ANTIRETROVIRAL ADHERENCE AND HIV VIROLOGICAL OUTCOMES IN HIV-POSITIVE PATIENTS IN UGU DISTRICT, KWAZULU-NATAL PROVINCE

by

KAPIAMBA MUTEBA GERMAIN

submitted in accordance with the requirements

for the degree of

MASTER OF PUBLIC HEALTH

at the

UNIVERSITY OF SOUTH AFRICA

SUPERVISOR: DR TE MASANGO

CO-SUPERVISOR: MR DD MPHUTHI

November 2014

DECLARATION

I declare that **ANTIRETROVIRAL ADHERENCE AND HIV VIROLOGICAL OUTCOMES IN HIV-POSITIVE PATIENTS IN UGU DISTRICT, KWAZULU-NATAL PROVINCE** 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.

Dr Kapiamba Muteba Germain   January 2015

FULL NAMES   **DATE**

ANTIRETROVIRAL ADHERENCE AND HIV VIROLOGICAL OUTCOMES IN HIV-POSITIVE PATIENTS IN UGU DISTRICT, KWAZULU-NATAL PROVINCE

Student Number: 37348639
Student: Dr MG Kapiamba
Degree: Master in Public Health
Department: Health studies, University of South Africa
Supervisor: Dr TE Masango
Co-supervisor: DD Mphuthi

ABSTRACT

Adherence to antiretroviral therapy is crucial to ensure viral suppression. In the scientific community it is widely accepted that an adherence level of at least 90% is necessary to achieve viral suppression. This study uses pharmacy refill records to describe antiretroviral adherence in HIV-positive patients in Ugu District and to describe pharmacy refill records as reliable monitoring method of antiretroviral therapy. In total, 61 patients' records were reviewed. Overall, 82% of participants (n=50) achieved an optimum adherence level of at least 90%. Although 38% (n=19) of these participants did not show any related viral suppression. A statistically significant relationship between adherence and viral suppression was not demonstrated. Therefore, pharmacy refill records cannot be recommended as an alternative method of monitoring response to antiretroviral therapy, but laboratory tests including CD4 cell count and or viral load must be combined to pharmacy refill method for monitoring of antiretroviral therapy in HIV-positive patients.

Key words

Adherence to antiretroviral therapy; pharmacy refill records; viral suppression; HIV-positive patients; Ugu District.

ACKNOWLEDGMENTS

Dedication

I dedicate this dissertation to my beautiful wife, Joelle LUKUSA and wonderful children, Joyce KAPIAMBA and Glory KAPIAMBA.

TABLE OF CONTENTS

CHAPTER 1

STUDY OVERVIEW

CHAPTER 2

LITERATURE REVIEW

CHAPTER 3

RESEARCH DESIGN AND METHOD

CHAPTER 4

ANALYSIS, PRESENTATION AND DESCRIPTION OF RESEARCH FINDINGS

CHAPTER 5

CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AACTG	Adult Aids clinical trials group
ADCs	AIDS defining conditions
AIDS	Acquired Immune Deficiency Syndrome
ART	Therapy
ARV	Antiretroviral
CAPRISA	Centre for the Aids programme of research in South Africa
CDC	Centre for Disease Control
CD4	Cluster of Differentiation
DOH	Department of Health
DOT	Directly observed therapy
FDC	Fixed-dose combination
HAART	Highly active antiretroviral therapy
HIV	Human Immunodeficiency Virus
HIV RNA	Human Immunodeficiency virus ribonucleic acid
IDPs	Internationally displaced persons
MDG	Millennium Development Goal
MTCT	Mother-to-child transmission
NSP	National Strategic plan
PEP	Pre-exposure prophylaxis
PMTCT	Prevention of mother to child transmission
KZN	KwaZulu-Natal
SA	South Africa
SANAC	South Africa National AIDS
SPSS	Statistical Package for Social Sciences
STI	Sexually transmitted infections
TB	Tuberculosis
UNAIDS	United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
UNISA	University of South Africa
VL	Viral load
WHO	World Health Organization

LIST OF ANNEXURES

CHAPTER 1

STUDY OVERVIEW

1.1   INTRODUCTION

Worldwide, the number of people newly infected with Human Immunodeficiency Virus (HIV) continues to decline (United Nations Programme on HIV/AIDS (UNAIDS) 2012:8). There were 2.3 (1.9-2.7) million new HIV infections globally in 2012, showing a 33% decline in the number of new infections from 3.4 (3.1-3.7) million in 2001 (UNAIDS 2013:4). Also, the annual number of people dying from AIDS-related causes declined by at least 50% from 2005 to 2011 because of scaled-up antiretroviral therapy and the steady decline in HIV incidence since the peak in 1997.

As programmatic scale-up has continued, health gains have accelerated and the number of life- years saved by antiretroviral therapy in Sub-Saharan Africa quadrupled in the last four years (UNAIDS 2012:12). In addition to the effects on Acquired Immune Deficiency Syndrome (AIDS) mortality and overall HIV prevalence, it is believed that improved treatment access could help to lower HIV incidence by reducing the viral load at the individual and community level (Centers for Disease Control and Prevention (CDC) 2013:1). Antiretroviral therapy (ART) aims to reduce and sustain plasma viral load levels to below the level of detectable limit of the assay. The sustained inhibition of viral replication results in partial reconstitution of the immune system in most patients, substantially reducing the risk of clinical disease progression and death (Benni, Sethi & Williams 2012:97-99).

Adherence to antiretroviral therapy is crucial to ensure viral suppression, and decrease the risk of disease progression and drug resistance (Rougemont, Stoll, Elia & Ngang 2009:2). The best biological marker of adherence is an undetectable viral load in patients on ART (Meintjes, Maartens, Boulle, Conradie, Goemaere, Hefer, Johnson, Mathe, Moosa, Regina, Rossouw, Van Cutsem, Variava, Venter & Spencer 2012b:165). In the scientific community, it is widely accepted that an adherence level of at least 90% is necessary to suppress the virus sufficiently, to avoid the risk of mutation, and to

prevent the development of drug resistant strains and drug failure (Van Dyk 2013:121). Improving the ability of providers to access adherence is essential for routine care of HIV-infected patients, especially in settings where viral load monitoring is limited.

Data are needed to inform policy makers on how best to use easily accessible methods such as pharmacy refill data for monitoring response to antiretroviral therapy and for identification of patients at risk of virological failure, especially in low-income countries. As a result, this study aimed to describe antiretroviral adherence in HIV-positive patients using pharmacy refill records and review of patients' files between January 2011 and December 2012 and to determine the ability of adherence to detect virological outcomes.

1.2   BACKGROUND TO THE RESEARCH PROBLEM

Sub-Saharan Africa remains most severely affected with nearly 1 in every 20 adults (4.9%) living with HIV and accounting for 69% of the people living with HIV worldwide. At the end of 2012, an estimated 25 million people were living with HIV in Sub-Saharan Africa, among which 1.6 million were newly infected with HIV (UNAIDS 2013:4). In addition, South Africa (SA) has a generalised epidemic of HIV, driven largely by sexual transmission. In 2009, an estimated 5.63 million people were living with HIV in South Africa. The HIV prevalence has stabilised in recent years with an estimated 5.26 million people living with the virus at the end of 2013. However, it is still significantly higher than in most countries in Sub-Saharan and the rest of the world (Moosa & Jeenah 2012:144; South Africa 2013:8; Statistics South Africa 2013:2).

In 2011, an estimated 56% of people eligible for HIV treatment in sub-Saharan Africa received it compared to a global average of 54%. South Africa achieved more than 60% coverage of HIV treatment (UNAIDS 2012:2). In 2012, 9.7 million people in low and middle-income countries were receiving antiretroviral therapy. Therefore, more people than ever are now receiving life-saving antiretroviral therapy, contributing to steady declines in the number of AIDS-related deaths and further buttressing efforts to prevent new infections. From 1996 to 2015, antiretroviral averted 5.5 million AIDS-related deaths in low and middle-income countries. The annual number of new HIV infections among adults in sub-Saharan Africa has declined by 34%. Despite these gains, the

epidemic continues to disproportionately affect sub-Saharan Africa, home to 70% of all new infections in 2012 (UNAIDS 2013:2-12).

The introduction of antiretroviral therapy has seen a decline in the morbidity and mortality associated with infection. This is a consequence of the ability of ART to suppress HIV viraemia to undetectable levels and allow immune restoration, resulting in an increase in circulating CD4 cells (Muzah, Takuva, Maskew, Delany-Moretlwe 2012:168). According to the study conducted by Pirkle, Boileau, Nguyen, Machouf, Aboubacrine, Niamba, Drabo, Koala, Tremblay and Rashed (2009:153), meticulous adherence to treatment is the most important factor in delaying the development of drug resistance and is crucial determinant of therapeutic success, as proper adherence is strongly correlated with virological and clinical outcome.

Ideally, viral load should be measured before starting therapy, 2 to 8 weeks later, and then at 4 to 8 week intervals until Human Immunodeficiency Virus ribonucleic acid (HIV RNA) is no longer detectable. At least a 1 log 10 reduction in viral load(VL) should be expected at 4 weeks, with decline in plasma HIV RNA to less than 50 copies/ml by 16 to 24 weeks of therapy (Tsibris & Hirsch 2010:5461). However, WHO has recommended the use of cluster of differentiation 4(CD4) count measurements and clinical outcomes for monitoring ART in the absence of viral load (Badri, Lawn & Wood 2008:89).

CD4 responses are highly variable and may fail to increase despite virological suppression, in about 10-20% of patients (Meintjes et al 2012a:119). In addition, patients with AIDS defining conditions (ADCs) take longer to regain their CD4 counts due to the defect in the immune system (Kigozi, Sumba, Mudyope, Namuddu, Kalyango, Karamagi, Odere, Katabira, Mugyenyi & Ssali 2009:7). A person with optimal virological suppression can in some cases have low CD4+Tcell count responses. Therefore, the CD4+Tcell count is not a good indicator of ART failure and should preferably not be used to indicate the effectiveness of ART (Van Dyk 2013:119).

Studies have shown that virological suppression is associated with adherence to antiretroviral medications (Pirkle et al 2009:153-154: Walshe, Saple, Mehta, Shah, Bollinger & Gupta 2010:190; Zaragoza-Macias, Cosco, Nguyen, Delrio & Lennox 2010:135). Study conducted by Ford, Darder, Spelman, Maclean Millis and Boulle (2010:1) has provided a confirmation of adherence as a primary determinant of

subsequent confirmed virological failure, and serves as a reminder of the importance of initial early investments in adherence counselling and support as an effective way to maximise long-term treatment success.

In Southern Africa, routine viral load monitoring is recommended to identify treatment failure but it is often not done with sufficient frequency, nor reacted to appropriately (Stoll, Michel & Oliveira 2013:24). Routine viral load monitoring, identifying patients with high viral loads and addressing adherence promptly are essential components of the ART programme in South Africa (Conradie, Cox & Wilkinson 2013:22).

1.3   STATEMENT OF THE RESEARCH PROBLEM

The South African antiretroviral treatment guidelines recommend monitoring viral load at six months after starting ART, one year and then annually to identify treatment failures and problems with adherence (South Africa 2013a:7). As a medical doctor working in Ugu district, a rural area in KwaZulu-Natal (KZN), the researcher has seen that despite standardised and supportive policy, plasma viral load measurements are not promptly done for HIV-positive patients on ART which could lead to the emergence of drugs resistance and result in therapeutic failure. Thus, the need for an alternative strategy method for monitoring the response to antiretroviral therapy in HIV-positive patients is imperative.

1.4   RESEARCH PURPOSE

The purpose of this study is to describe antiretroviral adherence in HIV-positive patients using pharmacy refill records and to describe pharmacy refill records as an alternative method of monitoring response to antiretroviral therapy.

1.5   RESEARCH OBJECTIVES

The objectives for this study are to

- describe adherence to antiretroviral therapy by HIV-positive patients in Ugu district

- describe pharmacy refill records as reliable monitoring method of HIV-positive patients on antiretroviral therapy

1.6   RESEARCH QUESTIONS

The study sought the answer the following research questions:

- To what extent do HIV-positive patients in Ugu District adhere to ART?
- Could pharmacy refill records be used as a reliable method of monitoring patients on antiretroviral therapy?

1.7   SIGNIFICANCE OF THE STUDY

The findings will help, ideally in clinical practice, to do the following:

- To assess the response to antiretroviral therapy by using a very simple measure of adherence. Pharmacy refill for clinics that do not have CD4 counts or viral load monitoring capabilities.
- For clinics able to perform viral load assessment in all patients routinely, adherence monitoring using pharmacy refill could guide decision-making on timing of these tests.
- For clinics unable to perform routine viral load measurement, the finding of this study will help to recommend the use of pharmacy refill as practical monitoring tool for early identification of patients at high risk of virological failure.

1.8   DEFINITIONS OF KEY CONCEPTS

The following terms will be used throughout this study and their meanings are defined so that the researcher and the readers can share the same understanding of these concepts.

Adherence refers to the willingness and ability of patients to follow health-related advice, take medication as prescribed, attend scheduled appointments, and complete recommended investigations (Moosa & Jeenah 2012:144). In this study, adherence is

measured as consistent collection of antiretroviral medications from the pharmacy at prescribed intervals.

Antiretroviral therapy (ART) consists of the combination of at least three antiretroviral (ARV) drugs to maximally suppress the HIV virus and stop the progression of HIV disease (WHO 2012:1).

Human immunodeficiency virus (HIV) is the virus that weakens the immune system, ultimately leading to AIDS: Acquired Immunodeficiency Syndrome (UNAIDS 2011:12). In this study, HIV refers to HIV-1 which is the predominant form of HIV in Southern Africa.

HIV-positive patient is used in this study to indicate a person that has the evidence of HIV via blood test or saliva test. An HIV-positive person is able to transmit the HIV virus during sex, through his or her blood, or during pregnancy, childbirth and breastfeeding (Van Dyk 2013:496).

Patient refers to an individual who is suffering from disease, injury, an abnormal state, or a mental disorder, and is engaged in related treatment (*Stedman's Medical Dictionary* 2012:1259). For the purpose of this study, a patient is a person who is 18 years and older ,who has had antibodies against HIV detected on a blood test or gingival exudates test commonly known as a saliva test and who is on antiretroviral therapy.

Virological failure refers to patients who have a confirmed HIV viral load of >1000 copies/ml in 2 measurements taken 1-3 months apart (Meintjes et al 2012a:119).

Virological suppression refers to patients achieving a viral load <50 copies/ml within 6 months of commencing ART and sustained thereafter (Meintjes et al 2012a:112).

1.9   RESEARCH DESIGN AND METHOD

1.9.1 Research design

The research design is the overall plan for obtaining answers to the questions being studied and for handling some of the difficulties encountered during the research

process. A design is the blueprint for conducting a study that maximises control over factors that could interfere with the validity of the findings (Polit & Beck 2008:66; Burns & Grove 2009:236). The researcher used a cohort study which was a quantitative, retrospective and descriptive in nature.

Quantitative research is a formal, objective, systematic process in which numerical data are used to obtain information about the world (Burns & Grove 2009:22). Descriptive research refers to research that has as its main objective the accurate portrayal of the characteristics of persons, situations, or groups, and/or the frequency with which certain phenomena occur (Polit & Beck 2008:752). Most importantly, the purpose of descriptive research is to explore and describe phenomena in real-life situations. In addition, this approach is used to generate new knowledge about concepts or topics about which limited or no research has been conducted (Burns & Grove 2009:45). Retrospective design involves collecting data on an outcome occurring in the present, and then linking it retrospectively to antecedents or determinants occurring in the past (Polit & Beck 2008:210). Baseline demographic, medical records on file, HIV viral load measurements as well as pharmacy refill records of HIV-positive patients who were initiated on ART between January 2011 and December 2012 were retrieved from the hospital' records. Therefore, the data collected are used to measure the adherence to antiretroviral therapy in HIV-positive patients.

This study systematically and objectively reviewed viral load measurements of HIV-positive patients who have been on ART and their pharmacy refill records in order to describe antiretroviral adherence in HIV-positive patients and to determine the ability of pharmacy refill adherence to detect virological outcomes.

1.9.2 Research setting

The researcher conducted the study at one of the district hospitals in Ugu Health District found in the lower south coast of the province of KwaZulu-Natal (KZN) in South Africa. The district provides health service to the population using the primary health care approach through the district health system and this is done at all levels of care. The district has three district hospitals, one regional hospital, one specialised hospital, two community health centres, 56 fixed clinics (including three gateway clinics) and 15 mobile clinics. The hospital where the study was conducted had about 1987 patients

who were still attending the institution for routine check-up and collection of antiretroviral drugs (ARV) at the end of December 2012.

1.9.3 Research population

The population is all the elements (individuals, objects, or substances) that meet certain criteria for inclusion in a given universe (Burns & Grove 2009:42). The population for this study are the records of HIV-positive patients who attended designated district hospital for antiretroviral therapy between January 2011 and December 2012, and that meet the eligibility criteria.

Sampling is a process of selecting subjects, events, behaviours, or elements for participation in a study (Burns & Grove 2009:35). A sample is a subset of the population that is selected for a particular study, and sampling defines the process for selecting a group of people, events, behaviours, or other elements with which to conduct a study (Burns & Grove 2009:42). The sampling plan specifies in advance how the sample will be selected and recruited, and how many subjects there will be (Polit & Beck 2008:67).

Probability sampling design using systematic sampling technique was used to select every 10th patients' records that meet the following criteria: 18 years and older; have completed at least 12 months of treatment and had at least two viral load measurements recorded after initiation of antiretroviral therapy. The medical records on file, HIV viral load measurements as well as pharmacy refill records were utilised as data sources of information for the study.

1.9.4 Data collection instrument

Quantitative researchers typically develop a detailed data collection plan; researchers often use formal data collection instruments (Polit & Beck 2008:390). The gathering of information to address a research problem was done by using a checklist as data collection instrument. It was developed by the researcher for recording the variables related to patient demographic information, medical information, and pharmacy refill records (Annexure D).

1.9.5 Data collection

In quantitative research, data collection involves obtaining numerical data to address the research objectives, questions, or hypotheses (Burns & Grove 2009:44). Data were collected by the researcher and the field workers using the checklist for recording of patient demographic data, clinical data and pharmacy drug information retrieved from patient's records (Annexure D).

1.9.6 Data analysis

Data analysis is defined as the systematic organisation and synthesis of research data (Polit & Beck 2008:751). Analysis of the data was carried out by using the Statistical Package for Social Sciences (SPSS) for Windows (Version 17) and a statistician assisted the researcher in analysing and interpreting collected data.

Descriptive statistics were used to describe key research variables and summarise sample characteristics in terms of frequency distribution, measures of central tendency and measures of variability. Once these features known, the researcher used bivariate descriptive statistics to describe the relationship between antiretroviral adherence and virological outcomes.

1.10   VALIDITY AND RELIABILITY

Validity provides a major basis for making decisions about which finding are sufficiently valid to add to the evidence base for patient care (Burns & Grove 2009:221). According to Polit and Beck (2008:287), internal validity concerns the validity of inferences that, given the existence of an empirical relationship, it is the dependent variable, rather than other factors, that caused the outcome. Conversely, external validity refers to the validity that inferences about observed relationship will hold over variations in persons, setting, time or measures of the outcomes.

Reliability refers to consistent and stable measurement of data as well as replicability (Welman, Kruger & Mitchell 2010:9). In contrast, validity of the research instrument is the degree to which an instrument measures what it is supposed to measure (Polit & Beck 2008:457).

In order to enhance the validity of the study, statistical analysis called analysis of covariance as well as probability (random) sampling method are used and the measuring instrument were pre-tested on the same population. Measures used to assure reliability and validity of data gathering instrument are described in Chapter 3.

1.11   ETHICAL CONSIDERATIONS

Ethics are a set of guidelines, principles and codes which in the case of research are used to guide the behaviour of the researcher when conducting research (Merrill & West 2009:168).

1.11.1 Protecting the rights of the participants

The data in this study were collected in such manner that subjects cannot be identified directly, the collection of data were done by reviewing a patient's medical and pharmacy records in the hospital. There are three primary ethical principles on which standards of ethical conduct in research are based namely the principle of beneficence, principle of respect for persons, and principle of justice guided the study (Polit & Beck 2008:170).

1.11.1.1 Principle of beneficence

The principle of beneficence imposes a duty on researchers to minimise harm and to maximise benefits (Polit & Beck 2008:170). In addition, participants were not subjected to any harm, discomfort, stigma or discrimination. The principal risk of harm could result in breaching of confidentiality or anonymity. Confidentiality is the researcher's management of private information shared by a subject that must not be shared with others without the authorisation of the subject (Burns & Grove 2009:196). Furthermore, anonymity, which is the most secure means of protecting confidentiality, occurs when even the researcher cannot link participants to their data (Polit & Beck 2008:180). Moreover, researchers have a responsibility to protect the anonymity of subjects and to maintain the confidentiality of data collected during a study (Burns & Grove 2009:197). In this study, the researcher investigated the record of existing data. To avoid the potential harm of breaching the confidentiality or anonymity, the information obtained

from patients' records is kept confidential and handled on anonymous basis. Most importantly, no participants can be identified, directly or through identifiers linked to them. To protect patients' anonymity, each patient record was given a code number generated from patient's number, the list of patient's number and their code had been kept separate from the data collected.

1.11.1.2 Principle of respect for persons

The principle of respect for persons holds that persons have the right to self-determination and the freedom to participate or not participate in research (Burns & Grove 2009:188). One particularly important procedure for safe-guarding participants and protecting their right to self-determination involves obtaining their informed consent (Polit & Beck 2008:176). It is essential that all participants enter the research process voluntarily and willingly through 'informed consent' and they are aware of their rights (Merril & West 2009:171).

Medical records and pharmacy records of HIV-positive patients were screened for eligibility; those who met the eligibility criteria were selected. Once selected, the potential participant were given explanation of the research and provided with a written consent form which they signed and dated. When obtaining informed consent from a participant who was physically unable to read, write, talk or were blind, a witness signed and dated the consent form attesting that the requirements for informed consent have been satisfied. However, the researcher reviewed data collected for clinical care that were in medical records; obtaining consent was impracticable for most of the participants for whom records were reviewed (Annexure E).

1.11.1.3 Principle of justice

The principle of justice includes participants' right to fair treatment and their right to privacy (Polit & Beck 2008:173). Patients' demographic, medical and pharmacy refill information collected are kept in strictest confidence.

Since the research involves patient's medical records in the hospital, ethical clearance from the Research Ethics Committee of the Department of Health Studies of the University of South Africa was obtained (Annexure A). In addition, permission to

conduct the study was requested (Annexure B) and full approval from Hospital Manager to access records was obtained before the collection of data. (Annexure C2).

1.11.2   Protecting the rights of the institution

Permission to conduct research was obtained from Hospital Manager, Ugu Health District (Annexure C2), and from the Provincial Health Research Committee in the KZN Department of Health (Annexure C1).

1.11.3   Scientific integrity of the research

Authors who are primary investigators for research projects must be responsible in their conduct, reporting and publication of research. Each researcher is responsible for monitoring the integrity of his or her research protocols, results and publications (Burns & Grove 2009:213). The structure of the research proposal has been taken into consideration. The primary data and findings of the research are fully, clearly and accurately documented and any authorised persons will have access to the primary data if needed. Any limitations or challenges encountered during collection, analysis and reporting of results are acknowledged. All individuals formally or informally involved in the study as well as all sources used are listed.

1.12   STRUCTURE OF THE DISSERTATION

This dissertation has been organised according to five chapters.

Chapter 1:   Study overview
Chapter 2:   Literature review
Chapter 3:   Research design and method
Chapter 4:   Analysis, presentation and description of the research findings
Chapter 5:   Conclusions and recommendations

1.13   CONCLUSION

This chapter provided background information about HIV/AIDS globally, in sub-Saharan Africa and South Africa. The following areas were discussed: the research problem,

purpose, objectives, questions, the significance of the study, research methodology, validity and reliability, ethical considerations, structure of the dissertation and conclusion.

The next chapter will discuss the literature reviewed on the concepts related to research topic in this study.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

The literature review will discuss information from publications; research studies; statistics and published reports related to research topic.

2.2 HIV GLOBAL EPIDEMIC

Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) are part of the daily life of vast numbers of people around the globe. Globally, an estimated 35.3 million people were living with HIV in 2012 compared to less than 10 million people being infected worldwide in 1990. In addition, the spread of HIV peaked in 1996 with an estimated 3.5 million new infections worldwide occurring in that year. At the end of 2012, the estimated number of people newly infected with Human Immunodeficiency Virus showed approximately 35% decline compared to the number at the epidemic's peak in 1996. There were 2.3 million new HIV infections globally in 2012 (Van Dyk 2013:7; UNAIDS 2013:4; United Nations Children's Fund (UNICEF) 2013:1).

The world's initial response to the AIDS epidemic was one of denial, blaming and moralising. It was believed that AIDS was a gay disease and that it would only affect homosexual people who brought it on themselves and that it would taper off and disappear in time. Today, HIV has established itself firmly in our communities and the effects of AIDS have devastated many families, communities and economies-especially in developing countries (Van Dyk 2013:9). In the developing world, HIV is spreading mainly through heterosexual intercourse. The epidemic in this region has been driven by a combination of poor economies and the absence of functioning health systems leading to lack of access to early diagnosis and antiretroviral therapy (Sultan & Alder, 2012:4). Although the growth of the epidemic has appeared to stabilise in most countries of the world, sub-Saharan Africa remains the most highly affected region in the world. The HIV incidence in 33 countries has decreased by 25% between 2001 and 2009, with 22 of these countries being in sub-Saharan Africa. However, in seven

countries there has been an increase of more than 25% in the same time period. These include five countries in Eastern Europe and Central Asia (Sultan & Adler 2012:2; Van Dyk 2012:7).

Globally, there are fewer AIDS-related deaths and a steady decline in the number of new HIV infections since the late 1990s. In 1995, the use of combination antiretroviral treatment (also known as Highly Active Antiretroviral Therapy (HAART) or multi-drug therapy) was introduced, and in 1997 deaths due to AIDS began to decline in developed countries as a result of the new antiretroviral treatment (Van Dyk 2013:11). From 1996 to 2012, antiretroviral averted 6.6 million AIDS-related deaths worldwide, including 5.5 million deaths in low and middle-income countries (UNAIDS 2013:6). Thirty years on and with the introduction of combination antiretroviral therapy, where it is widely available, the clinical picture of HIV has changed from a fatal illness to that of a chronic condition (Sultan & Adler 2012:1).

2.3   SUB-SAHARAN AFRICA HIV EPIDEMIC

Sub-Saharan Africa has experienced a disproportionate burden of the global HIV epidemic, with one third (34%) of all people living with HIV globally residing in the 10 countries of Southern Africa (UNICEF 2013:1). The number of people living with HIV in sub-Saharan Africa in 2012 was 25 million (23.5million-26.6 million) with an estimated 1.6 million (1.4 million-1.8 million) newly infected, accounting for 70% of all new HIV infections in 2012 and 1.2 million (1.1 million-1.3 million) Aids-related deaths in that year alone. However, since 2001, the annual number of new HIV infections among adults in sub-Saharan Africa has declined by 34% (UNAIDS 2013:12). Southern Africa remains the area most heavily affected by the epidemic and it is host to nine countries with the highest HIV prevalence rates among this age group (15-49 years) in the world, including Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia and Zimbabwe (UNICEF2013:1).

South Africa is the country with the largest population of people living with HIV in the world. In 2013, an estimated 5.26 million people living with HIV resided in South Africa, and it contributes to about 15% of the global number of HIV infections (Statistics South Africa 2013:2).

2.4   HIV EPIDEMIC IN SOUTH AFRICA

2.4.1   Modes of HIV transmission

South Africa has a generalised epidemic of HIV, driven largely by sexual transmission. HIV in South Africa is transmitted predominantly heterosexually between couples, with mother-to-child transmission being another main transmission route. Drivers of the epidemic in South Africa are intergenerational sex, multiple concurrent partners, low condom use, excessive use of alcohol and low rates of male circumcision (South Africa 2013b:30).

2.4.2   National HIV prevalence trends

The prevalence of the South African HIV remains huge. More HIV-positive people live in South Africa than in any other country. The HIV epidemic in South Africa until 1990 had a similar pattern to the European and American epidemics (Venter 2013:38). The total number of persons living with HIV in South Africa was estimated at approximately 5.26 million in 2013. For adults aged 15-49 years, an estimated 15.9% of the population is HIV positive. Approximately 17% of South African women in their reproductive ages are HIV positive (Statistics South Africa 2013:3-4). The prevalence of HIV in South Africa shows considerable variance across its nine provinces. In the past 20 years, the highest HIV prevalence among the 15-49 years olds has been recorded in KwaZulu-Natal, which remained stable at 39.5% in 2009 and 2010. Provinces with higher HIV prevalence after KZN were Mpumalanga (35.1%), Free State (30.6%) and Gauteng with 30.4% (South Africa 2013b:34).

2.4.3   National Response to the HIV epidemic

In South Africa, the initial response to HIV and AIDS was very similar to the worldwide one, tainted by government inaction, pseudoscience, denialism, dissident beliefs, conflict and harmful practices. The first major step forward was the creation of the National AIDS Convention of South Africa in 1993. The following years marked South Africa's darkest days in its response to AIDS epidemic until the new clinical guidelines for the management of HIV and AIDS in adults, adolescents and children, as well as guidelines to prevent mother to child transmission, were implemented on 1 April 2010

(Van Dyk 2013:9-11). The South Africa National AIDS Council (SANAC) responsible for coordination of the HIV response between government and civil society, was revived in 2011 and led the generation of National Strategic Plan 2012-2017 (Venter 2013:38-39). The National Strategic Plan (NSP) for HIV, sexually transmitted infections (STI) and tuberculosis (TB) (2012-2016) is a framework to guide the activities of all partners whose work is relevant to HIV, STIs and TB in South Africa. It provides goals and strategies for the country's response to these diseases during the period 2012 to 2016.

The National Strategic Plan has five goals:

- Halving the number of new HIV infections.
- Ensuring that at least 80% of people who are eligible for treatment for HIV are receiving it, at least 70% should be alive and still on treatment after five years.
- Halving the number of new TB infections and deaths from TB.
- Ensuring that the rights of people living with HIV are protected.
- Halving the stigma related to HIV and TB.

The NSP has identified four strategic objectives to reach its goals. These are:

- Address social and structural factors that drive these epidemics, influence their impact, and affect the way we care for affected people.
- Prevent new HIV, STIs and TB infections through a combination of interventions.
- Sustain health and wellness, primarily by reducing deaths and disability from HIV, AIDS and TB.
- Protect the human rights of people living with HIV and improve their access to justice.

The NSP aims to align with relevant international and regional obligations, commitments and targets. The targets of the Millennium development goals (MDGs) guide the NSP, specifically reversing the epidemics of HIV and TB (South Africa 2011:2-15).

The NSP implementation is measured by collecting the following key indicators:

- The percentage of young women and men aged 15-24 years who are HIV-positive.
- The percentage of key populations who are HIV-positive.
- The number and percentage of infants (born to HIV-positive mothers) who test HIV- positive at six weeks and 18 months after birth.
- Prevalence and incidence of TB.
- The percentage of adult deaths those are due to HIV and TB.
- The extent of stigma related to HIV and TB; retention on ART (South Africa 2011:24-25).

According to District Health Barometer, in 2013, an estimated 1.4 million people were accessing HIV treatment, making it the largest HIV treatment programme in the world (Statistic SA 2013:4; Venter 2013:207). The NSP aims to reduce mother to child transmission to less than 2% at six weeks after birth and less than 5% at 18 months by 2016. The national MTCT transmission rate at six weeks was at 2.7% among HIV-exposed infant in 2013. Transmission rates at 18 months are less certain as a result of low routine-testing coverage and challenges in following up infants (Bamford 2013:6).Thus, the implementation of the NSP will help South Africa to reverse the epidemics of HIV and TB.

2.4.4 The South African antiretroviral treatment guidelines

In 2003, the South Africa government decided to provide antiretroviral therapy free to all South Africans who visited public health services (Van Dyk 2013:10). Prior to 2004, ART was available only in the private sector, through private funding, workplace programmes, research projects and medical aid schemes. An estimated 100 000 people were on treatment through these mechanisms. The public ART programmes commenced officially in April 2004 in selected districts and sites. The local guidelines contained many restrictions on access, such as few selected sites per district with lengthy training preparation, onerous preparation for patient adherence, and prescribed staffing norms. However, initial access to ART for state-dependent patients was slow, very doctor-centred and generally confined to large central hospitals, despite large

numbers of ill patients that required immediate therapy. The years after 2008 mark the reorientation and scale-up of the programmes (Venter 2013:38-39). In 2010, the South African government revised its HIV treatment guidelines for the first time since the programme was launched in 2004. Among a host of changes to drug regimens, eligibility criteria, and monitoring protocols, the revised guidelines included a strategy of down referring stable, adult ART patients from a central hospital to nearby primary clinics and shifting strategy to enable nurses to initiate ARVs for treatment and prevention and to enable primary health care facilities to initiate, manage, monitor, and refer patients (Long, Brennan, Fox, Ndibongo, Jaffray, Sanne & Rosen 2011:1).

Since January 2010 to April 2013, the South African government have implemented new policies to increase universal access to free antiretroviral therapy in addition to the introduction of fixed-dose combination (FDC) ART tablet for patients initiated with ART for the first time. These interventions target all pregnant women who are HIV infected regardless of their CD4 count, all infants born to mothers who are HIV positive, all persons with CD4 of less or equal to 350 CD4 cells/mm3 and all persons with TB who are co-infected with HIV (Padayachee 2013:207; South Africa 2013a:5-6). South Africa has made remarkable progress in rolling out ART, with the largest number of people in the world enrolled on antiretroviral medication (Nyasulu, Muchiri, Mazwi & Ratshefola 2013:232). The total number of South African adults who remained on ART increased by about 33% from 1439445 at end of 2011/12 to 2161170 by the end of 2012/13 (Padayachee 2013:208).

2.5   KWAZULU-NATAL HIV EPIDEMIC

South Africa is made up of nine provinces. One of the provinces mostly affected by HIV/AIDS is KwaZulu-Natal, the setting where this study is conducted. It is the second most populous province in South Africa, with an estimated 10.6 million people of which approximately 54% of the population live in rural areas, and approximately 10% of the urban population live in under-developed informal settlements which as a result of under-development and non-availability of essential resources necessary to maintain health, have significant health and service delivery implications. The population is young with one third of the population younger than 15 years; an estimated 6.7% is 60 years or older; and 52.3% of the total population is female (KwaZulu-Natal Department of Health 2012:6-12).

The HIV prevalence in KZN increased from 11.7% in 2002 to 15.8% in 2008 compared with the national prevalence of 10.9% in 2008. Prevalence remains disproportionally high for females in comparison to males, and peaks in the 25-29 year age group with one in three found to be HIV positive in 2008. In the past 20 years, the HIV prevalence among the 15-49 year olds recorded in KZN has been consistently higher than in the rest of the country and continues to be one of the leading causes of mortality in KZN (KwaZulu-Natal Department of Health 2012:71; UNAIDS 2012:34). Ugu District Municipality in KwaZulu-Natal has the second highest prevalence in the country with HIV prevalence among clients tested during antenatal care at 41.9%. According to the 2012/13 District Health Barometer eThekwini Metropolitan District in KwaZulu-Natal had the most adults (207091) remaining on ART at the end of 2012/13 and Ugu District had 45588 adults remained on ART at the end of 2012/13 (Padayachee 2013:207 & Malaza 2013:301).

2.6   ANTIRETROVIRAL ADHERENCE

Adherence is a well-known problem in medicine. Especially in chronic, non-symptomatic diseases, keeping to the prescribed treatment has proven difficult for patients (Airoldi, Zaccarelli, Bisi, Bini, Antinori, Mussini, Bai, Orofino, Sighinolfi, Gori, Suter & Maggiolo 2010:115). Compared with other chronic illnesses requiring long-term therapy, adherence to ART required for viral suppression in HIV/AIDS is particularly challenging (Wise & Operario 2008:495).

Adherence refers to the willingness and ability of patients to follow health-related advice, take medication as prescribed, attend scheduled appointments, and complete recommended investigations (Moosa & Jeenah 2012:144). Medication adherence often accompanies other healthy behaviours such as diet and health care utilisation (Beer, Heffelfinger, Frazier, Mattson, Roter, Barash, Buskin, Rime & Valverde 2012:213). In addition, therapeutic effect is compromised when patients don't take their medications; take them in un-prescribed amounts or off the prescribed schedule, or fail to match the dose with food as directed. Furthermore, patients may take medications prescribed for family or friends, may share or sell their own medications, and may hoard medications for future use (Williams & Friedland 2010:1).

Non-adherence to antiretroviral, evidenced as missed doses, is associated with incomplete viral suppression and the development of drug resistant virus that will eventually limit therapeutic options (Wilson, Cotton, Bekker, Meyers, Venter & Maartens 2010:514). Many factors have been reported to either positively or negatively affect ART adherence. These factors are commonly divided into five intersecting categories: patient variables; treatment regimens; disease characteristics; patient-provider relationships; and clinical setting. Moreover, adherence rates have been shown to vary between individuals and within the same individual over time (Moosa & Jeenah 2012:147).

A number of studies have shown no change in adherence by level of education or gender. Adolescents and younger adults are less adherent than older adults. Disclosure of HIV status and support by a treatment partner or peer counsellor have been shown to have a great impact on adherence. Most importantly, individuals who start treatment should be well prepared, and a standard module of information should be offered to all patients, to the carers of children and of adults with mental illness (Maartens, Cotton, Wilson, Venter, Meyers & Bekker 2012:515-516). ART adherence rates of 90-100% are required to: ensure suppression of viral replication; maintain CD4 cell counts; prevent clinical progression to AIDS; and prevent the development of ART drug resistance and resistant HIV strains, which could leave drug-naïve patients with few effective treatment options (Moosa & Jeenah 2012:144). Anyone who has an adherence approaching 80% or less, or who has a viral load that is not suppressed at any time after baseline, should receive attention from the health care providers (Maartens et al 2012:518).

Many studies of ART adherence focused on missed doses, not on adherence to medications schedules and special instructions such as dietary restrictions. Failure to inquire about these may lead to inaccurate estimates of a patient's level of adherence and thus resulting to missed opportunities to address non-adherence issues as a cause of treatment failure. Therefore, successful ART requires clinicians to assess the risks of non-adherence before deciding on a regimen and to accurately monitor and support adherence throughout therapy (Beer et al 2012:213).

2.6.1 What is sufficient adherence?

Adherence close to 100% is ideal and will minimise the risk of developing resistant virus for all treatment regimens (Wilson et al 2010:514). The percentage adherence required for virological suppression varies from individual to individual, with different antiretroviral classes, and over time as higher adherence is needed to achieve virological suppression than to maintain suppression. Most combinations of medication require at least 85% adherence (Kalichman 2013:77). Adherence levels required in HIV are higher than in other chronic diseases, which are difficult to achieve (Maartens et al 2012:512). In her research on treatment adherence following the national antiretroviral rollout in South Africa, Van Dyk found that only 40.1% of the patients on ARVs could reach optimum adherence levels of 90% or above, while 49% reached adherence levels between 70% and 90%, 10.9% could not even reach adherence levels of 70% (Van Dyk 2013:121). In their study, Beer et al (2012:222) to describe the use of antiretroviral therapy and to assess the various measures of ART non-adherence in a large sample of HIV-infected patients in the United States found that the use of ART was high, but adherence to ART was suboptimal. Walshe et al (2010:190) compared physician estimates of their patients' ART adherence with participant's self-reported adherence in India. They found that by provider assessment, 40.1% of participants were considered adherent (for example, taking ≥ 95% of doses) as compared to 73.6% adherent by participant self-report.   Study on adherence to ART in conflict area in Uganda found no significant difference among patients living in and those outside the internationally displaced persons (IDPs) and non-IDPs (Garang, Odoi & Kalyango 2009:745).

Minimal levels of adherence needed to sustain viral suppression are not necessarily the same across compartments of the immune system. High concentrations of most nucleoside and non-nucleoside reverse transcriptase inhibitors are recovered from the genital tract, whereas protease inhibitors achieve lower drug concentrations in this compartment (Kalichman 2013:77).

In the scientific community it is widely accepted that an adherence level of at least 90% is necessary to suppress the virus sufficiently, to avoid the risk of mutation, and to prevent the development of drug resistant strains and drug failure (Van Dyk 2013:121).

Adherence to medication regimen in adults is an informed choice (Mc Master & Stokes 2012:95). Therefore, adherence is considered as a variable behaviour rather than a stable characteristic of an individual, and most people will exhibit low adherence some of the time (Moosa & Jeenah 2012:147). For example, the antiretroviral-based microbicide gel tested in the Centre for the AIDS Programme of Research in South Africa (CAPRISA) 004 trial demonstrated 54% reduction in risk for women who used the product more than 80% of the time as compared to 28% protection for women who used the gel less than 50% (Kalichman 2013:24).

2.6.2 The relationship between antiretroviral adherence and virological suppression

Adherence to antiretroviral is crucial to ensure viral suppression (Rougement et al 2009:21). The best biological marker of adherence is an undetectable viral load in patients on ART (Meintjes et al 2012b:165). In addition, Walshe et al (2010:190) found a correlation between participant adherence responses and plasma viraemia in their study to validate Adult AIDS Clinical trials group (AACTG) questionnaire. Measuring viral load can help to discriminate between treatment failure and non-adherence (WHO 2013:135); viral load should be measured before starting therapy, 2 to 8 weeks later, and then at 4 to 8 weeks intervals until Human Immunodeficiency Virus ribonucleic acid (HIV RNA) is no longer detectable. At least a log 10 reduction in viral load should be expected at 4 weeks, with a decline in plasma HIV RNA to <50 copies/ml by 16 to 24 weeks of therapy (Tsibris & Hirsch 2010:61).

The Southern African Clinicians Society recommends viral load at baseline before commencing ART, where possible, at three months after the commencement of ART. This early viral load is desirable to detect adherence problems early before resistance develops and at six months thereafter and then every six months in patients who are virologically suppressed for longer than 12 months and who demonstrate reliable adherence and follow up, it may be acceptable to reduce the frequency of viral load (VL) monitoring to annually (Meintjes et al 2012a:119). Thus, viral suppression should occur by six months. If this does not occur, then in nearly all cases the explanation will be poor adherence (Maartens et al 2012:470). However, even under optimal adherence, viral suppression is not always durable in the long run. Despite inhibition of viral replication in plasma, lymph nodes and at other sites, reservoirs of HIV infection in

latently infected resting T lymphocytes remain (Benn et al 2012:99). In addition, viral blips, or transient viral-load increases to between 50 to 1000 copies/ml in a patient with previously suppressed plasma HIV RNA are occasionally seen, and are estimated to last for short periods (<3 weeks) but do not appear to be associated with eventual virologic failure and do not necessitate a change in therapy (Tsibris & Hirsch 2010:61; CDC 2009:2). Moreover, viral suppression in blood plasma does not necessary mean that HIV is suppressed in the genital compartment (Kalichman 2013:62); virus persists within cells present in seminal fluid of some men who are on ART with undetectable plasma viral load. Thus, a person with an undetectable plasma viral load may still shed virus in genital fluid at higher levels, which poses risk for transmission (CDC 2009:1-2). A study by Sturmer, Doerr, Berger and Gale (2011:729) has documented a sexual transmission of HIV from an infected partner who was on ART with a repeatedly undetectable plasma viral load.

Without adequate adherence, antiretroviral agents are not maintained at sufficient concentration to suppress HIV replication in infected cells and to lower the plasma viral load (Foundation for Professional Development 2008:145). Therefore, non-adherence to antiretroviral therapy is associated with incomplete viral suppression and the selection of drug resistant virus that will eventually limit therapeutic options (Maartens et al 2012:512).

Pirkle et al (2009:153-154) found a decrease of at least 1 log 10 in plasma viral following the 1 month of modified directly administered antiretroviral treatment intervention on all cohort patients with more than 500 copies 6 months or more after starting treatment. The presence of a viral >1000 copies/ml in an individual who has been receiving ART for >6 months constitutes an adherence emergency, and should trigger a vigorous response from the health care provider, including increased adherence support, before the VL measurement is repeated (Meintjes et al 2012b:162).

2.6.3 Measuring adherence

There are different methods for assessing adherence and the level of adherence is specific not only to places and patient groups but also to the method of adherence measurement used (Reda & Biadgilign 2011:1). These methods fall into three categories, namely: subjective measures (self-report adherence, and medical chart

review); objective measures (pill counts, pharmacy refill records, and use of mechanical or electronic monitors of pill or drug use); and physiological methods or indicators (plasma assay and laboratory reports) (Moosa & Jeenah 2012:147). They include direct methods such as biologic markers and body fluid assays, or indirect methods such as self-report, interview, pill counts, pharmacy records, computerized medication caps, and viral load monitoring (Reda & Biadgilign 2011:1). All measures of adherence remain approximations; however, they can be used to target individuals who require more intense adherence interventions (Maartens et al 2012:515).

The hierarchy of adherence measures ranks physician and self-assessment reporting as the least accurate, pill count as intermediate and electronic drug monitoring as the most accurate adherence markers (Moosa & Jeenah 2012:147). Subjective adherence methods are notoriously insensitive, but better results are obtained by adopting non-judgmental attitudes and gaining the patient's trust (Maartens et al 2012:514). There are no gold standard methods for measuring adherence (Reda & Biadgilin 2011:2). In the absence of universally accepted criteria for establishing adherence, researchers diverge in their methods of defining and enumerating successful medication-taking behaviour. Adherence is commonly quantified as the percentage of doses taken as prescribed. However, variables such as frequency (number of doses per day) and quantity (number of pills per dose) as well as the complexity (number of medications) and specificity (meal indications, medication storage condition) of the regimen often are handled differently across studies (Martin, Desorbo, Calabrese, Wolters, Roby, Brennan & Wood 2009:594). Combination of these methods may be employed, patient self-report is the most widely used. In developing countries, pharmacy refill reports and self-reports are commonly implemented for adults (Reda & Biadgilign 2011:1).

2.6.3.1 Pharmacy refill records

Pharmacy refill records (data) refers to the number of times a patient receives medication over a fixed period, for example, a calendar year, is expressed as a percentage of the number of times they should have collected medications (Maartens et al 2012:514). Pharmacy refill records (data) require that patients always use the same pharmacy (Moosa & Jeenah 2012:147).

Pharmacy refill history gives no description of daily adherence to treatment, because patients may not take all prescribed medications. It could also be considered as a time consuming monitoring tool for the pharmacy staff (Rougemont et al 2009:7). Pharmacists' claims data may overestimate true adherence because the relationship between pharmacy refills and actual ingestion of medication is not clear (Ehlers, Tjipura & Ross 2009:24). Although, this is the simplest method of objectively recording adherence and it was previously reported to be as accurate as CD4 counts for predicting and detecting virological failure. Rougemont et al (2009:7) found that pharmacy refill irregularity is the most powerful predictor of virological failure compared with CD4 cell count increases at 6 months. Zaragoza-Macias et al (2010:135) have shown that virological suppression was associated with adherence with medication pick-up of more than 90%. The ability of adherence monitoring from the pharmacy to identify patients at risk of treatment failure may help health-care providers for early adherence counselling interventions (Rougemont et al 2009:7-9).

2.6.3.2   Pill counts

Pill counts: counting returned medication in order to estimate the number of doses taken is a method frequently used to calculate adherence (Maartens et al 2012:512). Most importantly, this method requires patient co-operation to bring their pills to the requested health visits, and not to share pills (Moosa & Jeenah 2012:144); this can be time consuming in a busy clinic. There is also a risk of people discarding their tablets to improve their adherence. Surprise or unannounced pill counts at home may decrease the risk of pill-dumping, but would require a dedicated team of counsellors to visit clients at home, and is not practical when monitoring adherence on a large scale (Maartens et al 2012:514). The pill count method may overestimate adherence (Moosa & Jeenah: 2012:148).

2.6.4.3   Electronic monitoring

Electronic monitoring is the use of electronic devices that record each time a bottle is opened; this is called the medication event-monitoring system (MEMS) that allows recording of when a drug container is opened via a micro-processor in the cap of container. This requires that patients only remove one dose at a time and caps only measure bottle opening and not medication ingestion (Moosa & Jeenah 2012:147).

Electronic monitoring is rare outside of the research environment and these devices (micro-processors) are expensive and require computers and software for downloading the information on return of the bottle (Maartens et al 2012:514). MEMS may overestimate adherence by about 10% (Moosa & Jeenah 2012:148).

2.6.4.4   Therapeutic drug monitoring

Therapeutic drug monitoring which is a low plasma concentration of antiretrovirals may be due to poor adherence, malabsorption or drug interactions. Patients tend to adhere best around their clinic visit, so-called white coat adherence; so, measuring drug concentrations overestimates adherence (Maartens et al 2012:514).

2.6.4.5   Recall questionnaires

Recall questionnaires is the subjective measure of patient self-report which is the commonly used measure of adherence in clinical settings. This measure is simple and inexpensive to administer. In this measure the patient is asked how many doses were missed in the past day, 2 days or 3 days and 2 weeks or alternatively, the percentage of prescribed doses taken in the past 4 days (Maartens et al 2012:514; Moosa & Jeenah 2012:148). This method may be more useful as research tool as more open, accurate responses might be expected when results are not reported to the clinical team (Maartens et al 2012:515).

A 30-day visual analogue scale (VAS) of doses taken may be a faster and more efficient means of obtaining similar information to the recall questionnaire. The patient is asked to mark on the line how well he took his medication in the last month. Remember, 0% means he does not take any medication at all and 100% means he was perfect (Maartens et al 2012:515). There may be overestimation of self-reported medication in early stages due to the desire to please when patients do not feel confident in a new environment (Fielding, Charalambous, Stenson, Pemba, Martin, Wood, Churchyard & Grant 2009:9).

Adherence must be monitored using at least one of the measures described above throughout an individual's time on antiretroviral therapy (Maartens et al 2012:518). No

single measure of adherence is appropriate for all settings or outcomes; therefore, the use of more than one measure is recommended (Moosa & Jeenah 2012:148).

2.7   CONCLUSION

The literature review discussed HIV Global epidemic, sub-Saharan Africa HIV epidemic, South African HIV epidemic, KwaZulu-Natal HIV epidemic and antiretroviral adherence including the importance of monitoring the response to ART in HIV-infected patients.

Monitoring the response to antiretroviral therapy means viral load is performed at baseline, at 3 months, at 6 months thereafter and then every 6 months and CD4 counts are performed every 6 months, and then annually. If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure (WHO 2013:133). Since viral monitoring is not available in most resource limited settings and antiretroviral treatment has been rapidly scaled up, monitoring patient in lifelong HIV care is a major challenge. Data are needed to inform policy makers on how best to use other easily accessible methods as alternative method for monitoring response to ART and for identification of patients at risk of virological failure.

Chapter 3 will describe the research design and research method.

CHAPTER 3

RESEARCH DESIGN AND METHOD

3.1   INTRODUCTION

The data were collected by the researcher and the field workers using a checklist developed by the researcher for recording the variables to be observed; patient demographic information, medical information, and pharmacy refill records.

A quantitative research methodology was followed in this study.

3.2   RESEARCH DESIGN

The research design is the overall plan for obtaining answers to the questions being studied and for handling some of the difficulties encountered during the research process. A design is the blueprint for conducting a study that maximises control over factors that could interfere with the validity of the findings (Polit & Beck 2008:66; Burns & Grove 2009:236).

A quantitative, retrospective, descriptive and cohort study design was used in this study. The researcher collected needed information without introducing an intervention for investigation of phenomenon of interest and the variables within the phenomenon. This research method was used to describe antiretroviral adherence in Human Immunodeficiency Virus (HIV)-positive patients using pharmacy refill records and to describe an alternative method of monitoring response to antiretroviral therapy.

3.2.1 Descriptive

A descriptive design may be used to develop theory, identify problems with current practice, justify current practice, make judgements, or determine what others in similar situations are doing (Burns & Grove 2009:237). This study was descriptive because the researcher systematically and objectively reviewed viral load measurements of HIV-positive patients who have been on antiretroviral therapy (ART) and their pharmacy refill

records in order to describe antiretroviral adherence in Human Immunodeficiency Virus (HIV) positive patients.

3.2.2 Retrospective

A retrospective design involves collecting data on an outcome occurring in the present, and then linking it retrospectively to antecedents or determinants in the past (Polit & Beck 2008:10). The researcher recorded retrospectively patient's baseline demographic information, clinical data, HIV viral load measurements as well as pharmacy refill records information from the hospital's records. The researcher used data from HIV-positive patients who were initiated on ART between January 2011 and December 2012.

3.2.3 Cohort

In a cohort study, the researcher identifies a group of people who have experienced a particular event. The cohort is evaluated to study outcomes (Burns & Grove 2009:298; Polit & Beck 2008:749). In this study, the researcher used a retrospective cohort study to follow a cohort of HIV-positive patients who were initiated on ART between January 2011 and December 2012 and attended the same designated hospital to describe adherence to antiretroviral therapy.

3.3   RESEARCH METHOD

This section covers the research population and sample, the sampling procedures adopted, data collection and data analysis.

3.3.1 Population

The population is the study object and consists of individuals, groups, organisations, human products and events, or the conditions to which they are exposed (Welman et al 2010:52). The study population for this study was the records of HIV-positive patients who were initiated on ART between January 2011 and December 2012, still attended the same designated district hospital for antiretroviral therapy, and that met the eligibility

criteria. Eligibility criteria include a list of characteristics essential for membership or eligibility in the target population (Burns & Grove 2009:345).

The records of patients who met the following eligibility criteria were selected:

- 18 years of age and over
- have completed at least 12 months of treatment
- have at least two viral load measurements recorded after initiation of antiretroviral therapy

At the end of December 2012, 1987 patients were still attending the designated hospital for antiretroviral therapy; the records of these patients were used as the study population.

3.3.2 Sample and sampling

A sample is a subset of the population that is selected for a particular study (Burns & Grove 2009:42). Sampling involves selecting a group of people, events, behaviours, or other elements with which to conduct a study. A sampling plan defines the process of making the sample selections (Burns & Grove 2009:343). The sampling plan specifies in advance how the sample will be collected and recruited, and how many subjects there will be (Polit & Beck 2008:67).

Probability sampling method using systematic sampling technique was used to select eligible patients' records that were used in this study. The term probability sampling method refers to the fact that every member (element) of the population has a probability higher than zero of being selected for the sample; there is less opportunity for systematic bias if subjects are selected randomly, thus increases the validity of the study (Burns & Grove 2009:349). Probability sampling involves random selection of elements (Polit & Beck 2008:340). In the case of probability sampling, the probability that any element or member of the population will be included in the sample can be determined (Welman et al 2010:56). An element is the most basic unit about which information is collected (Polit & Beck 2008:339).

In contrast, systematic sampling involves the selection of every kth case from a list; systematic sampling can be applied so that an essentially random sample is drawn (Polit & Beck 2008:347). Furthermore, systematic sampling can be conducted when an ordered list of all members of the population is available. The process involves selecting every kth individual on the list, using a starting point selected randomly (Burns & Grove 2009:352).

A sampling frame is a complete list in which each unit of analysis is mentioned only once; the sample should be representative of the sampling frame, which is the same as the population (Welman et al 2010:57). Sampling frame in this study was the list of all patients who were still attending the designated hospital at the end of December 2012.

The researcher got the assistance from HIV clinic staff to obtain the register in which all patients that had been initiated at designated hospital during the named period to randomly select the patient's records that were used in this study. The researcher randomly selected number 06 in a table of two-digit random numbers, using this number as starting point for selection of patient's files, the researcher systematically selected every 10th patient' records of HIV-positive that met the eligibility criteria for inclusion in the study. Out of 1987 patients who were still attending the designated hospital at the end of December 2012, the researcher systematically selected 198 records of patients for inclusion in the study. Of the 198 records of patients selected, 137 records were not included because patients were already transferred out to others health facilities, some were lost to follow up, some were younger than 18 years, some did not have at least two results of viral load measurements, some died before data collection. Only 61 records of HIV-positive patients were included in this study.

Quantitative researchers need to pay careful attention to the number of participants needed to achieve statistical conclusion validity; there are no simple formulas that can tell you how large a sample is needed in a given quantitative study (Polit & Beck 2008:348). Moreover, to some extent, the size of an adequate sample depends on how homogeneous or heterogeneous the population is how alike or different its members are with respect to the characteristics of research interest (Leedy & Ormrod 2010:214). In this study, a sample of 61 patient's records was obtained. The samples included participants who met the selection criteria (adults 18 years of age and over, have

completed at least 12 months of antiretroviral therapy and have at least two viral load measurements).

3.3.3 Research setting

The study was conducted at one of the district hospitals in Ugu Health District. The district is found in the lower south coast of the province of KwaZulu-Natal. This hospital was chosen based on accessibility and availability of hospital records.

3.3.4 Data collection

Research is a viable approach to a problem only when there are data to support it. Data are those pieces of information that any particular situation gives to an observer (Leedy & Ormrod 2010:88). Data collection involves obtaining numerical data to address the research objectives, questions, or hypotheses (Burns & Grove 2009:44). In this study, data were collected by the researcher and the field workers using the checklist for recording of patient demographic data, clinical data and pharmacy drug information retrieved from patient's records.

3.3.4.1 Data collection instrument

A checklist (Annexure D) was developed by the researcher for recording the variables related to research problem and pre-tested on five patients. The checklist is divided into three sections to cover patient information; medical information and pharmacy refill records.

SECTION A: This section covered: gender, age in years, marital status, population group, employment status, home address, disclosure of patient's HIV status to anyone.

SECTION B: This section covered: date of HIV diagnosis, significant past medical history, including opportunistic infections: Tuberculosis (TB); Sexually Transmitted Infection (STI); Herpes, previous antiretroviral exposure, including Pre Exposure Prophylaxis (PEP), Prevention of Mother to Child Transmission (PMTCT), Highly Active Antiretroviral Therapy (HAART); date of HAART initiation, months on Antiretroviral

Therapy (ART), Cluster of Differentiation 4 (CD4) count and viral load results, current antiretroviral therapy.

SECTION C: This section covered: date of Antiretroviral (ARV)'s collected from pharmacy and adherence level.

3.3.4.2 Data collection procedures

During the pre-testing of the measuring instrument, the researcher discovered that it was not possible to find the records of patients that have completed at least 24 months of treatment and still attending the designated hospital for routine check-up and collection of antiretroviral drugs. Because the reason was that most patients were already referred to their local clinic for continuation of care after being initiated at the hospital. The researcher has therefore selected the records of patients who have completed at least 12 months of treatment for this study. However, it was not possible to record the next appointment date of collection of the ARVs from the pharmacy; the ARV dispensing tool could only give the dates of pharmacy visits. In addition, the checklist was then revised and only dates of collection were recorded in revised checklist. Therefore, the researcher recorded the exact dates of ARVs collection and calculated adherence level by dividing the number of refills by the number of months on treatment and then multiplied by 100 to obtain the percentage of adherence.

The researcher numerically coded each patient's record by generating a code number. ART register has the name; surname and clinic number or folder number created from identification number of each patient. The clinic numbers and the generated code number were used for checking of data for correctness and reliability.

The patient demographic data, clinical data and pharmacy drug information retrieved from patient's records were transcribed from patient's records onto the checklists. A completed checklist is attached (Annexure D).

3.3.4.3 Ethical considerations related to data collection

Ethics are a set of guidelines, principles and codes which in the case of research are used to guide the behaviour of the researcher when conducting research (Merrill & West

2009:168). Ethical behaviour is important in research, as in any other field of human activity (Welman et al 2010:181). Three ethical principles are relevant to research involving human subjects, namely: the principle of beneficence, the principles of respect for persons and the principle of justice (Burns & Grove 2009:188).

The principle of beneficence imposes a duty on researchers to minimise harm and to maximise benefits (Polit & Beck 2008:170). In addition, the collection of data was done by reviewing patients' medical and pharmacy records in the hospital. Most importantly, the researcher ensured no harm came to the participants and their confidentiality and anonymity would be maintained by keeping confidential the information obtained from patients' records and by handling this information on anonymous basis. Each patient record was given a code number which was generated by the researcher, the list of patients' clinic number and their code are kept separately from the data collected to protect anonymity.

Principle of respect for persons holds that persons have the right to self-determination and the freedom to participate or not participate in research (Burns & Grove 2009:188). One particularly important procedure for safe-guarding participants and protecting their right to self-determination involves obtaining their informed consent (Polit & Beck 2008:176). Furthermore, the right to self-determination and informed consent were observed as the patients for whom the records were selected, were given the explanation about the study, the purpose, objectives, and benefits of the research, given assurance of confidentiality and asked to sign an informed consent form. When obtaining informed consent from participants who were physically unable to read, write, talk or were blind, a witness signed and dated the consent form attesting that the requirements for informed consent have been satisfied. However, the researcher reviewed data collected for clinical care that were in medical records; obtaining consent was impracticable for most of the participants for whom records were reviewed.

The principle of justice includes participants' right to fair treatment and their right to privacy (Polit & Beck 2008:173). Patients' demographic, medical and pharmacy refill information collected are kept in strictest confidence. Since the research involves patient's medical records in the hospital, ethical clearance from the Research Ethics Committee of the Department of Health Studies of the University of South Africa (Annexure A); full approval from the Provincial Health Research Committee in the KZN

Department of Health (Annexure C1) and from the Hospital Manager, Ugu Health District Manager (Annexure C2) to access records were obtained before the collection of data.

3.3.4 Data analysis

Data were collected from 05 August 2013 to 27 August 2013 and the records of 61 patients were reviewed for this study. Data were analysed using the Statistical Package or Social Sciences (SPSS) version 17. The researcher was assisted by a statistician from the Statistics Department from the University of South Africa in analysing and interpreting the data (see a letter from the statistician attached in Annexure F).

3.4 MEASURES TO ENSURE RELIABILITY AND VALIDITY

3.4.1 Reliability

Reliability refers to consistent and stable measurement of data as well as replicability (Welman et al 2010:9). An instrument is reliable to the extent that its measures reflect true scores, that is, to the extent that measurement errors are absent from obtained scores (Polit & Beck 2008:452). Reliable instruments enhance the power of a study to detect significant differences or relationships actually occurring in the population under study. Therefore, it is important to test the reliability of an instrument before using it in a study (Burns & Grove 2009:377). By comparing the transcribed data on the data collection instrument with that from the data sources for accuracy and correctness, the reliability of data collection instrument is assured. In addition, pre-testing of the instrument was also performed before the conduction of the study.

3.4.2 Validity

Study validity refers to a measure of the truth or accuracy of a claim; it is an important concern throughout the research process. Validity provides a major basis for making decisions about which findings are sufficiently valid to add to the evidence base for patient care (Burns & Grove 2009:221). There are many types of validity. What the researcher will be discussing here is measurement validity or validity of the research instrument, which is the degree to which an instrument measures what it is supposed to measure (Polit & Beck 2008:457).

To establish measurement validity, the research instrument was assessed based on three types of validity namely face validity, content validity and construct validity.

3.4.2.1 Face validity

Face validity refers to whether the instrument looks as though it is measuring the appropriate construct (Polit & Beck 2008:457). The required data on the checklist was correctly transcribed from the patients' medical records and pharmacy refill records. Therefore, systematic and objective collection of data from patients' records and their pharmacy refill records accurately represent what is really happening in the situation.

3.4.2.2 Content validity

Content validity concerns the degree to which an instrument has an appropriate sample of items for the construct being measured and adequately covers the construct domain (Polit & Beck 2008:458). In this study, all the elements of the variables to be described were all included in the checklist.

Adherence was measured as consistent collection of antiretroviral medication from the pharmacy at prescribed intervals. However, patients may not take all claimed medications and it is therefore very difficult to measure adherence accurately and correctly. It is assumed that if they collect the medication, they are likely to take their medication. If a patient failed to collect his antiretroviral medication then, it is assumed that the patient was not taking medication thus, non-adherent.

3.4.2.3 Construct validity

Construct validity determines whether the instrument actually measures the theoretical construct that it purports to measure (Burns & Grove 2009:693). Construct validity refers to the idea that a researcher already has ideas and models (constructs) about the topic they are researching. Therefore, it is important to use multiple ways of establishing that what they investigating is really going on, and is not just them imposing their existing constructs on the reality they are observing (Mcniff & Whitehead 2011:163). In this study, the pharmacy refill data was used to define antiretroviral adherence of HIV-

positive patients. Adherence to antiretroviral as measured by pharmacy refill data is to be associated with improved virological outcomes as measured by viral loads measurements.

The checklist developed by the researcher is valid because it only measured whether adherence to antiretroviral would lead to decrease of viral load measurement. If the pharmacy refill data show a regularity of pharmacy pick-ups, the checklist should show a decline in viral load measurement and if the patient does not collect his or her antiretroviral medication regularly, then there should be an increase in the viral load measurement.

3.5   CONCLUSION

This chapter covered the research design and method, including research design, research population and sample, the sampling procedures, data collection, data analysis and measures to ensure reliability and validity.

Chapter 4 presents analysis, presentation and description of the research findings.

CHAPTER 4

ANALYSIS, PRESENTATION AND DESCRIPTION OF RESEARCH FINDINGS

4.1   INTRODUCTION

This chapter presents and discusses the results of the study. The purpose of the study was to describe antiretroviral adherence of HIV-positive patients using pharmacy refill records and to describe pharmacy refill records as an alternative method of monitoring response to antiretroviral therapy.

These findings will be used to describe adherence to antiretroviral therapy by HIV-positive patients in Ugu District and to recommend the use of pharmacy refill as a reliable method of monitoring patients on antiretroviral therapy.

The researcher adopted a quantitative, retrospective, descriptive and cohort design for this study. Data were collected using the checklist divided into three sections so as to cover patients' demographics, medical information and pharmacy refill records. This analysis includes 61 records of HIV-positive patients who met the eligibility criteria. In addition, data were analysed using the Statistical Package for Social Sciences (SPSS) version 22 computer program and the results are presented in terms of frequency distributions, graphic presentations, measures of central tendency and bivariate statistical analysis.

The findings of this research suggest that the spread of the HIV in Ugu District is significantly influenced by demographic factors that included but not limited to gender, age, marital status, employment and disclosure of HIV status. In this study, all participants (100%) were black population who lived in rural area. The average duration of treatment was 22.02 (Std. Deviation: 5.886) while the shortest duration was 12 months on treatment and the longest duration was 31 months on antiretroviral therapy. Approximately 54% of participants had been on antiretroviral therapy for a period of

between 13-24 months. The findings also revealed that participants who collected the ARV's follow on pharmacy refill did not show any significant viral load suppression.

This section presents demographic data and addresses the research findings related to participants' gender, age, marital status, employment status and disclosure of HIV status.

4.2   DEMOGRAPHICS

A total of 61 (30.8%) records of HIV-positive participants who met the inclusion criteria were reviewed for this study. Out of 198 (100%) records of patients selected, 137 (69.2%) records were not included because the requirement of 18 years of age and over; have completed at least 12 months of treatment and have at least two viral load measurements recorded were not met. Out 61 (100%) of participants, about 41 (67.2%) of participant were initiated on antiretroviral therapy in year 2011, while 20 (32.8%) were initiated in year 2012.

4.2.1 Gender

Table 4.1   Gender distribution (n=61)

Gender	Frequency (n)	Percentage
Female	33	54.1
Male	28	45.9
Total	**61**	**100.0**

The table above shows that there were more females 33 (54.1%) than males 28 (45.9%) living with HIV. This confirms the inequalities between men and women that are created and reinforced by gender roles typically leaving women especially vulnerable to HIV infection. Women are more likely than men to become infected with HIV during unprotected vaginal intercourse. There are various biological, cultural, and social reasons which make women more susceptible to HIV infection than men. As the recipients of semen, women are exposed to semen for a longer time. Women also have a larger surface area of mucosa (the thin lining of the vagina and cervix) exposed to the partner's secretions during sexual intercourse. Apart from their biological vulnerability, women become more vulnerable in societies in which they are seen as having lower

status than men which makes women dangerously vulnerable in sexual relationships (Van Dyk 2013:39).

The result of this study are supported by the previous studies which found that in South Africa, just over 51% (27.08 million) of the population are females and the ration of new female infections to male for those aged 15-49 was 1.5 by 2013 (El-khatib, Ekstrom, Coovadia, Abrams, Petzold, Katzenstein, Morris & Kuhn 2011:1471-2458; Statistic 2013:4-6).

4.2.2 Age in years
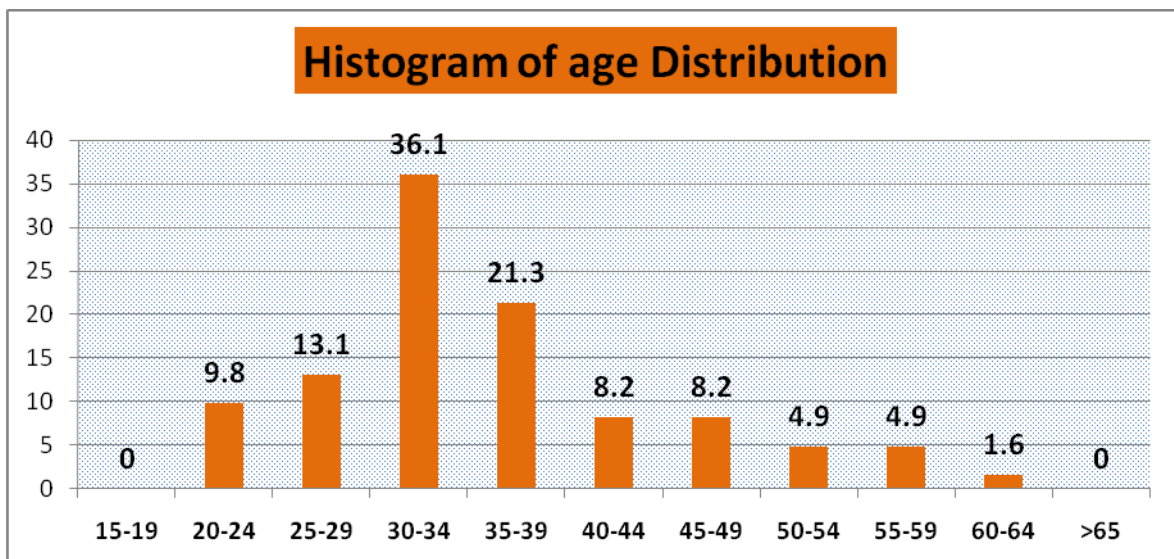
Figure 4.1   Histogram of the age distribution (n=61)

As reflected in the figure above, most participants 22 (36.1%) were aged between 30-34 years old. The key age group of adults aged between 20-49 years represents majority of participants with about 57 (93.4%), among these 31 (54.4%) were females and 26(45.6%) were males. This shows that there are higher HIV infection rates among young women especially those aged between 20 and 49 years compared to young men.

The finding of this study correlate with the evidences from South African studies which show that some gender norms related to masculinity encourage men to have more sexual partners and older men to have sexual relations with much younger women. In addition, this contributes to higher HIV infection rates among young people especially

those aged between 15 and 49 years compared to young men (Mutinta, Gow, George, Kunda & Ojteg 2011:100).

4.2.3 Marital status

Table 4.2   Marital status (n=61)

Marital status	Frequency (n)	Percentage
Single	37	60.7
Married	24	39.3
Total	**61**	**100.0**

Table 4.2 above shows that about 37 (60.7%) participants were single while 24 (39.9%) were married. This shows that in relation to the marital status and HIV infection, being single amplifies the risk of getting infected with HIV because single individuals are likely to be engaged into many risk-taking behaviours including casual sex, multiple and concurrent sexual partnership and do not use of condoms during sex. This finding agrees with a study in Zimbabwe which found that being single was associated with HIV infection (The Nation online 2013:1). In addition, Shisana, Rehle, Simbayi, Zuma, Jooste, Zungu, Labadarios, Onoya, Davids, Mbelle, Van Zyl and Wabiri (2014:125) found that in South Africa HIV infection varies considerably by marital status. Those that are married are less likely to be HIV positive compared to any other reported marital status.

4.2.4 Employment status
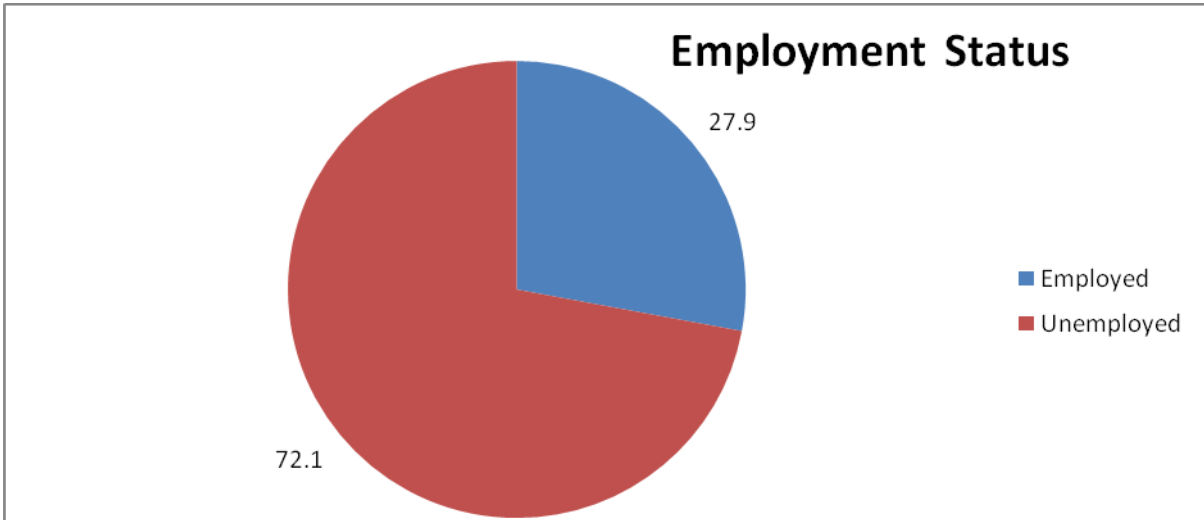
Figure 4.2   Employment status (n=61)

Figure 4.2 above depicts that about 72% (44) of all participants were unemployed with about 25 (56.8%) being females and 19 (43.8%) being males. This finding suggests that the socio-demographic context in which people live highly influence the individual risk of exposure to HIV-infection. In addition, this finding agrees with a study done by Blattman (2011:1) which found that being HIV positive is associated with increase in the likelihood of being unemployed.

Mc Laren (2011:1) found that in South Africa, individuals with HIV tend to be unemployed, and unemployed people are more likely to be HIV positive. Furthermore, Levinsohn, McLaren, Shisana and Zuma (2011:25) found that being HIV-positive is associated with a 6 to 7% point increase in the likelihood of being unemployed.

4.2.5 Disclosure of HIV status

Table 4.3   Disclosure of patient's to someone (n=61)

HIV disclosure	Frequency (n)	Percentage
No answer	1	1.6
Disclosed	56	91.8
Not disclosed	4	6.6
Total	**61**	**100.0**

Table 4.3 above shows that about ninety two percent (56) of participants had disclosed their HIV status to someone and only 6% had not disclosed their HIV status. This shows that majority of the participants had disclosed their HIV status to someone. This disclosure of the status to a confidant could improve adherence as participants will be reminded by the confidants. Sendagala (2010:58) alluded that, having disclosed their status, people living with HIV could adhere to the treatment as they will get both physical and psychological support. In addition, disclosure of HIV status and support by treatment partner or peer counsellor have been shown to have a great impact on adherence (Maartens et al 2012:516).

4.3   ADHERENCE LEVEL
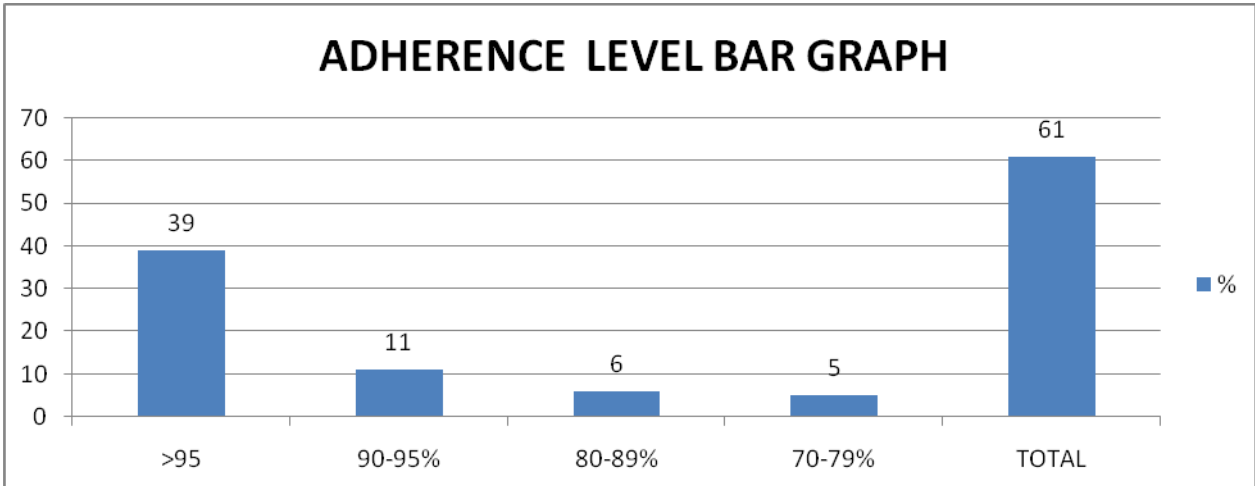
Figure 4.3   Adherence level (n=61)

Of the 61 records reviewed for this study, overall 50 (81.9%) of the participants achieved an optimum adherence level of 90% and above, while 6 (9.9%) reached an adherence level between 80-89% and 5 (8.2%) achieved an adherence level of between 70-79%. The mean adherence level was 94.8% ranging from 71% to 100%.

In this study, adherence is measured as consistent collection of antiretroviral medications from the pharmacy at prescribed intervals. It is assumed that if they collect the medication, then they are likely to take their medication. Adherence level is expressed as a percentage of the number of times they should have collected medication over the period of 12 months or more.

Adherence to antiretroviral therapy results in suppression in plasma viral load combined with increase in CD4 count. Therefore, the treatment adherence of antiretroviral should be monitored by checking at the plasma viral load and CD4 counts measurement.

In this study, the mean CD4 T cell count at antiretroviral therapy initiation was 250.67 cells/mm3. About 50% (31) of participants had severe immune suppression with recorded CD4 T cell count lower than 200 cells/mm3, about 31% (19) had CD4 T cell counts between 200-349 cells/mm3. After 12 months of antiretroviral therapy, the mean CD4 T cell count was 347.56 cells/mm3 with about 31% (19) of participants recorded CD4 T cell lower than 200 cells/mm3 and about twenty five percent (15) of participants achieved CD4 T cell count more than 500 cells/mm3. About 60% (37)

achieved sustained viral load of less than 50 copies/ml at 12 months of commencing antiretroviral therapy.

The finding in this study shows that despite overall 82% (50) of participants with adherence level of 90 or above. In addition, only around 25% (15) of participants achieved immunological recovery with CD4 T cells count of more than 500 cells/mm3 while around 31% (19) still had severe immune suppression with lower CD4 T cell of less than 200 cells/mm3. Only 37 (60.7%) of participants achieved sustained viral load less than 50 copies/ml after 12 months of antiretroviral therapy. However, the mean CD4 T cell count has increased from 250.67 cells/mm3 to 347.56 cells/mm3.

These findings suggest that patients may not take all claimed medications or they take them in not prescribed amounts or off the prescribed schedule, or fail to match the dose with food as directed. In addition, patients may share or sell their own medications and may hoard medications to avoid discrimination and stigma in the community/family. These findings are supported by the study done by Ehlers et al (2009:24) which found that the relationship between refills and actual ingestion of medications is not clear and it is therefore difficult to measure adherence in the outpatient setting accurately and correctly.

According to literature, antiretroviral therapy reduces the HIV viral load as much as possible, preferably to undetectable levels for as long as possible. By doing so, the CD4 T cell lymphocyte count usually increases progressively. Typically, the CD4 count increases rapidly by approximately 50-100 cells/mm3/year (Van Dyk 2013:110; Meintjes et al 2012a:119). In addition, CD4 responses are highly variable and may fail to increase despite virological suppression and a small proportion of patient who start antiretroviral therapy with a very high viral load may not be fully suppressed despite being adherent to the treatment (Meintjes et al 2012a:119; Wilson et al 2010:475).

4.4   RELATIONSHIP OF ADHERENCE LEVEL TO VIROLOGICAL SUPPRESSION
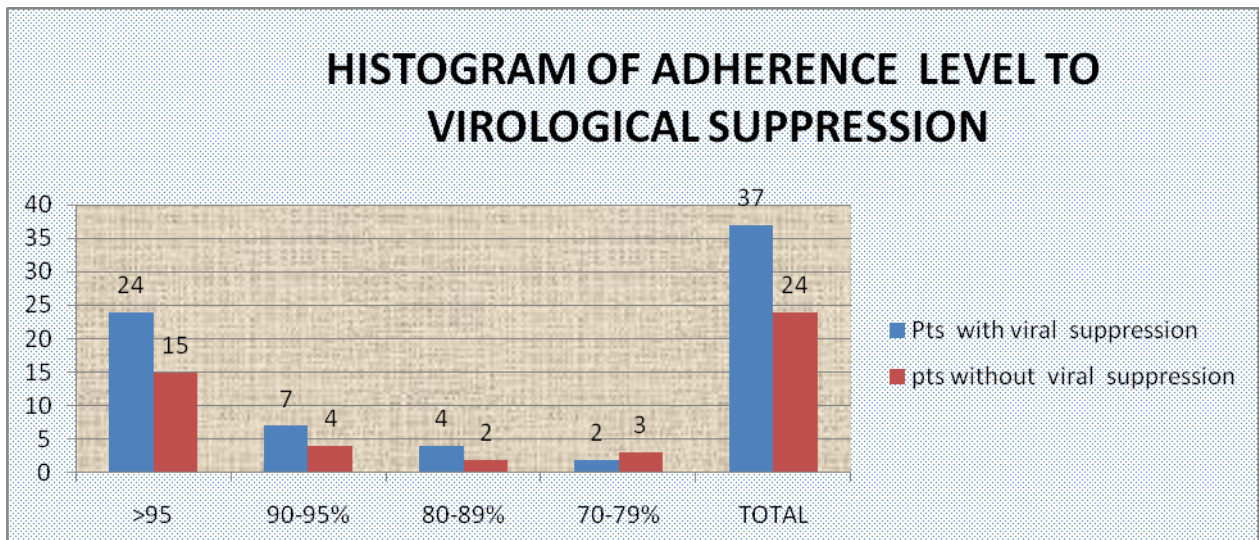
Figure 4.4   Adherence level to virological suppression (n=61)

Figure 4.4 shows that about 82% (50) of participants achieved at least 90% of treatment collection adherence. However, 38% (19) of these participants did not show any related viral suppression.

From the results, an examination of the relationship between adherence and virological suppression show that from the 61 records of patients reviewed, there were 37 (60.7%) who achieved virological suppression and 24 (39.3%) did not achieve a virological suppression. These findings show that majority of participants achieved a viral load measurement of less than 50 copies/ml.

Majority of participants (50) had an adherence level of at least 90% while, 11 participants did not achieve an adherence level of 90% or more. Among those who achieved adherence level of at least 90%, only 31 (62%) participants achieved a viral load measurement of less than 50 copies/ml and 19 (38%) did not achieve viral load measurement of less than 50 copies/ml within 12 months of commencing antiretroviral therapy. However, six participants that did not have an adherence level of at least 90% also achieved a viral load less than 50 copies/ml within 12 months of treatment.

These finding are supported by study done by Zaragoza-Macias et al (2010:135) and study by Henderson, Hindman, Johnson, Valuck and Kiser (2011:221) which have shown that virological suppression was associated with adherence with medication pick

up of more than 90%. In addition, Nachega, Hislop, Dowdy, Chaisson, Regensberg and Maartens (2007:564-573) identified a statistically significant dose-response relationship between viral load suppression and pharmacy claim adherence across all adherence strata. They found that every 10% increase in adherence beyond 50% was associated with a mean absolute increase of 0.10 in the proportion of patients with sustained virologic suppression (p<0.001). Even though, Sayles, Rurangirwa, Kim, Kinsler, Orugan and Janson (2012:463-470) found that despite high antiretroviral therapy (ART) coverage rates, a substantial portion of peoples living with HIV taking ART were not achieving HIV viral load suppression which leads to suboptimal treatment outcomes. In contrast, several studies using pharmacy based adherence measures with stratified adherence estimates failed to detect a threshold to achieve virological suppression (McMahon, Jordan, Bertagnolio, Hong, Wanke, Lewin & Elliott 2011:503).

The relationship between adherence level and virological suppression was investigated using bivariate statistical analysis and Pearson's correlation coefficient (r) was calculated. A statistically significant association between adherence and viral suppression is not demonstrated (r=0.094, p>0.05). Thus, there is no relationship between adherence and virological suppression. This finding agrees with a study done by Sayles et al (2012:463-470) which found no association between taking antiretroviral medications and achieving HIV viral load suppression. However, there are some studies that have shown a relationship between adherence level and virological suppression.

4.5   PHARMACY REFILL RECORDS ADHERENCE

Antiretroviral medication works only if they are taken regularly every day for the rest of the live. Adherence refers to the willingness and ability of patients to follow health-related advice, take medication as prescribed, attend scheduled appointments, and complete recommended investigations (Kalichman 2013:77; Moosa & Jeenah 2012:144). Conversely, non-adherence to antiretroviral, evidenced as missed doses, is associated with incomplete viral suppression and the development of drug resistant virus that will eventually limit therapeutic options (Wilson et al 2010:514).

In this study, the pharmacy refill records were used to measure adherence to antiretroviral by HIV positive patients in Ugu Health District. The method of using pharmacy refill records for estimation of adherence is related to the amount of drugs

actually ingested by the patients. As discussed in this chapter, the relationship between collection of medications and actual ingestion of medications is difficult to establish. Saberi, Caswell, Amodio-Groton and Alpert (2008:744) state that some advantages of utilising pharmacy refill records is that these data can easily be collected. However, they do not depend on patients' self-reports and accurate recall; they are inexpensive to acquire; they allow for retrospective assessment; and they are readily obtainable from computerised records.

In addition, pharmacy-based adherence measures are ideally suited to monitoring adherence because they are objective and can be easily derived from data routinely collected for other purposes, such as clinical care, medication billing, fulfilment of legal requirements, or drug supply management (McMahon et al 2011:503). In contrast, pharmacy refill records may overestimate actual pill taking if individuals discard or share pills. Therefore, estimate maximum possible adherence for this measurement methodology and threaten the internal validity of measurement method (Sattler, Lee & Perri III 2013:395; McMahon et al 2011:503).

In settings where frequent routine viral load monitoring is not available, pharmacy refill records can play an important role in monitoring individual and population level adherence to ART (Mahon et al 2011:503). Ndubuka and Ehlers (2011:1323) concluded that if single available measures, such as pharmacy refill records could be correlated with laboratory tests results for improved CD4 counts (indicating immunological recovery) and decreased viral load (indicating virological recovery), these could be used as preliminary measures of adherence.

In this study, about 82% (50) of participants achieved an adherence level of 90% or above with mean adherence level of 94.8%. In addition, the mean baseline CD4 counts at initiation of ART increased from 250.67 cells/mm3 to 347.56 cells/mm3 after 12 months of antiretroviral therapy while only about 60% (37) achieved undetectable viral load (below the detectable level of less than 50 copies/m within 12 months of treatment. It can be suggested that all claimed medications were not ingested. Therefore, pharmacy refill records should be implemented with laboratory tests for monitoring of patients' ART adherence. This is because it is difficult to predict who will take claimed medications as directed. In addition, directly observed therapy (DOT) strategy should be also implemented for patients who have problems taking medications correctly.

4.6   CONCLUSION

This chapter highlighted the demographic characteristics of participants in terms of gender, age, marital status, employment status and disclosure of patient's HIV status to someone. Most importantly, the findings in this study are supported by several previous studies related to use of pharmacy refill records in combination with others means or methods for monitoring of patients adherence of medication collection to antiretroviral therapy.

This study found that overall 81.9% of the patients achieved an optimum adherence level of 90 or above and there is no relationship between adherence and virological suppression.

The next chapter will present conclusions, limitations and recommendations.

CHAPTER 5

CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

5.1   INTRODUCTION

The purpose of this study was to describe antiretroviral adherence in HIV-positive patients in Ugu District using pharmacy refill records and to describe pharmacy refill records as an alternative method of monitoring response to antiretroviral therapy.

Furthermore, the findings of this study will be used to recommend the use of pharmacy refill records in clinical practice; to assess the response to antiretroviral therapy for clinics that do not have CD4 counts or viral load monitoring capabilities; to guide decision-making on timing to perform viral load measurement for clinics able to perform viral load assessment; and for early identification of patients at high risk of virological failure.

The research results discussed in Chapter 4 of this dissertation will be used to answer the following research questions:

- To what extent do HIV-positive patients in Ugu District adhere to antiretroviral therapy?
- Could pharmacy refill records be used as a reliable method of monitoring patients on antiretroviral therapy?

5.2   RESEARCH DESIGN AND METHOD

A quantitative, retrospective, descriptive and cohort study design was conducted at one of the district hospital in Ugu Health District in the lower south coast of the rural KwaZulu-Natal Province. A checklist developed by the researcher was used to retrospectively record patient's baseline demographic information, clinical data, HIV viral load measurement and pharmacy refill records information from the hospital's records; only the records of HIV-positive patients who were initiated on antiretroviral therapy

between January 2011 and December 2012 at the designated hospital that met the eligibility criteria were systematically and objectively reviewed in order to obtain numerical data to address the research purpose, objectives and questions.

At the end of December 2012, 1987 patients were still attending the designated hospital for antiretroviral therapy. The records of these patients were used as the study population. Using systematic sampling technique, out of these 1987 records, 198 were selected but only a sample of 61 patients' records was obtained for this study. However, 137 records were not included because some patients were already transferred out to other health facilities; some were lost to follow up; some were younger than 18 years; some did not have at least two results of viral load measurements; and some died before data collection.

The data retrieved from this sample were analysed using the Statistical Package for Social Sciences (SPSS) version 22 and the findings of this analysis were presented and discussed in Chapter 4.

5.3   SUMMARY AND INTERPRETATION OF THE RESEARCH FINDINGS

The findings of this research suggest that the spread of the HIV in Ugu District is significantly influenced by demographic factors such as gender, age, marital status, employment and disclosure of HIV status.

In this study, there were more females 33 (54.1%) than males 28(45.9%) who were infected with HIV. This confirms the inequalities between men and women that are created and reinforced by gender roles typically leaving women especially vulnerable to HIV infection. Most participants 22 (36.1%) were aged between 30-34 years old. The key age group of adults aged between 20-49 years represents majority of participants with about 57 (93.4%) among these, 31 (54.4%) were females and 26 (45.6%) were males. This shows that there was higher HIV infection rates among young women compared to young men in this key age group.

In relation to the marital status, about 37 (60.7%) participants were single while 24 (39.9%) were married. This shows that being single amplifies the risk of getting infected with HIV.

The finding in this study in relation to employment status showed that 72% (44) of all participants were unemployed with about 25 (56.8%) being females and 19 (43.8%) being males. This finding suggests that the socio-demographic context in which people live highly influence the individual risk of exposure to HIV-infection.

Ninety one percent (91%) (56) of participants had disclosed their HIV status to someone while only 6% had not disclosed their HIV status. This shows that disclosure of HIV status to treatment partner or to someone could have an impact on adherence.

In line with the first objective of this study, the results of the study have shown that about 81% of participant (50) achieved an optimum adherence level of 90% or above in Ugu District. About 10% (6) reached an adherence level between 80-89% and about 8% (5) achieved an adherence level between 70-79%. The mean adherence level was 94.8%.

Adherence to antiretroviral therapy measured as collection of antiretroviral medication should result in fall in plasma viral load combined with increase in CD4 cell count. In this study, the mean CD4 cell count of participants at initiation of antiretroviral therapy was 250.67 cells/mm3. After 12 months of antiretroviral therapy, the mean CD4 cell count increased to 347.56 cells /mm3 and about 60% (37) achieved sustained viral load of less than 50 copies /ml. The findings show that this is despite overall 82% of participants achieving an adherence level of at least 90%. Among those, only 31 (62%) had achieved a viral load of less than 50 copies /ml and 19 (38%) did not achieve undetectable viral load. However, our findings show that even at moderate level of adherence of 70% to 90% documented by pharmacy claims, 6 participants achieved a viral load less than 50 copies /mm3. This may suggest that there is no threshold of adherence level to achieve a virological suppression.

These findings could be explained by the fact that patients may not take all collected medications or they take them in not prescribed amounts or off the prescribed schedule; or fail to match the dose with food as direct; or patients may share or sell their own medications and patients may hoard medications to avoid discrimination and stigma in the community. Therefore, the relationship between collection of medication and actual ingestion of medications is difficult to establish.

In line with the second objective of this study, pharmacy refill records were used to measure adherence and the relationship between adherence and virological suppression could not be demonstrated at significance level of 5%. (Pearson's correlation coefficient(r)=0.094). Nevertheless, for estimation of adherence antiretroviral therapy by HIV positive patients, data from pharmacy records were easily accessible from hospital records and are inexpensive to acquire. Over and above this, the adherence level using these pharmacy refill records is simple to calculate.

5.4   CONCLUSIONS

In this study, the relationship between adherence to antiretroviral therapy using pharmacy refill records and virological suppression could not be determined. Multiple and varied means are more likely to identify patients with adherence problem than single method. Therefore, pharmacy refill records cannot be recommended as an alternative method of monitoring response to antiretroviral therapy. However, pharmacy refill records as simple available measure of adherence must be combined with laboratory tests results including CD4 cell count and or viral load measurement to monitor response to antiretroviral therapy and for early identification of patients at high risk of virological failure.

Good adherence to ART and corresponding high rates of sustained virological suppression can be achieved in a resource-limited area with improvement in the ability of health care providers to assess adherence in routine care of HIV infected persons.

5.5   LIMITATIONS

There are several limitations to this study. Firstly, it is retrospective cohort study in design and therefore reliance on records keeping which others that were incomplete; some were without all patients' CD4 counts and some without viral load measurement after 6 months of antiretroviral therapy initiation and necessitated using a sample of only 61 records out of a possible cohort of 198. In addition, all participants were black population who lived in rural area. As a result, patients' outcomes in this rural area may not be representative of those in urban areas. Moreover, the results of this study do not

necessarily reflect practices in other settings and may limit the generalization of these findings.

Secondly, this study used a pharmacy refill records, which do not reflect the dynamic nature of adherence. In addition, pharmacy claim does not describe the actual ingestion of medication, or the pattern of non-adherence (for example, frequency, duration). Therefore, there is an overestimation of the actual adherence because patients may not take all claimed medication.

Thirdly, this study used hospital records as source of information, obtaining informed consent from participants for whom records were reviewed was impracticable for most of the participants.

Fourthly, the research results are only applicable to one public hospital where the data had been collected. Consequently, these results might not be generalised to other ART services.

5.6   RECOMMENDATIONS AND FURTHER STUDIES

From the conclusions drawn above, the following recommendations are made:

For the National Department of Health and the Department of Social Development

The department should design and roll out a comprehensive combination package of interventions to address the conditions that are prevalent in rural areas such as poverty, unemployment, poor education, limited or no access to basic services such as water, sanitation, roads, transport and preventive health services.

Implementation of social and behavioural change communications campaigns targeting especially the key age which address risky behaviour such as having multiple sexual partnerships, inconsistent condom use, early sexual debut, age – disparate relationship, alcohol abuse and recreational drug use. In addition, structural issues and its impact on women need to be addressed with implementation of policy that addresses the inequalities between men and women.

For the health care providers

Health care providers should revive the health promotion campaign to educate the public about the basic message of abstain, be faithful, and use of condom.

They should also develop personal adherence plan and intensify counselling before antiretroviral therapy initiation with caution that patients should be willing to commit to lifelong treatment and should understand the importance of adherence.

There should be implementation of a comprehensive package of adherence support measures, including community outreach model, such as home-based weekly delivery of medication by peripheral health workers to the clients and collection of basic information on health status and adherence.

Comprehensive assessment of ART non-adherence should include measures of dose, schedule, and instruction, because accurate information is crucial for evaluating both the effectiveness of antiretroviral therapy regimens and interventions designed to increase adherence.

Pill count or patients' self-reported adherence level should be used in combination with the pharmacy refill records for measurement of adherence.

For further studies

Further research is needed to

- determine the threshold of adherence level necessary to achieve a virological suppression
- investigate the potential correlation between viral load and adherence in other setting (urban or private sector)
- investigate the relationship between pharmacy refill records and virological suppression at population level in resource limited settings
- assess antiretroviral adherence focusing on medications schedules, special instructions such as dietary restrictions, dosage

- elucidate what combination of methods of adherence measurements can produce the most reliable adherence level of patients on antiretroviral therapy

REFERENCES

Airoldi, M, Zaccarelli, M, Bisi, L, Bini, T, Antinori, A, Mussini, C, Bai, F, Orofino, G, Sighinolfi, L, Gori, A, Suter, F & Maggiolo, F. 2010. Once-pill one a day HAART: a simplification strategy that improves adherence and quality of life of HIV-infected subjects. *Dove Medical Press* 4:115-125.

Badri, M, Lawn, SD & Wood, R. 2008. Utility of CD4 cell counts for early prediction of virological failure during antiretroviral therapy in a resource-limited setting. *BMC Infectious Diseases* 8:89.

Bamford, L. 2013. *Maternal, new born and child health. South African Health Review*. Durban: Health Systems Trust.

Benni, P, Sethi, G & Willians, IG. 2012. Antiretroviral drugs. In *ABC of HIV and AIDS*. 6th edition. West Sussex: Blackwell.

Beer, L, Heffelfinger, J, Frazier, E, Mattson, C, Roter, B, Barash, E, Buskin, S, Rime, T & Valverde, E. 2012. Use of and adherence to antiretroviral therapy in a large U.S. sample of HIV-infected adults in care, 2007-2008. *The Open AIDS Journal* 6 (Suppl 1:M21):213-223.

Blattman, C. 2011. *The impact of HIV on poverty in South Africa*. *International development, economics, politics and policy*. From: www.chrisblattman.com (accessed on 29 March 2011).

Burns, N & Grove, SK. 2009. *The practice of nursing; appraisal, synthesis, and generation of evidence.* 6th edition. St Louis: Saunders/Elsevier.

CDC see Centers for Disease Control and Prevention.

Centers for Disease Control and Prevention. 2013. *Background* on *the prevention benefits of HIV treatment*.
From: http://www.cdc.gov/hiv/topics/treatment/resources/factsheets/tap.htm (accessed on 20 April 2013).

Centers for Disease Control and Prevention. 2009. *Effect of antiretroviral therapy on risk of sexual transmission of HIV infection and superinfection.* From: http://www.cdc.gov/hiv/topics/treatment/resources/factsheets/tap.htm (accessed on 13 July 2013).

Conradie, K, Cox, V & Wilkinson, L. 2013. Supporting adherence to antiretroviral treatment: a facility approach to reduce the risk of treatment failure. *Southern African HIV clinicians Society* 4(3):20-22.

El-Khatib, Z, Ekstrom, AM, Coovadia, A, Abrams, EJ, Petzold, M, Katzenstein, D, Morris, L & Kuhn, L. 2011. Adherence and virologic suppression during the first 24 weeks on antiretroviral therapy among women in Johannesburg, South Africa- a prospective cohort study. *Biomedcentral Public Health* 11:88.

Fielding, KL, Charalambous, S, Stenson, AL, Pemba, LF, Martin, DJ, Wood, R, Churchyard, GJ & Grant, AD. 2008. Risk factors for poor virological outcome at 12 months in a workplace-based antiretroviral therapy programme in South Africa: A cohort study. *BMC Infectious Diseases* 8:93.

Ford, N, Darder, M, Spelman, T, Maclean, E, Mills, E & Boulle, A. 2010. Early adherence to antiretroviral medication as a predictor of long-term HIV virological suppression: Five-year follow up of an observational cohort. *PloS ONE* 5(5):e10460.

Foundation for Professional Development. 2008. *Adherence counselling for ART*. 2nd edition. Lynnwood Ridge: Foundation for Professional Development.

Garang, PG, Odoi, RA & Kalyango, JN. 2009. Adherence to antiretroviral therapy in conflict areas: A study among patients receiving treatment from Lacor Hospital. *AIDS Patient Care & STDs* 23(9):743-747.

Henderson, KC, Hindman, J, Johnson, SC, Valuck, RJ & Kiser, JJ. 2011. Assessing the effectiveness of pharmacy-based adherence interventions on antiretroviral adherence in persons with HIV. *AIDS Patient Care and STDs* 25(4):221-228.

Kalichman, SC. 2013. *HIV treatment as prevention (TasP) primer for behavior-based implementation.* New York: Springer.

Kigozi, BK, Sumba, S, Mudyope, P, Namuddu, B, Kalyango, J, Karamagi, C, Odere, M, Katabira, E, Mugyenyi, P & Ssali, F. 2009. The effect of AIDS defining conditions on immunological recovery among patients initiating antiretroviral therapy at joint clinical research centre, Uganda. *AIDS Research and Therapy* 6:21.

KwaZulu-Natal Department of Health. 2012. *Annual report for the period 1 April 2012 to 31 March 2013.* Pietermaritzburg: KwaZulu-Natal Department of Health.

Leedy, PD & Ormrod, JE. 2010. *Practical research planning and design.* 9th edition. Boston: Pearson.

Levinsohn, J, McLaren, Z., Shisana, O. & Zuma, K. 2011. HIV status and labour market participation in South Africa. From:
levinsohn.commons.yale.edu/files/2010/10/HIV_labor_33.pdf (accessed on 05 October 2014).

Long, L, Brennan, A, Fox, MP, Ndibongo, B, Jaffray, I, Sanne, L & Rosen, S. 2011. Treatment outcomes and cost-effectiveness of shifting mangement of stable ART patients to Nurses in South Africa: An observational cohort. *Plos Medicine* 8(7):1.

Malaza, L. 2013. KwaZulu-Natal Province. *District Health Barometer.* Durban: Health Systems Trust.

Martin, S, Elliott-Desorbo, DK, Calabrese, S, Wolters, PL, Roby, G, Brennan, T & Wood, LV. 2009. A comparison of adherence assessment methods utilized in the Unites States: perspectives of researchers, HIV-infected children, and their caregivers. *AIDS Patient Care and STDs* 23(8):593-601.

McMahon, JH, Jordan, MR, Kelley, K, Bertagnolio, S, Hong, SY, Wanke, CA, Lewin, SR & Elliott, JH. 2011. Pharmacy adherence measures to assess adherence to antiretroviral therapy: Review of the literature and implications for treatment monitoring. *Clinical Infectious Diseases* 52(4): 493-506.

McLaren, Z. 2011. *HIV and unemployment cycle*. From: http://www.Sph.umich.edu/news_events/findings/spring_11/research/poverty.htm (accessed on 11 October 2014).

Mcniff, J & Whitehead, J. 2011. *All you need to know about research*. 2nd edition. London: Sage.

Meintjes, G, Maartens, G, Boulle, A, Conradie, F, Goemaere, E, Hefer, E, Johnson, D, Mathe, M, Moosa, Y, Regina, O, Rossouw, T, Van Cutsem, G Variava, E, Venter, F & Spencer, D. 2012a. Guidelines for antiretroviral therapy in adults. *Southern African Journal of HIV Medicine* 13 (3):114-133.

Meintjes, G, Maartens, G, Boulle, A, Conradie, F, Goemaere, E, Hefer, E, Johnson, D, Mathe, M, Moosa, Y, Regina, O, Rossouw, T, Van Cutsem, G Variava, E, Venter, F & Spencer, D. 2012b. The 2012 Southern African ARV drug resistance testing guidelines. *Southern African Journal of HIV Medicine* 13 (4):162-167.

Merril, B & West, L. 2009. *Using biographical methods in social research*. London: Sage.

Moosa, MYH & Jeenah, FY. 2012. Treating depression in HIV-positive patients affects adherence. *Southern African Journal of HIV Medicine* 13(3):144-149.

Mutinta, G, Gow, J, George, G, Kunda, K & Ojteg, K. 2011. The influence of socio-economic determinants on HIV prevalence in South Africa. *Review of Economics and Finance* 5:96-106.

Muzah, BP, Takuva, S, Maskew, M & Delany-Moretlwe, S. 2012. Risk factors for discordant immune response among HIV-infected patients initiating antiretroviral therapy: A retrospective cohort study. *Southern African Journal of HIV Medicine* 13(4):168-172.

Nachega, JB, Hislop, M, Dowdy, DW, Chaisson, RE, Regensberg, L & Maartens, G. 2007. Adherence to non-nucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. *Annals of Internal Medicine* 146(8):564-573.

Ndubuka, NO & Ehlers, VJ. 2011. Adult patients' adherence to antiretroviral treatment: A survey correlating pharmacy refill records and pill counts with immunological and virological indices. *International Journal of Nursing Studies* 48(11):1323-1329.

Nyasulu, JCY, Muchiri, E, Mazwi, S, & Ratshefola, M. 2013. NIMART rollout to primary health care facilities increases access to antiretrovirals in Johannesburg: An interrupted time series analysis. *South African Medical Journal* 103(40):232-236.

Padayachee, L. 2013. *HIV and AIDS. District health barometer.* Durban: Health Systems Trust.

Pirkle, CM, Boileau, C, Nguyen, VK, Machouf, N, Aboubacrine, Sag, Niamba, P A, Drabo, J, Koala, S, Tremblay, C & Rashed, S. 2009*.* Impact of a modified directly administered antiretroviral treatment intervention on virological outcome in HIV-infected patients treated in Burkina Faso and Mali*. HIV Medicine* 10:152-156.

Polit, DF & Beck, CT. 2008. *Nursing research. Principles and methods.* 7th edition. Philadelphia: JB Lippincott, Williams & Wilkins.

Rougemont, M, Stoll, BE, Elia, N & Ngang, P. 2009. Antiretroviral treatment adherence and its determinants in Sub-Saharan Africa: a prospective study at Yaounde Central Hospital, Cameroon. *AIDS Research and Therapy* 6:1-12.

Saberi, N, Caswell, M, Amodio-Groton, M & Alpert, P. 2008. Pharmacy refill measure of adherence to efavirenz can predict maintenance of HIV viral suppression. *AIDS Care* 20(6):741-745.

Sattler, EL, Lee, JS & Perri III, M. 2013. Medication refill adherence measures derived from pharmacy claim data in older Americans: A review of the literature. *Drug Aging* 30:383-399.

Sayles, JN, Rurangirwa, J, Kim, M, Kinsler, J, Oruga, R & Janson, M. 2012. Operationalizing treatment as prevention in Los Angeles country: Antiretroviral therapy use and factors associated with unsuppressed viral load in the Ryan White system of care. *AIDS Patient Care and STDs* 26(8):463-470.

Sendagala, S. 2010. Factors affecting the adherence to antiretroviral therapy by HIV positive patients treated in a community based HIV/AIDS care programme in rural Uganda. A case of Tororo district. MPH dissertation. Unisa: Pretoria.

Shisana, O, Rehle, T, Simbayi, LC, Zuma, K, Jooste, S, Zungu, N, Labadaries, D, Onoya, D, Davids, A, Mbelle, N, Van Zyl, J & Wabiri, N. 2014. *South African national HIV prevalence, incidence and behaviour survey. 2012*. Cape Town: Human Sciences Research Council.

South Africa (Republic). Department of Labour. 2014. *Job opportunities and unemployment in the South African labour market. 2012-2013.* Pretoria: Government.

South Africa (Republic). Department of Health. 2013a. *The South African antiretroviral guidelines*. Pretoria: Government Printer.

South Africa (Republic). Department of Health. 2013b. *The 2011 National Antenatal sentinel HIV & Syphilis prevalence survey in South Africa*. Pretoria: Government Printer.

South Africa (Republic). Department of Health. 2011. *National Strategic plan on HIV, STIs and TB: 2012-2016 summary*. Pretoria: SANAC.

Statistics South Africa. 2013. *Statistical release P0302 mid-year population estimates 2013*. Pretoria: Statistics South Africa.

Stedman's Medical Dictionary for the Health Professions and Nursing. 2012. Philadelphia: Lippincott Williams & Wilkins.

Stoll, K, Michel, J & Oliveira, TD. 2013. Principles of HIV drug resistance for clinical management in South Africa. *Southern African HIV Clinicians Society* 4(3):24-25.

Sturmer, M, Doerr, HW, Berger, A & Gale, P. 2011. Is transmission of HIV in non-viraemic serodiscordant couples possible? *Antiviral therapy* 13(5):729-732.

Sultan, B & Adler, MW. 2012. Development of the epidemic. In *ABC of HIV and AIDS.* 6th edition. West Sussex: Blackwell.

The Nation On line, 20 April 2013. For women marriage is risk factor for HIV infection. From: www.nation.com/for–women-marriage-risk-factor-for-hiv-infection (accessed on 18 August 2014).

Tsibris, AMN & Hirsch, MS. 2010. Antiretroviral therapy in the clinic. *Journal of Virology* 84(11):5458-5464.

UNAIDS. 2011. *Terminology Guidelines.* Geneva: UNAIDS.

UNAIDS. 2012. *Global AIDS response progress report 2012/SA.* Geneva: UNAIDS. From: www.unaids.org/en/region_countries/South_Africa (accessed on 21 November 2013).

UNAIDS. 2013. *Global Report: UNAIDS report on the global AIDS epidemic.* Geneva: UNAIDS.

UNICEF. 2013. Eastern and Southern Africa. UNICEF/ HIV and AIDS issues. Paris: UNICEF. From: www.unicef.org/esaro/5482_HIV_AIDS.html (accessed on 21 September 2013).

Van Dyk, A. 2013. *HIV and AIDS. Education, care and counselling. A multidisciplinary approach.* 5th edition. Cape Town: Pearson.

Venter, F. 2013. *HIV treatment in South Africa: the challenges of an increasingly successful antiretroviral programme, South African Health Review.* Durban: Health Systems Trust.

Walshe, L, Saple, DG, Mehta, SH, Shah, B, Bollinger, RC & Gupta, A. 2010. Physician estimate of antiretroviral adherence in India: Poor correlation with self-report and load. *AIDS Patient Care and STDs* 24(30):189-195.

Welman, C, Kruger, F & Mitchell, B. 2010. *Research methodology.* 3rd edition. Cape Town: Oxford University of Press.

Williams, A. & Friedland, G. 2010. Adherence, compliance, and HAART. *Journal Watch HIV/AIDS Clinical Care*:1-6.

Wilson, D, Cotton, M, Bekker, LG, Meyers, T, Venter, F & Meartens, G. 2008. *Hand book of HIV medicine.* 2nd edition. Cape Town: Oxford University Press.

WHO. 2012. *Use of antiretrovirals for treatment and prevention of HIV infection.* Geneva: WHO. From: www.who.in/entity/hiv/topics/treatment/en/ (accessed on 03 August 2013)

WHO. 2013. *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.* Geneva: WHO. From: www.who.int/hiv/pub/guidelines/arv 2013/en/index.html (accessed on 03 August 2013).

Zaragoza-Macias, E, Cosco, D, Nguyen, ML, Del Rio, C & Lennox, J. 2010. Predictors of Success with highly active antiretroviral therapy in an antiretroviral-naïve urban population. *AIDS Research and Human Retroviruses* 26(2):13.

ANNEXURE A

ETHICAL CLEARANCE CERTIFICATE, DEPARTMENT OF HEALTH STUDIES, RESEARCH AND ETHICS COMMITTEE, UNIVERSITY OF SOUTH AFRICA

UNISA | university of south africa

UNIVERSITY OF SOUTH AFRICA
Health Studies Higher Degrees Committee
College of Human Sciences
ETHICAL CLEARANCE CERTIFICATE

HSHDC/195/2013

Date: 3 July 2013   Student No: 3734-863-9

Project Title: Antiretroviral adherence and HIV virological outcomes in HIV-positive patients in UGU District, Kwazulu-Natal Province.

Researcher: Kapiamba Muteba Germain

Degree: Masters in Public Health   Code: DIS4986

Supervisor: Dr TE Masango
Qualification: PhD
Joint Supervisor: -

DECISION OF COMMITTEE

Approved   √   **Conditionally Approved**   ☐

Prof L Roets
CHAIRPERSON: HEALTH STUDIES HIGHER DEGREES COMMITTEE
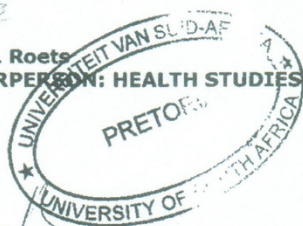
Prof MM Moleki
ACTING ACADEMIC CHAIRPERSON: DEPARTMENT OF HEALTH STUDIES

PLEASE QUOTE THE PROJECT NUMBER IN ALL ENQUIRES

ANNEXURE B

REQUEST TO CONDUCT RESEARCH

<div align="right">
PO BOX 28
HARDING
4680

15 July2013
</div>

TO WHOM IT MAY CONCERN

DEAR SI/MADAM

RE: REQUEST TO CONDUCT A STUDY.

I am a master student in public health (MPH) 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 conduct a research study on antiretroviral adherence and HIV virological outcomes in HIV-positive patients in Ugu district, KwaZulu-Natal province. The purpose of this study is to describe antiretroviral adherence in HIV-positive patients using pharmacy refill records and to describe an alternative method of monitoring response to antiretroviral therapy. Following are the objectives of this study: describe adherence to antiretroviral therapy by HIV-positive patients and determine if pharmacy refill records is reliable monitoring method of HIV-positive patients on antiretroviral therapy. I am therefore requesting permission to conduct the study.

The results obtained will be used for scientific purposes and may be published.

I trust that you will grant me permission to conduct research in your hospital.

Yours sincerely

Dr MG Kapiamba

Student

ANNEXURE C1

APPROVAL FROM THE KWAZULU-NATAL HEALTH RESEARCH COMMITTEE, DEPARTMENT OF HEALTH TO CONDUCT THE STUDY

health

Department:
Health
PROVINCE OF KWAZULU-NATAL

Health Research & Knowledge Management sub-component
10 – 103 Natalia Building, 330 Langalibalele Street
Private Bag x9051
Pietermaritzburg
3200
Tel.: 033 – 3953189
Fax.: 033 – 394 3782
Email.: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference : HRKM219/13
Enquiries : Mrs G Khumalo
Telephone : 033 – 395 3189

26 July 2013

Dear Dr M G Kapiamba

Subject: Approval of a Research Proposal

1. The research proposal titled '**Antiretroviral adherence and HIV virological outcomes in HIV positive patients in Ugu district, KwaZulu-Natal province**'was reviewed by the KwaZulu-Natal Department of Health.

The proposal is hereby **approved** for research to be undertaken at **St Andrews Hospital**.

2. You are requested to take note of the following:
   a. Make the necessary arrangement with the identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.

3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mrs G Khumalo on 033-395 3189.

Yours Sincerely

Dr. E Lutge
Chairperson, KwaZulu-Natal Health Research Committee
Date: 29/07/2013

uMnyango Wezempilo . Departement van Gesondheid

Fighting Disease, Fighting Poverty, Giving Hope

ANNEXURE C2

APPROVAL FROM THE HOSPITAL MANAGER, UGU HEALTH DISTRICT TO CONDUCT THE STUDY

HEALTH
KwaZulu-Natal

St Andrews Hospital
14 Moodie St
Private Bag X1010
HARDING
4680
Tel: 039 – 4331955
Fax: 039 - 4332439
E-mail: thandazile.ntleko@kznhealth.gov.za

Our Ref:SA/
Enquiries: Mrs T.L. Ntleko
Telephone: 0394331955 ext 266
25 July 2013

Dr MG Kapiamba

RE: LETTER OF SUPPORT: RESEARCH STUDY ON: ANTIRETROVIRAL ADHERENCE AND HIV VIROLOGICAL OUTCOMES IN HIV-POSITIVE PATIENTS IN UGU DISTRICT, KWAZULU-NATAL PROVINCE.

- I refer to your letter dated 25 July 2013 in the above matter.

- This is to confirm that as Hospital Manager, I support the project and agree that it can be conducted at St Andrews Hospital.

- Please note this is a letter of support only.

- Approval from Department of Health Ethics Committee is necessary before the research begins.

- Once you have obtained final approval from the Department of Health and ready to implement the project, please liaise with the Deputy Nursing Manager and Medical Manager to facilitate informing the relevant personnel in the institution.

Thank you,

T.L.NTLEKO
Chief Executive Officer
St Andrews Hospital

Cc: Ms N Vane
Cc: Dr SK Lumeya
Cc: Mrs Gugu Khumalo

ANNEXURE D

DATA COLLECTION INSTRUMENT

ANTIRETROVIRAL ADHERENCE AND HIV VIROLOGICAL OUTCOMES IN HIV-POSITIVE PATIENTS IN UGU DISTRICT, KWAZULU-NATAL PROVINCE.

CODE NUMBER:□□□

SECTION A: PATIENT INFORMATION

1. GENDER

M	
F	

.

2. AGE IN YEARS

20-24	
25-29	
30-34	
35-39	
40-44	
45-49	
50-54	
55-54	
55-59	
60-64	
≥ 65	

3. MARITAL STATUS

SINGLE	
MARRIED	
CO-HABITING	
DIVORCED	
SEPARATED	
WIDOWED	

4. POPULATION GROUP

AFRICAN	
WHITE	
COLOURED	
INDIAN	
OTHER	

5. EMPLOYMENT STATUS

EMPLOYED	
UNEMPLOYED	
SELF EMPLOYED	
VOLUNTEER	
STUDENT	

6. HOME ADDRESS

RURAL	
URBAN	

7. DISCLOSED OF PATIENT'S HIV STATUS TO ANYONE

YES	
NO	

SECTION B: MEDICAL INFORMATION

8. DATE OF HIV DIAGNOSIS

D	D	M	M	Y	Y	Y	Y

9. SIGNIFICANT PAST MEDICAL HISTORY, INCLUDING OPPORTUNISTIC INFECTIONS (TB, STI/HERPES)

DIAGNOSIS	DATE	TREATMENT RECEIVED	DURATION	OUTCOME

10. PREVIOUS ANTIRETROVIRAL EXPOSURE, INCLUDING PEP, PMTCT, HAART.

DRUGS	DATE TREATMENT STARTED	DATE TREATMENT ENDED	DURATION	REASON FOR DISCONTINUATION

11. DATE OF HAART INITIATION

D	D	M	M	Y	Y	Y	Y

12. MONTHS ON ART

13. CD4 COUNT & VIRAL LOAD RESULTS

DATE	CD4 COUNT(cells/mm)	VIRAL LOAD (copies/ml)

14. CURRENT ANTIRETROVIRAL THERAPY

MEDICATION	DOSE	DURATION(months)

SECTION C: PHARMACY REFILL RECORDS

15. DATE OF ARV'COLLECTED FROM PHARMACY

DATE	YES	NO	DATE	YES	NO

16. ADHERENCE LEVEL

Adherence level=no of times collected medication/no of times expected X 100.

› 95%	
90-95%	
80-90%	
70-89%	
60-69%	
50-59%	
0-49%	

ANNEXURE E

CONSENT FORM

CONSENT FORM

Study title: *Antiretroviral Adherence and HIV Virological Outcomes in HIV-positive Patients in Ugu District, KwaZulu-Natal Province.*
Researcher: Kapiamba Muteba Germain.

Dr Kapiamba is a registered master student in public health at University of South Africa conducting a research study aims to describe antiretroviral adherence in HIV-positive patients using pharmacy records and to describe an alternative method of monitoring response to antiretroviral therapy. This study will not benefit you directly, but it will help to inform policy markers on how best to use other easily accessible methods for monitoring response to antiretroviral therapy.

The structure of this research project has been approved by the health facility authorities, the provincial health research committee of KZN department of health and by the ethical committee of the department of health studies (UNISA).

Participants will not be subjected to any harm, discomfort, stigma or discrimination. The potential risk would be a breach of confidentiality or anonymity. The collection of data in this study will be done using a check list for recording of patient demographic information, medical information, and pharmacy refill records (data).

Your participation in this study is entirely voluntary and free. Your record will be coded; all study data will be kept confidential and will be handled anonymously. The results obtained at the end of this study will be used for scientific purpose and may be published.

The study has been explained to me, I have read and understand this consent form and voluntarily consent to participate in this study.

....
Signature of Participant   Date

(if Appropriate) ·

....
Signature of Witness   Date

I have explained this study to the above participant and to have sought his/her understanding for informed consent

....
Signature of Researcher   Date

ANNEXURE F

LETTER FROM THE STATISTICIAN

UNISA | university of south africa
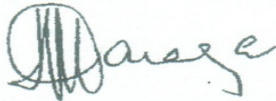
To Whom It May Concern:

This letter is to confirm that I (Miss M.A Managa) and Prof P Ndlovu assisted Dr. MG kapiamba with data analysis.

Should you have any questions, you may contact me at 0794924078 or 011 670 9252 or 9250.

Sincerely,

[signature]

24/07/14