PERSONAL FACTORS INFLUENCING PATIENTS' ANTI-RETROVIRAL TREATMENT ADHERENCE IN ADDIS ABABA, ETHIOPIA

by

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DECLARATION

I declare that **PERSONAL FACTORS INFLUENCING PATIENS' ANTI-RETROVIRAL TREATMENT ADHERNECE IN ADDIS ABABA, ETHIOPIA** is my own work and 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.

....

Tefera Girma Negash

13/06/2011

Date

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PERSONAL FACTORS INFLUENING PATIENTS' ANTI-RETROVIRAL TREATMENT ADHERNECE IN ADDIS ABABA, ETHIOPIA

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ABSTRACT

This study attempted to identify personal (patient-related) factors influencing anti-retroviral therapy (ART) adherence in Addis Ababa, Ethiopia. A quantitative, descriptive, cross-sectional and analytical design was used. Structured interviews were conducted with 355 ART patients.

The findings revealed that stigma, discrimination, depression and alcohol use negatively affected patients' ART adherence levels. However, patients' knowledge levels had no influence on their ART adherence levels, contrary to other researchers' reports.

Addressing stigma and discrimination at community levels might enhance patients' abilities to take their medications in the presence of others. Healthcare professionals should be enabled to diagnose and treat depression among ART patients during the early stages. Non-adherent ART patients should be counseled about possible alcohol abuse.

KEY CONCEPTS
Anti-retroviral treatment (ART) adherence, AIDS, anti-retroviral drugs (ARVs), ART in Ethiopia, depression among ART patients, discrimination against ART patients, HIV, stigmatisation of ART patients

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LIST OF ABBREVIATIONS

ABC   Abacavir

ALERT   All African Leprosy, TB, Rehabilitation, Research, and Training Center

ART   Anti-retroviral therapy

ARV   Anti-retroviral

ATV/r   Azatanavir/ritonavir

AZT   Zidovudine

ddI   Didanosine

DNA   Deoxi-ribonucleic acid

DOTS   Directly observed treatment

D4T   Stavudine

EFMOH   Ethiopian Federal Ministry of Health

EFV   Efavirenz

FTC   Emtricitabine

HAART   Highly active anti-retroviral therapy

HAPCO   HIV/AIDS prevention and control office

HBM   Health Belief Model

HCT   HIV/AIDS counseling and testing

HIV   Human immune deficiency virus

IRB   Institutional review board

3TC   Lamivudine

LPV/r   Lopinavir/ritonavir

MEMS   Medication event monitoring system

NNRTI   Non-nucleoside reverse transcriptase

NRTI   Nucleoside/nucleotide reverse transcriptase inhibitor

NVP   Nevirapine

PI   Protease inhibitor

PLHIV   People living with HIV

RNA   Ribonucleic acid

TDF   Tenofovir

UK   United Kingdom

UNAIDS   The Joint United Nations Programme on HIV/AIDS

UNISA   University of South Africa

USA	United States of America		
WHO	World	Health	Organization

Chapter 1

ORIENTATION TO THE STUDY

1.1 INTRODUCTION

Adherence can be described as taking pharmaceuticals according to the medical standards after a voluntary agreement has been made between the patient and the health care provider. However, adherence beyond this definition also encompasses other health-related behaviours. "It is the extent to which a person's behaviour in taking medications, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider" (WHO 2003:3). An adherence rate of at least 95.0% is necessary to maximise the benefits of antiretroviral therapy (ART). These benefits include improved clinical, immunological and virological parameters (WHO 2006:70). Adherence below 95.0% is associated with a high level of viral drug resistance which has public health implications, and poor personal health outcomes (WHO 2003:95). Adherence can be measured using different techniques including medication event monitoring systems (MEMS), pill counts, biological markers, pharmacy refill data and patients' self-reports (WHO 2003:4-5).

The MEMS cap system utilises a computer chip embedded in a specially designed pill-bottle cap to record the time and duration of each bottle opening. MEMS adherence usually is calculated by dividing the number of time-appropriate bottle openings by the number of expected doses over the study period. Pill counts can be conducted in clinics or at unannounced home visits. Pill count adherence is usually calculated by counting the remaining doses of medication and assuming that the remaining pills are in excess of what is expected, representing the missed doses. Biological markers of adherence refer primarily to plasma concentrations of antiretroviral drugs (ARVs). Pharmacy refill data can serve as an adherence measure by providing the dates on which antiretroviral medications were dispensed (WHO 2003). The study considered ≥95.0% adherence level as adherent

and <95.0% non-adherent. In Ethiopia there are limited studies available to understand adherence determinants and adherence status of patients on ART, required for ART programme effectiveness. According to Arnsten, Demas, Farzadegam, Grant, Goureritch, Chang, Buon, Echholdt, Howard and Schoenbaun (2001:1423) high levels of adherence rates are associated with viral suppression and improved CD4 counts among patients who were >95.0% adherent (Wood, Hogg, Yip, Harrigan, O'Shaughnessy & Montaner 2004:267).

Ethiopia uses first-line and second line ARVs for HIV/AIDS patients who fulfill the ART initiation criteria. ART is initiated in Ethiopia based on clinical and immunological assessment. Immunological assessment is done using CD4 count; it is best to start ART when CD4 count is 200-350cells/ml. In situations where immunological assessment is not possible, ART is initiated based on clinical grounds only. Second line ARVs are reserved for those patients who show treatment failure while on first line drugs. Two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase (NNRTIs) are used as first line drugs while protease inhibitors (PIs) are reserved for second line ARVs. Rather than using single ARV doses, Ethiopia uses fixed dose combinations (triple or double doses together), which is believed to promote patient convenience and adherence to ART (Ethiopian Federal Ministry of health HIV/AIDS prevention and control office (EFMOH/HAPCO) 2008:63-82).

There are five interacting dimensions affecting adherence to ART; these include health system, patient-related, socioeconomic, therapy-related, and condition-related dimensions (WHO 2003:27-30). The independent variables that were analysed in this study are patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression, and alcohol use.

1.2 THE RESEARCH PROBLEM

1.2.1 Source of the research problem

In Ethiopia, since there are few published reports about factors influencing ART adherence, little is known about specific strategies to address this issue for HIV positive

patients on ART. There are no currently standardised adherence guidelines used throughout the country, so each programme and facility develops and follows its own unique method for retaining patients on treatment and follow up adherence counseling. This has been observed and documented during multiple site visits to hospitals and health centers throughout the country. Some health facilities have separate adherence counselors while others do not; even health care providers are not quite sure about their patients' levels of ART adherence, and the patient-related factors influencing ART adherence. This research topic was selected based on observation from health facilities, experiences of ART adherence counselors and the need to fill the gap of research for this topic. The factors that were studied are patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression, and alcohol use and their influence on ART adherence

1.2.2 Background information

In 2007, 33.2 million people globally were estimated to be living with HIV. Two and half million people became newly infected and 2.1 million people died of AIDS. In the same year 22.5 million people were estimated to be living with HIV, 1.7 million were
newly infected and 1.6 million had died of AIDS in Sub-Saharan Africa (SSA) (UNAIDS/WHO 2007).

HIV prevalence in the overall Ethiopian population is 2.4% but the urban prevalence is 7.7% while the rural prevalence is 0.9% (EFMOH/HAPCO 2007a). The first evidence of HIV/AIDS in Ethiopia was reported in 1984. Ethiopians living with HIV/AIDS number about 777 500, of whom 242 500 need ART. Of the people in need of ART, 61% live in urban areas, yet urban dwellers constitute an estimated 15.5% of the total population. This makes urban areas a potential high yield recruitment area for ART patients to participate in research projects (EFMOH/HAPCO Road Map 2007b:09). The adult HIV/AIDS deaths accounted for 35.0% of young adults' deaths. By 2010, there could be 41.0% fewer deaths due to the scale-up of ART programmes in the country, provided the ART adherence rates remain adequate (EFMOH/HAPCO 2006). Addis Ababa is the capital city of Ethiopia and the adult prevalence rate of HIV/AIDS in this area is 9.2% (EFMOH/HAPCO 2007a). This

figure is higher than the national prevalence rate, making Addis Ababa a highly affected area in the country.

Standard treatment of HIV is the provision of at least three medications to HIV/AIDS patients. These medications are known as antiretroviral (ARV) drugs (Ethiopian AIDS Resource Center 2009). ART, also known as Highly Active Anti Retroviral Therapy (HAART), does not cure but slows down the progression of HIV and improves the health outcomes of patients. Once ART is started it should be taken for life with greater than 95.0% adherence (Ethiopian AIDS Resource Center 2009). Provision of ART is challenging in resource limited countries like Ethiopia. However, the country started fee-based single ARVs initiatives in 2003 and in 2005 providing free ARVs for those HIV positive patients eligible to receive ART (EFMOH/HAPCO. 2008: 0*8*). By February 2009, there were reportedly 136 344 HIV/AIDS patients on ART (EFMOH/HAPCO 2009) in Ethiopia.

In order to obtain the desired health outcomes of ART, adherence plays a key role. Adherence refers to voluntary participation of the patient in taking medications according to the agreement made with the health care providers. When patients fail to follow the instructions about the amount, frequency and duration of ART, the result will be poor health outcomes. ART adherence rates of less than 95.0% can result in the development of drug resistant mutant viruses which cannot be treated successfully by first line ARVs. The first-line ARVs destroy the sensitive viral strains while leaving the resistant ones unaffected. These mutants replicate and can be transmitted to the community via sex partners, mother-to-child transmission (MTCT), breastfeeding and through shared injection needle use which make treatment of HIV/AIDS more challenging. As the number of mutants increase, the individual taking ARVs derive fewer benefits from the treatment (Ethiopian AIDS resource center 2009).

It has been postulated that there are at least five interacting dimensions affecting ART adherence (WHO 2003). These include socioeconomic, patient-related, condition-related, therapy-related and health system factors. In developing countries low socioeconomic status forces patients to allocate their resources to other competing priorities. There are few studies about the health system factors' influences on adherence. Therapy-related

factors are those which are due to medical regimen complexities. Patient-related factors influencing adherence to ART, are patients' knowledge and beliefs about the illness and effects of treatment, presence or absence of psychosocial stress, use of alcohol, expectation from the treatment and feelings about being stigmatised (WHO 2003). The focus of this study is on investigating personal factors' influences on ART adherence in Addis Ababa, Ethiopia.

With the introduction of ART, the previously rapidly fatal HIV/AIDS illness is now becoming a chronically manageable illness, which requires taking doses of ARVs every day for the rest of the person's life. A study conducted in Zambia showed that patient-related factors facilitating adherence included looking and feeling better, the support of the patients' family and physical reminders and support, in the form of watches or clocks, to take drugs (Grant, Logie, Masura, Gorman & Murray 2008:1158). Patient-related factors are personal characteristics that determine adherence or non adherence to treatment. These characteristics have different variables that can be categorised as alcohol factors, affective factors, cognitive factors and social factors (Parsons, Rosof & Mustanski 2007:359). Among these factors it has been observed that only alcohol and cognitive factors differed for those adherent versus non-adherent to the HIV medication. A significant relationship between non-adherence and alcohol abuse has been reported (Chander, Lau & Moore 2006: 414; Parsons et al. 2007:366; Samet, Cheng, Libman, Nunes, Alperen & Saitz 2007:198). In a cohort study across 18 primary health care (PHC) centers providing ART in Lusaka, Zambia, mortality decreased among those HIV/AIDS patients who adhered to ART. It was observed that mortality among HIV patients receiving ART, with less than 80.0% adherence status, was higher after 12 months than for those patients with more than 81.0% adherence (Chi, Cantrell, Zulu, Mulenga, Levy, Tambatamba, Reid, Mwango, Mwinga, Bulterys, Saag & Stringer 2009: 751). Patients with lower adherence levels have higher viral load levels making them more likely to transmit the HI virus to their partners in comparison to those with lower viral loads (Wutoh, Brown, Kumoji, Daftary, Jones, Barnes & Powell 2001:248).

Adherence to ART in Addis Ababa among children is relatively higher in comparison to other similar facilities. Reportedly the paediatric ART adherences rates were 93.1% for three days and 86.9% for a seven days recall period. This adherence rate was higher

among those who used co-trimoxazole prophylaxis (Biadgiligh, Deribew, Amberbir & Deribe 2008:8). A study conducted in the southern part of Ethiopia at Yirgalem Hospital found that the adherence level was better than that of developed countries. The main reasons for non-adherence included being busy or simply forgetting, changes in daily routine, and being away from home (Markos, Worku & Davey 2008: 174). A study done in the USA found that 29.0% of people taking ART, adhered differentially, implying that they had missed one or more of the ARVs while taking the other class of ART medication. Adherence in this study was associated with the clinically relevant outcomes of virological failure and development of drug resistance (Gardner, Sharma, Peng, Hullsiek, Burman, MacArthur, Chesney, Telzak, Friedland & Mannheimer 2008: 77).

ART has become more affordable in developing countries as more people are being enrolled in HIV care and treatment. To improve adherence to ART, directly observed treatment (DOTS) has been suggested, even though the method has had only limited success in the treatment of Tuberculosis (TB) in Africa. Some researchers maintain that other methods for improving ART adherence need to be developed and evaluated (Stevens, Kaye & Corrah 2004). In Mozambique, it has been learned that recruiting and involving specially trained health care providers in public health facilities, who spoke the local language, facilitated the involvement of the patients, and motivated them to take responsibility for their own treatment. This increased ART patients' knowledge and adherence and improved their health status (Marazzi, Bartolo, Gialloreti, Germano, Guidotti, Liotta, San Lio, Mancinelli, Modolo, Narciso, Perno, Scarcella, Tintisona & Palombi 2005: 40).

1.3 STATEMENT OF THE PROBLEM

Ethiopia has higher prevalence rates in urban areas versus the rural areas of the country. As a result, urban areas have more patients taking ART (EFMOH/HAPCO Road Map 2007b). By February, 2009, in Addis Ababa alone there were 32 577 patients taking ART, out of the total 133 344 national ART clients in Ethiopia (Monthly HIV Care and ART Update 2009). This number shows that 24.0% of all ART clients in the country were found in Addis Ababa. From this, one could infer that there might be more problems with adherence to ART in the capital city. Different variables under patient-related factors were

studied to identify their effects on adherence or non-adherence to ART. The factors that were studied included patient's knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression and alcohol use.

1.4 PURPOSE OF THE STUDY

This study proposed to identify patient-related factors related to ART adherence for HIV people living in Addis Ababa. The results would contribute to the body of knowledge of adherence in Ethiopia and provide recommendations and directions towards solving adherence problems.

1.5 RESEARCH OBJECTIVES

The objectives of this study were to:
- Determine the adherence status of ART patients in Addis Ababa, Ethiopia.
- Identify the influence of patients' knowledge of HIV and ART on adherence to ART in Addis Ababa, Ethiopia.
- Assess the influence of HIV stigma and discrimination on adherence to ART in Addis Ababa, Ethiopia.
- Evaluate the influence of depression on adherence to ART in Addis Ababa, Ethiopia.
- Identify the influence of alcohol use on adherence to ART in Addis Ababa, Ethiopia.

1.6 ASSUMPTIONS UNDERLYING THE STUDY

This study assumed that ART patients with adherence level of ≥ 95.0% or more would have good health outcomes, improved immunological response and suppressed viral loads. Optimal adherence of 95.0% or more, might in turn be influenced by patients' knowledge about HIV and ART, minimal stigma and discrimination, absence of depression and low level of alcohol intake. Structured interviews were conducted with patients while they collected their ARVs from the pharmacy.

1.7 SIGNIFICANCE OF THE STUDY

The ART programme's scaling up throughout Ethiopia, resulted in increasing numbers of ART patients (EFMOH/HAPCO 2006:35). This study, although specific to Addis Ababa, would contribute to the existing knowledge of adherence to ART in Ethiopia. The study will inform both programme managers and clinicians about the existing challenges of patient-related factors influencing adherence to ART and the possible solutions. Policy-makers who have the major responsibility for designing and managing the health care programme also need to understand these factors. This study could also increase the understanding of health professionals in their important role of encouraging maintenance of healthy behaviours among their patients.

1.8 DEFINITION OF KEY CONCEPTS

Adherence: The extent to which a person's behaviour in taking medications, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider (WHO 2003:3). In this study, adherence refers to compliance of the patient's behaviour in taking ARV medication.

AIDS: It defines the acquired immune deficiency syndrome and is used to describe the various clinical syndromes, specific opportunistic infections or malignancies that occur with HIV infection, and signals those in whom advanced HIV infection has occurred (WHO 2005:10). AIDS is clinically diagnosed for any person with any one of a specific list of diseases (stage 4 conditions), with confirmed HIV infection or immunological diagnosis with confirmed HIV infection and first ever documented CD4 count less than 200 per mm^3 (WHO 2007: 9).

Anti-retroviral drugs (ARVs): These are medications which are used in the treatment of HIV. The main classes of anti-retroviral drugs are NRTI, NNRTI and PIs. Monotherapy or dual therapy with these types of ARVs is not recommended since it is associated with virological failure. ART requires the administration of at least three types of ARVs. The first-line ARV regimen for adults and adolescents contain two NRTI and one NNRTI. For

patients who develop treatment failure, the preferred second-line ARV regimen includes two NRTIs and one PI (WHO 2006:17-23). Figure 1.1 indicates the preferred two NRTI/NNRTI first-line ARVs and Figure 1.2 shows the possible combination of ARVs that make up possible second-line regimens. The ARVs found at the intersection of the rectangle and circle, are PIs that constitute the major component of the second-line regimen.

AZT or D4T

3TC or FTC

TDF or ABC

EFV

NVP
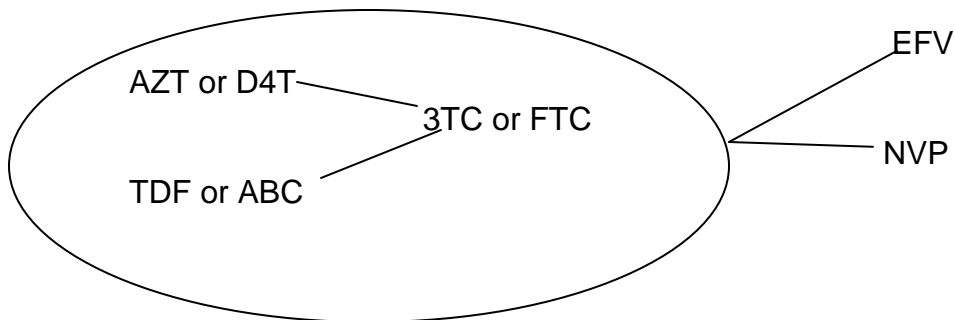
Figure 1.1 Preferential two NRTI/NNRTI first-line ARVs (WHO 2006: 19).

Standard second-line option if NRTI/NNRTI Approach used in first-line therapy (WHO 2006: 41)

ddI or TDF

ABC or 3TC (+-AZT)

PI/r

EFV or NVP
NRTI sparing option if triple NRTI approach used in first-line therapy (WHO 2006: 41)
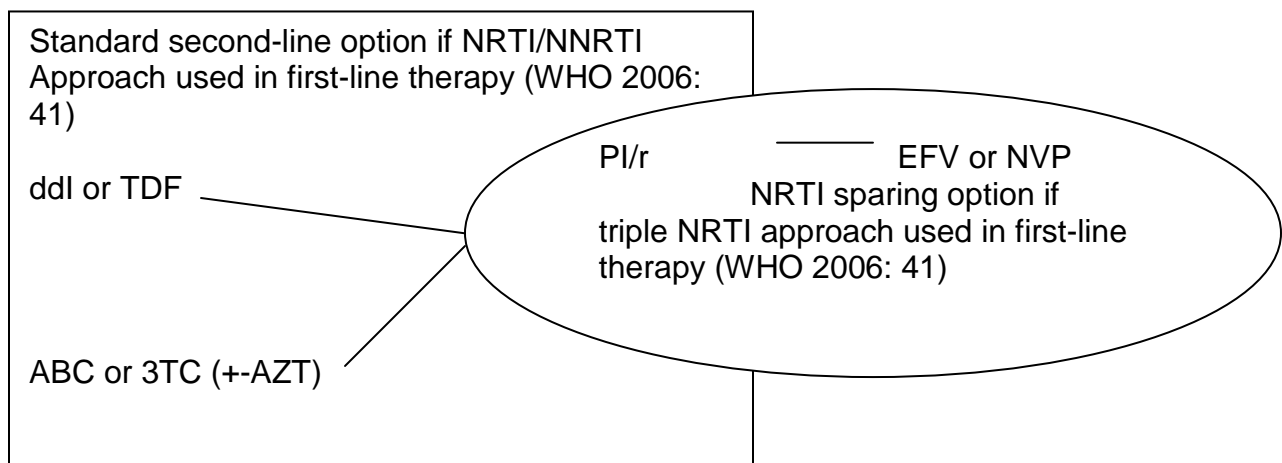
Figure 1.2 second line ARV regimens (WHO 2006:41)

Anti-retroviral therapy (ART): The administration of at least three different ARVs, in order to suppress the replication of HIV (WHO 2006:18). Treatment with these combinations of drugs is also known as highly active antiretroviral therapy (HAART) (Fauci & Lane 2005:1124).

Depression: It is having a depressed mood on a daily basis for a minimum duration of two weeks. It can be also manifested in the form of loss of interest or pleasure in nearly all activities including enjoyable activities (Reus 2005:2553).

Discrimination: Includes both negative attitudes, or particular behaviours or actions towards others; often described as a distinction that is made about persons resulting in them being treated unfairly and unjustly on the basis of their belonging, or being perceived to belong, to a particular group (ENGENDERHEALTH 2004:15). The operational definition is unfair treatment of HIV/AIDS patients by their community or health care providers.

HIV: The human immune deficiency virus that damages the body's immune system, the system that fights infections (Longo & Fauci 2005: 1071-1075). HIV is diagnosed among adults and children 18 months or older based on positive HIV antibody testing (rapid or laboratory-based enzyme immune-assay). This is confirmed by a second HIV antibody test (rapid or laboratory-based immune-assay) and/or positive virological test for HIV or its components (HIV-RNA or HIV-DNA or ultrasensitive HIV p24 antigen) confirmed by a second virological test obtained from a separate determination (WHO 2007: 8). In Ethiopia HIV is diagnosed once the client follows the processes of HIV counseling and testing services (HCT). The HCT process encompasses pre-test counseling, testing and post-test counseling. Test results are given in post-test counseling. If a person becomes HIV positive then he/she is linked to HIV care and treatment services. Results are disclosed to the client on the same day of HIV testing (EFMOH/HAPCO 2007c:09).

Stigma: an undesirable or discrediting attribute that a person or group possesses that results in the reduction of that person's or group's status in the eyes of society (ENGENDERHEALTH 2004:15). The operational definition applicable to this study is a person's or group's undesirable feelings towards HIV patients.

1.9 CONCEPTUAL FRAMEWORK

According to the WHO (2003:27) there are different dimensions affecting adherence to ART. These are health system, condition-related factors, therapy-related factors, socioeconomic and patient-related factors. The adapted conceptual model for this study is the Health Belief Model (HBM). "The HBM contains several primary concepts that predict why people will take actions to prevent, to screen for, or to control illness or conditions. These include susceptibility, seriousness, benefits and barriers to a behaviour, cues to action, and self efficacy" (Champion & Skinner 2008: 46-47). The authors also defined the following concepts which construct the HBM. **Perceived susceptibility** is a belief about the chances of getting a disease or condition. **Perceived severity** is the belief about how serious a disease or a condition or its consequences could be. **Perceived benefits** refer to the beliefs about the advantages of a proposed action. **Perceived barriers** refer to the beliefs about possible disadvantages of the advised action and/or obstacles to be overcome to utilise the service/treatment. **Cues to action** are strategies that activate readiness, and self-efficacy is confidence in one's ability to take action.

The HBM examines how health behaviour changes result after evaluation of the benefits to and barriers of action (Munro, Lewin, Swart & Volmink 2007:5). These constructs are related to this study, given that if individuals feel that they are susceptible to HIV infection then they should perceive the seriousness of the disease and get tested. Once their status is confirmed, they should start to think about the benefits available and the associated barriers. Perceived barriers include stigma and discrimination. Cues to action in this case are information on the availability of ART and the importance of ART adherence. Finally, self efficacy is realised when the individual decides to receive ARVs and adhere to the treatment. The following diagram is adapted from Champion and Skinner (2008:49) and shows these concepts succinctly.

| Age
Gender
Ethnicity
Personality
(Depression)
Socioeconomics
Knowledge about
HIV and ART | → | Perceived susceptibility (I am not at risk of HIV; not engaged in risky behaviours) |

```
┌─────────────────────────┐      ┌──────────────────────────────┐
│ Age                     │      │ Perceived                    │
│ Gender                  │  →   │ susceptibility               │
│ Ethnicity               │      │ (I am not at risk of         │
│ Personality             │      │ HIV; not engaged in          │
│ (Depression)            │      │ risky behaviours)            │
│ Socioeconomics          │  →   ├──────────────────────────────┤
│ Knowledge about         │      │ Perceived severity           │
│ HIV and ART             │      │ (HIV is a fatal              │
│                         │      │ disease)                     │
│                         │      ├──────────────────────────────┤
│                         │  →   │ Perceived benefits           │
│                         │      │ (The medication will         │
│                         │      │ make me better)              │
│                         │      ├──────────────────────────────┤
│                         │  →   │ Perceived barriers           │
│                         │      │ (Alcohol use, stigma         │
│                         │      │ and discrimination)          │
└─────────────────────────┘      └──────────────────────────────┘
```

Health behaviour (I will take and adhere to the medication)

Cues to action (Information on availability of ART and the importance of ART adherence)

Figure 1.3 Concepts of the Health Belief Model (adapted from Champion and Skinner 2008:49).

1.10 RESEARCH METHODOLOGY

The research methodology provides an entire strategy and defines structures within which the study is implemented (Burns & Grove 2005: 211). The research methodology of this study is described in detail in chapter 3 of the dissertation.

1.10.1 Research design

The research design followed was cross-sectional, analytical, quantitative, exploratory and observational. These design concepts will be addressed in chapter 3 of the dissertation.

1.10.2 Research setting

The research was conducted at one hospital in Addis Ababa, Ethiopia. The hospital had
4 708 patients on ART by the end of February, 2009 (EFMOH/HAPCO 2009). The patients
on ART during December 2009 who were included in the study provided they had started
ART at least twelve months previously (during or prior to 1 December 2008).

1.10.3 Population, sample and sampling

The participating hospital, a health facility providing ART services in Addis Ababa, was
selected because of logistical and financial reasons. By February, 2009 there were
reportedly 4 708 patients taking ARVs from the participating hospital out of a total of 37
286 patients taking ART in Addis Ababa (Monthly HIV Care and ART Update 2009). The
Inclusion criteria for this study were: PLHIV age >=18 years, started ART at least twelve
months previously, both males and females. The exclusion criteria were those ART
patients younger than 18 years of age and those who had used ART for less than twelve
months. According to Burns and Grove (2004:342) the target population is the entire set of
individuals who meet the sampling (inclusive) criteria. The sampling frame is a list of all
ART patients taking ARVs at the selected hospital at a specific point in time and who met
the inclusion criteria. Those patients were chosen using simple random sampling
techniques. Population and sampling issues will be discussed in chapter 3 of the
dissertation in more detail.

1.10.4 Data collection instrument

An interview schedule was developed to collect data from patients. Before the interview
schedule was initially used as a data collection instrument, pre-testing was done. Individual
questions were well structured in order to avoid ambiguity; interviewers were trained to ask
questions in a uniform way.

1.10.5 Data collection

Structured interviews were used for this data collection. Trained data collectors interviewed patients when collected their ARVS from the pharmacy. The questions asked were in line with the objectives of the research, allowing calculation of patients' adherence levels. Other information was also collected and included patient's knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression and alcohol use.

1.10.6 Data analysis

For the statistical analysis procedures the Statistical Package for the Social Sciences (SPSS version 17.0) computer software was used. The services of a statistician were employed to do the actual statistical calculations and to assist with the interpretations of the statistical results.

1.10.7 Ethical considerations

The research proposal was submitted to the Research and Ethics Committee of the Department of Health Studies, Unisa and to the participating hospital's institutional review board clearance (IRB). This was done to confirm that the rights and welfare of the individuals involved were protected, the appropriate methods were used to secure informed consent and the potential benefits of the investigation were greater than the risks. Permission was obtained before data collection started.

1.11 SCOPE AND LIMITATIONS OF THE STUDY

By February 2009, there were reportedly 37 286 ART patients taking ARVs in Addis Ababa (Monthly HIV care and ART update 2009). Reaching the representative sample of 37, 286 ART patients is difficult due to logistical and financial reasons. As a result, the study was conducted only at one health facility. The sample taken from only one facility is not representative of the whole of Addis Ababa and cannot be used to make inferences to the

other health facilities and regions of the country. However, inferences made from the sample are applicable to ART patients in the selected health facility.

1.12 ORGANISATION OF THE REPORT

This dissertation has been organised according to five chapters.

Chapter 1 provided an orientation to the study and background information about HIV/AIDS in the world, SSA and Ethiopia. It also introduced adherence concepts and the research design adopted for the study.

Chapter 2 describes literature reviewed on adherence to ARVs.

Chapter 3 mentions the research design and method used in the study.

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

Chapter 5 discusses the conclusions and limitations of this study and provides recommendations for minimising patient-related factors influencing adherence to ARTand for conducting similar studies in the future.

1.13 CONCLUSION

This chapter presented background information on HIV/AIDS globally, at SSA and at country level (Ethiopia) and Addis Ababa city. The following areas were discussed: the research problem, purpose of the study, research objectives, assumptions underlying the study, significance of the study, definition of key concepts, conceptual framework, research methodology, scope and limitation of the study. The study was conducted at one hospital, in Addis Ababa. Chapter 2 provides a discussion on literature review of adherence to ARVs.

CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

The literature review will cover reports within the context of HIV/AIDS, ART, adherence to ART and patient-related factors influencing adherence to ART. Reviewed documents were obtained from websites, journals articles, WHO publications and EMOH publications. The literature review covered the period from 2002-2010

2.2 INITIATING ANTIRETROVIRAL THERAPY

The WHO (2007:12) classifies HIV-associated clinical disease as stage 1 (asymptomatic), stage 2 (mild symptoms), stage 3 (advanced symptoms) and stage 4 (severe symptoms). According to the WHO (2006:13-16), in resource limited countries, ART should be initiated based on clinical and immunological assessments. It is important to have clinical staging and CD4 count for monitoring patients' responses to taking ART. Additionally, the process of initiating ART involves assessment of patients' readiness and understanding that ART involves life-long therapy, excellent adherence and associated toxicities. ART brings about improvements in clinical and immunological outcomes. The optimal time to initiate ART is before a patient develops opportunistic infections. Immunological monitoring can be done by the use of CD4 counts. When the CD4 count is <200cells/mm^3, ART is started irrespective of the patient's clinical stage. When the CD4 count is between 200 cells/mm^3 and 350 cells/mm^3 treatment is considered and can be initiated depending on the patient's WHO stage. However, if the CD4 count is above 350 cells/mm^3 ART should not be initiated. Plasma viral load assessment is not necessary in resource limited countries for initiating ART once clinical and CD4 count assessments have been made.

The preferred first-line ARV regimen consists of NRTI drugs as the backbone with one of the NNRTIs. For treatment-naïve patients TDF and ZDV are preferred first-line NRTIs. These drugs can be combined with either 3TC or FTC and given with one of NNRTIs. Fixed dose combinations are preferable since they facilitate patient convenience and improved adherence. When there is first-line treatment failure a second-line ARV regimen is started. Treatment failure can be diagnosed clinically, immunologically and virologically. Clinically diagnosed treatment failure occurs when there is clinical progression of HIV infection despite documented ART adherence. Immunological diagnosis is made by documenting a decline in CD4 counts. Virologic treatment failure occurs when there is a rise in viral load. The major component of a second-line ARV regimen is based on PIs such as LPV/r or ATV/r. ATV/r with an equivalent efficacy with LPV/r (EFMOH/HAPCO 2008:50-62).

2.3 ADHERENCE TO ARVS

Key words used in this research were: adherence to anti-retroviral (ARVs), antiretroviral drugs, antiretroviral therapy (ART), depression, stigma and discrimination, alcohol use and patient's knowledge about HIV and ART.

2.3.1 Defining adherence

Usually adherence is defined as the extent to which a patient's taking of his/her medication matches the prescribed drug regimen (Ingersoll & Cohen 2008:213). Adherence requires informed consent and participation in care and treatment. The patient agrees to follow the instructions of the health care provider regarding a drug regimen (Ethiopian AIDS resource center 2009). ART patients need to be supported in a variety of ways to adhere to their medications: these are client-centered counseling and support; support from peer educators and community treatment supporters. These interventions encourage ART patients to disclose their HIV status (WHO 2009:42). An adherence rate of ≥95% is needed to obtain the benefits of ART; these benefits include better clinical, immunological and virological parameters (WHO 2006:70). An adherence level of <95.0% is associated with a high level of viral drug resistance, which has public health implications, and poor personal health outcomes (WHO 2003:95).

In the absence of universally accepted criteria for defining adherence, researchers adopt different methods of defining and enumerating appropriate medication-taking behaviour. Adherence is commonly measured as a percentage of prescribed medication doses taken over a given period of time (Martin, Deborah, Calabresse, Wolters, Rogby, Brennan & Wood 2009: 594). Medication adherence can also be described as taking medications according to the health care provider's prescriptions (Cauldbeck, O'Conner, Mortimer, Saunders, Rao, Mallesh, Kotehalappa, Kumar, Mamtha, McGoldrick, Laing & Satish 2009:3).

For this study, adherence refers to compliance of the patient's behaviour in taking ARVs. The adherence level was calculated by dividing self reported ARVs taken by the total drugs prescribed over a seven day period. Taking ≥95.0% of the prescribed drug (adherence level) was considered as optimal and less than 95.0% suboptimal.

2.3.2 Scope of the problem

Adherence to treatments for chronic diseases in general, tends to be 60% while adherence to ART ranges from 55.0% in American patients to 77.0% for African patients (WHO 2009b:32). Suboptimal adherence has both individual and public health implications. The individual implications are poor clinical outcomes and the public health implications are the development of drug resistant viral strains.

In another study done in the USA, which assessed ≥95% adherence levels among 244 HIV patients aged 50-plus, the rate was found to be 80.0% (Johnson, Heckman, Hanson, Kochman & Sikkema 2009:541-551). There were also other studies in the USA reporting lower adherence levels; one showed that only 71% of ART patients took their prescribed doses and another reported 96.0% of ART patients being adherent less than 95.0% (Golin, Liu, Hays, Miller, Beck, Ickovics, Kaplan & Wenger 2002:761). Another USA study showed that overall adherence to ART among HIV-infected veterans, starting combination ART, was 63.0%: adherence to efavirenz-based ART being 67.0%; nevirapine-based ART 65%; and boosted PI 59% (Braithwaite, Kozal, Chang, Roberts, Fultz, Goetz, Gibert, Rodriguez-Barradas, Mole & Justice 2007:1579-1589). However, according to a study done in

Tanzania, a resource poor country, it showed that patients can achieve high levels of adherence through persistence adherence counseling in a clinic setting (Mugusi, Mugusi, Bakari, Hedgemann, Josiah, Janabi, Aboud, Aris, Swai, Mhalu, Biberfeld, Rollangry & Sandstrom 2009:1226-1232). A Zambian study reported that at least 95.0% adherence level was documented for 83.7% out of 409 patients for whom pill counts were done (Carlucci, Kamanga, Shenberger, Shephered, Jenkins, Spurrier & Vermund 2008:618).

According to the Kip, Ehlers and Van der Wal's (2009:149-157) study done in Botswana, different factors were identified that affected adherence to ARVs both positively and negatively. The negative ART adherence factors were travel expenses, ARVs' side effects, lack of social support, use of traditional medicines, alcohol abuse, and long waiting times at ART clinics. The positive ART adherence factors were health workers ensuring that ART doses fit into the daily routines of ART patients and explaining to patients how to take ART and what side effects to expect from ARVs.

ART adherence may also change over time. In a study done in China the mean level of adherence was 91.0% at baseline, 89.0% at month three, and 88.0% at month six, showing slight decreases over time. The four most common reasons for missing doses or discontinuing treatment were forgetfulness (45%), being away from home (44.0%), being too busy (33.0%), and having side effects (30.0%) (Wang, Zhou, He, Luo, Li, Yang, Fennie & Williams 2009:759).

It has been suggested that ART adherence in Addis Ababa at least among children is relatively higher in comparison to other similar facilities in the rest of Ethiopia. Adherence levels of 93.1% for three days; recall and 86.9% for seven days recall period were documented. Those who used co-trimoxazole prophylaxis showed a relatively higher level of adherence (Biadgilign et al 2008:8). A study conducted in the southern part of Ethiopia at Yirgalem Hospital found that the adherence level was better than that of developed countries. Being busy or simply forgetting, changes in daily routine, and being away from home were the main reasons for non-adherence (Markos et al 2008:174).

2.3.3 Role of adherence to ARVs in HIV/AIDS

According to the WHO (2006:9) "ART should be delivered as part of a package of care interventions, including the provision of co-trimoxazole prophylaxis, the management of opportunistic infections and co-morbidities, nutritional support and palliative care". Ethiopia started fee-based ART initiatives in 2003 and free ART in 2005 (EFMOH/HAPCO. 2008:0*8*). The first free ARV service in Ethiopia began at hospitals in March, 2005. The government of Ethiopia then started accelerated access to ART in 2006 which had reached 260 ART sites against a target of 89 (EFMOH/HAPCO Road Map 2007a: 10). By February 2009, there were reportedly 136 344 HIV/AIDS patients on ART in Ethiopia (EFMOH/HAPCO 2009).

There are challenges in the scaling up of access to ART nationally. The main challenge is patient attrition from ART treatment. The three underlying causes are treatment stoppage, death and being lost to follow-up actions. Treatment stoppage refers to permanent or temporary interruption of ART as decided by the health care provider with the patient such as in cases of drug toxicities. Death is calculated from the number of patients alive after a period compared to the total number of people who started treatment; in many low and middle income countries the information is not easily available. An ART patient is considered lost to follow-up when he or she fails to return for refills of their ARVs. These challenges highlight that ART requires close follow-up actions and monitoring since the treatment needs life-long adherence to ARV medications (WHO 2009c:61).

Adherence to ART is recognised as the key to both programmatic and individual level treatment success. Adherence is helpful for delaying or avoiding resistance to first-line ARVs. For this, adherence counseling of patients helps them to understand how to take the medications, and what to do in case of developing ARVs' side effects. For adherence counseling, family or community members should be engaged to build patient support, and to avoid stigma and discrimination (WHO 2006:70-71)

Suboptimal adherence is the most common cause of developing viral resistance. Accurate and reliable measures of adherence are needed for transition from reactive prevention to proactive prevention of viral resistance in the management of HIV. There are promising

approaches to improving adherence monitoring including interviewing patients about recent missed doses, reviewing pharmacy-dispensing information and using medication containers with electronic monitoring (MEMS). Even though adherence may decline overtime the best approach of predicting future adherence is past adherence (Bangsberg 2008:272).

2.3.4 The relationship between adherence and treatment outcomes

According to a study done in Lusaka, Zambia by Chi, Cantrell, Zulu, Mulenga, Levy, Tambatamba, Reid, Mwanga, Mwinga, Bulterys, Sage and Stringer (2009:748) high levels of adherence to ART are associated with favourable patient outcomes. The authors conducted a cohort study among 27 115 treatment-naïve patients who initiated and continued ART for ≥12months: 17 060 (62.9%) demonstrated optimal adherence, 7682 (28.3%) had suboptimal adherence and 2373 (8.8%) had poor adherence. Mortality risk was similar for those who optimally and sub optimally adhered to ART but higher among those with poor adherence. CD4 increases were relatively good for those optimally and sub optimally adherent but appeared to be worse for those who adhered poorly.

Adherence to ART reduces viral replication and prevents the emergence of drug resistant strains of HIV. Different studies have shown that high levels of adherence in Africa are possible despite resource limitations. An additional study conducted in Lusaka, Zambia revealed that decreased adherence levels (measured by medication possession ratio) among ART patients is associated with detectable HIV viremia (Goldman, Cantrell, Mulenga, Tambatamba, Reid, Levy, Limbada, Taylor, Saag, Vermund, Stringer & Chi 2008:1032). Braithwaite et al (2007:1579-1589) reported similar findings: a higher level of adherence to ART was associated with viral suppression and increased CD4 cell counts.

A study conducted in South Africa suggested that the type of health service delivery site is associated with suppression of virological measures in addition to good adherence. The factors which may influence virological outcome negatively at a health facility include long waiting times for clients; using staff members without specialised training in HIV care; failure to contact individuals who do not attend clinic and lack of communication between pharmacy and clinic staff members (Fielding, Charalambous, Stenson, Pemba, Martin,

Wood, Churchyard & Grant 2008:4-7). Compared with HIV positive adults in Southern Africa, adolescents are less adherent and have lower rates of viral suppression, immunological recovery and a higher rate of viral rebound (Nachega, Hislop, Nguyen, Dowdy, Chaisson, Regensberg, Cotton & Maartens 2009:69).

Virologic failure was associated with low CD4 cell count, low past adherence, shorter duration of prior suppression and intravenous drug use. A study in the USA showed that while high levels of adherence are required for viral suppression in the long term, the range of adherence capable of sustaining viral suppression is wider after extended periods of viral suppression (Rosenblum, Deeks, van der Laam & Bangsberg 2009:6).

2.3.5 Factors affecting adherence to ARVs

According to the WHO (2003:27-35) there are five interacting factors that influence adherence to medication. The five factors are socioeconomic factors, therapy-related factors, patient-related factors, condition-related factors and health care and system-related factors. Patient-related factors include forgetfulness, schedule, attitude and knowledge about HIV treatment, and whether patients need to take medication in secret. Patient-related factors are just one dimension and not the sole factor responsible for influencing adherence to medication. When designing programmes that address adherence to medication, it is important to take into consideration all other factors. Socioeconomic factors are related to food security, employment and degree of social support. Therapy-related factors are complexities of drug regimens, side-effects, toxicities and their management. Condition-related factors are associated with the stage of the disease, severity of symptoms and occurrence of co-morbidities. Health care and system-related factors are health care reimbursement systems and the cost of medications and consultations, drug distribution systems and the availability of medicines, access to health services, levels of confidentiality in the health care setting and the conditions of the medical encounter.

Other patient-related factors affecting adherence include the patients' mental health status, income levels and gender. A multivariate analysis study conducted in Stockholm, Sweden, found that anxiety interfered with adherence dose instructions. The study further

mentioned that suboptimal adherence might be a symptom of psychological distress or a coping strategy of adjusting ART to one's daily living in addition to a behavioural pattern (Schonnesson, Williams, Ross, Bratt & Keel 2007:181-183). A study at the Yaonde central hospital in Cameroon found out that 70% of patients who had started ART six months prior to the data collection, were still returning to the hospital for pharmacy refills, 17% disappeared, 9% died and 4% were referred to other health facilities. As compared to the poorest and richest ART patients, people with middle income were more adherent while female gender and having fewer side effects from ARVs were associated with higher rates of pharmacy adherence (Rougemont, Stoll, Elia & Ngang 2009:7-9).

Stigma has been associated with suboptimal adherence both in resource poor and rich countries and this relationship is partially mediated by lower mental status (Sayles, Wong, Kinsler, Martins & Cunningham 2009:1105-1108). A cross sectional and descriptive study done in South East Nigeria reported different factors associated with non-adherence: 75% of the respondents were not fully adherent to ART. In addition to previously mentioned factors of non-adherence including ART side effects, non-availability of drugs at treatment site, forgetting to carry drugs during the day, other associated factors included fear of social rejection, treatment being a reminder of HIV status, and selling of own drugs to those unable to enroll in the projects. Additionally being female, over 35 years old and high education status were significantly associated with non-adherence (Uzochukwu, Onmujekwe, Onoka, Okoli, Uguru & Chukwuogo 2009:192).

According to Golin et al (2002:759), a US-based multivariate analysis study, being of African-American ethnicity, having lower income and education, alcohol abuse, having a higher medication dose frequency and fewer adherence aids (such as pillboxes, timers) were independently associated with poor adherence. On the other hand, Carlucci et al 2008:620 in a study done in rural Zambia found that travel-related factors did not predict adherence. Patients in rural Zambia achieved adherence rates well-matched with good clinical outcomes despite long travel distances. A study conducted in southwest Ethiopia at the ART unit of Jimma University specialist hospital, showed that depression was associated with non-adherence. Adherence was common among those who had social support systems. More than 75% of the respondents reported that they missed doses due

to forgetting, feeling sick or ill, being busy, and running out of medications (Amberbir, Woldemichael, Getachew, Girma & Deribe 2008:6-7).

The literature review has shown that adherence to ART can be affected by various factors. This study focused on personal factors influencing adherence to ART. The variables that were analysed in this study are patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression, and alcohol use.

2.3.5.1 Stigma and discrimination

A study conducted on Zambian women revealed stigma to be one of the major barriers to adherence to ART. Even though ART is to be taken life-long once started, significant social stigma may partially or completely disrupt patients' drug adherence levels. The studied women described stigma in different ways: shyness, fear of being laughed at, fear of being embarrassed or that others would know their status, fear of being seen as a prostitute. Finally the study discussed ways for addressing stigma to bring about successful ART adherence (Murray, Semrau, McCurely, Thea, Scott, Mwiya, Kankasa, Bass & Bolton 2009:82). In another study done in the USA, the association between stigma and ART adherence was reported to be mediated by the patients' mental health status.

Poor mental health status coupled with stigma, resulted in suboptimal adherence to ART. Self-reports of poor medical care were associated with experiencing stigma. PLHIV diagnosed within the last five years experienced greater levels of stigma as compared to those who had been diagnosed for more than five years. This suggests that stigma might reduce over time (Sayles et al 2009:1104-1105). A study done in five African countries (Lesotho, Malawi, South Africa, Swaziland and Tanzania) found that stigma interfered with adherence to ART. Percieved stigma was correlated with missed ART doses. Accordingly the study suggested that health care providers should be expected to discuss stigma-related issues with their patients before the commencing ART (Dlamini, Wantland, Makoae, Chirwa, Kohi, Greeft, Naidoo, Mullan, Uys & Holzemer 2009:384).

2.3.5.2 Knowledge about HIV and ART

A Zambian study conducted among urban women, found that lack of information regarding HIV and ART was associated with non-adherence to ART. In the absence of adequate information about HIV and ART, when patients felt better, they discontinued ART, thinking that their HIV had been cured. Not enough patient information was given when health workers were overburdened and had limited time with each patient (Murray et al 2009:84). The South African study in Soweto found that knowledge scores among HIV positive people attending clinical care, was 86%. Their knowledge was evaluated in terms of cause, mode of transmission and progression of HIV. The knowledge gained through media and during counseling sessions at health facilities was well understood by HIV patients. Among patients taking ART, a high level of knowledge regarding ART and its importance in controlling the infection was observed (Nachega, Lehman, Hlatswayo, Mothopeng, Chaisson & Karstaedt 2005:196-201). Another study done in Rio de Janeiro, Brazil, reported that HIV patients who had been taught by health care providers how to take ARVs, had better adherence levels. This study suggested that interventions that help to improve patient-health care provider interactions were necessary for better adherence to ART (Filho, Nogueira, Machado, Abreu, De Oliveira, Evangelista & Hofer 2008:687).

2.3.5.3 Alcohol use

According to Ruthlind, Greenfield, Bruce, Meyerhoff, Flenniken, Lindgren & Weiner (2005:80) a study done in the USA, heavy drinking among HIV-infected individuals was associated with adverse effects on neuropsychological functioning and reduced self-reports of adherence to ART. The observed neuropsychological effects included deficits in processing and auditory working memory, balance and executive functions. A USA based study showed that moderate and hazardous alcohol use was associated with poor adherence to ART. This relationship was further aggravated by concurrent use of drugs and alcohol (Chander et al 2006:415). Another study in the USA found differences in levels of adherence among those who used alcohol and those who did not do so. The amount of drinking affected adherence to ART; frequent and heavy alcohol drinkers were less ART adherent than infrequent and light alcohol drinkers (Parsons et al 2007:366).

2.3.5.4 Depression

In a multiple logistic regression analysis study done in Ethiopia, PLHIV who were not depressed, adhered two times more than those who were depressed. Social support was also positively associated with adherence to ART (Amberbir et al 2008:5). A South African study, conducted among black women, also revealed the same result that suboptimal adherence was associated with depression (Aspeling & van Wyk 2008:7). A prospective, observational cohort study among past or current alcohol problems in Spain, found that patients with depressive symptoms were twice more likely to discontinue ARVs after six months of follow-up treatments. Therefore the management of depressive symptoms among HIV patients with alcohol problems is important to improve adherence to ART (Kim, Palepu, Cheng, Libman, Saitz & Samet 2007:1042-1044). A quantitative cross-sectional study done in India also showed similar findings, that depression was associated with poor adherence. Health care providers were advised to identify the presence of depression and manage it accordingly as early as possible in order to improve adherence to ART (Sarna, Pujari, Sengar, Garg, Gupta & Van Dam 2008:34-35).

2.3.5.5 Gender differences

In a study done in the US, women initiating ART, spent more time off therapy than men, and women were more likely to discontinue or change ARV regimens due to neurologic, dermatologic or symptoms such as rash, peripheral neuropathy, fatigue, weight loss, and feelings of vertigo/dizziness. The number of people off therapy was higher in black women than white women, white men and black men. The study further suggested that adherence strategies and interventions needed to target African American women (Kempf, Pisu, Dumcheva, Westfall, Kilby & Saag 2009:339-340). Another study done in Nigeria also showed that being female, single and having a higher educational status were significantly associated with non-adherence to ART (Uzochukwu et al 2009:192)

2.3.5.6 ARVs' side effects

According to Canestri, Sow, Vray, Ngom, M'boup, Kane, Delaporte, Gueye, Peytavin, Girard & Landman (2007:5-6) in a study conducted in Senegal, different side effects from

ARV could occur affecting adherence levels. These include EFV-related central nervous system symptoms (mainly dizziness), peripheral nuerophathy and severe neuropathies with incapacitating and intolerable discomforts. A different study by De Padua, Cesar, Bonolo, Acurcio & Guimaraes (2007:23) in Brazil showed that 92.2% of the studied sample had at least one and 52.6% had four or more different types of adverse reactions in the initial period of ART. The most frequently reported adverse reactions were gastrointestinal effects. There were increased frequencies of reported regimen switches as a result of having adverse reactions. The patients' perceptions of having adverse reactions could contribute to non-adherence and discontinuation of ART. According to Uzochukwu et al (2009:192) side effects of ARVs and unavailability of drugs from the treatment site were associated with non-adherence to ART in Nigeria. According to Johnson and Neilands (2007:583) a study done in the USA found that patients on ART intentionally skipped their medications in order to avoid side effects from the treatment. Skipping of medication has been observed among those with limited understanding of how ART works, those who had poor interactions with their health care providers, those with limited disclosure of their HIV status to their family members and friends and those with greater intrusiveness of HIV treatment on their lives.

2.3.5.7 Socioeconomic status

A study done in the USA compared ethnicity and risks of AIDS and death among HIV infected patients with access to care. Among the studied ethnic groups, lower adherence rates were observed for Hispanic and Blacks as compared to Whites. There was also a surprising result that better survival was observed among Hispanics despite poor adherence to ART, reduced immunological responses and lowered census-based socio-economic status as compared to Whites. This might be explained based on differences in diet, genetics and extended family support (Silverberg, Leyden, Quesenberry & Horberg 2009:2070).

A different USA study examined the role of neighborhood socioeconomic context on racial/ethnic differences in AIDS treatment and survival in San Francisco. The relative risk

of mortality from AIDS was higher among residents of the lower neighborhood socioeconomic context. However, this effect was reduced after ART initiation. Blacks demonstrated greater delays in obtaining or having no treatment relative to other groups (Arnold, Hsu, Pipkin, McFarland & Rutherford 2009:8-9).

2.3.6 Measuring adherence

Adherence can be measured using different techniques including MEMS, pill counts, biological markers, pharmacy refill data and patient self-reports (WHO 2003:4-5). The MEMS cap system utilises a computer chip embedded in a specially designed pill-bottle cap to record the time and duration of each bottle opening. MEMS adherence usually is calculated by dividing the number of time-appropriate bottle openings by the number of expected doses over the study period. Pill counts can be conducted in clinic or at unannounced home visits. Pill count adherence is usually calculated by counting the remaining doses of medication and assuming that the remaining pills are in excess of what is expected and represent the missed doses. Biological markers of adherence refer primarily to blood or urine concentrations of non-toxic biological markers. Pharmacy refill data can serve as an adherence measure by providing the dates on which antiretroviral medications were dispensed. Patient-self-report measurements are done by asking patients for their subjective rating of their adherence behaviours (WHO 2003:4).

2.3.6.1 Medication event monitoring system (MEMS)

The South African study on pediatric patients compared the adherence rate measured by MEMS and care giver self-report with virologic suppression. For 73 children followed, the median adherence measured by MEMS was 87.5% and the median caregiver self-report adherence was 100%. Overall 65% of children achieved virologic suppression and MEMS adherence was significantly associated with virologic suppression (Muller, Bode, Myer, Roux & Von Steinbucher 2008:257). Another study done in Botswana, supports the finding that MEMS is a more reliable measure of adherence level as compared to self-report. It can be used to measure adherence levels in low resource-limited countries (Vriesendrop, Cohen, Kristanto, Vrijens, Rakesh, Anand, Iwebor & Stiekema 2007:1119). MEMS has an advantage of being sensitive in detecting non-adherence and useful for pharmacokinetic

studies. However, MEMS is costly, relies on the assumption that pills are taken when, and only when the pill cap is removed and is feasible only in specific contexts (WHO 2009b:37).

2.3.6.2 Pill counts

According to Paterson, Potoski and Capitano (2002:103-206), pill counts are usually performed at clinic when patients bring their bottles with them. A health care provider counts the number of pills remaining in the bottle and computes the number of missed doses by comparing the difference between the actual and expected number of pills remaining in the bottle. The disadvantage of pill count is that patients may dispose pills before coming to the clinic hoping to appear as being ART adherent. An unannounced pill count may solve this problem. A US-based study investigated the use of announced pill counts to calculate the adherence status; the study found that there is a high correlation between an announced pill count and a visual analogue scale of adherence administered to patients. This suggests that both measurements of adherence provide similar findings for the same patients (Giordano, Guzman, Clark, Charlebois & Bangsberg 2004:76).

Phone call pill counts provide the same adherence levels as home-based pill counts. Phone call pill counts could save time and money needed to undertake home-based pill count. This requires that ART patients do not give wrong numbers of missed doses while the evaluator conducts the phone call pill counts. However, the time does not allow the patient to calculate the expected numbers of missed doses from the previous call to the current call while the assessor is on the phone (Kalichman, Amaral, Stearns, White, Flanagan, Pope, Cherry, Cain, Eaton & Kalichman 2007:1006).

2.3.6.3 Biological markers

Non-toxic biological markers can be added to the patients' medications and their detected presence in the blood or urine could provide evidence that the required doses had been taken. The drawback of this is that these measurements might be misleading and influenced by a variety of individual factors such as diet, absorption and rate of excretion (WHO 2003:5).

2.3.6.4 Pharmacy refill data

Pharmacy databases can be used to check the time of prescription being initially filled, refilled over time, or if prematurely discontinued. From these dates and prescribed dosages, adherence levels can be measured. The problem associated with pharmacy refill data is that picking up the drug does not ensure its ingestion (this would overestimate adherence if not accounted for). Pharmacy information might be incomplete, since patients might use more than one pharmacy and this data might not be captured, and if captured, it might not be available to different pharmacies (WHO 2003:5). Adherence measures, using pharmacy refill data, can be conducted easily but relies on accurate and complete record keeping (WHO 2009b:37). According to a study conducted among nine Southern African countries, adherence measurements using pharmacy refill data, were as accurate as CD4 count changes for detecting virologic failure. This finding suggested that pharmacy refill data adherence measurements could be considered as alternatives to CD4 counts for the monitoring of patients with high probabilities of virologic failures (Bisson, Gross, Bellamy, Chittams, Hislop, Regensberg, Frank, Maartens & Nachega 2008:785).

2.3.6.5 Self-reports

Patients' self-reports are practical measures of adherence and using 3-4 day recalls of pills taken divided by the total number of pills prescribed for that period, had been used to calculate adherence estimates (Jerant, Dimatteo, Arnsten, Moore-Hill & Franks 2008:1134). According to a US-conducted adherence study, patients usually tell their physicians why they are taking ART. However, half of the participants who were not adherent to ART did not tell their physicians the reasons for missed doses, because they anticipated that the physician would not support their decisions, lacked trust in the physicians' opinions and were unable to discuss their feelings or spiritual or moral issues (Kremer & Ironson 2006:526). Another study done in Italy used self-report for measuring adherence to ART on patients taking PI based ARVs and found that missed doses of drugs were associated with low plasma drug levels. This suggests that patient self-reports might be a valid method for identifying non-adherence (Murri, Ammassari, Gallicano, De Luca, Cingolani, Jacobson, Wu & Antinori 2000:123-128).

A study done in the USA showed that self-reports of <95.0% adherence levels were associated with higher concentrations of HIV RNA. This suggested the usefullness of self-reports for measuring adherence (Sullivan, Campsmith, Nakamura, Begley, Schulden & Nakashima 2007:3). A different USA study found out that self-reports on adherence to ART using 3-day recalls and 7-day recalls had similar virologic and immunologic outcomes. The adherence levels measured by these two recall periods were the same (Mannheimer, Thackeray, Hullsiek, Chesney, Gardner, Wu, Telzak, Lawrence, Baxter & Fiedland 2008:165).

2.4 SUMMARY

Adherence levels of ≥95.0% are required for optimal clinical and immunological ART outcomes. If patients fail to have at least 95.0% adherence to ART the result can be a poor clinical outcomes, immunological responses and treatment failures. Poor adherence can also result in the development of viral resistant strains which can be transmitted among members of the community through unsafe sexual practices, mother-to-child transmission or blood transfusions. Generally, adherence to ART is higher than adherence to treatment for other chronic illnesses. Studies on ART adherence in developing countries dispelled previous conceptions that high adherence levels in resource poor countries were unachievable.

Different factors affect adherence to ART and can be classified as socioeconomic therapy-related, patient-related conditions and health care and system-related factors. Patient-related factors are the focus of this study. Adherence can be measured by MEMS, pill-counts, biological markers, pharmacy refill data and patient self-reports. This study used patient-self-report as a measure of adherence to ART.

Chapter 3 will discuss the research methodology to identify the relationship between patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression, and alcohol use and adherence to ART.

CHAPTER 3

RESEARCH DESIGN AND METHOD

3.1 INTRODUCTION

The data were collected by a health worker trained by the researcher. The data collection instrument was a structured interview schedule which had been designed by the esearcher and used to collect information about only the variables of interest. Quantitative research methodology was followed.

3.2 STUDY DESIGN

A quantitative, descriptive, cross-sectional and analytical study was conducted. Applied research is one type of quantitative research that contributes to the improvement of clinical or public health practice. Its purpose is to solve problems that exist in real life practice situations like public health or medical practice (Burns & Grove 2005:33). This study investigated the determinants of Anti-Retroviral Therapy (ART) adherence and involved addressing some of the challenges affecting patients when using the public health approach to delivering ART and proposed possible solutions for addressing these challenges. The study could be considered to be applied research contributing to identifying and addressing patient-related factors affecting ART adherence in Ethiopia.

3.2.1 Cross-sectional

A cross-sectional design is used to examine groups of subjects in various stages of development simultaneously with the intent to describe changes in the phenomenon

across stages (Burns & Grove 2005:236). People living with HIV (PLHIV), who started ART at different times were studied simultaneously in this case. The two groups of people identified in the study were those who adhered to ART and those who did not adhere to ART. Adherence rates of more than or equal to 95.0% were considered as adherent, while adherence rates of less than 95.0% were considered to be non-adherent. In this study the association between patient-related factors, adherence status and adherence behaviour were examined.

In a cross-sectional study, the researcher usually selects the sample without reference to exposure; often the sample is drawn at random from a defined population (Morroni & Myer 2007:85). The chosen exposure variables were patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression, and alcohol use. These variables were not considered during the selection of respondents.

The cross sectional analytical design allowed evaluation of the relationship between exposures and outcomes and it was useful for assessing the health care needs of populations. The disadvantage of the cross-sectional design is, compared to cohort and case control studies, that it provides weaker evidence about the causation of disease (Morroni & Myer 2007:87).

3.2.2 Quantitative

Burns and Grove (2005: 23) described quantitative research as "a formal, objective, systematic process in which numerical data are used to obtain information about the world". Quantitative research helps to understand variables and examine relationships between dependant and independant variables. Statistical tests were used to examine the relationship between variables. Creswell (2003:18) defined the quantitative approach as where "the investigator primarily uses postpositivist claims for developing knowledge (such as cause and effect thinking, reduction to specific variables and hypotheses and questions, the use of measurements and observations, and the testing of theories), employs strategies of inquiry such as experiments and surveys, and collects data on predetermined instruments that yield statistical data". Applied research is one type of quantitative research that contributes to the improvement of clinical or public health practice. Its

purpose is to solve problems that exist in real life practice situations like public health or medical practice (Burns & Grove 2005: 33). This study was an investigation of the patients' determinants of ART adherence. Hence, it involves dealing with some of the challenges affecting the public health approach to delivering ART and proposing possible solutions. The study could be considered to be applied research that contributes to identifying and addressing patient-related factors affecting adherence to ART.

3.2.3 Descriptive

This study, intending to identify the patients' ART adherence levels, was best approached using a descriptive study. Descriptive studies are used to measure the extent of a health problem or the burden of disease in a population. It describes the occurrence of disease in a population such as prevalence or incidence (Morroni & Myer 2007:78).

3.2.4 Analytical

An analytical study design is used to find the factors that predict or cause health problems. In the case of a cross sectional study, an analytical design can be used in combination with a descriptive study. While a descriptive study describes the outcome of interest, an analytical design examines the relationship between an exposure and an outcome (Morroni & Myer 2007:78-79). In this study the outcome is ART adherence level while the exposures are patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression, and alcohol use.

3.3 RESEARCH METHOD

This Section covers the steps involved in the data collection and sampling. It also provides information about the research setting and population.

3.3.1 Research setting

The research was conducted at one hospital in Addis Ababa, Ethiopia, because it provided treatment to a large number of ART patients during the study period. There were reportedly 4 708 patients on ART by the end of February, 2009 at this hospital (EMOH/HAPCO 2009). The patients receiving ART came from different backgrounds,

used ART for different periods of time, had different adherence levels, ages, education status and included both males and females.

3.3.2 The research population

According to Burns and Grove (2005:342) the target population is defined as the entire set of individuals who meet the sampling (inclusion) criteria. The participating hospital, a health facility providing ART services in Addis Ababa, was conveniently selected for logistical and financial reasons. By February, 2009 there were reportedly 4 708 ART patients at this hospital from the total 37 286 patients taking ART in Addis Ababa (EFMOH/HAPCO 2009). These patients comprised the accessible population, which is the subset of target population that the researcher can access (Burns & Grove 2005: 342).The inclusion criteria for this study were: PLHIV age ≥18 years and started ART at least twelve months previously. The exclusion criteria were those ART patients younger than 18 years of age and those who had used ART for less than twelve months.

3.3.3 The sampling process and the sample

The sampling frame is a list of all ART patients at the selected hospital at a specific point in time who met the inclusion criteria. Those patients were chosen using simple random sampling techniques. In simple random sampling, each individual is chosen by chance and subjects have a known chance of being included in the sample (Joubert & Katzenellenbogen 2007:96*)*. Potential respondents were identified using their ART unique numbers. These numbers were obtained from the ART clinic and randomly chosen using a table of random numbers until the desired sample size had been reached. The selected ART numbers were cross checked with patients' identifications and each chosen patient was contacted when he or she came to the hospital for ART refills. The data were gathered from these patients following their voluntary agreement to participate and their signing of the informed consent forms.

The formula used for the sample size calculation was $S=p(1-p)z^2/d^2$ where p stands for anticipated population proportion, z refers to the cut-off value of the normal distribution and d is the precision required on either side of the proportion (Sayed 2007:347). The

assumptions for sample size calculations were 95.0% confidence interval, 50.0% frequency of adherence and 5.0% worst acceptable result. Hence S became 384 but when the adjusted sample size was calculated, using S/ (1+S/Pop), it resulted in 355 patients comprising the sample. Where Pop is the known number of a population (The survey system 2007), the adjusted sample size was used considering the size of the target population of 4 798.

3.4 DATA COLLECTION

The data were collected from ART patients by conducting structured interviews; and using an interview schedule prepared for this purpose. Two data collectors were recruited and trained by the researcher. The data collectors were health professionals with prior knowledge of adherence to ART. They received training in data collection for two days; the training including both theoretical instruction and practical exercises. The exercises were conducted using the structured interview schedule with each other. The theoretical part of the training covered different topics relevant to this study's and data collection procedures. Specific topics included ART, adherence to ART, factors influencing adherence to ART with particular focus on patients' knowledge about ART and HIV/AIDS, stigma and discrimination, alcohol use and depression. Additionally, components of the data collection tool and how to explain the survey questions to the participants were discussed. The two data collectors divided the number of participants in to 178 and 177 and gathered the information in alternating fashion. The researcher controlled the data collection process through providing supportive supervision. The data collection process took two months to complete.

3.4.1 The research instrument

Structured interviews were used for data collection. A structured interview is an oral communication between the data collector and the subject, in order to obtain information for the researcher. A structured interview is a flexible technique that allows researchers to ask questions in a way that is understood by the respondents. Response rates to structured interviews are higher than self-completion questionnaires. Besides, it allows getting information from those respondents who are unable to complete questionnaires

because of blindness, or their inability to read and write. The disadvantages of this technique include longer time to collect data and more costs compared to using postal questionnaires (Burns & Grove 2005: 396-397). The purpose of the structured interviews was to ask respondents about their ART adherence and to determine which patient-related-factors affected ART adherence.

A structured interview schedule was developed to collect data from patients. The interview schedule is a data collection document for collecting specific information from respondents (Fathalla 2004:57). Before the interview schedule was initially used as a data collection instrument, it was pre-tested. During the pre-testing phase ambiguous words and sentences were identified by the data collectors. The respondents were also asked at the end of the interview how they felt about the nature, style and timing of the questions. All identified problems were addressed during the revision of the data collection instrument. Individual questions were structured to avoid ambiguities; interviewers were trained to ask questions in a uniform way. The language of interview was Amharic as this is the national language of Ethiopia and well understood by the patients. The originally developed interview schedule in English was translated in to Amharic with a licensed translator. The data collectors are well versed both in English and Amharic communication. They were recruited based on their college level education and prior experience of data collection. Hence, the data collectors accurately documented the respondents' Amharic responses in English. The interview schedule was divided in to the following six components.

<u>Section A</u>: General and demographic questions, including background information of the respondents, were asked in this introductory section. Aspects covered included the ART patients' unique codes, ages, gender, residence types, levels of education and marital status.

<u>Section B</u>: The questions in this section pertained to the duration of time since the each patient's HIV positive status had become known to him/her, and to the patient's adherence levels on his/her ART regimen. The adherence level is obtained by dividing medication doses taken by medication doses prescribed.

<u>Section C</u>: This section covered questions about the patient's knowledge about HIV and ART, using seven questions. The questions focused on patients' knowledge of HIV transmission, HIV prevention knowledge and HIV in-depth knowledge which included ART.

<u>Section D</u>: These questions addressed stigma and discrimination experienced by the ART patient, focusing on the ART patients and their perceptions of their feelings of stigma and discriminatory actions experienced by them.

<u>Section E</u>: This section's questions pertained to symptoms of depression. The questions were asked in such a way that patients could respond to each question as either 'yes' or 'no'. The total number of 'yes' responses were added to reach a potential diagnosis of depression. Depression was diagnosed if five or more of the following symptoms occurred nearly every day for two weeks with at least one of the symptoms being depressed mood or loss of interest or pleasure (Reus 2005:2553):

- Depressed mood most of the time
- A dramatic change in appetite resulting in a 5% change in weight (gain or loss),
- Over sleeping or sleep disturbance
- Inability to concentrate, think clearly or make decisions
- Agitation, restlessness, and irritability
- Diminished interest or inactivity and withdrawal from pleasurable activities
- Fatigue or loss of energy nearly everyday
- Feelings of worthlessness and helplessness and
- Thoughts of death or suicide.

<u>Section F</u>: The section asked questions about alcohol use, to gather data on the type, frequency and amount of alcohol consumed by each ART patient. Munne (2005:36) classified the frequency of alcohol drinking in the past 12 months and the amount of drinking as five or more drinks, by using the following typology:

- Current abstainer: never had a drink or had none in the past year
- Infrequent light drinker: drinking less often than weekly, always less than five drinks per one occasion
- Frequent light drinker: drinking weekly and less than five drinks per occasion

- Infrequent heavy drinker: drinking less than weekly, sometimes more than five drinks per occasion.
- Frequent heavy drinker: drinking weekly and more than five drinks per occasion

There were also open ended questions in the above mentioned sections that enabled ART patients to explain their personal experiences about factors influencing their ART adherence levels. These were questions about patients' knowledge about ART and HIV/AIDS and stigma and discrimination.

3.4.2 Data collection procedures

The structured interviews were conducted in the pharmacy since this was the last place the patients visited before leaving the ART clinic. Nine patients were interviewed per day over for a period of two months. The two data collectors alternated doing patient interviews. On average it took 25 minutes to interview a single respondent. The researcher controlled the data accuracy by observing whether the data collectors recorded the exact information.

3.4.3 Data management and analysis

The completed hard copy interview schedules were kept locked up the researcher. No patient's name was written on the interview schedule. Although each patient's file number had been recorded, only the researcher could trace any specific file should it be necessary to check any recorded information.

Different statistics and measures of association were applied to test a null hypothesis at P-value of <0.05. 95.0% confidence levels were used to calculate a range of likely values for the difference in mean outcome (adherence level) of the population. Since the sample size was larger than 60, z-tests were used to calculate p-values (Sterne & Kirkwood 2003: 60-61). There were also exposure variables with more than two categories and hence analysis of variance (ANOVA) was employed; specifically in comparison of adherence levels between different expectations of the patients. Odds ratios (ORs) were considered,

since this was a cross-sectional analytic study. The alternative hypothesis stated that a relationship exists between patient-related factors influencing adherence levels. The dependant variable was adherence level while the independent variables were patients' knowledge about HIV and ART, HIV/AIDS stigma and discrimination, depression and alcohol use. The data gathered had both categorical and numerical figures. Measures of association (odds ratio) across the different independent variables were used to assess the association between those who adhered to ART and those who did not.

Simple linear regressions and multiple linear regression analyses were used to examine the dependency of adherence level on one and on several different exposure variables. Since different variables were considered, multivariate analysis was used to examine these associations. Correlation coefficients were used to determine whether the relationships between these independent and dependant variables were positive. The type and number of factors associated with either of the two levels of adherence were analysed. The percentage of adherence was calculated for each drug by dividing the number of pills taken by the number of pills prescribed. For these statistical analysis procedures the Statistical Package for the Social Sciences (SPSS version 17.0) computer software was used. The services of a statistician were employed to do the actual statistical calculations and to assist with the interpretations of the statistical results.

3.4.4 Reliability

The precision of a study indicates consistent results in its measurement or finding and whether the same result would be found, if the measurements were taken or the study was conducted repeatedly. Precision is also called reliability. Factors that influence precision of study results including random sampling error and random measurement error (Abdool Karim & Myer 2007). Reliability is used to indicate the consistency of a particular instrument in measuring the concept of interest (Burns & Grove 2005:374-375). That means if different data collectors are used to measure a particular concept, the data should be comparable. Reliability testing is also considered to be a measure of the amount of random error in the measurement technique. It is concerned with characteristics such as dependability, consistency, precision, and comparability. A reasonable sample size was calculated assuming 95.0% confidence interval, 50.0% frequency of adherence and 5.0%

worst acceptable result (Sayed 2007:347). During the pre-test phase of the data collection instrument, the interviewer identified and recorded words and sentences that were not understood and questions that required prompting or further explanations. The interviewer also recorded the time taken to complete each interview. At the end of each pre-test interview, the respondent was asked how he or she felt about the nature, style and timing of the questions. Finally, all the observed shortcomings were addressed during the revision of the data collection instrument.

3.4.5 Validity

According to Ulin, Robinson and Tolley (2005:25) validity is the extent to which a measurement could be trusted. Validity can also be mentioned as the closeness of a measurement towards a true finding. Factors that influence validity of study results include selection bias, information bias and the presence of confounding variables (Abdool Karim & Myer 2007). The best method of preventing selection bias is to ensure that the participants sampled are representative of the target population of interest. This study ensured that the sample was a random selection of the target population because the inclusion and exclusion criteria were used to identify the population from which a random sample had been selected. Information bias in this study was prevented by ensuring that variables were measured (by how questions were asked and variable defined) in the same way for all participants.

3.4.5.1 Content validity

According to Burns and Grove (2005: 377-378) content validity examines the extent to which the instrument measures the major elements that needed to be considered. For this particular study, content-related validity was achieved through two steps. An extensive literature search was done to ensure that the data collection instrument had all the necessary questions for addressing ART-related adherence issues. The second step was consultation with experts who were working as ART trainer, HIV/AIDS programme manager, statistician with experience in data collection tool development, health researcher and research advisor. A total of three experts from health background and one

expert from statistics consulted for this purpose. Their comments were included to ensre that the instrument addressed all the major elements.

3.4.5.2 Construct validity

Construct validity occurs when the theoretical constructs of cause and effect accurately reflect the real world model. It ensures that the data collection instrument measures what it intends to measure (Types of validity 2010). For this study all exposure and outcome variables were carefully written in the instrument so that the questions were clearly understood by the respondent and data collectors. Besides, the data collectors were adequately trained to collect all the needed information. The relationship between patient-related factors and adherence to ART were in agreement with other studies. This indicated that construct validity of the instrument had been achieved.

3.4.5.3 Face validity

Face validity is a measure of how representative the measure is at face value. It is a more general measure and often potential respondent have input (Face validity 2010). During the pre-test phase of this study, respondents were asked about their opinions of the instrument. The questions were clearly structured and the responses were easily recorded by the data collectors.

3.5 MEASUREMENT

The measurement used for adherence to ART was based on patients' self reported answers in response to specific questions. The literature review indicates that self-reports could be used to measure adherence levels (Murri et al 2000:123-128; Sullivan et al 2007:3; Mannheimer et al 2008:165). Questions enquired about patients' duration on ART, specific ARV regimens, three day and seven day recalls of ART adherence and reasons for missing ARV doses. The adherence level was calculated by dividing ARVs taken by prescribed drugs. Even though questions were asked about the recall periods at three and seven days, adherence level calculations were done for the seven day recall periods only. The cutoff point for considering someone adherent was at the 95.0% level (those who

adhered ≥95.0% were considered to be optimally adherent while those who adhered <95.0% were regarded as being sub optimal ART adherent).

3.6   ETHICAL CONSIDERATIONS

The proposal was submitted to the Research and Ethics Committee of the Department of Health Studies, Unisa and to the participating hospital's institutional review board (IRB) clearance. This was done to confirm that the rights and welfare of the individuals involved were protected, the appropriate methods were used to secure informed consent and the potential benefits of the investigation were greater than the risks. Informed consent must ensure that participant understands the following things: possible risks and benefits, voluntary participation, assurance of confidentiality, the purpose of the research, how he/she was chosen to participate, data collection procedures and whom to contact with questions and concerns (Ulin et al 2005:58). The different human rights that required protection in research are; the right to self determination, the right to privacy, the right to anonymity and confidentiality, the right to fair treatment and the right to protection from discomfort and harm (Burns & Grove 2005:181). The information sheets and the interview schedules were available in both English and Amharic.

The right to self determination was protected through treating subjects as autonomous agents by informing them about the proposed study and allowing them to voluntarily choose to participate or not. They were also informed that they had the right to withdraw from the study at any time without incurring any penalties. The right to privacy was protected by not disclosing the patient's information to any third party during interviewing; this was achieved through finding an appropriate room for each interview. The right to anonymity was protected through anonymous collection of information. Respondents were not identified by their key identifiers like name, home number, telephone number or postal address when the research report was written. Patients' interview schedule were marked consecutively beginning with 001. Even through the patients ART unique numbers were recorded, the right to confidentiality was protected by not sharing this private information with others.

The right to fair treatment was protected through fair selection and treatment of respondents by using simple random sampling. The right to protection from discomfort and harm was achieved since the study had minimal to no risk for physical, emotional, social or economic harm. Informed consent was obtained from every respondent of the study to the degree that they were capable, and documented that they had the opportunity to choose whether or not to participate in this research. In other words, informed consent was obtained after the objectives of the study and the right to participate or not to participate was explained to each respondent. Benefits and risks were balanced as the research respondents would benefit when the findings would be shared with the decision makers and interventions might be designed and implemented based on such information.

3.7 LIMITATIONS

REVIEW AND DECIDE TO MOVE TO CHAPTER 5

- The sample was selected from only one hospital from a total of 9 public hospitals and 17 private hospitals providing ART services in Addis Ababa. This makes it unrepresentative of the whole population of ART patients in Ethiopia and Addis Ababa. Hence, the findings are only generalisable to the participating hospital.

- The 355 sample respondents were selected using simple random sampling technique. As a result both the exposures and outcome variables were collected simultaneously. This limits establishing temporal relationship between the two variables and assessing causal associations.

- Because the participating hospital provided free ARV services, the ART patients might have been of lower socio-economic status. Those patients from higher economic status might receive their care from private hospitals. Therefore the sampled patients might be different from the general ART patients in Addis Ababa.

- Only structured interviews were used to collect data from patients.

- No family members and no health care workers were interviewed.

- In-depth qualitative interviews with the ART patients might have provided information about these patients' lived experiences of being HIV positive and about the challenges faced to remain ART adherent.

3.8 SUMMARY

The data collection was done on patients at Alert Hospital who have taken ART for at least 12 months of period. A quantitative, descriptive, cross-sectional and analytical study was used to collect data using self report adherence measurement and structured interviews. The data were collected from 355 ART patients by conducting structured interviews designed for this specific purpose. The data were analysed using the statistical package for the social science (SPSS version 17.0).

Chapter 4 presents the analysis and discussion of the data obtained by conducting structured interviews with 355 ART patients.

CHAPTER 4

ANALYSIS AND DISCUSSION OF RESEARCH RESULTS

4.1 INTRODUCTION

Chapter 4 presents and discusses the results of this study. The overall purpose of the study was to identify personal factors influencing patients' ART adherence in Addis Ababa, Ethiopia. The study's findings will be used to address those personal factors that could present barriers to effective ART adherence.

The specific objectives of this study were to:

- Determine the adherence status of ART patients in Addis Ababa, Ethiopia.
- Identify the influence of patients' knowledge of HIV and ART on adherence to ART in Addis Ababa, Ethiopia.
- Assess the influence of HIV stigma and discrimination on adherence to ART in Addis Ababa, Ethiopia.
- Evaluate the influence of depression on adherence to ART in Addis Ababa, Ethiopia.
- Identify the influence of alcohol use on adherence to ART in Addis Ababa, Ethiopia.

4.2 PATIENTS' LEVELS OF ART ADHERENCE

At least 95% ART adherence is required to suppress viral replication, show clinical improvement and increase the CD4 count (WHO 2006:70). If this adherence level is not maintained then it has public health implications and poor personal health outcomes (WHO 2003:95). Adherence was calculated using ART patients' self reports in this study for the preceding seven days. The actual figure was obtained by dividing the total

number of pills reportedly ingested by the total number of pills prescribed for the preceding seven days.

Out of the 355 patients, 94 (26.5%) were non-adherent, with less than 95% adherence level, and 261 (73.5%) of them were adherent at a 95-100% adherence level. There were 6 (1.7%) patients with 0-5% adherence level. The adherence levels ranged from 0% to 100%; the lowest, 0% indicated that the patient did not take any pills during the preceding seven days and the highest 100% indicated that the patient took all pills prescribed for the past seven days.

Table 4.1 Adherence levels (n=355)

Adherence level	Frequency	Percent	Cumulative percent
0-5%	6	1.7	1.7
55-59%	5	1.4	3.1
60-64%	1	0.3	3.4
65-69%	1	0.3	3.7
70-74%	3	0.8	4.5
75-79%	2	0.6	5.1
80-84%	14	3.9	9.0
85-89%	35	9.9	18.9
90-94%	27	7.6	26.5
95-100%	261	73.5	100.0
Total	**355**	**100.0**	

More than two thirds (73.5%; n=261) of the respondents took their ARVs as prescribed. This study supports the findings of other studies that patients in resource-poor countries can adhere to their ARVs as prescribed (Mugusi et al 2009:1231; Carlucci et al 2008:618).
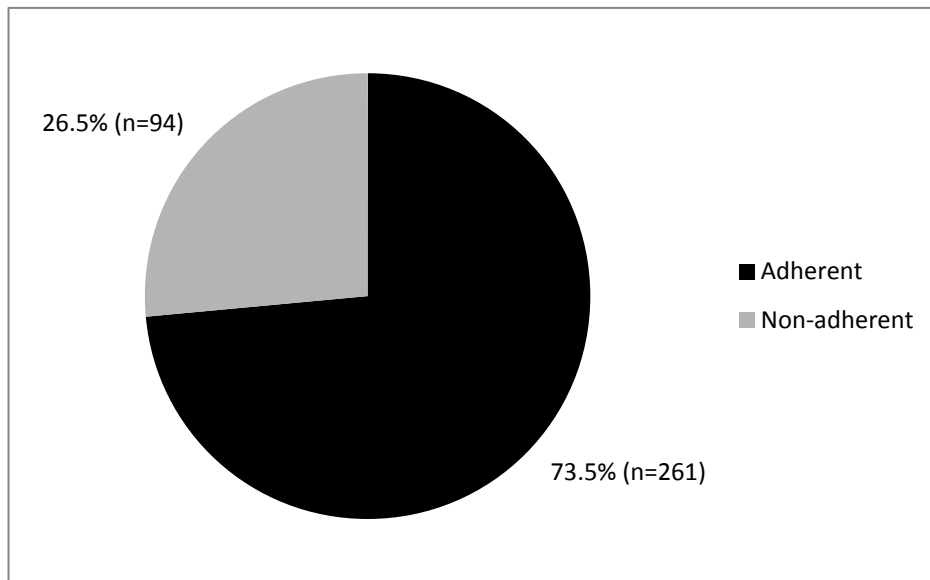
Figure 4.1 Adherence/non adherence percentages among ART patients (n=355)

4.3 DEMOGRAPHIC DATA

This section presents demographic data, followed by clinical data with discussions about the adherence levels in association with personal factors. All figures are rounded off to the first decimal place. The demographic section addresses the results pertaining to the participants' gender, ages, educational levels and marital status.

A total of 355 (100%) ART patients, 130 (36.6%) males and 225 (63.4%) females, who were PLHIV ≥18 years of age and who had started ART at least twelve months previously were selected for the study using simple random sampling. Those patients excluded by study criteria upon sampling were substituted with other patients to attain the required power. Table 4.2 shows the key characteristics of the respondents.

Table 4.2 Characteristics and profile of respondents (n=355)

Variables	Values
Age range (years)	20-67
Mean age (years)	36.43
Female (number)	225
Male(number)	130
Baseline CD4 cell count range (cells/mm^3)	4-478
Most recent CD4 cell count range (cells/mm^3)	17-1053

4.3.1 Gender

Although in Ethiopia the overall percentage of males (50.5%) and females (49.5%) are almost equal, the proportion differs between urban and rural areas. In urban areas the male to female proportion is 49.7% to 50.3% and in rural areas 50.6% to 49.4% respectively. In urban areas females are more in number but in rural areas the reverse is true. In Addis Ababa the total percentage of males is (47.6%) and females (52.4%) (FDRE/PCC 2008:7-14).
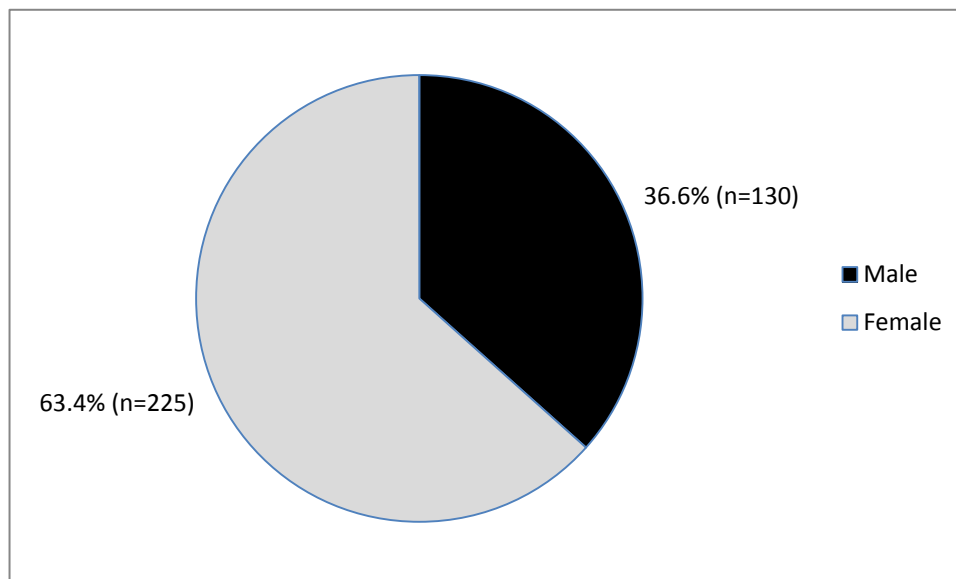
Figure 4.2 Proportion by gender of sampled patients on ART (n=355)

In this study there were more females 63.4 % (n=225) than males 36.6% (n=130) which reflects the higher HIV prevalence among females normally seen in the urban areas of Ethiopia. The adult HIV prevalence rate in urban areas is higher among females, 9.25% compared to males (6.2%) (EFMOH/HAPCO 2007a:07).

Out of the 94 non adherent respondents, 43.6% (n=41) were males and 56.4% (n=53) were females (see figure 4.3). Among the 261 adherent patients, 34.1% (n=89) were males. The adherence level of males was significantly different from that of females (p= 0.05, 95%CI= -6.40,-0.01). This result could indicate that females were more ART adherent than males. This difference could possibly be explained by the fact that more males than females were employed outside their homes, working as drivers and/or farmers, and might be less unlikely to take their medications with them to their workplaces.
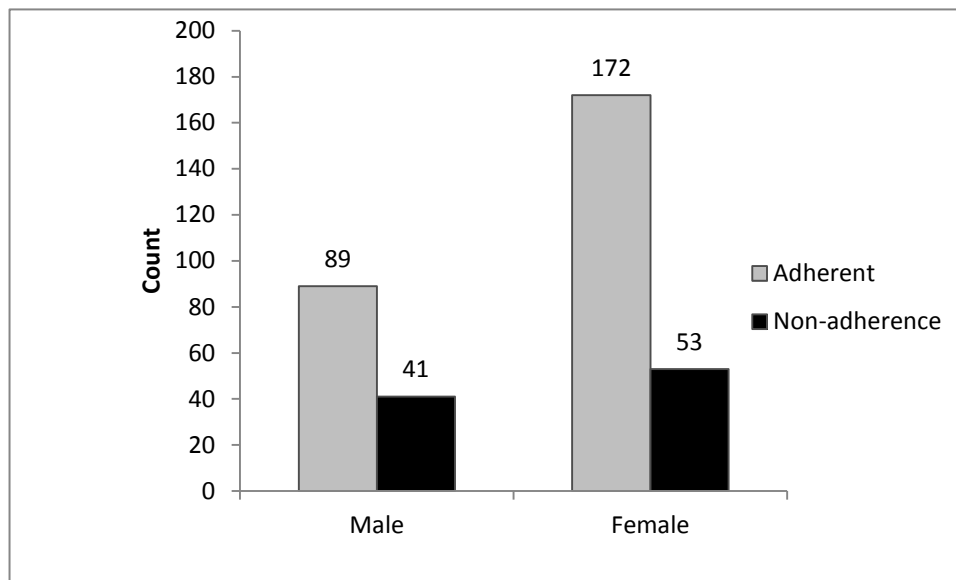
Figure 4.3 Relationship between ART adherence and gender (n=355)

This finding is supported by a South African study showing that women were more adherent than men based on self reported adherence rates validated by virological suppression, CD4 counts and clinical outcomes (Boulle, Michaels & Hildebrand 2004). There is also a contradictory study from Nigeria, showing that females were less adherent. According to Uzochukwu et al (2009:192) females in Nigeria who were single

and had higher educational status, had significantly higher levels of ART non-adherence.

Table 4.3 Gender versus adherence (n=355)

| | | | Adherence | | |
			Non adherent (<95%)	Adherent (95-100%)	Total
Gender	Male	Count	41	89	130
		% within gender (males)	31.5%	68.5%	100.0
		% of total	11.5%	25.1%	36.6%
	Female	Count	53	172	225
		% within gender (females)	23.6%	76.4%	100.0
		% of Total	14.9%	48.5%	63.4%
Total		Count	94	261	355
		% within gender	26.5%	73.5%	100.0

4.3.2 Age

The patients' ages ranged from 20 to 67 with an average of 36.4. The age 30-34 year group constituted the largest group of patients (n=77), followed by the age 35-39 year group (n=72). Accordingly the most adherent patients were identified in the age group 30-34 years (n=55), followed by those aged 35-39 (n=53). In the age group 25-29 there were 47 adherent respondents.

Age was not significantly associated with adherence (p=0.15), as shown in table 4.4. This result is similarly reported from a study done in Nigeria showing no significant association between age with ART adherence levels (Afolabi, Ijadunola, Fatusi & Olasode 2009:9). According to Uzochukwu et al (2009:192) being female, over 35 years old and having higher educational status were significantly associated with non-adherence, contrary to this study's findings.

Table 4.4 Relationship between adherence and age (n=355)

Age	Count	Non-adherent (<95%)	Adherent (95-100%)	TOTAL
18-24	Count	6	14	20
	% within adherence	6.5%	5.3%	5.6%
25-29	Count	21	47	68
	% within adherence	22.3%	18.0%	19.2%
30-34	Count	22	55	77
	% within adherence	23.4%	21.1%	21.7%
35-39	Count	19	53	72
	% within adherence	20.2%	10.3%	20.3%
40-44	Count	12	27	39
	% within adherence	12.8%	10.3%	11.0%
45-49	Count	4	40	44
	% within adherence	4.3%	15.3%	12.4%
50-54	Count	7	13	20
	% within adherence	7.4%	5.0%	5.6%
55-59	Count	3	3	6
	% within adherence	3.2%	1.1%	1.7%
60-64	Count	0	6	6
	% within adherence	.0%	2.3%	1.7%
65-69	Count	0	3	3
	% within adherence	.0%	1.1%	.8%
	Count	94	261	355
	% within adherence	100.0%	100.0%	100.0%
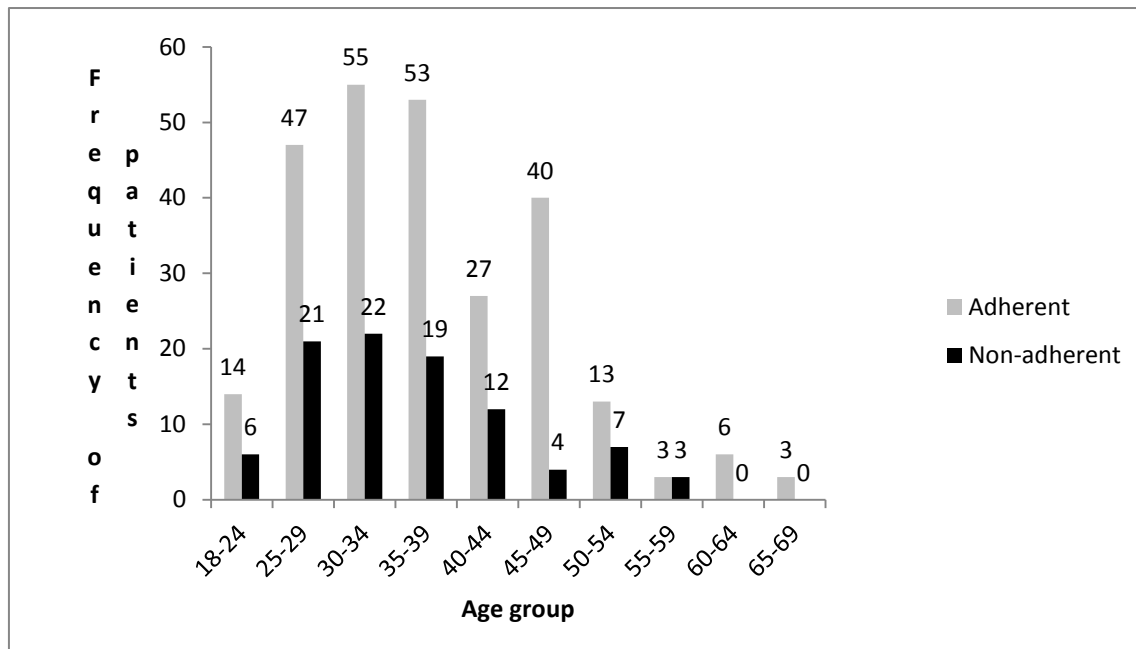
Figure 4.4 Relationship between adherence and age (n=355)

4.3.3 Education levels

Out of 355 respondents, 38 (10.7%) had never been to school, 133 (37.5%) had attended primary school, 52 (14.6%) secondary school, 104 (29.3%) high school and 28 (7.9%) higher education institutions. Out of the 261 adherent patients, 103 (39.5%) attended primary education, 73 (28.0%) school, 40 (15.3%) secondary school and 26 (10.0%) had never been to school. There was no association between education level and adherence status (p=0.638, two tailed tests). Higher levels of education were not associated with higher levels of ART adherence.

Table 4.5 Level of education attained versus ART adherence (n=355)

Highest level of education		Non-Adherent (Less than 95%)	Adherent (95-100%)	TOTAL
Not been to school	Count	12	26	38
	% within highest level of education passed	31.6%	68.4%	100.0%
Grade 1-6 (Primary)	Count	30	103	133
	% within highest level of education passed	22.6%	77.4%	100.0%
Grade 7-8 (Secondary)	Count	12	40	52
	% within highest level of education passed	23.1%	76.9%	100.0%
Grade 9-12 (High school)	Count	31	73	104
	% within highest level of education passed	29.8%	70.2%	100.0%
University/college (Higher institution)	Count	9	19	28
	% within highest level of education passed	32.1%	67.9%	100.0%
TOTAL	Count	95	261	355
TOTAL %	% within highest level of education passed	26.5%	73.5%	100.0%

According to this study there was no evidence that a person's educational level affected his/her ART adherence level. Whether a person had been educated or not, he/she could take his/her ARVs as prescribed by the healthcare provider. This finding is consistent with another study which indicated that low literacy levels were not associated with low levels of ART adherence (Paasche-Orlow et al 2006:838).
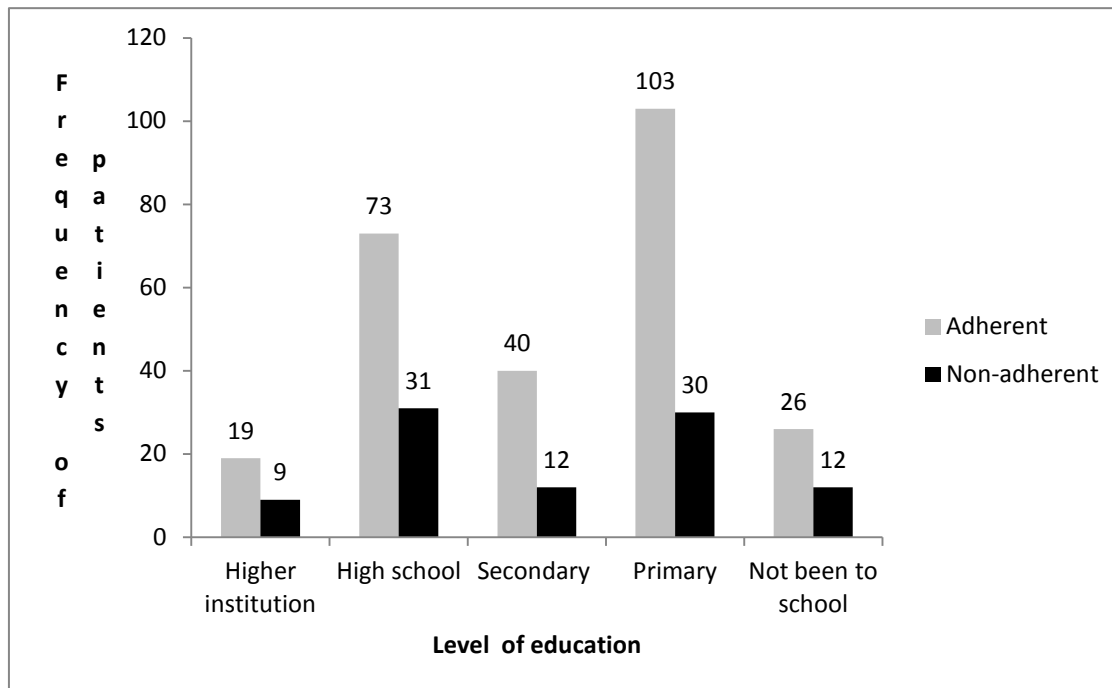
Figure 4.5 Relationship between adherence and education level (n=355)

4.3.4 Marital status

Of the 355 patients, 156 (43.9%) were married, 89 (25.1%) widowed, 48 (13.5%) single, 37 (10.4%) divorced and 25 (7.0%) separated. Among the 261 adherent patients the largest number was found among the 115 (44.1%) married respondents, followed by the 67 (25.7%) who had been widowed. However, there was no association between marital status and adherence levels (p=0.30, two tailed test of chi-square). This finding related to whether or not a person was married, divorced, single, separated or widowed, but it did not indicate whether the person was living alone or with others. A single, separated or widowed person could be living with other individuals, and this might have impacted on his/her ability to adhere to his/her ART.

Table 4.6 Marital status versus adherence (n=355)

Marital status	Count and %	Non-adherent(<95%)	Adherent (95-100%)	TOTAL
Single	Count	10	38	48
	% within marital status	20.8%	79.2%	100.0%
	% within optimal suboptimal adherence	10.6%	14.6%	13.5%
Married	Count	41	115	156
	% within marital status	26.3%	73.7%	100.0%
	% within optimal suboptimal adherence	43.6%	44.1%	43.9%
Divorced	Count	10	27	37
	% within marital status	27.0%	73.0%	100.0%
	% within optimal suboptimal adherence	10.6%	10.3%	10.4%
Separated	Count	11	14	25
	% within marital status	44.0%	56.0%	100.0%
	% within optimal suboptimal adherence	11.7%	5.4%	7.0%
Widowed	Count	22	67	89
	% within marital status	24.7%	75.3%	100.0%
	% within optimal suboptimal adherence	23.4%	27.7%	25.1%
TOTAL	Count	94	261	355
	% within marital status	26.5%	73.5%	100.0%

According to Knodel, Kespichayawattana & Wiwalwanich (2010:6) in a study conducted at Thailand, family members could support the patient to take his or her medication on time. Smith and Mbakwem's (2007:38) study done in Nigeria, found that ART programmes need to acknowledge and create enabling environments for marriage and reproduction; while addressing disclosure, adherence to ART and prevention issues.
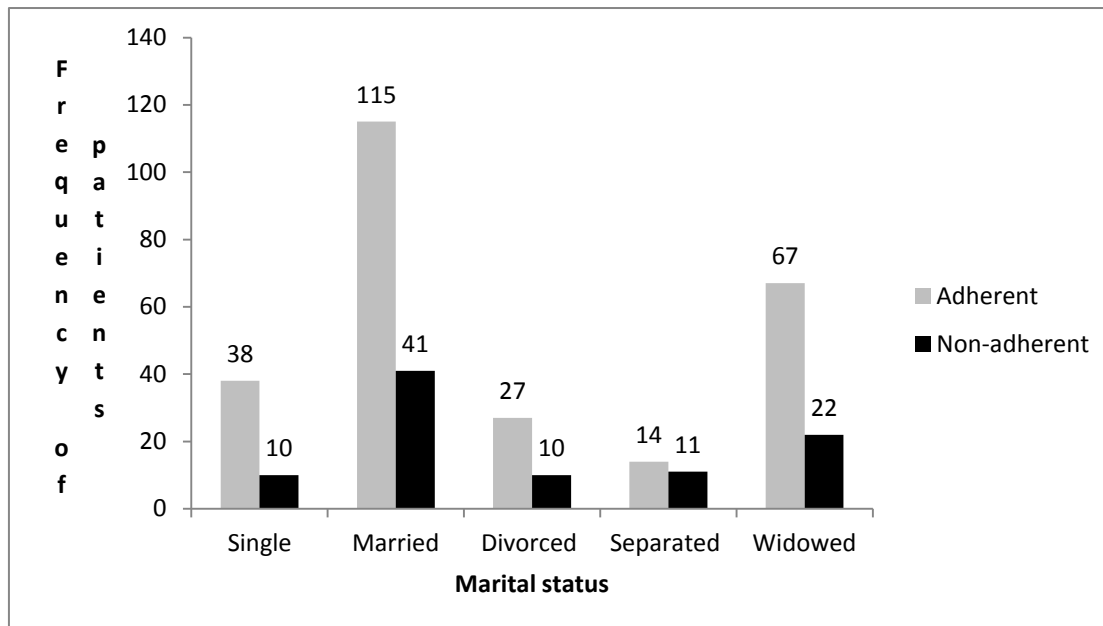
Figure 4.6 Relationship between adherence level and marital status (n=355)

4.4   CLINICAL DATA

This section presents the clinical data gathered from participants' records.

4.4.1 CD4 cell count values

Patients are initiated on ART based on their CD4 cell count and their WHO HIV/AIDS clinical stage (WHO 2006:13-16). ART is initiated when the CD4 cell count is <200cells/mm^3, irrespective of the clinical stage. When the CD4 count is between 200 cells/mm^3 and 350cells/mm^3, ART is initiated based on the patient's WHO stage. The severity of the illness increases as the stages progress from 1 to 4 (WHO 2007:12). The CD4 cell counts, gathered at baseline and most recently available in the patients' charts, were used for this analysis. The baseline CD4 count ranged from 4 to 478 cells/mm^3 and the most recent CD4 cell count ranged from 17 to 1053 cells/mm^3.

Figure 4.7 shows the result of changes in CD4 cell count from the baseline (before treatment was started) to the most recent for the respondents. There appears to be a

weak positive relationship between the baseline CD4 count and the most recent CD4 count with a Pearson Correlation Coefficient of 0.417, meaning the higher pre-treatment cell count, the higher the post treatment cell count. The regression line of the most recent CD4 count on the baseline CD4 cell count is y=0.977x+271.565, where y is the most recently counted CD4 cell and x is baseline CD4 cell count. The gradient of the regression line is 0.977 which means as the baseline CD4 count increase by one then the most recent CD4 count rise by 0.977.
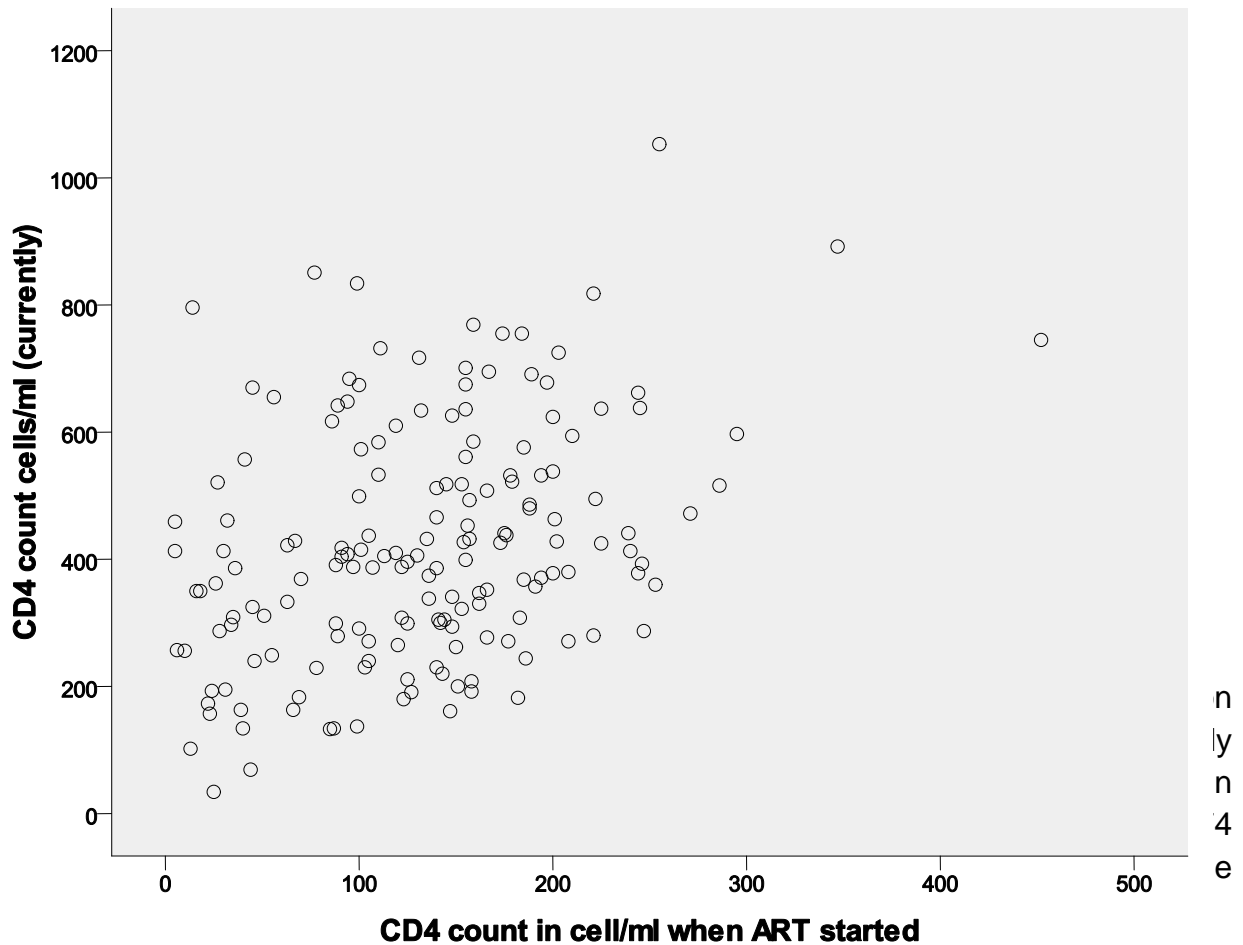
Table 4.7 Statistics: CD4 cell count at baseline versus CD4 cell count most recently

| Model | Unstandardised Coefficients | | Standardised Coefficients | | |
	B	Std. Error	Beta	t	Sig.
(Constant)	271.565	18.515		14.668	.000
CD4 count in cell/mm^3 when ART started	.977	.113	.417	8.616	.000

4.4.2 WHO HIV/AIDS stage

WHO classifies HIV/AIDS infection into four stages and this is used in deciding ART initiation. The stages are stage I (asymptomatic), stage II (mild symptoms), stage III (advanced symptoms) and stage IV (severe symptoms) (WHO 2007:12). Out of 355 respondents, 179 were classified as being in WHO's HIV/AIDS stage I; 83 (23.4%) in WHO's stage II; 57 (16.1%) in stage III and 14 (3.9%) in stage IV. The rest, 22 (6.2), did not have any WHO staging reported in their records. A higher number of patients who were ART-adherent were found in WHO stage I (n=141; 57.8%) followed by WHO stage II (n=56; 23.0%). There was a significant association between WHO HIV/AIDS staging and adherence (p=0.039). The proportion of patients who adhered to treatment increased as the WHO clinical stage decreased, indicating that when patients adhered to ART, the associated severity of their illness could be reduced.
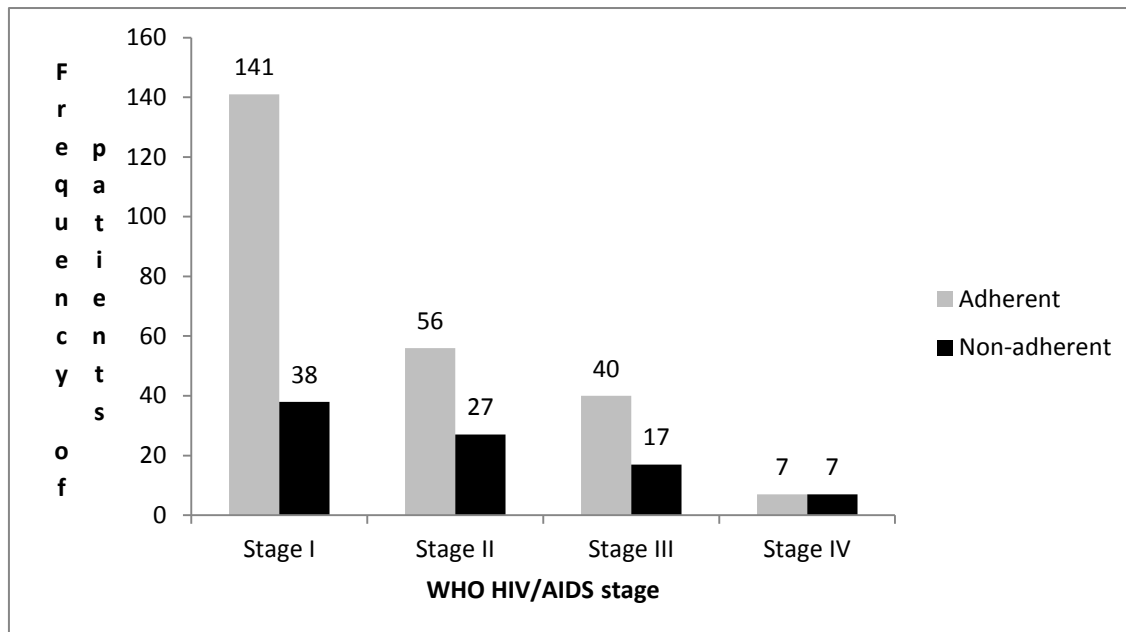
Figure 4.8 Relationship between adherence and WHO HIV/AIDS stage (n=333)

4.5   CORRELATION BETWEEN ADHERENCE AND PATIENTS' KNOWLEDGE LEVELS

Patients' knowledge levels were assessed using questions pertaining to HIV/AIDS and ART. Nine questions were asked and the knowledge was scored out of 100%. The questions focused on the mode of transmission of HIV, difference between HIV and AIDS, benefits and adherence to ART. The mean knowledge score was 61.84% (range 18.89% to 86.66%; standard deviation of 10.92). Figure 4.9 does not show a linear relationship between adherence and knowledge score. Spearman's Correlation Coefficient is -0.002, suggesting no association. Hence, there no association was found between adherence level and knowledge score. Additionally, at the 5% significance level, the results indicated no statistically significant association (p=0.967). People with higher knowledge score (good knowledge of HIV and ART), were reportedly not more likely to be adherent to ART compared to those with poorer knowledge levels, as measured in this study.

Table 4.8   Knowledge score versus adherence level (n=355)

			Adherence		
			Non-adherent (<95%)	Adherent (95-100%)	Total
Grouped knowledge Score	18-24%	Frequency	1	0	1
	25-29%	Frequency	0	1	1
	30-34%	Frequency	1	2	3
	35-39%	Frequency	3	4	7
	40-44%	Frequency	2	10	12
	45-49%	Frequency	8	12	20
	50-54%	Frequency	13	36	49
	55-59%	Frequency	10	29	39
	60-64%	Frequency	10	54	64
	65-69%	Frequency	18	64	82
	70-74%	Frequency	12	22	34
	75-79%	Frequency	11	22	33
	80-84%	Frequency	3	5	8
	85-89%	Frequency	1	0	1
Total		Frequency	94	261	355
		% of total	26.5%	73.5%	100%

A Zambian study found that lack of information about HIV and ART among females was associated with poor adherence (Murray et al 2009:84). The same finding was documented in a South African study with a knowledge score of 86% at Soweto (Nachega et al 2005:199). Both studies contrast with the finding of this study indicating no association between knowledge and ART adherence level.
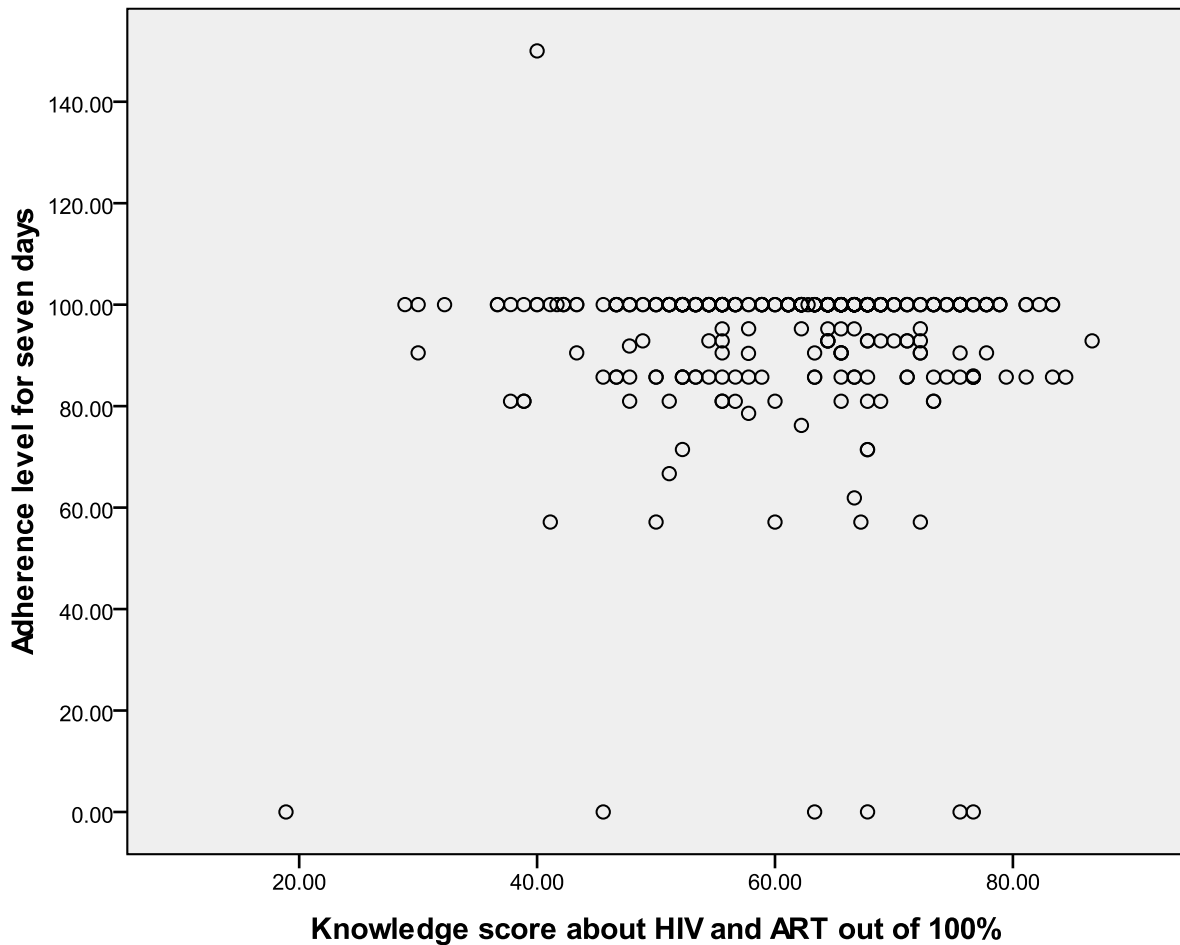
Figure 4.9 Scatterplot: Relationship between adherence and knowledge score

4.6 ADHERENCE, STIGMA AND DISCRIMINATION

Stigma and discrimination were divided into internalised stigma, perceived stigma and experienced discrimination to facilitate the analysis of this research. Each stigma type was presented in association with adherence in this section.

4.6.1 Relationship between adherence and internalised stigma

Stigma is a negative attitude towards a group of people due to their unique attributes (such as HIV status) (Luna-Cadena et al 2004:01). The authors further discussed that a

patient develops internalised stigma when he/she treats himself differently or develops stigmatizing feelings due to fear of reactions by other people based on his/her specific attribute(s). This stigma is related to shame, fear and guilt, and can lead to isolation, deception, and camouflage.

In this study internalised stigma was identified based on the patients' responses to three internal stigma questions. Out of the 355 patients, 161 (45.4%) had reportedly developed internalised stigma while 194 (54.6%) did not. Out of the 261 adherent patients, 161 (61.7%) did not develop self stigma. Out of the 94 non-adherent respondents, 61 (64.9%) developed internalised stigma. Adherence level ranged from 0-100% for both internalised stigma and non-internalised stigma patients. However, out of the 8 patients with adherence levels of 0-5%, 4 (50.0%) had experienced internalised stigma and 2 (25.0%) patients had not experienced internalised stigma.
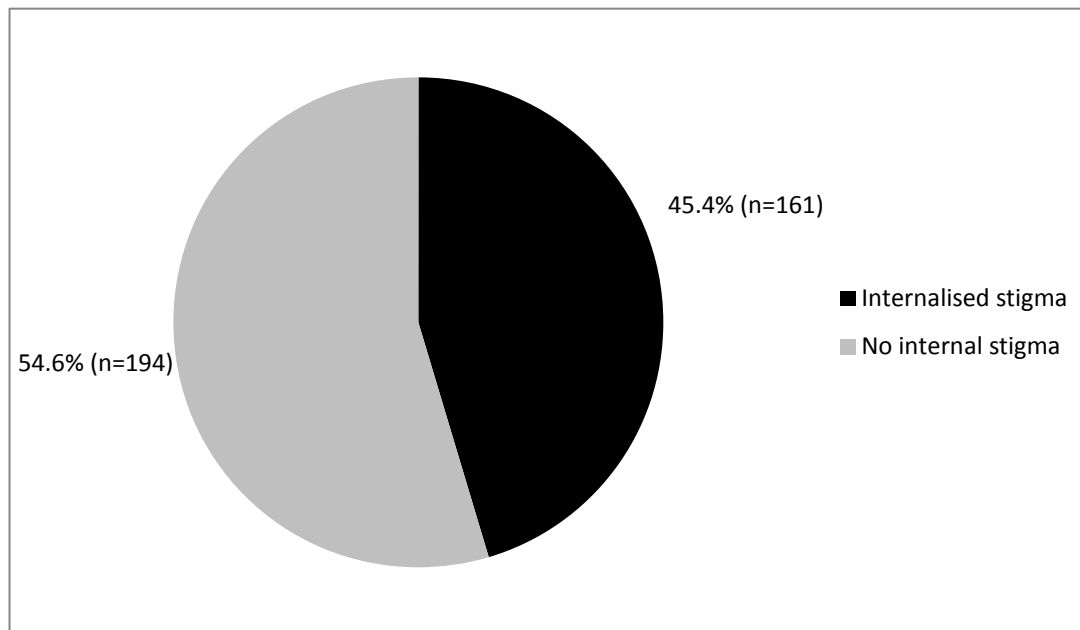
Figure 4.10 Internalised stigma status (n=355)

At a 5% significance level, the z-test statistic showed a significant association between internalised stigma and adherence (p=0.003; 95%CI= -7.70,-1.55). Further adherence levels were grouped into adherent and non-adherent categories and the strength of

association with internalised stigma was calculated from odds ratio (OR) of 2.89 and 95% CI of 1.77, 4.74. This indicated that people with internalised stigma were less likely to take ARVs as prescribed. This finding is consistent with other results. According to a study in the USA, internal stigma and other factors such as denial, life stress and adverse ARVs' side-effects were barriers to ART adherence (Konke-Parker et al 2008:98). Another study found that people with internalised stigma were three times as likely to report suboptimal adherence to HIV medications (Sayles et al 2009:1103).

Table 4.9   Logistic regression: internalised stigma versus adherence

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
								Lower	Upper
Step 1[a]	StigmaInternal	1.064	.251	17.951	1	.000	2.898	1.772	4.742
	Constant	-.543	.378	2.068	1	.150	.581		

Figure 4.11 Adherence level versus internal stigma (n=355)

4.6.2 Relationship between adherence and perceived stigma

Perceived stigma is due to another person thinking negatively about an individual because of something s/he develops, such as HIV (OVC support: 2011). In this study, perceived stigma was identified based on the patients' response to three perceived stigma questions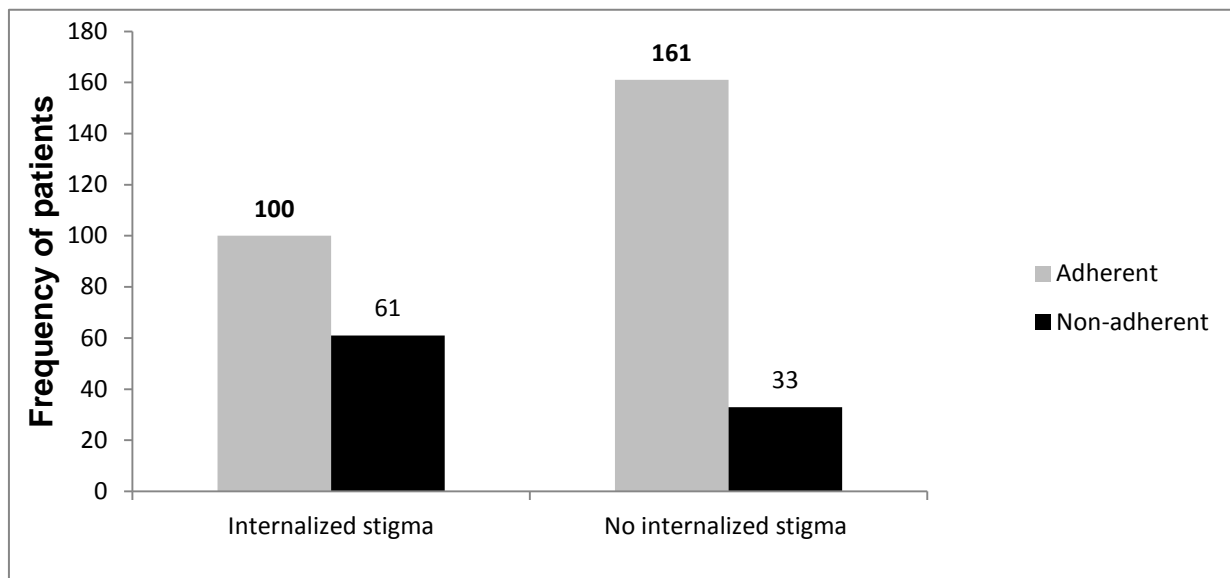. From the 355 respondents, 60 (16.9%) developed perceived stigma and 295 (83.1%) did not. Among the 94 non-adherent patients, 34 (36.2%) had perceived stigma and of the 261 adherent patients, 235 (90.0%) did not have perceived stigma. Adherence levels ranged from 0-100% for both groups who developed perceived stigma or did not develop perceived stigma. However, of 6 patients with an adherence level of 0-5%, 2 (33.3%) developed perceived stigma and 4 (66.7%) did not do so.

Table 4.10 Adherence vs. perceived stigma (n=355)

| | | | Adherence | | |
			Non-adherent (<95%)	Adherent (95-100%)	Total
Perceived Stigma	Perceived stigma	Count	34	26	60
		% within perceived stigma	56.7%	43.3%	100.0%
		% within optimal or suboptimal adherence	36.2%	10.0%	16.9%
	No perceived stigma	Count	60	235	295
		% within perceived stigma	20.3%	79.7%	100.0%
		% within optimal or suboptimal adherence	63.8%	90.0%	83.1%
Total		Count	94	261	355
		% within perceived stigma	26.5%	73.5%	100.0%
		% within optimal or suboptimal adherence	100.0%	100.0%	100.0%

The z-test shows a statistically significant association at a 5% significance level between perceived stigma and adherence (p=0.01; 95%CI=-11.66,-3.54). This finding

supports that adherence tends to be lower with people having perceived stigma. Perceived stigma is associated with patients not taking their pills, possibly because of fears of social rejection. This finding is congruent with a study done in five other African countries (Lesotho, Malawi, South Africa, Swaziland and Tanzania) which found that perceived stigma interfered with adherence to ART and correlated with missed doses of HIV/ADS medications (Dlamini et al 2009:384).
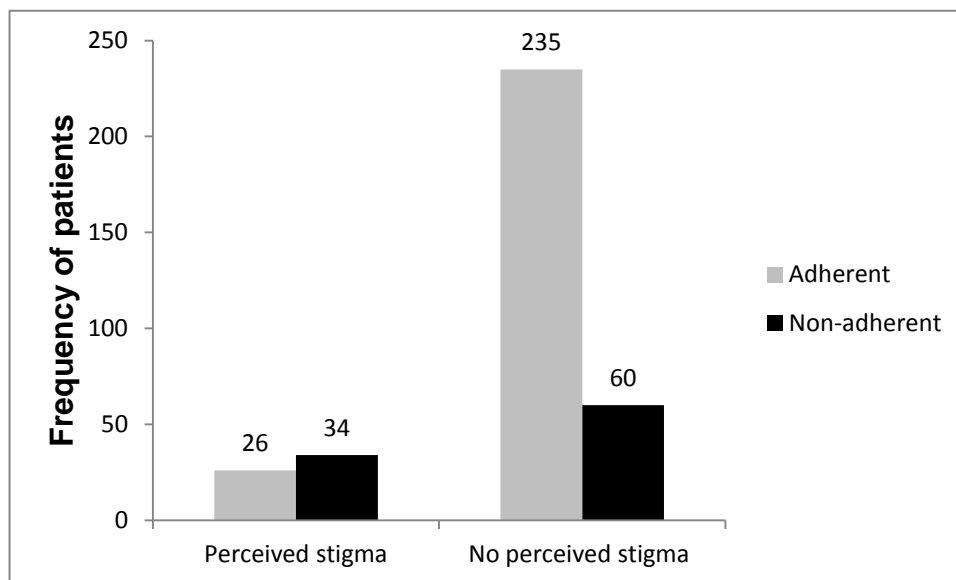
Figure 4.12 Adherence level versus perceived stigma (n=355)

4.6.3 Relationship between adherence and discrimination

Stigma when acted upon becomes discrimination. Discrimination encompasses action or omissions that are derived from stigma and directed towards those stigmatised individuals (UNAIDS 2005:09). In this study discrimination was identified based on patients' responses to eleven discrimination questions. Among the 355 patients, 62 (17.5%) experienced discrimination and 293 (82.5%) did not experienced discrimination. Of the total 62 discriminated patients, 24 (38.7%) were non-adherent and out of the 293 non-discriminated patients, 70 (23.9%) were non-adherent. Adherence levels ranged from 0-100% for both discriminated and non-discriminated patients. Out of 6 patients

with an adherence level of 0-5%, 3 (50.0%) had faced discrimination and 3 (50.0%) did not face discrimination. Out of the 261 patients with an adherence level of 95-100%, 38 (14.6%) faced discrimination and 223 (85.4%) did not face discrimination.

Table 4.11 Statistics: discrimination versus adherence (n=355)

	Z-test				
				95% confidence interval of the difference	
	Z	Df	Sig. (2-tailed)	Lower	Upper
Equal variances assumed	-2.727	353	0.007	-9.638	-1.561
Equal variances not assumed	-1.906	69.225	0.061	-11.459	0.259

The z-test shows there is a statistically significant association between discrimination and adherence at the 5% significance level (p=0.007; 95%CI= -9.6,-1.6). Patients who experienced discrimination had lower levels of adherence. This finding is supported by another study which indicated that ; because of stigma and discrimination, people living with HIV may not take their medications at the correct time or in the correct way, in order to hide their positive status from others (DFID 2007:02).
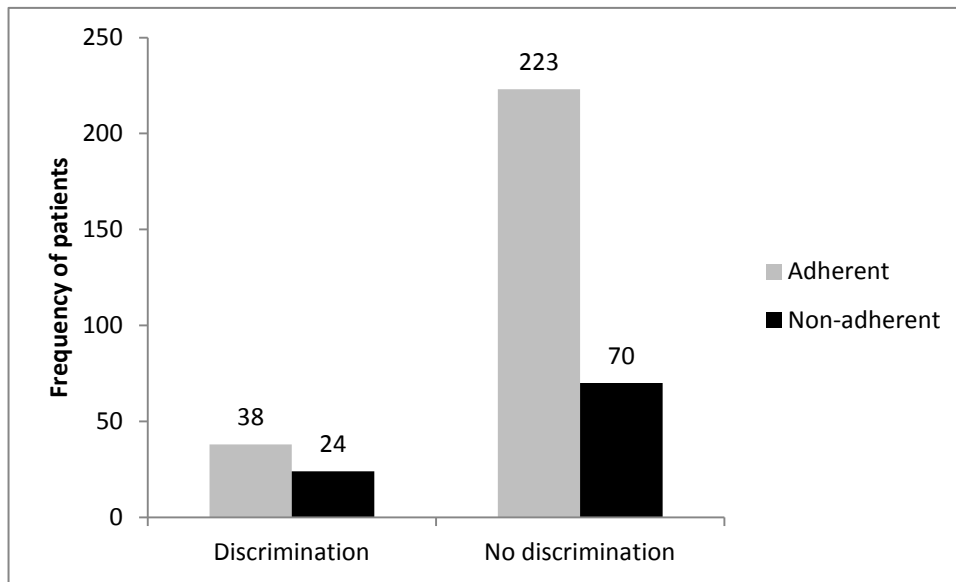
Figure 4.13 Adherence versus discrimination (n=355)

4.7   ADHERENCE AND DEPRESSION

Out of the 355 respondents, 19 (5.4%) developed depression. Among these 19 depressed patients 15 (78.9%) were non-adherent and 4 (21.1%) were adherent. ART adherence levels ranged from 0-100% for non-depressed patients and 57-100% for depressed patients. Adherence levels were grouped into intervals and frequency of depressed and non-depressed patients calculated for each level. The highest number of depressed patients 6 (31.6%) was observed for an adherence level of 85-89%. For non-depressed patients, the highest number was 257 (76.5%) with an adherence level of 95-100%.

Table 4.12 Statistics: depression versus adherence (n=355)

	Z-test			95% confidence interval of the difference	
	Z	df	Sig. (2-tailed)	Lower	Upper
Equal variances assumed	-2.001	353	0.046	-13.809	-0.120
Equal variances not assumed	-2.823	11.683	0.10	-12.071	-1.857

There was a statistically significant association between adherence and depression at the 5% significant level (p=0.046; 95%CI=-13.81,-0.12). The strength of the association was also determined using an odds ratio (OR=12.40; 95%CI=4.00, 38.46). The odds ratio is more than 1 and indicates that depression was a risk factor for adherence to ART.

5.4% (n=19)

■ Depressed
■ Not depressed

94.6% (n=336)
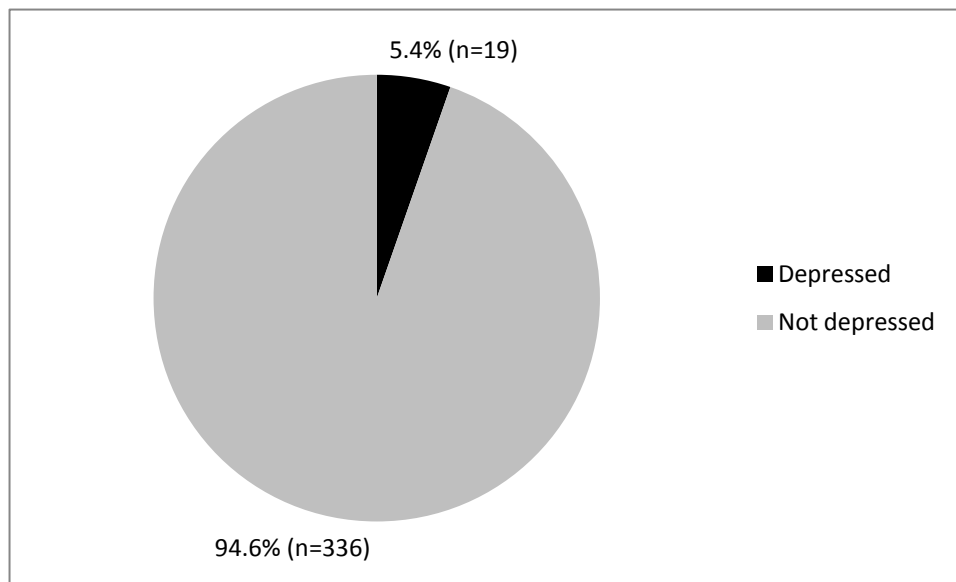
Figure 4.14 Frequency and percentage of depressed and non-depressed patients (n=355)

This finding is supported by other studies. An Ethiopian study (Amberbir et al 2008:5) reported that non-depressed patients adhered to ART twice more than depressed

patients. Depressed patients had poor moods, even if good things were happening to them. As a result depressed patients were not motivated to take their pills as agreed to with their health care providers. The same result was also identified in an Indian study (Sarna et al 2008:34) that showed depression to be associated with non-adherence to ART. This suggests that healthcare providers should identify depression among HIV patients as early as possible and manage it to improve ART adherence levels.
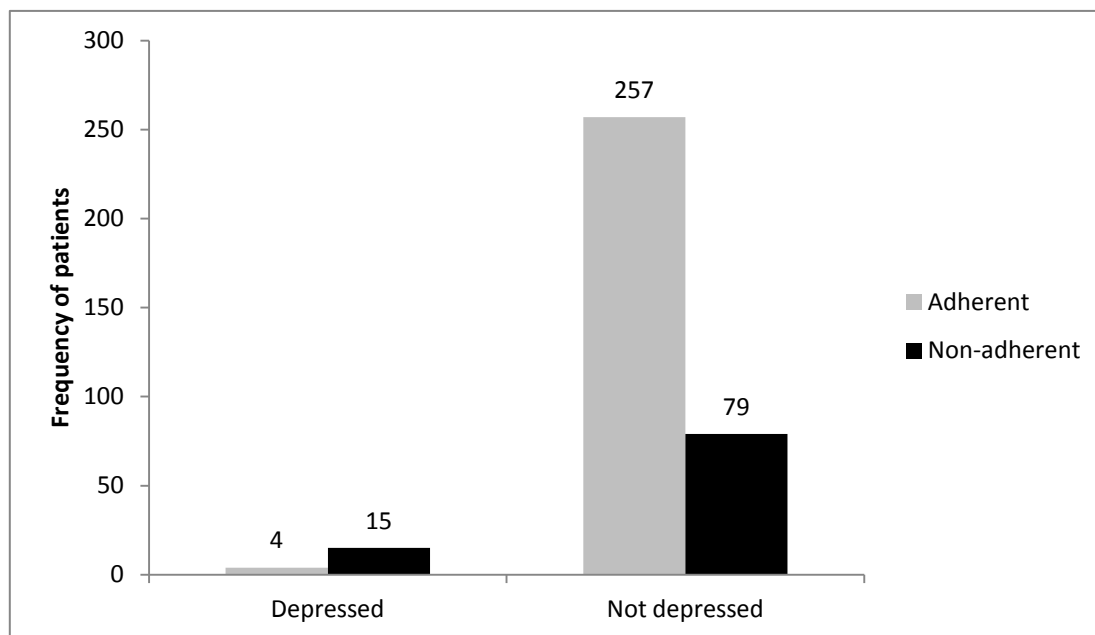
Figure 4.15 The relationship between adherence and depression (n=355)

4.8 ART ADHERENCE AND ALCOHOL USE

Based on the frequency and amount of alcohol use, alcohol drinkers were classified into five categories. The majority of participants in this study were classified as current abstainers, 283 (79.7%), followed by infrequent light drinkers 66 (18.6%). There were 2 (0.6%) frequent light drinkers and 4 (1.1%) infrequent heavy drinkers. There were no frequent heavy drinkers. Of the total 261 adherent patients, 233 (88.3%) were current abstainers, 26 (10.0%) infrequent light drinkers, 1 (0.4%) frequent light drinker and 1 (0.4%) infrequent heavy drinker. Out of the 94 non-adherent respondents, 40 (42.6%) were infrequent light drinkers, 50 (53.2%) current abstainers, 1 (1.1%) frequent light

drinker and 3 (3.2%) infrequent heavy drinkers. Adherence levels ranged from 0-100% for both current abstainers and infrequent light drinkers; 86-95% for frequent light drinkers and 67-95% for infrequent heavy drinkers.

Since the alcohol variable had five categories, one way analysis of variance (ANOVA) was used to assess the association between adherence and alcohol. There was a statistically significant association between alcohol use and adherence at the 5% significance level (p=0.001). This indicated that when the frequency and amount of alcohol consumption is high, the probability of ART non-adherence is also high.

Table 4.13 ANOVA: association between alcohol use and ART adherence

	Sum of Squares	Df	Mean Square	F	Sig.
Between Groups	4674.620	3	1558.207	7.483	.000
Within Groups	73085.309	351	208.220		
Total	77759.929	354			

This finding is supported by other studies. Alcohol use is associated with ART non-adherence even though it cannot be concluded that alcohol consumption was causal in nature (Hendershot, Stoner, Pantalone & Simoni 2009:08). In a different study in the USA, both moderate and hazardous levels of alcohol use were associated with non-adherence to ART (Chander et al 2006:414).
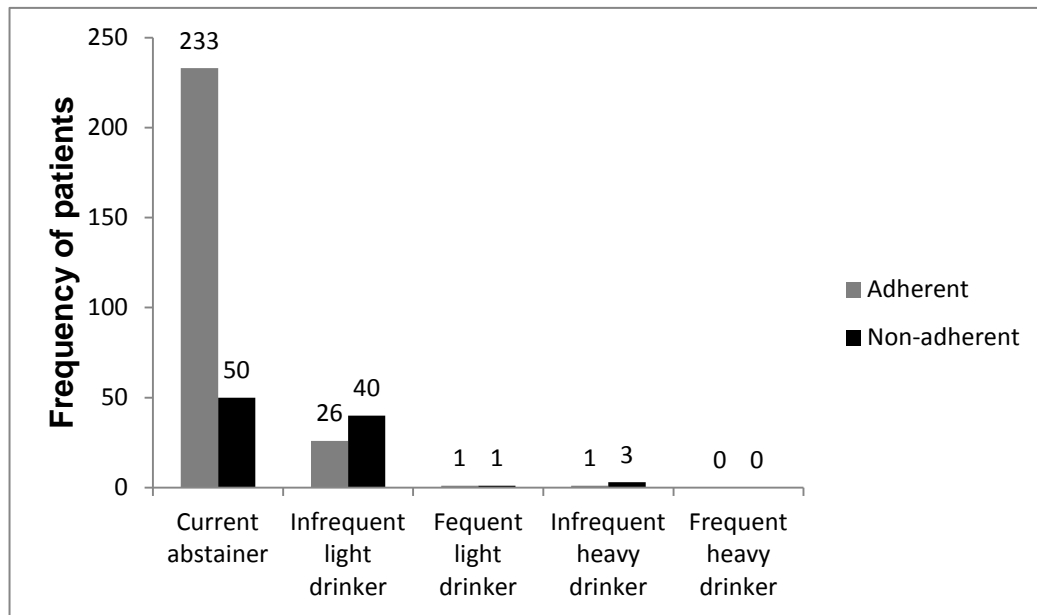
Figure 4.16 Alcohol consumption versus ART adherence (n=355)

4.9 CONCLUSION

This chapter presented the results of the association between patient ART adherence (defined for the last seven days) and demographic, clinical and personal factors. Gender was significantly associated with adherence, but there was no association with age. Both higher levels of education and knowledge score were not related to higher levels of adherence. Marital status alone did not have an effect on increased adherence level, however, his study did not investigate the role of other family supports on adherence. Baseline CD4 cell count and the most recent CD4 cell counts had a weak positive association. WHO HIV/AIDS stage was also associated with adherence to ART showing patients with better adherence had less severe illness.

Stigma and discrimination when sub categorised into three types, were all found to be associated with adherence. People adhere better to their medication in the absence of any type of stigma and discrimination. Alcohol use and a depressed mood were related to suboptimal adherence.

In summary, the study found that 73.5% of the respondents had optimal adherence and 26.5% had sub optimal adherence. From the personal factors studied, stigma and discrimination, depression and alcohol use were associated with adherence to ART, while no association was found with knowledge.

The next chapter will present the conclusions, limitations and recommendations of this study and proposed areas for possible future research.

CHAPTER 5

CONCLUSIONS, LIMITATIONS AND RECOMMENDATIONS

5.1 INTRODUCTION

The main purpose of the study was to identify the associations between personal factors and patients' adherence to anti-retroviral treatment. Adherence was measured by self report among treatment experienced patients (aged 18 and older) at the ALERT hospital. The results will be used to make recommendations to address personal barriers of adherence to ART. Specifically the conclusions, detailed in chapter 4, were used to answer the following research questions:

- What is anti-retroviral treatment adherence level at one government hospital?
- What is the association of knowledge, stigma and discrimination, depression and alcohol use on adherence to anti-retroviral treatment adherence at ALERT hospital?

5.2 OBJECTIVES

The objectives of the study were assessed as to whether or not they had been attained. Each objective is listed and then the conclusions are given along with related implications and applications.

5.2.1 Determine adherence status of ART patients in Addis Ababa, Ethiopia

Optimal adherence level was set at 95% which is necessary for desired clinical outcomes, adequate immunological response and suppressed viral replication. An adherence level of 95-100% was found among 73.5% of the respondents at one participating hospital. Suboptimal adherence level, less than 95%, was documented among 26.5% of patients. This finding aligns with results from other studies of patients

in resource limited countries and indicates that patients in these countries are capable of adhering as required.

5.2.2 Identify the influence of patients' knowledge of HIV and ART on adherence to ART in Addis Ababa, Ethiopia

In this study, patients had a mean knowledge score of 61.84% when rated on questions about HIV/AIDS and ART. There was no correlation between patients' knowledge and adherence to ART with a spearman's correlation coefficient of -0.002, suggesting that patients' level of HIV/AIDS and ART knowledge was not associated with adherence to ART.

Implication: Further study in different health facilities in Ethiopia, if possible prospectively over a longer time period, is recommended to investigate the relationship between knowledge and adherence to ART.

5.2.3 Assess the influence of HIV stigma and discrimination on adherence to ART in Addis Ababa, Ethiopia

Stigma and discrimination were divided into internal stigma, perceived stigma and discrimination. The number of respondents with internal stigma was highest (161 out of the 355 patients), followed by those experiencing discrimination (n=62) and finally those with perceived stigma (n=60). Each of the categories of stigma was associated with adherence to ART. People with stigma and discrimination were less likely to adhere to their ARVs.

Implication: This finding indicates the necessity to address stigma and discrimination by mobilising leaders (religious, secular and government) to promote and foster respect and compassion for people living with HIV/AIDS; empowering people living with HIV/AIDS to take the lead in diverse support and advocacy activities; mobilising community leaders to encourage openness around sexuality and HIV-related issues

within communities by building on positive social norms; raising awareness through media, mobilising organisations to implement non-discriminatory policies; ensuring redress where cases of discrimination occur and promoting understanding among people living with HIV/AIDS of their rights.

5.2.4 Evaluate the influence of depression on ART adherence in Addis Ababa

Depression as mentioned by different studies as well as this research has a negative influence on adherence to ART. Among the 19 depressed patients, 78.9% of them were found to be non-adherent. The depressed patients showed low levels of adherence and did not take their medications as the healthcare providers prescribed.

Implication: Healthcare providers should screen ART patients for depression before starting ART. When depressed patients are identified they should get appropriate therapy for their depression along with ART adherence counseling.

5.2.5 Identify the influence of alcohol use on adherence to ART in Addis Ababa

The majority of the 355 ART patients were current abstainers from alcohol (n=283; 79.7%). However, there were 66 infrequent light drinkers, 2 frequent light drinkers and 4 infrequent heavy drinkers. This study found that greater frequencies and amounts of alcohol consumed were associated with lower ART adherence levels. There was also a statistically significant association between alcohol use and adherence to ART at the 5% significance level.

Implication: Healthcare providers should counsel ART patients about the effects of alcohol use on ART adherence and on ART outcomes. Healthcare professionals should also teach the general community about the harmful effects of alcohol, including informally produced alcohol.

5.3   LIMITATIONS OF THE STUDY

- The sample was selected from only one hospital from a total of 9 public hospitals and 17 private hospitals providing ART services in Addis Ababa. This makes it unrepresentative of the whole population of ART patients in Ethiopia and Addis Ababa. Hence, the findings are only generalisable to the participating hospital.

- The 355 sample respondents were selected using simple random sampling technique. As a result both the exposures and outcome variables were collected simultaneously. This limits establishing temporal relationship between the two variables and assessing causal associations.

- Because the participating hospital provided free ARV services, the ART patients might have been of lower socio-economic status. Those patients from higher economic status might receive their care from private hospitals. Therefore the sampled patients might be different from the general ART patients in Addis Ababa.

- Only structured interviews were used to collect data from patients.

- No family members and no health care workers were interviewed.

- In-depth qualitative interviews with the ART patients might have provided information about these patients' lived experiences of being HIV positive and about the challenges faced to remain ART adherent.

5.4   RECOMMENDATIONS FOR IMPROVING ADHERENCE TO ART IN ETHIOPIA

Adherence level might be improved if the following recommendations were implemented.

- Assessment of adherence level is feasible and can be done by the healthcare providers using the patients' self report. This can be done routinely when the patient comes for medication refills. Patients can be supported and counseled to take their medications if they have difficulty with adherence.

- Male adherence supporters can be employed as one strategy to support male patients to adhere to their medications given female patients were more adherent than male patients.

- It is important to consider the implementation of facility-based and community based programs to alleviate stigma and discrimination. There is a need to timely

identify those patients with stigma and discrimination and provide support accordingly. It is also important to consider how stigma affects prevention strategies in order to improve patients' adherence to ART adherence.

- Depression is also a problem that needs to be screened for among all patients and treated accordingly, or referred for psychiatric follow up. Depression should be emphasised as it presents double problems (the disease itself and its impact on adherence to ART).

- Alcohol use lowers the level of adherence to ART. To improve patients' health condition through better adherence to ART, alcohol use prevention programs should be implemented both at the patient, health facility and community levels.

5.5   RECOMMENDATIONS FOR FURTHER STUDIES

Future researchers should investigate the following areas to improve adherence to ART in Addis Ababa and other parts of Ethiopia.

- This study should be duplicated in other health facilities of Addis Ababa and Ethiopia since this study was conducted at a single hospital and cannot be generalised to the whole of the country.

- ART adherence levels seen among patients at hospital facilities might not be the same as health center adherence levels. The differences between adherence levels among hospitals and health centers in Ethiopia should be assessed.

- As this study was conducted only at a public hospital, it is important to further study ART adherence levels at private hospitals and also identify the barriers of adherence specific to these facilities.

- Investigations should be done to identify other factors that are barriers to adherence to ART, in addition to those personal factors identified in this research. It is also important to consider that barriers of adherence may vary among the different regions of Ethiopia.

- Barriers to adherence among children and adults might not be the same. Adherence to ART barriers among children should also be investigated.

- It is also important to investigate the prevalence of depression among ART patients. This helps to understand the burden of the problem and propose appropriate solutions for its prevention.

- The rate of hospital admissions among ART patients and this relationship to non-adherence to ART should be studied.

- As other outcome measures, the prevalence of opportunistic infections among ART patients and their survival and the associated relationship with non-adherence could be examined.

5.6   CONCLUSION

Among the demographic factors, female gender was associated with greater ART adherence levels, whereas age, educational level and marital status did not have any association with ART adherence. Baseline CD4 cell counts and the most recent CD4 cell counts had weak positive associations. WHO HIV/AIDS staging was also associated with adherence to ART, indicating that adherent patients experienced less severe illnesses. These adherence level findings are similar to those reported by other studies in other resource poor countries, confirming that even in resource-limited countries patients can maintain high levels of ART adherence. To improve ART adherence and subsequent improved health outcomes, it is necessary to design and implement practically sound programmes that alleviate the burdens of stigma and discrimination, depression and alcohol use among ART patients.

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List of annexures

Annexure A: Letter of approval from ALERT hospital ethical committee

AHRI-ALERT ETHICAL REVIEW COMMITTEE
APPROVAL SHEET

TITLE OF THE PROJECT

"personal factors influencing patients anti-retroviral treatment adherence in Addis Ababa, Ethiopia."

PI: Tefera Girma

Project Reg. No. | P 017/10

Recommendation of the AHRI-ALERT Ethics Review Committee

The above mentioned research project was duly considered and approved by AHRI/ALERT Ethics Review Committee on September 22, 2010. The PI should submit progress report of the work every 6 months and the final report upon completion. The PI should also notify AAERC ahead any amendments or modifications in the protocol or premature suspension or termination of the study

Signature: _____   Signature: _____

CHAIRPERSON   SECRETARY

NAME: Dr Ruth Leekassa   NAME: Ms Martha Zewdie

D/Director of AHRI

Signature: _____

Date: _____
12.11.10

Abraham Aseffa, MD, Ph.D
Scientific Director

Annexure B: Letter to ALERT hospital ethical committee requesting permission

To: ALERT Hospital

Addis Ababa/Ethiopia

20/09/2010

Subject: **request for permission to carry out a research for academic purposes**

Dear Sir/Madam,

I am master of public health (MPH) student at University of South Africa (UNISA) and currently doing research as part of the fulfillment of my degree. The title of my research is "Personal factors influencing patients' anti-retroviral treatment adherence in Addis Ababa, Ethiopia". I would like to conduct my research in your hospital; the details of sampling, representativeness and ethical considerations are addressed in my research proposal which is attached with this letter of request. I have got ethical clearance from UNISA Ethical Review Committee which is attached herewith. The objectives of my study are to:

- Determine the adherence status of ART patients at ALERT in Addis Ababa, Ethiopia.
- Identify the influence of patients' knowledge of HIV and ART on adherence to ART at ALERT in Addis Ababa, Ethiopia.
- Assess the influence of HIV stigma and discrimination on adherence to ART at ALERT in Addis Ababa, Ethiopia.
- Evaluate the influence of depression on adherence to ART at ALERT in Addis Ababa, Ethiopia.
- Identify the influence of alcohol use on adherence to ART at ALERT in Addis Ababa, Ethiopia.

I hereby kindly request your esteemed hospital for ethical approval to conduct this research as part of my academic requirements.

Yours sincerely,

Tefera Girma Negash

Annexure C: Ethical clearance from UNISA

UNISA | university of south africa

College of Human Sciences
16 September 2010

Proposed title: Personal factors influencing patents' anti-retroviral treatment adherence in Addis Ababa, Ethiopia

Principal investigator: Mr TG Negash (student no. 42014735) **Degree:** Master of Public Health

Reviewed and processed as: Class approval (see paragraph 10.7 of the UNISA Guidelines for Ethics Review)

Approval status recommended by reviewers: Approved

The Ethics Subcommittee of the College of Human Sciences has reviewed your proposal and considers the methodological, technical and ethical aspects of the proposal to be appropriate to the tasks proposed. Approval is hereby granted for the candidate to proceed with the study in strict accordance with the approved proposal and the ethics policy of the University of South Africa.

In addition, the candidate should heed the following guidelines:
- To only start this research study after obtaining informed consent from the research participants.
- To carry out the research according to good research practice and in an ethically sound manner.
- To maintain the confidentiality of all data collected from or about research participants, and maintain security procedures for the protection of privacy.
- To work in close collaboration with your supervisor(s) and to record the way in which the ethical guidelines as suggested in your proposal has been implemented in your research.
- To notify the Ethics Subcommittee in writing immediately if any change to the study is proposed and await approval before proceeding with the proposed change.
- To notify the Ethics Subcommittee in writing immediately if any adverse event occurs.

Approvals are valid for ONE academic year after which a request for a continuation of the approval must be submitted to your supervisor(s).

Kind regards

Prof LI Zungu
Chair: Ethics Subcommittee: College of Human Sciences

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Annexure D: Map of Ethiopia
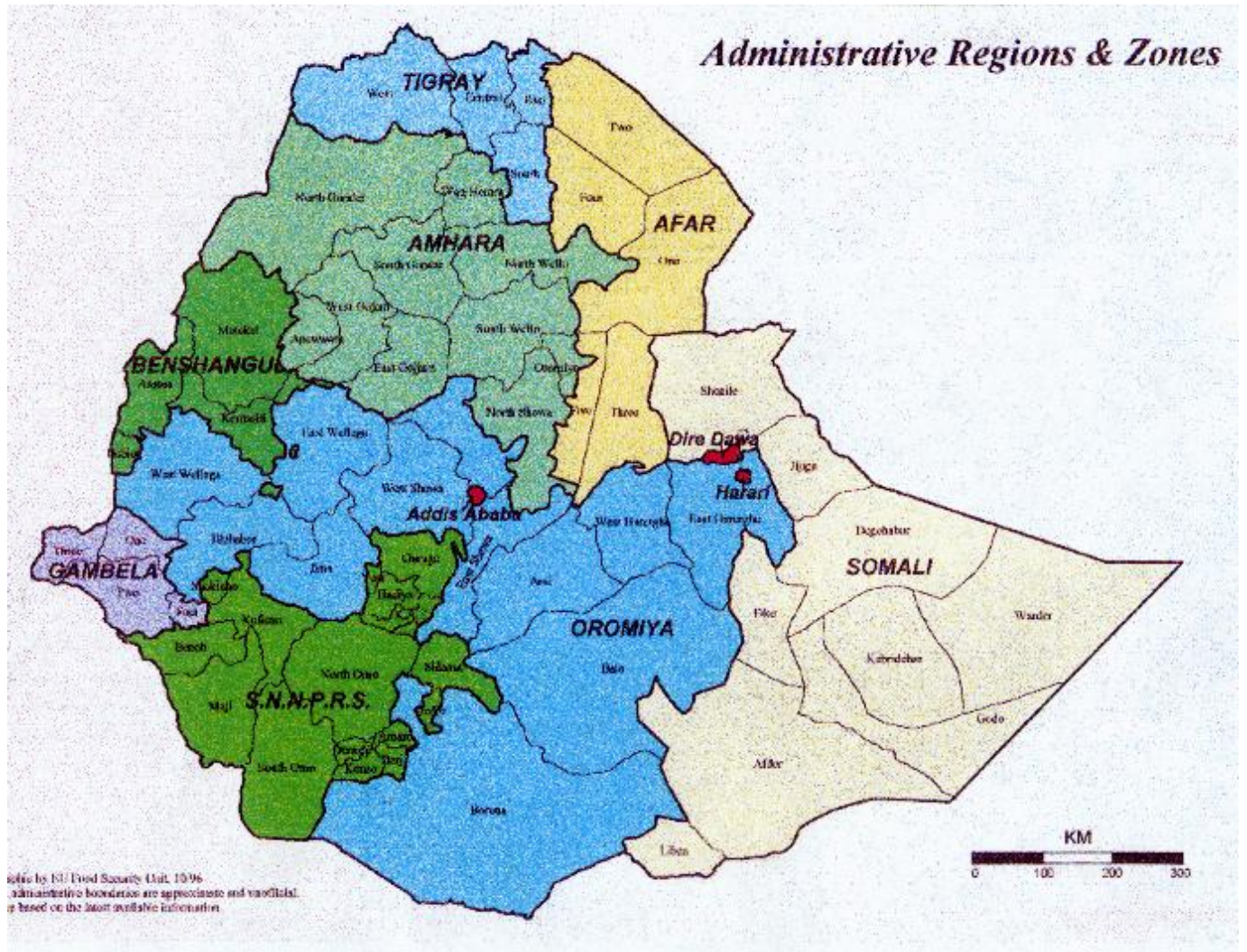
Annexure E: Structured interview schedule used for data collection (English version)

Section A: General questions		
1. Interview ID number in the form of 001, 002, 003…		
2. ART unique code		
3. CD4 count (when ART started)		
4. CD4 count (Currently)		
5. Viral load (when ART started)		
6. Viral load (currently)		
7. WHO stage when ART started		
8. WHO stage currently		
9. Interviewer's name		
10. Date of interview DD/MM/YYYY		
11. Age in years at last birthday		
12. Gender	Male	Female

13. What is your religion?		Muslim	Christian	Other

14. Where do you live	Region	Sub city/woreda	Kebele (lower level administrative unit in Ethiopia)

15. How far do you live from the hospital?

16. Can you afford to pay money for transportation to come to this hospital?

17. What is the highest level of education that you passed?	Not educated	Grade 1-6	Grade 7-8	Grade 9-12	University/College

18. Marital status	Single	Married	Divorced	Separated	Widowed

19. What kind of work do you do?

20. What is your monthly income in Ethiopian Birr?

21. With whom do you live? Mark all that apply.

With Father

With mother

With father+mother

With father+mother+siblings

With wife

With husband

With wife+children

With husband and children

With friends

Other, please specify:

Section B: Adherence

| 1. When were you informed that you are HIV positive? Please give date or say how many months ago you obtained this knowledge | |
| 2. When did you first start taking ART to manage your HIV? (Date or number of months) | |

3. ART regimen (prescribed doses)

Name of medication	Morning dose	Midday dose	Evening dose	Daily total
	# of pills	# of pills	# of pills	# of pills
1.				
2.				
3.				

4. Three-day recall of adherence: Many patients find it difficult to take all their medications as prescribed. We would not be surprised if you have missed taking some of your medications over the last few days. We are trying to find out how difficult it is for patients to take their medication, and what things make it difficult. Please answer these questions as honestly as you can about your own experiences.

Name of medication	# of pills prescribed	Yesterday	Day before yesterday	3 days ago
		# of pills taken	# of pills taken	# of pills taken
1.				
2.				
3.				

5. What circumstance led you to miss taking your medication as prescribed?

Missed dose # 1…………………………………………………………………….

Missed dose # 2…………………………………………………………………….

Missed dose # 3…………………………………………………………………..

6. Some people find it difficult to take their antiretroviral therapy medications on the weekends. Thinking about the past seven days, how many times did you miss taking a dose of your medication?

Never

Once

Twice

Three or more times

7. We know that it is difficult to take all your ART just as the Doctor prescribed. Would you

say that in the past month you:

Totally followed prescriptions

Generally followed prescriptions but with some deviations

Often modified timing and quantities

Almost never followed prescriptions

Interrupted treatment

8. Circumstances and reasons for non adherence in the past month

In general, what helps you take your medications on time?

What circumstances led you to miss taking your pills on time?

What other things make it difficult to take all your medications on time?

9. During the past month, how often did you take a double dose of ART medication after missing a dose?

Never

Once

Twice

More than twice
10. Did you ever stop taking your ART for 48 hours or longer? If yes: how long did you stop taking ART? For more than 48 hours and less than a week From one to two weeks For more than two weeks and less than one month For more than one month
Section C: HIV/AIDS and ART Knowledge
1. Please tell me about all the ways in which HIV can be transmitted to persons
2. Please tell me about all the ways which HIV cannot be transmitted to other persons
3. How can people protect themselves from getting HIV?

4. What is the difference between HIV and AIDS?
5. Can a healthy- looking person have HIV? Please give a reason for your answer
6. Can a healthy-looking person have AIDS? Please give a reason for your answer

7. Is there a cure for AIDS?	Yes	No	Do not know

8. What are the benefits of the ARV drugs you are taking?

9. What could happen if you do not take the ARV drugs as prescribed by your doctor?

Section D: Stigma and discrimination

1. Do you feel guilty because you are HIV+ve?

2. What do you feel due to your HIV positive?

a. Angry

b. despondent

c. Hopeful for a long happy life

d. scared of getting very sick

e. Worthless

f. Other

3. In the past 12 months, have you ever found yourself avoiding or isolating yourself from

friends or family?		
Indicate your opinion about the following judgements of people in your community.		
4. Do some people act as though it is your fault you have HIV?		
5. Do people say that you deserve being HIV positive for things you have done?		
6. Do people seen uncomfortable being around you once they learn you have HIV?		
Have you faced any of the following in the last 12 months because you were known to have, or suspected of having, HIV or AIDS?		
7. Excluded from a social gathering (wedding, funeral, party, community association group)	Yes	No
8. Treated differently/shunned at social gathering	Yes	No
9. Abandoned by your family/ sent away-to the village.	Yes	No

10. Isolated in household for example being made to eat alone/ made to use separate eating utensils/ made to sleep in own room.	Yes	No
11. Teased, insulted, or sworn at	Yes	No
12. Lost customers who bought my products/goods or lost a job	Yes	No
13. Lost housing or being un-able to rent housing	Yes	No
14. Given poorer quality health services for example: being passed from provider to provider, not given medicines, denied treatment	Yes	No
15. Had property (land, household or other goods) taken away	Yes	No
16. Lost respect/standing within the family and/or community	Yes	No

17. Physically assaulted (i.e., hit, kicked, punched)	Yes	No

Section E. Depression

1. Do you feel depressed even when good things happen to you.	Yes If yes for how long and please explain in what way(s) you feel depressed	No
2. Have lost interest or pleasure in aspects of your life that used to be important to you	Yes If yes for how long And please give examples	No
3. Have you lost or gained body weight	Yes: how many kilograms did you lose/gain	No
4. Are you getting a sufficient number of hours' restful sleep	Yes If yes for how many hours do you sleep out of a 24-	No please explain why you regard you sleeping as being inadequate or too much

	hour day	
5. Do you do things more slowly than before you became HIV positive	Yes If yes for how long have you had this experience and please give an example where your activities take longer now than previously	No
6. Do you feel tired with minimal activity	Yes If yes for how long have you experienced this tiredness; please give an example of what makes you tired easily	No
7. Is it hard for you to concentrate on reading or thinking	Yes If yes for how long and please give an example	No

	of such difficulties				
Section F. Alcohol					
1. During the last 12 months, how often did you drink alcohol?	Never	Monthly or less	2 to 4 times a month	2 to 3 times a week	4 or more times a weeks
2. What type of alcohol you usually drink?					
3. What was the size of the typical can, bottle, or glass of your alcoholic drink during the last 12 months?	1 or 2	3 or 4	5 or 6	7, 8 or 9	10 or more
4. On the days when you drank alcohol in the last 12 months, how many (cans/bottles/glasses) did you usually drink in a single day?	1 or 2		3 or 4		5 or more
5. During the last 12 months, what was the largest number of (can/bottles/glasses) of					

alcohol that you drank in a single day?			
6. How often did you drink (number reported in previous question) (cans/bottles/glasses) alcohol in a single day?			
7. Has a relative or friend or a doctor or any health worker suggested that you reduce your alcohol intake?	No	Yes, but not in the last year	Yes, during the last year

Thank you very much indeed for answering the questions. Your answers will contribute towards helping the health care workers to supply better ART services in Ethiopia.   You have my contact telephone numbers on the card I gave you. If you have any questions or worries, you are welcome to contact me, or your usual health care provider(s).