, Trotta, Murri, Castelli, Narciso, Noto, Vecchiet, Monforte, Wu and Antinori (2002:S125), argued that although several studies revealed better adherence in persons with high CD4 cell counts, no direct causal effect of this association had been clarified. It is not clear if patients with less advanced HIV
related symptoms manage better adherence to ART or whether persons who adhere worse fail to achieve viral suppression and immunological recovery.

Though most studies cited were in clinical settings, the studies were in agreement that there was a relationship between adherence and good clinical outcomes. The clinical outcomes were proven by increased CD4 cell counts, reduced viral loads and/or improved clinical outcomes, including weight gain, decreased numbers of opportunistic infections, and enhanced feelings of general well-being.

2.2.5 Factors affecting adherence to ARVs

Many factors including behavioural, socio-demographic and provider characteristics have been reported to influence non-adherence to HAART. Chesney (2000:S172), stated that before measures are implemented to improve adherence, it was essential to identify the main factors that contribute to the inability of patients to take their medications.

Factors affecting adherence are normally grouped in the following categories:

- patient-related factors
- treatment regimens
- patient-provider relationships
- clinical settings, and

A qualitative study conducted in the USA in 1998 among people living with HIV/AIDS to understand barriers to adherence revealed eight common barriers, namely:

• frequency and severity of side effects
• conflicts with daily routines
• dietary requirements
• frequency of taking medications
• number and dosages of medications
• psychosocial factors (for example stress, feeling good, bad news)
• pharmacy refills and
• physiological needs (sleep, hunger or thirst) (Proctor, Testa & Tompkins 1999).

The characteristics of the ARV regimens contribute to non-adherence because the regimens are complex and comprise many pills per day taken at different times with different dietary requirements. Many of these medicines have unpleasant side effects such as diarrhoea, nausea, vomiting and peripheral neuropathy (Goudge at al 2004:4).
According to Weiser et al (2003:285-7), a study among 109 patients in Botswana revealed that adherence rates in Botswana were comparable with adherence rates in most developed countries but patients in Botswana had to overcome the following barriers to ARV adherence: financial constraints (44%), stigma (15%), travel/migration (10%) and side effects (9%).

A study among hospital attendees in Tanzania cited that factors that contributed to non-adherence to ARVs were lack of knowledge about the consequences of irregular dosing, taking alcohol, logistics at clinics, economic constraints and use of alternative medicines (Ndayango, Kwesigabo, Mugusi, Majigo, Almeida & Munubhi 2005).

A study of patients receiving HAART in Thailand used a visual analogue scale to ask patients to report their pill taking behaviours over the past month. They cited the following as the most common reasons for missing medications: forgetting (34%), activity outside/not home (31.3%), sleeping through (24.6%), don’t want to be noticed (20%), too busy (18%) and change in routine (9.9%). The less adherent patients also reported less academic education and less social support (Maneesriwongul, Williams & Tulathong 2002).

Ammassari et al (2002:S126) reviewed published studies conducted in different settings that reported that the most common reasons for skipping HAART included complexity of medication regimens (7-52%), difficulty of integrating
treatment schedules into their daily activities (36%-57%), fear of side effects (13%-42%), worries about disclosure (14%-33%), and forgetfulness about taking medications (30%-66%)

The literature review indicated that adherence may be affected by various factors of which some might be beyond the control of the patient. In the case where a patient does not have money to pay for transport or buy food to eat, these factors will prevent the patient from collecting and/or taking ARVs.

2.2.6 Measuring adherence

The key to improving clinical and virological outcomes in the treatment of HIV/AIDS is the development of practical methods to increase adherence to antiretroviral regimens (AIDS Read 2000).

Literature provides numerous adherence measurement instruments in HAART that have been used in clinical (experimental) settings, but their use in real settings have not been tested. The main problem in studying adherence is that there is no measurement tool that is found to be of higher standard than the other. When reading any study on adherence to HAART, there is always a need to ascertain how adherence was measured (AIDS Read 2000; Ammassari et al 2002:S126; Goudge et al 2004:6). Different adherence measures applied to the same patients suggested different levels of adherence. It has been reported that adherence might be underestimated by MEMS and overestimated by pill count.

A multi-method adherence assessment tool was developed based on previously validated elements including self report, pill identification test, visual analogue scale and pill count. The effort needed to administer the tool was easy to use in a busy ART clinic in South Africa and can be used in other resource-constrained countries (Steel, Banoo, Paterson & Van Rooyen 2006).

There might not be an ideal ARV adherence measurement tool but various strategies are available and have been used in clinical settings to monitor adherence to HAART (AIDS Read 2000; Jani 2004:17 & Paterson et al 2000:25).

2.2.6.1 **Self reports**

This is the most frequently used measurement tool whereby a patient is asked how many doses he/she missed in the last day or two days or two weeks. The format of the questions may vary from study to study and non-adherence rates are higher in studies where a longer recall time is used. Answers to the questions are influenced by patients’ desires to provide socially acceptable answers or mere forgetfulness on the part of the patients (Goudge et al 2004:6; Nieuwkerk & Oort 2005:445). These measures include surveys, interviews and
diaries that are easy and inexpensive but studies show that self reports tend to overestimate patients' actual adherence.

A study on adherence rates among hypertensive patients found that 67% of the patients overestimated their adherence when the data were compared with data from MEMS records (Jani 2004:17). The study also found that 30% of the diary entries differed from the MEMS recordings. Chesney (2000:S171) argued that this method assumes that patients can accurately recall their behaviours and provide honest answers. A limitation to this method was that self reports reflect only short-term or average adherence and may overestimate adherence but some studies showed significant relationships between adherence self reports and viral loads. Though the method has limitations, it has been used in ARV adherence studies by Weiser et al (2003:282).

Though self report is considered to be very subjective and that patients may fabricate medication taking history, there is a clear correlation between self reports of not missing tablets and undetectable viral loads and increased CD4 cell counts (Paterson et al 2000:30).

2.2.6.2 Pill counts

According to Chesney (2000:S171), Jani (2004:17) and Ostenberg and Blaschke (2005:<88), pill counts have been widely used where a patient is required to bring
back actual pill containers in order for health practitioners to count left over pills. Excess pills provide evidence of non-adherence. However, this method has limitations because patients either forget to bring the pill containers or deliberately remove and dump some pills before their next hospital visit. As a result pill counts may also overestimate adherence.

A study in the USA revealed that the reported percentages of adherence to prescribed medications taken by patients ranged from 96% reported adherence for self report, 85% for pill counts and 73% for MEMS. That result suggested that pill counts could be a more accurate method of assessing adherence to HAART than self reports (AIDS Read 2000).

2.2.6.3 Pharmacy refill records

Pharmacy refill records are also used to assess adherence to ARVs. Pharmacists may work with other healthcare providers and patients to indicate if ARVs are collected as directed (Jani 2004:18). This is considered to be an accurate measure of overall adherence. If the records are computerised, they can provide clinicians and researchers with valuable information about the rates of refilling to assess a patient’s adherence to the regimen (Ostenberg & Blaschke 2005:488).
A study by Fairly et al (2005:368) compared long-term adherence to HAART as measured by two practical inexpensive methods (self reports and pharmacy refill records) at a HIV clinic in Melbourne, Australia. The study found clinically useful levels of adherence required to suppress viral load in most patients. It showed correlations between self reports and pharmacy refill records, using <95% as non adherent for pharmacy records and <97% as non-adherent for self reports. Pharmacy refill records identified about twice as many individuals to be non adherent as had been identified with self reports (27% versus 14%).

Pires, Ventura and Magdalena (2005) assessed the hospital pharmacy database in Portugal to analyse the correlation between pharmacy refill data and virological response. The study concluded that pharmacy refill data is a simple and useful method to assess adherence of HIV/AIDS patients to HAART. Over 90% adherence assessed by pharmacy refill data was associated with lower viral load and increased rates of virological responses.

The pharmacy refill records are used at KIH to trace defaulters and alert the other health care workers. The pharmacy refill records are computerised and it is assumed that when medicines are collected they are taken as prescribed. However, this method requires close working relationships between the pharmacists and clinicians which might be non existent and in some cases, patients are also required to collect their ARVs at the same pharmacy which might be problematic for migrant workers.
2.2.6.4 **Electronic devices**

In a study of 57 patients in the USA, the relationship between adherence, as measured by MEMS, and the likelihood of achieving undetectable viremia discovered that it was roughly linear. The proportion of patients with 95% adherence or better who had achieved undetectable viral loads was greater than the proportion among those with 90% to 95% adherence rates (AIDS Read 2000).

MEMS are examples of electronic monitoring systems that are inserted into the caps of the medication bottles containing computer chips. The chip records the date and time whenever the bottle is opened and closed. Data are retrieved by downloading the information from the cap device to the computer. Interpretation of the data assumes that a single dose was removed each time the cap was removed but this may be incorrect because multiple doses may be removed at once or a cap may be removed without taking any pills (AIDS Read 2000; Chesney 2000:S172; Jani 2004:18; Ostenberg & Blaschke 2005:488). Other authors, Paterson et al (2000:24) also used this method in their study on measuring adherence and have demonstrated decreased virological responses with increased adherence rates as measured by MEMS. Though this method is found to be of more benefit over the others, these devices are expensive and not affordable in resource constrained countries such as Namibia.
2.2.6.5 Directly Observed Therapy (DOT) or Directly Administered Anti-retroviral Therapy (DAART)

DOT has been widely used in the management of TB. In this strategy someone should supervise the patient actually taking the drugs. Previously the main challenge in using this method in HIV patients was that ARVs were taken three to four times per day and therefore DOT or DAART was not feasible. Once medications become available that can be taken once or twice per day, DOT or DAART can be considered to be used for measuring adherence to ARVs (Jani 2004:19).

A randomised controlled two armed study is being conducted in Mombassa, Kenya by Sarna, Hawken, Geibel, Kaai and Mandaliya (2005) where DAART is used to measure adherence to ARVs. The DAART group visits the clinic twice per day while the non-DAART group only visits the clinic on a monthly basis. Preliminary data after four months showed that there was high adherence and improvements in weight gain and CD4 counts in both groups. Further analysis of the data could determine if there were differences in CD4 cell counts and other variables to determine if DAART patients were responding better to ART than the non-DAART patients.

2.2.6.6 Provider estimate
Some clinical studies have used provider estimates of adherence and several studies even confirmed that such estimates independently predicted virological response to HAART. But other investigations have found that clinicians are frequently inaccurate in assessing adherence to HAART. Therefore, a clinician’s subjective assessment of adherence may be as problematic as a patient’s self reported adherence (AIDS Read 2000).

According to Goudge at al (2004:6), assessment by the health care providers are often inaccurate because providers do not have the time to collect detailed adherence assessment data to determine which pills were taken less frequently, why and at what times. That leads to providers missing opportunities to help patients to find solutions for their adherence challenges/problems.

2.3 CONCLUSION

The literature reviewed emphasised the importance of adherence to ARVs in the effective treatment of HIV/AIDS. High levels (>95%) of adherence are required to suppress the HI virus to an undetectable level and to increase immunological responses. Though this strict adherence is required, the experiences of adherence to treatment in other chronic diseases have been below optimal levels and studies have shown that similar levels of adherence are experienced by HIV/AIDS patients. Therefore it is a serious challenge to attain and maintain high levels of adherence to ARVs due to their complexities and side effects.
It is important that each country assesses the adherence measuring tool(s) used in its ART programme to estimate patients' adherence to ARV regimens. The KIH, being in a developing country, requires a simple inexpensive adherence measuring tool. Therefore, the pharmacy refill records need to be assessed to determine whether it is effective in predicting CD4 cell counts, indicating patients' levels of adherence to ARV regimens.

Chapter 3 will address the research methodology adopted to study the potential correlation between patients' ARV adherence (as portrayed in their pharmacy refills) and increased CD4 cell counts.
CHAPTER 3
RESEARCH METHODOLOGY

3.1 INTRODUCTION

The data were collected solely by the researcher using a checklist designed by the researcher specifically for this study addressing only the variables of interest. The study followed a quantitative research methodology.

3.2 STUDY DESIGN

A research design is defined as the plan or blue print which stipulates how the researcher intends to collect the data. It can also be defined as a specification of the most adequate operations to be performed in order to test a specific hypothesis under given conditions (Strydom, Fouche & Delport 2002:137).

A quantitative, retrospective, descriptive and cohort study design was used because the researcher was interested in analysing available quantifiable data to investigate a phenomenon that already happened. The aim of the study was to determine the relationship between adherence to HAART, as measured by pharmacy refill records and the CD4 cell counts.
3.2.1 Descriptive

This study was descriptive in nature because the researcher observed a situation and then described what had been observed (Babbie & Mouton 2001:80-81). The description of the phenomenon was the correlation between adherence and CD4 cell counts in HAART patients at KIH.

3.2.2 Retrospective

The researcher used data from patients who were started on ARVs from the 1st of February 2006 and who have been on treatment for at least 12 months by 31 March 2007. The month of January 2006 was not included because no patients were started on HAART during January of every year in Namibia.

3.2.3 Quantitative

Burns and Grove (1997:808) describe quantitative research as a "... formal, objective, systematic process to describe and test relationships..." This study systematically and objectively reviewed patients' records and their pharmacy refill records to identify any correlation between adherence as reflected in pharmacy refill records and enhanced immunity (increased CD4 cell counts). Statistics were used to summarise and describe the data.
3.2.4 Cohort

A cohort can be described as a sample of people participating in a study who meet specific time requirements (Burns & Grove 1997:792). In this study the cohort had to be on HAART for at least 12 months by 31 March 2007.

3.3 RESEARCH METHOD

This section covers the exact steps followed in data collection. These include the research population and the research setting.

3.3.1 The research population

Power et al (1985:235) as cited by Strydom et al (2002:198) defined the population as a set of entities in which all measurement of interest to the researcher are represented. KIH had two groups of patients: those that were registered as potential candidates to start HAART and those who were receiving HAART. The records of patients who were started on HAART at KIH from the 1\textsuperscript{st} of February 2006 and who were on treatment for at least 12 months by 31 March 2007 were reviewed for inclusion based on the following criteria.
Inclusion criteria:

- Adult patients who had been on HAART for at least 12 months from 1 February 2006 to 31 March 2007.
- Adult patients who had received the results of least two CD4 cell counts (at baseline and most recent).
- Adult patients who have been on HAART for at least 12 months by 31 March 2007.

Exclusion criteria:

- Adult patients who had not been on HAART at KIH for 12 months
- Adult patients who did not have two CD4 cell counts results
- Adult patients who started with HAART before 1 February 2006

The medical records of 308 patients who had started with HAART during February and March 2006 were reviewed to select those who met the inclusion criteria. Of the 308 patients, 122 patients were excluded because some were younger than 18 years, some were not on HAART for at least 12 months and the rest did not have at least two results of CD4 cell counts. Only 176 patients were included in this study because 10 patients whose records had been used in the pre-test were excluded from the actual study.
3.3.2 Research setting

The study was conducted at KIH which is a public health institution in Windhoek, the capital city of Namibia. The researcher conducted the study at this hospital because it was one of the two public health facilities where HAART was piloted during September 2003. The patients who received HAART at KIH were from diverse backgrounds in terms of race, gender, education and income.

3.4 DATA COLLECTION

The researcher transcribed data from the ARV dispensing tool and patients' medical records onto the checklist designed specifically for the study.

3.4.1 The research instrument

A checklist (annexure E) was designed by the researcher, based on findings from the literature review and was pre-tested on 10 patients. The checklist is divided in the following four sections:

Section A: This section covered: the patients' ARV and pharmacy reference numbers, gender, age, education, employment, residence type and the person chosen to support the patient with use of ARVs.
Section B: This section covered the patient’s TB status and at least two CD4 cell count results.

Section C: This section covered: date of HAART initiation, WHO HIV/AIDS stage, ARV therapy, changes to therapy if any and reasons for change.

Section D: This section covered: pharmacy refill dates, adherence level and any additional information.

3.4.2 Data collection procedures

During the piloting of the checklist, the researcher discovered that some variables were not possible to collect based on the information recorded on the patients' medical records. It was impossible to record the highest grade attained because on the patients’ medical records the education levels had already been categorised. All patients' addresses were recorded as living in Windhoek and therefore the permanent residential address was found to be of no added value as all of them were living in an urban area. The weight of the patient before and after being on ARVs for at least 12 months were also omitted because there was no consistency in the recording and most patients’ weight were not recorded at each visit. It was also not possible to record when the next appointment was to collect the ARVs from the pharmacy. The ARV dispensing tool could only give the latest appointment date and there was no history of previous pharmacy visits.
The researcher therefore only recorded the exact dates when the ARVs had been collected and calculated adherence by dividing the number of refills by 12 months and then multiplied by 100 to obtain the percentage adherence. The checklist was amended and data collection started using the revised checklist.

The researcher numerically numbered each checklist before data collection commenced. The ARV pharmacy number and the ART clinic numbers were both entered on the checklist in order to allow easy cross checking of data for correctness and reliability.

The following information was transcribed from patients' ARV dispensing tool (electronic) and manual medical records on the checklists. A completed checklist is attached (annexure F):

- Patients' ARV reference numbers
- Demographic profiles: age, gender, education, employment, residence type and treatment supporter
- CD4 cell counts value
- If patient was on TB treatment and if he/she was, when treatment was initiated
- Date when HAART was initiated.
- The ARV regimen the patient was on. The switch from first to second line ARV treatment can give an indication as to whether the patient was resistant to ARV and/or non-adherent.
- The reason for changing an ARV treatment regimen, if applicable
- The dates when the ARVs were collected from the ARV pharmacy.
- Compared the pharmacy refills with CD4 cell counts. This served to validate the KIH adherence measurement instrument.

3.4.3 Data management

The completed checklists were kept locked up. These checklists contained no names but were handled in a very confidential manner to prevent use of ARV reference numbers to trace and obtain the name of the patient.

3.4.4 The use of routine data

This data is usually collected on an ongoing basis either for monitoring or evaluation of services and to give guidance to policy makers to formulate appropriate interventions (Katzenellenbogen et al 1997:133). The data used for the study were routinely collected as part of service provision and also to monitor patients’ adherence to HAART.
3.4.4.1 Advantages of using routine data

This data can provide a rich source of information to the researcher who will then spend less time on data collection and more time on thorough analysis of the data (Katzenellenbogen et al 1997:133).

3.4.4.2 Disadvantage of using routine data

The researcher did not play any part in data collection, only in recording the relevant data from the patients’ records onto the checklist. Routinely available data can also be of poor quality because of incomplete records, incorrect recordings and/or unavailability of some records or some aspects (Katzenellenbogen et al 1997:133). The researcher encountered poor recording of the data and some variables could not be recorded because of missing data on some patients’ medical records.

3.4.5 Data analysis

The data were analysed using the Statistical Package for Social Sciences (SPSS) version 13. The researcher was assisted by a statistician from the statistics department from the University of Namibia. (Please see a letter from the statistician to this effect attached to this dissertation as annexure G).
3.5 MEASUREMENT

The outcome measure that was considered crucial was the effectiveness of the pharmacy refill record in measuring adherence to HAART.

3.5.1 Adherence measure

The adherence measuring tool used was the pharmacy refill records. Data captured on the ARV dispensing tool are: ARV reference number, age, gender, residential address, the name of treatment supporter, ARV regimen, date HAART was initiated, next pharmacy follow up date and actual date prescription was filled. If a patient’s ARV reference number is entered, the history of the patient is displayed this can give an indication on the history of prescription refills. This allows the pharmacist to alert other health care workers in case of defaulters and to be able to trace the patient telephonically or through home visits.

The initial date when HAART was started, the type of regimen and the dates the ARVs were collected from the ARV pharmacy were recorded on the checklist. Missing pharmacy refill data gave an indication that the patient was defaulting from prescribed treatment.
3.5.2 Outcome measure

The outcome measure of interest was the consistent pharmacy refill record of a patient and assessing if that can predict CD4 cell counts after twelve months of HAART. However, the measurement may be affected by poor record keeping as routinely collected data were used.

3.5.3 Bias due to confounding variables

The following variables could bias the findings of this study:

- Recording error may be caused by transcribing data from one patient on another patient’s checklist.
- Some patients may have a HIV virus that is resistant to HAART so even though they are adherent, their immunological status might remain poor.
- Some patients may have poor absorption of the medicines due to gastrointestinal diseases. Patients may experience a fall in CD4 cell counts even if they are adherent.
- Patients may not respond to HAART because of other medications they may be taking for other diseases that make ARVs ineffective and not necessarily due non-adherence. This is known as drug-drug interaction(s).
• Some patients may already have a high CD4 cell counts especially if they are in WHO stage IV. Because they are clinically ill, they are started on HAART irrespective of their CD4 cell counts.

3.6 VALIDITY

Validity refers to the degree to which a measure adequately reflects the actual meaning of the concept that is considered (Babbie & Mouton 2001:122). The checklist’s validity was tested based on face validity, content validity and construct validity. The checklist was also assessed based on sensitivity, specificity, positive predictive value and negative predictive value (See section 4.7 of chapter 4).

3.6.1 Content validity

The measure should include or account for all the elements of the variables that are being investigated (Katzenellenbogen et al 1997:92). The variables of measure were all included in the measuring tool. Adherence was measured as consistent collection of ARVs from the pharmacy at prescribed intervals. If a patient failed to collect ARVs then that patient was considered to be non-adherent.
3.6.2 Face validity

It refers to how much a measure covers the range of meanings included within the concept (Babbie & Mouton 2001:123). The required information on the checklist was easily transcribed from the patients' medical records and was also clear.

3.6.3 Construct validity

It is based on the reasonable relationships among variables (Babbie & Mouton 2001:122). In this study the pharmacy refill records were used to determine if there was a relationship between adherence to HAART and immunological response, as measured by the CD4 cell counts. The checklist was valid because it only measured whether adherence to HAART would lead to immunological recovery. If the patient adheres, the measurement should detect the increase in CD4 cell counts and if the patient does not adhere, then there should be a decrease in the CD4 cell counts.

3.7 RELIABILITY

Babbie and Mouton (2001:119-20) and Katzenellenbogen et al (1997:90) defined reliability as a matter of whether a specific method if applied several times to the same object would give the same result. There is normally no proof on how
much reported data originated from the observed situation and how much was just from the observer. Burns and Grove (1997:327) also stated that reliability is concerned with how consistently the measurement methodology measures the concept of interest. That implies that if the same data collection instrument is used by different data collectors to obtain the same information, the recorded data should be comparable. Reliability testing is also considered to be a measure of the amount of random error in the measurement technique and it is concerned with such characteristics as dependability, consistency, accuracy and comparability. Reliability estimates are only specific to the sample being tested and therefore high reported reliability values on an established instrument do not guarantee that reliability will be satisfactory in another sample or with a different population. It is therefore important that reliability testing needs to be performed on each instrument used in a study prior to performing other statistical analysis. Stability is concerned with the consistency of repeated measures which is referred to as test-retest reliability. The test-retest method is a procedure that is used to establish the reliability of the instrument (Strydom et al 2002:168).

The researcher recorded the patient’s ARV number from the patients’ medical files at the ART clinic and the ARV pharmacy number from the ARV dispensing tool at the ARV pharmacy. The collected data can easily be verified for accuracy and correctness by comparing the transcribed data on the checklist with that from the two data sources. The instrument was pre-tested on ten patients that were
initially piloted and the data for the 10 patients were analysed before the data collection commenced from the 176 patients’ records.

3.8 CONCLUSION

Data collection covered the period 1st February 2006 to 31 March 2007 and included patients who completed at least 12 months of HAART and who had at least two CD4 cell count results. A quantitative, descriptive, retrospective and cohort study was used to collect data from patients’ medical records and ARV dispensing tool. The study collected data from records of 176 patients using the checklist that was specifically designed for the study. The collected data were analysed using the Statistical Package for Social Science (SPSS) version 13.

Chapter 4 presents the analysis and discussion of the data obtained by completing the designed checklist for 176 patients’ records.
CHAPTER 4

ANALYSIS AND DISCUSSION OF RESEARCH RESULTS

4.1 INTRODUCTION

This chapter presents and discusses the results of the study. The overall purpose of the research was to determine the effectiveness of the adherence measurement practices at KIH in predicting CD4 cell counts. This information will be used to recommend an effective ARV adherence measurement tool at KIH in order to increase adherence to ARVs among ART experienced patients.

Specific objectives of this study were to:

- determine if there is a correlation between adherence to ARVs as measured by pharmacy refill and CD4 cell counts
- determine if ARV pharmacy refills are effective adherence measurement tools at KIH
- recommend a simple adherence measurement tool at KIH
4.2 DEMOGRAPHIC DATA

A total of 176 patients who met the inclusion criteria, as explained in chapter 3 of this dissertation, were enrolled in the study. These formed the total number of patients who could meet the inclusion criteria from the 306 patients who were started on HAART during February and March 2006 and who completed at least 12 months of treatment by the end of March 2007. The requirement of at least 12 months’ treatment experience and the other inclusion criteria reduced the number of patients’ records that would have qualified for the review. Many records could not qualify for inclusion because of poor record keeping; missing CD4 cell count results and missing pharmacy refill data. The results shown in Table 4.1 highlight some of the key baseline characteristics and profiles of patients whose records were reviewed.

Table 4.1: Baseline characteristics and profile of patients (N=176)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range</td>
<td>19-62</td>
</tr>
<tr>
<td>Mean age</td>
<td>35.4</td>
</tr>
<tr>
<td>Female</td>
<td>93</td>
</tr>
<tr>
<td>Male</td>
<td>83</td>
</tr>
<tr>
<td>Baseline CD4 cell count range</td>
<td>6-784</td>
</tr>
<tr>
<td>Mean baseline CD4 cell count</td>
<td>167.8</td>
</tr>
</tbody>
</table>

The section that follows will present demographic data, followed by clinical and HAART data, discussion on adherence and CD4 cell count and assessment of
the pharmacy refill adherence measurement methodology. All figures will be rounded off to the nearest decimal point.

This section will address the research results pertaining to participants’ gender, age, education levels, employment, residence type and person chosen to support a patient with the use of ARVs.

4.2.1 Gender

There were more females 52.8% (n=93) than males 47.2% (n=83) who initiated treatment during the period of the study. Women constitute 55% of Namibia’s adult population. Unlike men, women have weaker powers than men to negotiate safe sexual practices within their sexual relationships which can lead to higher rates of HIV infections among women (MoHSS 2005a:4). Of the 176 patients 64.2% (n=113) had an adherence level of >95% while 35.8% (n=63) had an adherence level of <95%. Of the 113 patients who were adherent, 53.1% (n=60) were females while 46.9% (n=53) were males. There is not enough evidence at the 5% level of significance to suggest that the proportion of adherence among females is different from that among males (P=0.04).
Table 4.2: Gender versus adherence

<table>
<thead>
<tr>
<th>Gender</th>
<th>Adherence Crosstabulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adherence</td>
</tr>
<tr>
<td>Male</td>
<td>Count</td>
</tr>
<tr>
<td>Female</td>
<td>Count</td>
</tr>
<tr>
<td>Male</td>
<td>% within Gender</td>
</tr>
<tr>
<td>Female</td>
<td>% within Gender</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
</tr>
<tr>
<td></td>
<td>% within Gender</td>
</tr>
</tbody>
</table>

Figure 4.1: Relationship between adherence and gender
Adherence predicts immunological response which is shown in the increase in CD4 cell counts. The average male CD4 cell counts before treatment was 151.3 cells/mm$^3$; after treatment the average male CD4 cell counts became 335.7 cells/mm$^3$. Therefore there was an average immune recovery in terms of CD4 count gain for males in the study of 184.4 cells/mm$^3$ whereas the average female CD4 cell counts before treatment was 182.6 cells/mm$^3$ and after treatment this value became 349.5 cells/mm$^3$. The average gain in CD4 cell counts for female patients was 166.92 cells/mm$^3$ compared to 184.4 cells/mm$^3$ for the males. The difference in CD4 cell counts gained by gender is not statistically significant at 5% level of significance (P=0.19).

The findings in this study correlated with those of other studies which reported no difference in adherence rates between females and males. However, Mehta et al (1997:1666) found an association between adherence and gender where females were reportedly less adherent than males. Women might be more non-adherent than men because women are prone to depression which is one of the main causes of non-adherence in patients on HAART (Starace, Ammassari, Trotta, Murri, De Longis, Izzo, Scalzini, Monforte, Wu & Antinori 2002:S136).

4.2.2 Age at previous birthday

The age range of patients participating in the study was from 19 years to 62 years, with mean age of 35.4 years. Patients aged 25-44 years constituted the majority (n=156; 88.6%). This is in line with results from the 2006 Namibian
national HIV sentinel survey conducted among pregnant women visiting antenatal clinics which revealed that the same age group was the most affected by HIV infection (MoHSS 2007:11). The most adherent patients were in the age group 35-39 (n=36 or 31.9%), followed by the 30-34 (n=30 or 26.5%). In the age group 15-24, there were 6 patients and 2 were adherent which is 1.8% of the adherent group. There were 14 patients in the age group 45 – 64 and 11 were adherent. At 5% level of significance, age was found to be significant (P=0.1). The older the patient, the more adherent they were (See table 4.3). Though Altice and Friedland (1998:503) found that adherence is not predicted by age, the results of this study agree with findings reported by Mehta et al (1997:1666) as well as Paterson et al (2000:26) who found that adherence increases with age.
Table 4.3: Relationship between adherence and age

<table>
<thead>
<tr>
<th>Age-group</th>
<th>Count</th>
<th>Non-adherent</th>
<th>Adherent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>1.6%</td>
<td>.0%</td>
<td>.6%</td>
<td></td>
</tr>
<tr>
<td>20-24</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>4.8%</td>
<td>1.8%</td>
<td>2.8%</td>
<td></td>
</tr>
<tr>
<td>25-29</td>
<td>6</td>
<td>18</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>9.5%</td>
<td>15.9%</td>
<td>13.6%</td>
<td></td>
</tr>
<tr>
<td>30-34</td>
<td>23</td>
<td>30</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>36.5%</td>
<td>26.5%</td>
<td>30.1%</td>
<td></td>
</tr>
<tr>
<td>35-39</td>
<td>19</td>
<td>36</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>30.2%</td>
<td>31.9%</td>
<td>31.3%</td>
<td></td>
</tr>
<tr>
<td>40-44</td>
<td>8</td>
<td>16</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>12.7%</td>
<td>14.2%</td>
<td>13.6%</td>
<td></td>
</tr>
<tr>
<td>45-49</td>
<td>2</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>3.2%</td>
<td>6.2%</td>
<td>5.1%</td>
<td></td>
</tr>
<tr>
<td>50-54</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>1.6%</td>
<td>2.7%</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>60-64</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>.0%</td>
<td>.9%</td>
<td>.6%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>113</td>
<td>176</td>
<td></td>
</tr>
<tr>
<td>% within Adherence</td>
<td>100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>
4.2.3 Educational levels

Twenty eight (15.9%) patients had not been to school. Fifty six (31.8%) had primary education, 60 (34.1%) had secondary education, 24 (13.6%) had high school education, 2 (1.1%) had higher education while for 6 (3.4%) patients the level of education was not stated. Of the total of 113 patients who were adherent, 17.7% (n=20) have not been to school and 31.9% (n=36) had primary education.
### Table 4.4: Level of education attained

<table>
<thead>
<tr>
<th>Education</th>
<th>Adherence</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-adherent</td>
<td>Adherent</td>
<td>Percent within Education</td>
<td>Total</td>
</tr>
<tr>
<td><strong>Not been to school</strong></td>
<td>Count</td>
<td>8</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td>% within Education</td>
<td>28.6%</td>
<td>71.4%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Primary</strong></td>
<td>Count</td>
<td>20</td>
<td>36</td>
<td>56</td>
</tr>
<tr>
<td>% within Education</td>
<td>35.7%</td>
<td>64.3%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td>Count</td>
<td>27</td>
<td>33</td>
<td>60</td>
</tr>
<tr>
<td>% within Education</td>
<td>45.0%</td>
<td>55.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>High school</strong></td>
<td>Count</td>
<td>5</td>
<td>19</td>
<td>24</td>
</tr>
<tr>
<td>% within Education</td>
<td>20.8%</td>
<td>79.2%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Higher institution</strong></td>
<td>Count</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>% within Education</td>
<td>50.0%</td>
<td>50.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Not stated</strong></td>
<td>Count</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>% within Education</td>
<td>33.3%</td>
<td>66.7%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>Count</td>
<td>63</td>
<td>113</td>
<td>176</td>
</tr>
<tr>
<td>% within Education</td>
<td>35.8%</td>
<td>64.2%</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

Some studies have stated that an increase in education does not predict enhanced adherence rates while others found a positive correlation between education and adherence (Ickovics & Meade 2002:S98). In this study better education did not predict better adherence as shown in table 4.4 and figure 4.3. (In Namibia secondary school is from grade 8 to 10 while grades 11 and 12 are classified as high school. As the patients’ education levels had been grouped on their records, these had to be accepted as stated on these records).
Figure 4.3: Relationship between adherence and level of education

4.2.4 Type of employment

The study revealed that as many as 78 (44.3%) patients on ARVs were unemployed, 51 (29.0%) were working for private companies, 11 (6.3%) were self-employed and 22 (12.5%) patients’ records failed to indicate their employment status. Those working for the parastatal organisations and government institutions were in the minority (n=9; 5.1%) and (n=3; 1.7%) respectively (see table 4.5 and figure 4.4). This can be explained by the fact that government and parastatal organisations offer medical aid benefits for their employees who can afford to visit private health facilities and obtain their ARVs from private pharmacies. Therefore, these employees might have been excluded
from this study conducted at KIH, a state institution. The unemployed may have
time to visit the hospital and collect their ARVs because ARVs are provided at no
cost to the patients but these patients need money to pay for transport to the
hospital.

Table 4.5: Type of employment

<table>
<thead>
<tr>
<th>Type of Employment</th>
<th>Frequency</th>
<th>Percent</th>
<th>Valid Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>78</td>
<td>44.3</td>
<td>44.3</td>
<td>44.3</td>
</tr>
<tr>
<td>Self-employed</td>
<td>11</td>
<td>6.3</td>
<td>6.3</td>
<td>50.6</td>
</tr>
<tr>
<td>Government Institution</td>
<td>3</td>
<td>1.7</td>
<td>1.7</td>
<td>52.3</td>
</tr>
<tr>
<td>Private company</td>
<td>51</td>
<td>29.0</td>
<td>29.0</td>
<td>81.3</td>
</tr>
<tr>
<td>Parastatal Organisation</td>
<td>9</td>
<td>5.1</td>
<td>5.1</td>
<td>86.4</td>
</tr>
<tr>
<td>Student</td>
<td>1</td>
<td>.6</td>
<td>.6</td>
<td>86.9</td>
</tr>
<tr>
<td>Other</td>
<td>22</td>
<td>12.5</td>
<td>12.5</td>
<td>99.4</td>
</tr>
<tr>
<td>Not stated</td>
<td>1</td>
<td>.6</td>
<td>.6</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td>100.0</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

Altice and Friedland (1998:504) found that adherence does not seem to be predicted by socioeconomic status while Mehta et al (1997:1666) found that lower socioeconomic status (low income) could influence non-adherence levels detrimentally. Ickovics and Meisler (1997:S388) argued that concerns about patients confidentiality may be heightened by the fear of stigmatisation. These fears may affect adherence if the patient does not want to be seen at an ART clinic, or taking medications, or is unwilling to take time off from work for clinic appointments. The finding in this study is in agreement with another study which
found that unemployment per se did not predict non-adherence (Ammassari et al 2002: S125).

![Bar graph](image)

**Figure 4.4: Relationship between adherence and type of employment**

### 4.2.5 Residence type

Of the 113 patients who were adherent, as many as 58 (51.3%) were living with others, followed by those owning houses (n=37; 32.7%) then those renting accommodation (n=15; 13.3%). The one patient who lived with a partner was non-adherent probably because he/she did not inform the partner and it was not
easy to regularly visit the pharmacy to collect the ARVs (see table 4.6 and figure 4.5).

Table 4.6: Type of residence

<table>
<thead>
<tr>
<th>Type of Residence</th>
<th>Adherence</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Non-adherent</td>
<td>Adherent</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Own house</td>
<td>Count</td>
<td>19</td>
<td>37</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Type of Residence</td>
<td>33.9%</td>
<td>66.1%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Renting</td>
<td>Count</td>
<td>5</td>
<td>15</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Type of Residence</td>
<td>25.0%</td>
<td>75.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Living with others</td>
<td>Count</td>
<td>38</td>
<td>58</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Type of Residence</td>
<td>39.6%</td>
<td>60.4%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Living with partner</td>
<td>Count</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Type of Residence</td>
<td>100.0%</td>
<td>.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Not stated</td>
<td>Count</td>
<td>0</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Type of Residence</td>
<td>.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>63</td>
<td>113</td>
<td>176</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% within Type of Residence</td>
<td>35.8%</td>
<td>64.2%</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

Of the 63 patients who were non-adherent, 60.3% (n=38) were living with others. Individuals with unstable living circumstances may not be able to carry their medications with them and may not have a private place to take them out of view of their co-inhabitants.
Figure 4.5: Relationship between adherence and type of residence

4.2.6 Persons chosen to support the patient with ARV treatment

Seventy three patients (41.5%) were supported by people in the category other, while 30 (17.0%) had their spouses/partners as their supporters, 7.4% (n=13) were supported by their relatives, 8.0% (n=14) by their friends. For the 21.6% (n=39) of the patients the treatment supporters were not stated, 2.8% (n=5) were
supported by their parents, 1.1% (n=2) were supported by their employers and 0.6% (n=1) had no supporter (See figure 4.6 for details).

Figure 4.6: Relationship between adherence and treatment supporter

The ART guideline requires that each patient who is started on HAART should have a treatment supporter (MoHSS 2003:7). The essence is to enhance adherence to ARVs because the patient on HAART might forget or be too sick to collect the ARVs from the pharmacy. There was only one patient who did not have a treatment supporter but the patient was adherent. The spouses or partners seemed to have provided good support because 20 out of these 30 patients were adherent. Friends do not seem to be good treatment supporters
because 8 out of these 14 patients were non-adherent. A friend could be living far from the patient and find it difficult to remind or encourage the patient to regularly collect the ARVs from the pharmacy. Kumarasamy, Safren, Raminani, Pickard, James, Sri Krishnan, Solomon and Mayer (2005:533) also concluded that social support is a predictor of adherence.

Generally socio-demographic factors do not predict adherence behaviour, although some studies have found that being male, white, older, having a higher income, higher education and higher literacy levels correlate with better adherence. In clinical trials the patients who were adherent reported greater social, emotional and economic support from staff members and significant others (Ickovics & Meisler 1997:387).

4.3 CLINICAL DATA

This section presents results on the pre-clinical assessment transcribed from patients' medical records.

4.3.1 Current use of TB medicines

Only 2.3% (n=4) patients were on both TB and ARV therapies. This is in compliance with the ART guideline which states that a patient with TB should complete the TB therapy first prior to beginning ARV therapy unless there is a
high risk of HIV/AIDS progression and death while completing the TB treatment (MoHSS 2003:15). This is to reduce the pill burden which is a major cause of non-acherence (see figure 4.7 for details) among patients with chronic diseases especially HIV/AIDS.

![Distribution of ARV Patients by Whether They Are on TB Medicines](image)

**Figure 4.7: Patients currently using TB medicines**

### 4.3.2 CD4 cell count values

Starace et al (2002:S137) defined immunological failure as the persistent decline in the CD4 cell count which is measured at least on two separate occasions or
immunological can be the failure to increase CD4 cell counts by at least 25-50 cells/mm³ above baseline within the first year of HAART.

Though patients are generally started on HAART when the CD4 cell count is below 200 cells/mm³ (WHO HIV/AIDS stage I, II and III), those patients who have the HIV virus and are clinically ill (WHO HIV/AIDS Stage IV), are started on HAART irrespective of their CD4 cell counts. Therefore not all patients were started on HAART with baseline CD4 cell counts of less than 200 cells/mm³. In this study, changes in CD4 cell counts were calculated as the difference between the count at baseline and the most recent count.

The results showed that the lowest baseline CD4 cell count was 6 cells/mm³ and after 12 months the lowest was 80 cells/mm³ while the highest baseline was 788 cells/mm³ and the highest after 12 months was 2000 cells/mm³. The mean CD4 cell counts at baseline was 167.8 cells/mm³ with standard deviation of 105.5 and after 12 months on HAART, the CD4 cell counts was 343.1 cells/mm³ with standard deviation of 238.3. That is interpreted as a mean gain of 175.1 cells/mm³ for all 176 patients.
Figure 4.8: Scattergram: CD4 cell count baseline versus most recent CD4 cell count

Figure 4.8 shows a positive relationship between the baseline (pre-treatment) to the most recent (post-treatment) CD4 cell counts ($Y=0.679$ and $X = 228.993$ (regression Line)); $X =$ baseline CD4 cell counts; $Y =$ most recent CD4 cell count.)
Table 4.7: Baseline CD4 cell count versus most recent CD4 cell count

<table>
<thead>
<tr>
<th>Correlations</th>
<th>Most recent CD4 cell count</th>
<th>Baseline CD4 cell count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Correlation</td>
<td>Most recent CD4 cell count</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Baseline CD4 cell count</td>
<td>.301</td>
</tr>
<tr>
<td>Sig. (‘-tailed)</td>
<td>Most recent CD4 cell count</td>
<td>.</td>
</tr>
<tr>
<td></td>
<td>Baseline CD4 cell count</td>
<td>.000</td>
</tr>
<tr>
<td>N</td>
<td>Most recent CD4 cell count</td>
<td>176</td>
</tr>
<tr>
<td></td>
<td>Baseline CD4 cell count</td>
<td>176</td>
</tr>
</tbody>
</table>

Table 4.7 shows a weak positive association between the baseline CD4 cell counts and the most recent CD4 cell counts (r=0.301).

4.4 ANTI-RETROVIRAL THERAPY DATA

This section presents results transcribed from the patients’ ART clinic medical records, providing information about each patient’s HIV/AIDS progress and treatment.

4.4.1 WHO HIV/AIDS status

As presented in figure 4.9, 46.0% (n=81) of the patients were in the WHO’s HIV/AIDS stage III. There were 31.0% (n=55) in stage II, followed by stage I (10.2%; n= 18), stage IV (8.5%; n= 18) and for the rest of the patients (4.0%;
n=7), the stage was not stated. Most of the patients who were adherent were in stage III (46.0%; n= 52) and the same applies for those who were non-adherent (46.0%, n=29). The 8.5% (n=15) patients who were in stage IV were clinically sick irrespective of their CD4 cell counts which could be more or less than 200 cells/mm³. Of these 15 patients in stage IV, 53.3% (n=8) were adherent while 46.7% (n=7) were non-adherent. Though other studies such as Ammassari et al (2002:S125), Ickovics and Meisler (1997:388) as well as Singh, Squier, Sivek, Wagener, Hong-Nguyen and Yu (1996:266) stated that disease progression predicts non-adherence. In this study, no correlation between adherence and WHO HIV/AIDS stage was found.

![Graph showing adherence and WHO HIV/AIDS stage](image)

**Figure 4.9: Relationship between adherence and WHO HIV/AIDS stage**
4.4.2 Current ARV therapy

As discussed in chapter 1 of this dissertation, the regimens included 2 NRTIs plus 1 NNRTI (1st line) or 2 NRTIs plus 1 PI (2nd line). While 170 patients were on first line ART regimens only 6 patients were on second line ARV regimens. Most patients (n=162; 92.0%) of the patients’ ARVs were not changed from the original prescription, 5.7% (n=10) were changed and for 2.3% (n=4) the records did not state whether the regimens had been changed or not (see figure 4.10).

![Graph showing ARV regimen changes](image1)

Figure 4.10: ARV regimen changes
The 5.7% (n=10) patients whose regimens were changed, was due to toxicity (3.3%; n=6), immunological failure (1.1%; n=2), clinical failure (0.6%; n=1) and 0.6% (n=1) hepatitis (see figure 4.11). Due to these reasons, their regimens were changed from 2 NRTIs plus 1 NNRTI (1st line) to 2 NRTIs plus 1 PI (2nd line). The fact that 166 of the 176 patients were still on the 1st line regimen 12 months after the initiation of HAART, indicates that the majority adhered well and there was a good immunological response to the 1st line ARV regimen.

This finding indicates that the clinicians complied with the ART guidelines because the majority of patients were on 1st line compared to those on the 2nd line ARV regimens. The results are also in agreement with another study which documented that 2/3 of patients on HAART remained on the original regimes 12 months after starting HAART (Jani 2004:9).
Figure 4.11: Reasons for change of ARV regimens

4.5 ADHERENCE LEVEL

An adherence level of >95% is required to suppress the HIV virus. In the absence of virological testing, a CD4 cell count can indicate the level of the virus in the blood at KIH, the CD4 cell counts is the only test routinely used to prove immunological recovery after HAART initiation. Adherence is an important predictor of morbidity and mortality in clinical trials of drugs for cancer and coronary heart disease and the rates of non-adherence with medical regimens range from 15-93% with average rates of non-adherence estimated at 50%. The costs of non-adherence may be substantial in terms of illness, relapses and recovery (Ickovics & Meisler 1997:385-6).
In this study, adherence to ARVs was calculated from the pharmacy refills which do not necessarily mean that the ARVs were indeed ingested. Of the 176 patients 64.2% (n=113) had an adherence level of >95% while 35.8% (n=63) had an adherence level of <95%. The mean adherence level was 96.4% for the 176 patients enrolled in the study with the lowest being 75% and highest 100%. Table 4.8 shows the strata of adherence of all the patients in the study.

Table 4.8: Adherence levels

<table>
<thead>
<tr>
<th>Adherence</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;95%</td>
<td>113</td>
</tr>
<tr>
<td>90-95%</td>
<td>52</td>
</tr>
<tr>
<td>80-89%</td>
<td>10</td>
</tr>
<tr>
<td>&lt;80%</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
</tr>
</tbody>
</table>

4.6 CORRELATION BETWEEN ADHERENCE AND CD4 CELL COUNTS

Adherence is critical to obtain the full benefits of HAART, including maximal and durable suppression of viral replication, reduced destruction of CD4 cells, prevention of viral resistance, promotion of immune reconstitution and slowed progression to AIDS (Ickovics & Meade 2002:S98).

A study by Paterson et al (2000:27) on adherence to ARVs, stated that patients with 95% or greater adherence, had superior virological outcomes, greater increases in CD4 cell counts and lower hospitalisation rates than those with
lower levels of adherence. Ickovics and Meisler (1997:388) stated that adherence rates were lower among patients with lower CD4 cell counts, suggesting that as the disease becomes more severe, adherence may be compromised. Generally, better adherence rates are observed in patients with higher CD4 cell counts but no direct causal effect of adherence and CD4 cell counts has been established. It is also not clear whether patients with less advanced HIV disease adhere better because of fewer HIV related symptoms or patients who adhere worse fail to achieve viral suppression and immunological recovery (Ammassari et al 2002:S125).

From the results, an examination of the relationship between adherence and CD4 cell counts show that from the 176 patients enrolled in the study, there were 113 adherent patients and 87 of those achieved a CD4 cell count of equal to or more than 200 cells/mm$^3$ within one year of commencing HAART. This means that though 64.2% of patients were adherent and 77.0% had immunological recovery (CD4 cell count of equal to or more than 200 cells/mm$^3$). This indicates a positive relationship between adherence and increasing CD4 cell counts.

The baseline mean CD4 count was 167.8 cells/mm$^3$. Therefore there was a gain of an average of 175.3 cells/mm$^3$ CD4 cells in the total study population which comprised 176 patients.
Table 4.9: Correlations between adherence, age, baseline CD4 cell count, most recent CD4 cell count

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Baseline CD4 cell count</th>
<th>Most recent CD4 cell count</th>
<th>Adherence level (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Pearson correlation Sig. (2-tailed)</td>
<td>1</td>
<td>-0.096</td>
<td>-0.007</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>176</td>
<td>176</td>
<td>176</td>
</tr>
<tr>
<td></td>
<td>Baseline CD4 cell count</td>
<td>Pearson correlation Sig. (2-tailed)</td>
<td>-0.096</td>
<td>**0.301</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>176</td>
<td>176</td>
<td>176</td>
</tr>
<tr>
<td></td>
<td>Most recent CD4 cell count</td>
<td>Pearson correlation Sig. (2-tailed)</td>
<td>-0.007</td>
<td>**0.301</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>176</td>
<td>176</td>
<td>176</td>
</tr>
<tr>
<td></td>
<td>Adherence level (%)</td>
<td>Pearson correlation Sig. (2-tailed)</td>
<td>0.072</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>176</td>
<td>176</td>
<td>176</td>
</tr>
</tbody>
</table>

** Correlation is significant at the 0.01 level (2 tailed)

The results of correlation in table 4.9 indicate that there is a weak positive association between adherence and age (r= 0.07); adherence and baseline CD4 cell counts (r=0.001); adherence and most recent CD4 cell counts (r=-0.125).

Table 4.10: Relationship of adherence to most recent CD4 cell count

<table>
<thead>
<tr>
<th>Number of patients (176)</th>
<th>CD4 cell counts</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥200</td>
</tr>
<tr>
<td>Adherent</td>
<td>113</td>
</tr>
<tr>
<td>Non-Adherent</td>
<td>131</td>
</tr>
</tbody>
</table>
Figure 4.12: Relationship of adherence to CD4 cell count.

Table 4.10 and figure 4.12 show the ability of the pharmacy refill adherence score in predicting CD4 cell counts of equal to or more than 200 cells/mm³. The tool was able to predict that 77% of the patients who were adherent achieved immune recovery (CD4 cell counts of equal to or greater than 200 cells/mm³). More patients in the adherent group had CD4 cell counts of equal to or more than 200 cells/mm³. The non-adherent group had fewer patients with CD4 cell counts equal or greater than 200 cells/mm³. However, 69.8% of patients in the non-adherent group also attained CD4 cell counts equal to or more than 200 cells/mm³. A weak positive relationship exists between adherence and CD4 cell counts.
Table 4.11: Post treatment adherence versus CD4 cell count (N=176)

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>176</td>
<td>100</td>
</tr>
<tr>
<td>Adherent patients (&gt;95% adherence)</td>
<td>113</td>
<td>64.2</td>
</tr>
<tr>
<td>Non-adherent patients (&lt;95% adherence)</td>
<td>63</td>
<td>35.8</td>
</tr>
<tr>
<td>CD4 cell count &gt;200</td>
<td>131</td>
<td>74.4</td>
</tr>
<tr>
<td>CD4 cell count &lt;200</td>
<td>45</td>
<td>25.6</td>
</tr>
</tbody>
</table>

The results in table 4.11 indicate that though non-adherent patients represented 35.8% (n=63), the patients with CD4 cell counts of equal to or less than 200 cells/mm$^3$ represented only 25.6% (n=45).

Table 4.12: Adherence versus mean most recent CD4 cell count

<table>
<thead>
<tr>
<th>Adherence</th>
<th>Mean CD4</th>
<th>Number of patients</th>
<th>Std, Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherent</td>
<td>362.1</td>
<td>113</td>
<td>274.5</td>
</tr>
<tr>
<td>Non-adherent</td>
<td>308.8</td>
<td>63</td>
<td>149.4</td>
</tr>
<tr>
<td>Total</td>
<td>343.0</td>
<td>176</td>
<td>238.3</td>
</tr>
</tbody>
</table>

The mean CD4 cell counts increased between baseline and most recent CD4 cell counts was as high as 175.3 cells/mm$^3$ (n=176). However, the mean CD4 cell
counts between the adherent (362.1) and non-adherent (308.8) groups at 12 months showed no significant difference.

If the causes of non-adherence are with memory, memory aids can be used, including beepers, cell phone reminders, or watches that will alarm when it is time to take medication and display the name of the pill and the number to be taken. Similar methods can be used to alert patients to collect medications when the due date is nearing. These devices have been used in clinical trials on small populations but are too expensive to give to all patients on HAART in a real life setting because the patients are too many and the resources are scarce (Tennenberger 1999). After therapy has been started, ongoing assessment and reinforcement of adherence is critical because the goal is for patients to live longer and better. Thus, researchers are interested not only in determining what strategies optimise adherence but also to optimise a range of outcomes including virological, immunologic and clinical aspects. Because adherence is not directly observable, the best that can be done is to estimate the extent of adherence. The most useful answer may be from composite methods that combine multiple measurements into a single score (Wu et al 2002:S95-S97).

As discussed in chapters 1 and 2 of the dissertation, there could be confounding variables that might have biased the findings of this study. These include patient metabolic profile (including gastrointestinal diseases), data recording errors, viral resistance to treatment, drug-drug interaction and patients with CD4 cell counts
of equal to or more than 200 cells/mm$^3$ because of being in WHO HIV/AIDS stage IV.

Apart from accurate measurement of adherence, there are other key issues in the study of adherence to ARVs, such as assessment of the impact of adherence on viral load and clinical outcome, determination of the factors that affect adherence and the development of interventions (Chesney 2000:S171). Patients also experience problems with adherence due to factors beyond their control, such as depression which has been associated with HAART non-adherence. Singh, Squier, Sivek, Wagener, Hong-Nguyen and Yu (1996:262) as well as Starace, Ammassari, Trotta, Murri, De Longis, Izzo, Scalzini, Monforte, Wu and Antinori (2002:S137) reported that depression has been associated with HIV infection since the beginning of the HIV/AIDS epidemic and that depression has a significant impact on the quality of life of people living with HIV/AIDS and it is also associated with worse treatment outcomes. In general depressed people’s behaviours have been associated with self-neglect, apathy and forgetfulness all of which may lead to non-adherence and therefore to a greater decline in CD4 cell counts and possibly also to an accelerated mortality.

Accessibility and affordability have been identified as factors leading to non-adherence (Ndayango et al 2005 & Weiser et al 2003:286). Though, at KIH ARVs are provided free of charge to the patients, they have to travel to KIH and may have to pay for transport. This may also be a factor leading to non-
adherence to ARVs at KIH because the majority of patients are either unemployed or in low paying jobs. These patients might not have the financial means to pay for transport to collect their ARVs or purchase food or food with the required nutrients and may therefore take ARVs on empty stomachs or miss pills because of their fears of side effects. These factors may influence non-adherence in patients on HAART at KIH.

There is a positive but weak relationship between adherence and CD4 cell counts equal to or more than 200 cells/mm$^3$. The increase in the study’s mean CD4 cell count post-treatment of 343.1 cells/mm$^3$ is an indication of the positive outcome of HAART treatment as an intervention to reduce morbidity and mortality rates. This can also be considered as a great improvement in immune recovery because the patients in the study population have only been on HAART for 12 months.

4.7 ASSESSMENT OF THE PHARMACY REFILL ADHERENCE MEASUREMENT METHODOLOGY

The pharmacy refill records were used to calculate the adherence level for each patient. The total number of prescriptions filled from the date of HAART initiation over a 12 month period of HAART was divided by 12 and the answer was multiplied by 100 to obtain the percentage adherence for each patient.
The optimal way to assess adherence to anti-retroviral therapy is not known because various studies used different methods to assess adherence and therefore, the best method to assess adherence remains unclear. Wu et al (2002:S95), stated that research on adherence measurement is crucial and that there is a problem because the measure of adherence is not standardised and studies used different adherence measurement methodologies.

In this study, the pharmacy refill adherence measurement tool was evaluated in order to improve the sensitivity of the KIH adherence measurement methodology. It has been documented that non-adherence leads to immunological and virological failure in patients on HAART and that optimal adherence improves survival and the durability of regimens (Paterson et al 2000:27). Clinical trial settings may employ direct observation of pill taking and rigorous follow-up on patients but that is hard to achieve in every day practice. Similarly the accurate quantification of taken and missed pills in every day practice is a daunting task, but benefits may be obtained with the use of a combination of adherence measurement methods.

The relationship between pharmacy refills and actual ingestion of medications is not clear and it is therefore very difficult to measure adherence in the outpatient setting accurately and correctly. As discussed in section 2.2.6 of chapter 2 of this dissertation, the various adherence measurement methodologies were found to have limitations such as over-estimation of adherence especially by the self
report methodology. This is the case because clinicians rely heavily on what the patient reports which might not necessarily be true. This necessitates the use of combination adherence measurement methods.

In any HAART programme, adherence needs to be measured and adherence measurement methodology needs to be studied in a real life setting and not only in a clinical trial (experimental) setting where patients are vigorously followed up and where methodologies that are not affordable in a HAART programme with a big population could be used. This study investigated adherence rates in a real life situation at KIH, serving many underprivileged people in a resource-poor country. The figures and calculations provided in table 4.13 should be read in conjunction with those of table 4.11. (All the numbers in table 4.13 add up to 176, which is the total number of patients’ records used in these calculations).

Table 4.13: Validity for predicting CD4 ≥200

<table>
<thead>
<tr>
<th>Adherence Measurement</th>
<th>CD4 cell counts</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD4 &gt;200</td>
<td>CD4 &lt;200</td>
</tr>
<tr>
<td>Adherent</td>
<td>87 [A]</td>
<td>26 [B]</td>
</tr>
<tr>
<td>Non-adherent</td>
<td>44 [C]</td>
<td>19 [D]</td>
</tr>
<tr>
<td>Total</td>
<td>131</td>
<td>45</td>
</tr>
</tbody>
</table>

Table 4.13 shows results of the assessment of the pharmacy refills in terms of the validity to predict CD4 cell counts equal to or more than 200 cells/mm$^3$.
Results:

Sensitivity \((A/A+C \times 100) = 66.4\%\), Specificity \((D/B+D) = 42.2\%\), Positive predictive value \((A/A+B) = 77.0\%\), Negative predictive value \((D/C+D) = 30.2\%\)

Sensitivity (true positive rate) in this study defines the percentage of CD4 cell counts equal to or more than 200 cells/mm\(^3\) in patients who were identified as adherent by the pharmacy refills adherence measuring method used at KIH. The sensitivity for adherence scores predicting CD4 cell counts equal to or more than 200 cells/mm\(^3\) is 66.4\%. Though this seems to be a high sensitivity value, it is not as high as other validated instruments used in screening for disease conditions. However, this appears promising considering that pharmacy refill records’ claims do not necessarily measure the actual ingestion of pills.

Specificity (true negative rate) of the instrument (pharmacy refills at KIH) translates to proportion of CD4 cell count below 200 cells/mm\(^3\). The specificity value of the instrument was 42.2\% for CD4 cell count. This is a low value and therefore confirms that the adherence measurement methodology may not be able to guide clinicians to detect early immunological failure.

The positive predictive value is the percentage of positive test results that are truly positive. The positive predictive value of the pharmacy refill was 77.0\% for predicting the percentage of CD4 cell counts, that are equal or more than 200
cells/mm$^3$ and that were truly equal or more than 200 cells/mm$^3$. This percentage is considered to be high.

The negative predictive value is the percentage of negative test results which are truly negative. The pharmacy refill has a negative predictive value of 30.2% for predicting the percentage of CD4 cell count results that are less than 200 cells/mm$^3$ and which were truly less than 200 cells/mm$^3$. This percentage is low and it might be better to use the instrument in combination with other more reliable adherence measurement methods.

The changes in the CD4 cell count results was used only as a measure of the validity of the adherence measurement instrument in this study because other studies such as Paterson et al (2000:23) already found that immunological and virological failures are associated with non-adherence. The pharmacy refill is able to measure adherence and predict the immunological outcome. Therefore, in the absence of another adherence measurement instrument, pharmacy refills can be used to monitor adherence but it should be used in combination with other adherence measures. Other quantitative adherence measures exist as discussed in chapter 2 of this dissertation, apart from pharmacy refills such as electronic monitoring devices, self reports and pill counts which can be used in combination with the pharmacy refills adherence measurement, to enhance validity of the tool.
There is a relationship between adherence as measured by pharmacy refills and immunological response, as shown in changes in the CD4 cell counts of the patients in the study population. However, the association is weak and it would be better to use this adherence measurement methodology in combination with other methods which have been proven to increase adherence and predict immunological responses.

This result is of this study is comparable to findings in a study on adherence to HAART, as assessed by pharmacy refill records, claims to predict survival in HIV-infected South African adults. That study concluded that pharmacy based records are valid indicators of HAART adherence in settings where other more labour intensive or expensive methods are impractical (Nachega, Hislop, Dowdy, Lo, Omer, Regensberg, Chaisson & Maartens 2006:84). Pharmacy refill records may provide a simple and effective population tool for monitoring adherence in a large HAART programme.

4.8 CONCLUSION

This chapter highlighted the level of adherence in terms of demographic factors and CD4 cell counts. There was no significant difference in terms of adherence and gender but a relationship was found between adherence and age. Adherence and CD4 cell counts increased with age. Unemployment was also not associated with non-adherence. Those who were living with others, renting or owning their own houses were more adherent users of ARVs. The patients
supported by their spouses or partners were more adherent and those supported by friends were the least adherent. Most patients were not on TB medication at the initiation of HAART. There was a significant increase in CD4 cell counts as noticed in the changes between the mean baseline CD4 cell counts and the mean of the most recent CD4 cell counts. The stage of WHO HIV/AIDS did not correlate with adherence and the majority of the patients were on 1st line ARVs compared to the few whose treatment was changed to 2nd line ARVs because of ARV toxicity, clinical and immunological failure and hepatitis. Most patients had an adherence level of >95% with a mean adherence level of 96.5% and a weak association between adherence level and CD4 cell counts was found. The pharmacy refill adherence measurement methodology scored high on sensitivity and positive predictive values but low on specificity and negative predictive values.

Thus, the study concludes that though the pharmacy refill records can predict immunological response, it should be used in combination with other adherence measurement tools. The reasons for non-adherence and why some adherent patients had CD4 cell counts of less than 200 cells/mm³, were not investigated in this study and this could be an area for future research.

The next chapter will present the conclusions, limitations and recommendations of this study as well as propose areas for possible future research.
supported by their spouses or partners were more adherent and those supported by friends were the least adherent. Most patients were not on TB medication at the initiation of HAART. There was a significant increase in CD4 cell counts as noticed in the changes between the mean baseline CD4 cell counts and the mean of the most recent CD4 cell counts. The stage of WHO HIV/AIDS did not correlate with adherence and the majority of the patients were on 1\textsuperscript{st} line ARVs compared to the few whose treatment was changed to 2\textsuperscript{nd} line ARVs because of ARV toxicity, clinical and immunological failure and hepatitis. Most patients had an adherence level of >95\% with a mean adherence level of 96.5\% and a weak association between adherence level and CD4 cell counts was found. The pharmacy refill adherence measurement methodology scored high on sensitivity and positive predictive values but low on specificity and negative predictive values.

Thus, the study concludes that though the pharmacy refill records can predict immunological response, it should be used in combination with other adherence measurement tools. The reasons for non-adherence and why some adherent patients had CD4 cell counts of less than 200 cells/mm\textsuperscript{3}, were not investigated in this study and this could be an area for future research.

The next chapter will present the conclusions, limitations and recommendations of this study as well as propose areas for possible future research.
CHAPTER 5
CONCLUSIONS, LIMITATIONS AND
RECOMMENDATIONS

5.1 INTRODUCTION

The main purpose of the study was to determine the relationship between adherence to ARVs as measured by pharmacy refills and immunological response as indicated by an increase in CD4 cell counts in treatment experienced patients (aged 18 and older) at KIH.

Furthermore, the pharmacy refill adherence measurement methodology used at KIH was assessed for validity in predicting changes in CD4 cell counts. The results have been used to recommend an appropriate adherence measurement methodology at KIH and the possibility of recommending for its use at other public health facilities providing HAART. The conclusions, based on the research results discussed in chapter 4 of this dissertation, will be used to answer the research questions which were formulated in Chapter 1 as follows:

- Are pharmacy refill records good predictors of CD4 cell counts?
- Is pharmacy refill an accurate ARV adherence measuring tool?
5.2. OBJECTIVES

The objectives of the study were evaluated to determine whether they have been attained. Each objective will be listed and the conclusions given in relation to that specific objective.

- To determine if there is a correlation between adherence to ARVs as measured by pharmacy refill and CD4 cell counts

The results of the study have shown that there is a correlation between adherence and CD4 cell counts because the patients who had adherence of >95% as measured through the pharmacy refills had immunological response as shown through an increase in their CD4 cell counts from baseline to when measured after 12 months of HAART. However, there were few patients who were non-adherent but whose CD4 cell counts were more than 200 cells/mm³ after being on HAART for 12 months. This could be explained by the fact that the patients' were started on HAART because they were clinically ill even though their CD4 cell counts were more than 200 cells/mm³ (WHO HIV/AIDS stage IV). Though the study established that a relationship between adherence and CD4 cell counts existed, this relationship was weak.
• To determine if ARV pharmacy refills are effective adherence measurement tools at KIH.

The assessment of the pharmacy refill adherence measurement methodology revealed that the tool has a sensitivity of 66.4% and is therefore able to identify patients who were adherent and who had CD4 cell counts of equal to or more than 200 cells/mm³. The pharmacy refill adherence measurement tool is reliable and can be predictive of the CD4 cell count results. However, there is a need for more studies to evaluate why the tool has a low sensitivity and also investigate the relationship between adherence and other clinical outcomes such as morbidity and mortality. The study concluded that pharmacy refill records are valid indicators of HAART adherence in settings where other more reliable and expensive adherence measurement methodologies are not available. Pharmacy refill is a simple and effective population tool for monitoring adherence in a large HAART programme because other methodologies have mainly been used in research settings and not in a big HAART population programme such as the one at KIH with 2600 patients.

• To recommend a simple adherence measurement tool at KIH

The pharmacy refill records presented a simple adherence measurement tool which can be used to monitor adherence at KIH. Because the tool is not sensitive enough, it is recommended that another simple tool such as pill count
or self reports should be used in combination to increase the validity and reliability of the measurement methodology.

5.3 LIMITATIONS OF THE STUDY

The limitations that were identified during the course of the study included that:

- The research results might only be limited to the KIH where the study was conducted and since the sample was small and represented only one hospital out of the 36 public health hospitals which provide HAART and is not a representative sample of all HAART patients in Namibia.

- The patients were from a cohort of patients who were enrolled during the same period, 3 years after the ART programme had been initiated.

- The researcher only recruited 176 patients. Out of the 306 patients who had started using ARVs during February and March 2006 and who were on treatment until 31 March 2007, only 176 could be recruited because the rest of the patients did not meet the inclusion criteria. Poor record keeping was the main contributing factor to the small sample because some patients’ medical records lacked important information such as CD4 cell count results and pharmacy refills.

- Patients who were enrolled on HAART at KIH are from a lower socio-economic class and most of them are unemployed and therefore do not
measurement and reporting. This is important to ensure reliability of the result of the measurement because observation of same adherence levels using different measurement tools can be scored differently.

- It is also crucial that factors contributing to non-adherence are explored and interventions developed to eliminate the barriers to adherence in order to improve adherence.

- The HAART programme is only provided at all public sector district and referral hospitals. These health facilities are mostly overcrowded and not easily accessible due to distance. Therefore, there is a need to roll out HAART to health centres and clinics to increase accessibility to HAART and promote adherence.

- To reduce the travel costs to hospital to collect the ARVs on monthly basis which has been cited to be a barrier to adherence, the patients who adhere should be given three months’ supplies. This will imply that the patient will come to the hospital only once per quarter and not every month.

- Adherence counselling should be repeated at every ART clinic and ARV pharmacy visits to reinforce the importance of adherence to ARVs.

- Virological tests should be routinely conducted on all patients on HAART so that if the HI virus is resistant to the ARVs, the regimen can be changed. This will reduce wastage of resources because if the virus is resistant to the ARVs and it is not determined by doing virological tests,
the health practitioner may continue to prescribe the same ARVs and may also wrongly regard the patient to be non-adherent.

5.5 RECOMMENDATIONS FOR FURTHER STUDIES

Future researchers should investigate the following aspects pertaining to adherence to ARVs, to enhance adherence rates at KIH and at other sites.

- Duplicate of this study in other public health facilities prior to generalisation of these research results to all HIV/AIDS experienced patients.
- Investigate correlation between CD4 cell counts and adherence in the private sector using medical aid scheme records for ARV refills and laboratory results.
- Investigate the reasons why ARV experienced patients do not adhere to ARVs.
- Identify and implement interventions that could be put in place to increase adherence to ARVs.
- Find reasons why non-adherent patients also have increased CD4 cell count results.
- Find reasons why adherent patients also have decreased CD4 cell count results.
- Study the use of traditional or complementary medicines in combination with ARVs and its relations with CD4 cell counts.
• Study the behaviours of health professionals at public health facilities with specific emphasis on the treatment of HIV/AIDS patients.

• Investigate the perceptions of ARV experienced patients towards public health professionals.

• Conduct qualitative research to determine the knowledge, attitudes and perceptions of people in the community concerning ARVs in an attempt to get their support in reducing discrimination and stigmatisation and increase adherence among all patients at KIH.

• Conduct research on the knowledge, attitudes and perceptions of HIV/AIDS counsellors at KIH.

• Evaluate the quality of HIV/AIDS counselling and education provided at KIH.

• Study the extent of depression among patients on HAART at KIH and its link to non-adherence.

• Study the rate of hospitalisation among patients on HAART at KIH and its correlation with non-adherence.

• identify the major opportunistic infections experienced among patients on HAART at KIH.

• Study the extent of TB and HIV/AIDS co-morbidity.

• Study the extent of morbidity and mortality among patients on HAART at KIH.
5.6 CONCLUSION

The study revealed a weak relationship between adherence and CD4 cell counts. The pharmacy refill adherence measurement methodology was able to predict immunological recovery as shown in changes in the CD4 cell counts. Though there was a relationship between adherence and CD4 cell counts, this relationship was weak and it is recommended that the pharmacy refill adherence measurement methodology should be used in combination with other more sensitive adherence measurement tools to increase validity. The pharmacy refill adherence measurement methodology is therefore recommended to be used to monitor adherence in ARV experienced adult patients at KIH. However, before this tool is rolled out to other public health facilities, another study should be conducted to determine the factors leading to non-adherence.


Katutura Intermediate Hospital ARV pharmacy. 21 February 2006. Personal Interview


KIH – see Katutura Intermediate Hospital


MoHSS – see Ministry of Health and Social Services (Namibia)


Proctor, VE, Testa, A & Tompkins, DC. 1999. Barriers to highly active anti-retroviral therapy as expressed by people living with HIV/AIDS.

SADC see Southern Africa Development Community


WHO see World Health Organization.


Annexure A

Letter to the MOHSS requesting permission to conduct the study
Annexure A
Dr Kalumbi Shangula
Permanent Secretary
Ministry of Health and Social Services
Private Bag 13198
Windhoek

Dear Dr Shangula

RE: REQUEST TO CONDUCT A STUDY

I am a final year Master of Public Health (MPH) student at the University of South Africa (UNISA) in Pretoria. I am required to complete a dissertation of limited scope before obtaining the above-mentioned qualification.

I intend to do a study on CORRELATION BETWEEN CD4 CELL COUNT AND ADHERENCE TO ANTIRETROVIRALS IN TREATMENT EXPERIENCED PATIENTS AT KATUTURA INTERMEDIATE HOSPITAL (KIH). The proposed study requires CD4 cell counts results and the pharmacy refill data of patients who have been on ARVs at KIH between September 2003 and June 2006. The required data are available from the Ministry’s HIS and the ARV pharmacy at the said hospital.

I am therefore requesting permission to conduct the study. This study is quite significant because the findings cannot only be used for academic qualification but can also be used to develop interventions to improve or strengthen the ART programme not only at KIH but for the entire public health facilities providing ART.

The issue of ethics have been seriously considered and covered in the attached proposal. All information will be handled confidentially and all copied information (no names of patients) will be destroyed once the data analysis has been completed.

Let me assure you that if permission is granted and the study is completed, findings will be disseminated to the Ministry.

Sincerely

Dinah Jorokee Tjipura (A.K.A Tjiho)
P.O.Box 32289
Pionierspark
Windhoek
203 2391 (W)/223782 (H)/08-128-6359
Annexure B

Letter of approval from the MOHSS granting permission to conduct the study
OFFICE OF THE PERMANENT SECRETARY

Ms. D.J. Tjipura
P.O. Box 32289
Pionerspark
Windhoek

Dear Ms. Tjipura,

**Correlation between CD4 cell count and adherence to antiretroviral in treatment experienced patients at Katutura Hospital.**

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:
   3.9.1 The data collected is only to be used for your degree;
   3.10 A quarterly progress report is to be submitted to the Ministry’s Research Unit;
   3.11 Preliminary findings are to be submitted to the Ministry before the final report;
   3.12 Final report to be submitted upon completion of the study;
   3.13 Separate permission to be sought from the Ministry for the publication of the findings.

Wishing you success with your project.

Yours sincerely,

[Signature]

DR. K. SHANGULA
PERMANENT SECRETARY

*Forward with Health for all Namibians by the Year 2000 and Beyond!*
Annexure C

Ethical clearance from Unisa
ANNEXURE C

UNIVERSITY OF SOUTH AFRICA
Health Studies Research & Ethics Committee
(HSREC)
Faculty of Humanities and Social Sciences
CLEARANCE CERTIFICATE

Date of meeting: 8 February 2007
St No: 0860-597-1

Project Title: CORRELATION BETWEEN CD4 CELL COUNTS AND
ADHERENCE TO ANTIRETROVIRAL THERAPY IN TREATMENT
EXPERIENCED PATIENTS AT KATUTURA INTERMEDIATE HOSPITAL,
WINDHOEK, NAMIBIA.

Researcher: Ms DJ Tjipura
Supervisor/Promoter: Dr VJ Ehlers
Joint Supervisor/Joint Promoter: Dr JH Roos
Department of Health Studies
Degree: Master’s in Public Health

DECISION OF COMMITTEE

Approved
Date: 8 February 2007

Prof TR Mavundla
RESEARCH COORDINATOR

Prof SM Mogotlane
ACADEMIC CHAIRPERSON: DEPARTMENT OF HEALTH STUDIES
Annexure D

Map of Namibia
ANNEXURE D: MAP OF NAMIBIA
Annexure E
DATA COLLECTION INSTRUMENT: CHECKLIST

Correlation between CD4 cell counts and adherence to Antiretroviral therapy in treatment experienced patients at Katutura Intermediate Hospital, Windhoek, Namibia

Checklist number

SECTION A: Patient Information

1. Patient’s ARV reference number:

2. Pharmacy reference number

3. Gender:
   M
   F

4. Age at your previous birthday

5. Education:

   None
   Primary
   Secondary
   High school
   Higher institution
   Other
6. Home language

<table>
<thead>
<tr>
<th>Language</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lozi</td>
</tr>
<tr>
<td>Rukwangali</td>
</tr>
<tr>
<td>English</td>
</tr>
<tr>
<td>Afrikaans</td>
</tr>
<tr>
<td>Otjiherero</td>
</tr>
<tr>
<td>Nama/Damara</td>
</tr>
<tr>
<td>German</td>
</tr>
<tr>
<td>Tswana</td>
</tr>
<tr>
<td>Oshiwambo</td>
</tr>
<tr>
<td>Other (please specify)</td>
</tr>
</tbody>
</table>

7. Type of employment

<table>
<thead>
<tr>
<th>Employment Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unemployed</td>
</tr>
<tr>
<td>Self-employed (please specify)</td>
</tr>
<tr>
<td>Government institution</td>
</tr>
<tr>
<td>Private company</td>
</tr>
<tr>
<td>Parastatal organisation</td>
</tr>
<tr>
<td>Other (please specify)</td>
</tr>
</tbody>
</table>

8. Permanent physical address

<table>
<thead>
<tr>
<th>Address Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural</td>
</tr>
<tr>
<td>Urban</td>
</tr>
</tbody>
</table>

9. Residence type

<table>
<thead>
<tr>
<th>Residence Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Own house</td>
</tr>
<tr>
<td>Rent</td>
</tr>
<tr>
<td>Live with others</td>
</tr>
<tr>
<td>Other (please specify)</td>
</tr>
</tbody>
</table>

10. Person chosen to support patient with ARV use

<table>
<thead>
<tr>
<th>Parent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child</td>
</tr>
<tr>
<td>Spouse/partner</td>
</tr>
<tr>
<td>Friend</td>
</tr>
<tr>
<td>Employer</td>
</tr>
<tr>
<td>Other (please specify)</td>
</tr>
</tbody>
</table>

SECTION B: Clinical Information

11. Date of HIV diagnosis

\[
\text{dd/mm/yyyy}
\]

12. Currently on TB medicines

<table>
<thead>
<tr>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
</tr>
</tbody>
</table>

13. If yes, date on which TB treatment was initiated

\[
\text{dd/mm/yyyy}
\]

14. CD4 cell count values

<table>
<thead>
<tr>
<th>Date (dd/mm/yyyy)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>Most recent</td>
<td></td>
</tr>
</tbody>
</table>
SECTION C: ART Information

15. Date of HAART initiation

\[ \text{dd/mm/yyyy} \]

16. WHO HIV/AIDS stage at start of HAART

| I |  
| II |  
| III |  
| IV |  

17. Current ARV therapy

<table>
<thead>
<tr>
<th>Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
</tr>
<tr>
<td>(30) Stavudine (D4T)</td>
</tr>
<tr>
<td>(40) Stavudine (D4T)</td>
</tr>
<tr>
<td>Didanosine (ddl)</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-Nucleoside Analogue Transcriptase Inhibitors (NNRTIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine (NVP)</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protease Inhibitors (PI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indinavir (IDV)</td>
</tr>
<tr>
<td>Lopinavir (LPV)</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
</tr>
</tbody>
</table>

18. Is this current ART regimen:

<table>
<thead>
<tr>
<th>First line</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2nd line</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>

19. Was the regimen changed?

<table>
<thead>
<tr>
<th>YES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td></td>
</tr>
</tbody>
</table>

20. Reason for regimen change if applicable

<table>
<thead>
<tr>
<th>ARV toxicity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Active TB disease</td>
<td></td>
</tr>
<tr>
<td>Clinical failure</td>
<td></td>
</tr>
<tr>
<td>Immunological failure (decrease in CD4 cell)</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>

SECTION D: Pharmacy refill record for the period 1st February 2006 to 31st March 2007

21. Date ARVs collected from ARV Pharmacy

| 1. |  |
| 2. |  |
| 3. |  |
| 4. |  |
| 5. |  |
| 6. |  |
| 7. |  |
| 8. |  |
| 9. |  |
| 10 |  |
| 11 |  |
| 12 |  |
22. Adherence level

23. Remarks

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
Annexure E

Checklist used for data collection
Annexure F

Completed checklist
DATA COLLECTION INSTRUMENT: CHECKLIST

Correlation between CD4 cell counts and adherence to Antiretroviral therapy in treatment experienced patients at Katutura Intermediate Hospital, Windhoek, Namibia

Checklist number 010

SECTION A: Patient Information

1. Patient’s ARV reference number:

   4959A

2. Pharmacy reference number

   135852

3. Gender:

   M X
   F

4. Age at your previous birthday

   32

5. Education:

<table>
<thead>
<tr>
<th>None</th>
<th>Primary</th>
<th>Secondary</th>
<th>High school</th>
<th>Higher institution</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>V</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6. **Home language**

<table>
<thead>
<tr>
<th>Language</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lozi</td>
<td></td>
</tr>
<tr>
<td>Rukwangali</td>
<td></td>
</tr>
<tr>
<td>English</td>
<td></td>
</tr>
<tr>
<td>Afrikaans</td>
<td></td>
</tr>
<tr>
<td>Otjiherero</td>
<td>✔</td>
</tr>
<tr>
<td>Nama/Damara</td>
<td></td>
</tr>
<tr>
<td>German</td>
<td></td>
</tr>
<tr>
<td>Tswana</td>
<td></td>
</tr>
<tr>
<td>Oshiwambo</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>

7. **Type of employment**

<table>
<thead>
<tr>
<th>Employment Type</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unemployed</td>
<td>✔</td>
</tr>
<tr>
<td>Self-employed (please specify)</td>
<td></td>
</tr>
<tr>
<td>Government institution</td>
<td></td>
</tr>
<tr>
<td>Private company</td>
<td></td>
</tr>
<tr>
<td>Parastatal organisation</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>

8. **Permanent physical address**

<table>
<thead>
<tr>
<th>Category</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural</td>
<td>✔</td>
</tr>
<tr>
<td>Urban</td>
<td>✔</td>
</tr>
</tbody>
</table>

9. **Residence type**

<table>
<thead>
<tr>
<th>Type</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Own house</td>
<td></td>
</tr>
<tr>
<td>Rent</td>
<td></td>
</tr>
<tr>
<td>Live with others</td>
<td>✔</td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>
10. Person chosen to support patient with ARV use

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent</td>
<td></td>
</tr>
<tr>
<td>Child</td>
<td></td>
</tr>
<tr>
<td>Spouse/partner</td>
<td></td>
</tr>
<tr>
<td>Friend</td>
<td>✓</td>
</tr>
<tr>
<td>Employer</td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
</tr>
</tbody>
</table>

SECTION B: Clinical Information

11. Date of HIV diagnosis

<table>
<thead>
<tr>
<th>dd/mm/yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/3/2015</td>
</tr>
</tbody>
</table>

12. Currently on TB medicines

<table>
<thead>
<tr>
<th>YES</th>
<th></th>
</tr>
</thead>
</table>

12. Currently on TB medicines

<table>
<thead>
<tr>
<th>NO</th>
<th></th>
</tr>
</thead>
</table>

13. If yes, date on which TB treatment was initiated

<table>
<thead>
<tr>
<th>dd/mm/yyyy</th>
</tr>
</thead>
</table>

14. CD4 cell count values

<table>
<thead>
<tr>
<th></th>
<th>Date (dd/mm/yyyy)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4/5/6</td>
<td></td>
</tr>
<tr>
<td>Most recent</td>
<td>6/4/4</td>
<td></td>
</tr>
</tbody>
</table>
SECTION C: ART Information

15. Date of HAART initiation

\[dd/mm/yyyy\]

16. WHO HIV/AIDS stage at start of HAART

<table>
<thead>
<tr>
<th>Stage</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></td>
</tr>
</tbody>
</table>
| III   |   | ✔
| IV    |   |

17. Current ARV therapy

<table>
<thead>
<tr>
<th>Nucleoside Analogue Reverse Transcriptase Inhibitors (NRTIs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
</tr>
<tr>
<td>(30) Stavudine (D4T)</td>
</tr>
<tr>
<td>(40) Stavudine (D4T)</td>
</tr>
<tr>
<td>Didanosine (ddl)</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
</tr>
</tbody>
</table>

Non-Nucleoside Analogue Transcriptase Inhibitors (NNRTIs)

<table>
<thead>
<tr>
<th>Nevirapine (NVP)</th>
</tr>
</thead>
</table>
| Efavirenz (EFV)    | ✔

Protease Inhibitors (PI)

<table>
<thead>
<tr>
<th>Indinavir (IDV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopinavir (LPV)</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
</tr>
<tr>
<td>Saquinavir (SQV)</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
</tr>
</tbody>
</table>
18. Is this current ART regimen:

| First line | ✓ |
| 2nd line |   |
| Other (please specify) |   |

19. Was the regimen changed?

| YES | ✓ |
| NO |   |

20. Reason for regimen change if applicable

| ARV toxicity |   |
| Active TB disease |   |
| Clinical failure |   |
| Immunological failure (decrease in CD4 cell) |   |
| Other (please specify) |   |

SECTION D: Pharmacy refill record for the period 1st February 2006 to 31st March 2007

21. Date ARVs collected from ARV Pharmacy

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>6 Mar 06</td>
</tr>
<tr>
<td>2.</td>
<td>2 Apr 06</td>
</tr>
<tr>
<td>3.</td>
<td>9 May 06</td>
</tr>
<tr>
<td>4.</td>
<td>21 May 06</td>
</tr>
<tr>
<td>5.</td>
<td>23 Jun 06</td>
</tr>
<tr>
<td>6.</td>
<td>24 Jun 06</td>
</tr>
<tr>
<td>7.</td>
<td>25 Jun 06</td>
</tr>
<tr>
<td>8.</td>
<td>27 Sept 06</td>
</tr>
<tr>
<td>9.</td>
<td>4 Nov 06</td>
</tr>
<tr>
<td>10.</td>
<td>8 Dec 06</td>
</tr>
<tr>
<td>11.</td>
<td>8 Jan 07</td>
</tr>
<tr>
<td>12.</td>
<td>8 Jan 07</td>
</tr>
</tbody>
</table>
22. **Adherence level**

\[ \begin{array}{c}
\end{array} \]

23. **Remarks**

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]

\[ \begin{array}{c}
\end{array} \]
Annexure G

Letter from the statistician